

UNIVERSITY OF LJUBLJANA

FACULTY OF ECONOMICS

ÖNER TULUM

**INNOVATION AND FINANCIALIZATION IN THE U.S.
BIOPHARMACEUTICAL INDUSTRY**

DOCTORAL DISSERTATION

Ljubljana, 2018

AUTHORSHIP STATEMENT

The undersigned Öner Tulum, a student at the University of Ljubljana, Faculty of Economics, (hereafter: FELU), author of this written final work of studies with the title “Innovation and financialization in the U.S. biopharmaceutical industry” prepared under supervision of Professor William Lazonick

DECLARE

1. this doctoral dissertation to be based on the results of my own research;
2. the printed form of this written final work of studies to be identical to its electronic form;
3. the text of this doctoral dissertation to be language-edited and technically in adherence with the FELU's Technical Guidelines for Written Works, which means that I cited and / or quoted works and opinions of other authors in this doctoral dissertation in accordance with the FELU's Technical Guidelines for Written Works;
4. to be aware of the fact that plagiarism (in written or graphical form) is a criminal offence and can be prosecuted in accordance with the Criminal Code of the Republic of Slovenia;
5. to be aware of the consequences a proven plagiarism charge based on the this doctoral dissertation could have for my status at the FELU in accordance with the relevant FELU Rules;
6. to have obtained all the necessary permits to use the data and works of other authors which are (in written or graphical form) referred to in this doctoral dissertation and to have clearly marked them;
7. to have acted in accordance with ethical principles during the preparation of this doctoral dissertation and to have, where necessary, obtained permission of the Ethics Committee;
8. my consent to use the electronic form of this doctoral dissertation for the detection of content similarity with other written works, using similarity detection software that is connected with the FELU Study Information System;
9. to transfer to the University of Ljubljana free of charge, non-exclusively, geographically and time-wise unlimited the right of saving this doctoral dissertation in the electronic form, the right of its reproduction, as well as the right of making this doctoral dissertation available to the public on the World Wide Web via the Repository of the University of Ljubljana;
10. my consent to publication of my personal data that are included in this doctoral dissertation and in this declaration, when this doctoral dissertation is published.

Ljubljana, April 9th, 2018

Author's signature:



ACKNOWLEDGMENTS

*To Oliver Ömer, Everett Hasan, and to their mother,
an amazing woman, and the love of my life, Christina Birmingham*

This thesis is the product of a nearly decade-long research effort, which benefited immensely from collaborative efforts with, and invaluable support from, a number of people and institutions that I am proud to acknowledge here. All the facts, arguments, and viewpoints expressed herein, as well as any errors observed, are solely my responsibility as the author of this study.

I must start with William Lazonick, whose involvement at every stage of this project has been instrumental, and whose theoretical perspective on the operation and performance of the innovative enterprise in a productive economy constitutes the basis for this doctoral research. As a scholar with tremendous academic integrity, who has a great dedication to science and a devotion to his students, fellow scholars, and society, Bill has been a role model. I am privileged to have had him as my mentor, colleague and friend. It is his courage to think critically, audacity to challenge the status quo, and commitment to new learning that inspired me to pursue this research and to pursue an academic career.

I also wish to thank the members of my thesis evaluation committee, Mateja Drnovšek and Boštjan Antončič, both of the University of Ljubljana, and Antonio Andreoni of SOAS University of London, for their time and effort in helping me to take this thesis from proposed topic to final defense. I also wish to thank Lawrence King of the University of Massachusetts Amherst and the members of the doctoral research committee at the Faculty of Economics of the University of Ljubljana, namely Marko Pahor and Irena Ograjenšek, for their constructive criticism, feedback, and recommendations, which were instrumental in the process of transforming a set of complex ideas and questions into a fully-fledged thesis proposal.

I also wish to thank Tea Petrin, Patricia Kotnik, Lidiya Urek and Petra Vranješ, all of the University of Ljubljana, whose support has been critical. I am indebted to my colleagues at the Academic-Industry Research Network (theAIRnet), Ken Jacobson and Marie Carpenter, for their insights, which strengthened my arguments and brought greater clarity to the text. I also wish to thank Matt Hopkins, Mustafa Erdem Sakinc, Satyasiba Das, Paul Ryan, Michael Best, Phil Moss, Hal Salzman, and many other colleagues, for the many discussions and debates that pushed forward my thinking and helped me to better articulate the complexities that this work aims to convey.

I am particularly grateful for the intellectual and financial support that the Academic-Industry Research Network (theAIRnet) has provided me over the years. The theoretical arguments and analyses that inform various chapters of this thesis were developed through research projects financially supported by the Institute for New Economic Thinking (INET), namely “Collective and Cumulative Careers: Foundations for Sustainable

Prosperity” (INO15-00018); “Financialization of the US Pharmaceutical Drug Industry, and What Can Be Done About It” (INO16-00024); “Value Creation and Methods of Value Extraction in US Firms” (INO17-00013); and “Innovation versus Financialization: Europe and the United States” (INO17-00016). I wish also to express my gratitude to Thomas Ferguson, Research Director of INET, who showed great interest in this project and ensured that my research received the necessary support. I also want to acknowledge the financial support received from Horizon 2020, the latest European Union Framework for Research and Innovation, through the project, “Innovation-fueled Sustainable and Inclusive Growth” (ISIGrowth GA No. 649186), which enabled me to complete the analyses of European biopharmaceuticals.

I am forever indebted to my parents, Sema and Ömer Tulum, who have been the source of my strength; and my mother-in-love Alberta Bermingham. I am thankful to Naciye and Kemal Oguz Kalafat for their invaluable support and encouragement in making sure that I persevered through the prolonged and arduous process of researching and writing this thesis. I also wish to express enormous gratitude to other family members and friends in Istanbul, Ordu, Berlin, Galway, and Massachusetts, whose emotional support was invaluable. I would not have been able to manage the stresses of doctoral research without their support.

“Time is an illusion,” says Albert Einstein, but what one can or cannot capture in time is very real: the satisfaction of a joyful moment, or the regret of missing such moments. “Time is the most valuable thing a man can spend,” says Theophrastus, but what is the value of the hours that one borrows from his loved-ones? A great deal of time that went into building this project from the ground up was time borrowed from those closest to me, so they deserve credit for this work as they bore the burden of making it happen. The joy and happiness that my sons, Oliver Omer and Everett Hasan, radiate around the house have been the source of my strength and inspiration to complete this work.

And last but certainly not least, I need to express my deepest and greatest gratitude to Christina Bermingham. At times I was so preoccupied with this research that I was physically or mentally absent from our family life, and she took on more than her share of parenting so that I could continue. I could not conclude my remarks without also acknowledging her many intellectual contributions to this project, in addition to sharing all the pains and burdens that putting this work together has involved. Christina Bermingham, this work would not have been possible without your endless support, from the very first moment that I decided to pursue a doctoral study until the writing of this final sentence, which brings this thesis and a bittersweet chapter in our lives to an end. My love, we finally did it.

Öner Tulum
University of Ljubljana, April 2018

SUMMARY

Driven by the ideology of maximizing shareholder value (MSV), the US biopharmaceutical industry has adopted a highly financialized business model. Its key performance metrics are stock price, earnings per share, and dividend yield, supported by distributions to shareholders in the forms of dividends and stock buybacks. Incentivized by stock-based executive pay, this value extraction can be at the expense of productivity in drug innovation (Lazonick et al., 2017). Yet with government support for drug development through the National Institutes of Health and various forms of intellectual property protection and financial subsidies as well as unregulated drug prices that can provide high profits for reinvestment in drug development, US economic institutions should be highly conducive to innovation in drug development (Lazonick & Tulum, 2011). Despite all these supports and incentives to develop innovative new drugs, many US biopharmaceutical companies are facing a deep productivity crisis. At the same time, many of their European rivals are making use of the US institutional environment to outcompete the US companies in their home market. This dissertation adduces the evidence that the financialized business model is the main reason why US biopharmaceutical companies face an ongoing productivity crisis. The dissertation then assesses the evidence that the less-financialized European biopharmaceutical companies, which are subject to price regulation in their home markets, augment their innovative capabilities by tapping into the immense US knowledge base and selling their products in the United States at high, unregulated, prices. Recognizing that all business corporations confront a tension between innovation and financialization—or, alternatively stated, between value creation and value extraction—this dissertation employs William Lazonick's theory of the innovative enterprise to examine how the social conditions of innovative enterprise influence the direction of this tension in US and European biopharmaceutical companies operating in the same institutional environment. Recognizing as well that the operation of the tension between innovation and financialization is to some extent company-specific and that within a particular company the tension evolves over time, the analysis presented in this dissertation focuses on the US company Merck and the Swiss company Roche Holding. The two-company cross-national comparison presented here is part of a larger-scale project that, eventually, seeks to integrate the findings on innovation, financialization, and productivity from in-depth case studies of all of the world's major biopharmaceutical companies.

Keywords: Financialized US biopharma business model, the theory of innovative enterprise, productivity of European biopharma, crisis in drug R&D, historical-transformation methodology

POVZETEK

Biofarmacevtska panoga ZDA je pod vplivom ideologije maksimiranja vrednosti premoženja delničarjev povzela zelo financializiran poslovni model. Ključna merila uspešnosti takšnega modela predstavljajo cena delnice, čisti dobiček na delnico in dividendna donosnost, podprta z distribucijo delničarjem v obliki dividend in odkupov lastnih delnic. Tak način ekstrakcije vrednosti, spodbujen z načinom plačilom izvršnih direktorjev na podlagi delnic, je lahko velikokrat na račun zmanjšane produktivnosti in inovacij zdravil (Lazonick et al., 2017). Toda z vladno podporo razvoju zdravil prek Nacionalnih inštitutov za zdravje in številnih oblik zaščite intelektualne lastnine ter finančnih subvencij kot tudi nereguliranih cen zdravil, ki lahko omogočijo visoke dobičke za reinvestiranje v razvoj zdravil, bi morale gospodarske institucije veliko prispevati k inovativnosti v razvoju zdravil (Lazonick & Tulum, 2011). Kljub vsem tem podporam in spodbudam za razvoj novih zdravil se mnoga biofarmacevtska podjetja soočajo s krizo produktivnosti. Istočasno veliko evropskih tekmecev izkorišča institucionalno okolje ZDA, da bi prehiteli ameriška podjetja na njihovem domačem trgu. Disertacija postreže z dokazi, da je financializacija poslovnega modela glavni vzrok, zakaj se biofarmacevtska podjetja v ZDA soočajo s stalno krizo produktivnosti. Prav tako oceni dokaze, ki kažejo na to, da so manj financializirano evropska biofarmacevtska podjetja, ki so podvržena cenovni regulaciji na svojih domačih trgih, povečala svoje inovacijske sposobnosti z izkoriščanjem ogromne baze znanja ZDA in prodajo svojih proizvodov v ZDA po visokih, nereguliranih cenah. Na podlagi spoznanja, da se vse poslovne družbe soočajo s pritiskom ozziroma dilemo med inovativnostjo in financializacijo, ozziroma alternativno, med ustvarjanjem vrednosti in ekstrakcijo vrednosti, disertacija uporablja Teorijo inovativnega podjetja Williama Lazonicka, za preučevanje kako socialne razmere v inovativnem podjetju vplivajo na smer tega pritiska v ameriških in evropskih farmacevtskih podjetjih, ki delujejo v istem institucionalnem okolju. Ob upoštevanju, da je delovanje pritiska med inovativnostjo in financializacijo do neke mere odvisno od posameznega podjetja in da se znotraj določenega podjetja napetosti pojavi skozi čas, se analiza predstavljena v disertaciji osredotoča na ameriško podjetje Merck & Co. in švicarsko podjetje Roche Holding AG. Tu predstavljena mednacionalna primerjava med dvema podjetjema je del večjega projekta, ki poskuša postopoma povezati ugotovitve s področja inovativnosti, financializacije in produktivnosti na podlagi poglobljenih študij primerov vseh največjih svetovnih farmacevtskih podjetij.

Ključne besede: Financializirani poslovni model biofarmacevtskih podjetij ZDA, teorija inovativnega podjetja, produktivnost evropskih biofarmacevtskih podjetij, kriza v raziskovah in razvoju zdravil, metodologija zgodovinskega preoblikovanja

TABLE OF CONTENTS

INTRODUCTION	1
The productivity paradox and the financialization of the US biopharmaceutical industry	4
Transition from innovation to financialization	6
Analyzing the tension between innovation and financialization	6
The theory of innovative enterprise	7
Thesis outline	9
1 THEORY AND CONCEPTUAL FRAMEWORK	11
1.1 The theory of market economy and varieties of resource allocation modes.....	12
1.2 Transition from managerial-capitalism to shareholder-capitalism	14
1.2.1 Capital markets emerging as corporate locksmiths that “unlock” value for shareholders.....	15
1.2.2 Capital markets vs corporate management for allocating resource	16
1.3 The theory of innovative enterprise (TIE) and the social conditions of innovative enterprise (SCIE)	18
1.3.1 Schumpterian, Penrosioan, and Chandlerian Antecedents to TIE.....	20
1.3.2 From innovation to financialization: the shift from the Old Economy business model (OEBM) to the New Economy business model (NEBM)	22
1.3.3 Analyzing the “innovative enterprise”	26
1.4 Financialization and the drug innovation crisis	27
1.4.1 Financialization in the context of biopharmaceutical industry.....	30
1.4.2 Identifying the innovation crisis in the biopharmaceutical industry	35
1.4.3 Maximizing shareholder value (MSV) ideology and the transition into Blockbuster-driven New Economy Business Model in the US biopharmaceutical sector	47
1.5 Research implication and contributions	48
2 RESEARCH DESIGN AND METHODOLOGY	50
2.1 Historical-transformation and case study methods	53
2.2 Sampling and data collection	55
2.3 Purposeful sampling.....	56
2.4 Data for market analysis	61
2.5 Data for case analysis.....	62

2.6	Methodological contributions and future implications	64
3	AN OVERVIEW OF THE CHANGES IN THE INSTITUTIONAL ENVIRONMENT AND THE CONDITIONS OF THE PHARMACEUTICAL INDUSTRY IN THE UNITED STATES	64
3.1	Governance institutions	66
3.2	Employment institutions	70
3.3	Investment institutions	75
3.3.1	The rise of product-less IPOs (PLIPOs) as New Economy pharmaceutical businesses	77
3.3.2	Big pharma's financialized "blockbuster" model.....	80
3.4	Creating the national innovation system.....	82
4	AN ANALYSIS OF THE TRANSITION FROM INNOVATION TO FINANCIALIZATION: MERCK & CO., INC.	107
4.1	Strategic Control	117
4.1.1	Transformation of German Merck into an "Americanized" enterprise	119
4.1.2	Transformation into an innovative enterprise (building core competence).	122
4.1.3	Vagelos is the chief scientist: A new era for drug research at Merck	152
4.1.4	Transformation out of Old-Economy enterprise, early-1990s.....	160
4.1.5	Transformation into a New Economy enterprise, late 1990 and 2000s.....	167
4.2.	Organizational Integration	176
4.2.1	Surging productivity and expansion of the workforce at Merck.....	178
4.2.3	Market diversification and setbacks in R&D productivity.....	181
4.2.4	From Major to Vagelos, building a century of research tradition at Merck.....	182
4.2.5	Changing labor relations and diminishing productivity at Merck.....	184
4.2.7	Ending "career-with-one-company" (CWOC) as pervasive employment norms at Merck	190
4.3	Financial Commitment.....	197
4.3.1	Transforming Merck into a science-driven innovative enterprise	199
4.3.2	Financing innovation at Merck under Horan and Vagelos	201
4.3.3	Financial windfall for Merck shareholders and executives.....	211
4.3.4	Shopping for innovation! Frazier and Perlmutter seek acquisitions for future products	214

5 AN ANALYSIS OF THE EUROPEAN BIG PHARMA: THE US NATIONAL INNOVATION SYSTEM AND THE PRODUCTIVITY OF EUROPEAN PHARMA	219
5.1 The growth of European biopharmaceutical companies in the US market	220	
5.2 An analysis of product portfolios and clinical pipelines of the leading European biopharmaceutical companies.....	223	
6 AN ANALYSIS OF THE TRANSITION FROM INNOVATIVE ENTERPRISE TO GLOBAL LEADER: ROCHE HOLDING AG	231
6.1 Strategic Control	233	
6.1.1 Evolution of dual-share structure at Roche	235	
6.1.2 Evolution of Fritz Hoffman-La Roche & Co. into innovative enterprise....	245	
6.1.3 Shifting the focus of drug discovery from chemistry to biology: Factors requiring drug manufacturers to transform drug R&D in the 1960s and 1970s	249	
6.1.4 Penetrating the early biotechnology network: Roche joins the cloning rush on the West Coast.....	254	
6.2 Organizational Integration	268	
6.2.1 Dealing with New Economy biotech: Integrating Genentech into Roche... 270		
6.2.2 Changing structure of the executive pay at Roche?	273	
6.3 Financial Commitment.....	276	
6.3.1 Genentech: Roche's most productive investment	279	
6.3.2 A different kind of stock repurchases: maintaining strategic control of Genentech after the merger	282	
6.3.3 Growing shareholder payouts at Roche	284	
7 DISCUSSIONS ON ANALYSIS AND FINDINGS	286	
7.1 Strategy, ownership, and control	290	
7.3 Finance, innovation, and stock repurchases.....	297	
7.4 Organization.....	301	
CONCLUSION	305	
Research Contributions	310	
Limitations of the research.....	315	
Future Research	317	
REFERENCES	318	

APPENDICES.....344**LIST OF FIGURES**

Figure 1: Changes in the FDA Review time (standard vs priority) and R&D productivity, between 1995 (index year) and 2015.....	38
Figure 2: Industry (PhRMA) and government (NIH) funding for R&D, New Drug Application (NDA), New Molecular Entity (NME) approvals and the productivity of R&D, per \$B spent, 1995-20.....	40
Figure 3: Changes in the PhRMA members annual sales (domestic and abroad), National Health Expenditures (Total vs prescription drugs), and Consumer Price Index (All city vs. prescription drugs), 1986-2015.....	43
Figure 4: R&D Funding for [poverty-related] neglected diseases by institution, 2007-2014	44
Figure 5: Accessibility of innovative therapies in high-burden disease areas, 2015.....	45
Figure 6: Top shareholder value creators in 2016, ranked by major industry groups, average annual TSR 2011-2015 (%)	48
Figure 7: Concentration of prescription drug sales in the US (left) and worldwide markets (right), % shares in market total by companies grouped in sales	57
Figure 8: Employment and Average Annual Earnings in NAICS 54171 Biotechnology Research (2000\$)	73
Figure 9: Employment in Major Life Sciences Manufacturing Industries	74
Figure 10: Wage Growth Index in Major Life Sciences Manufacturing Industries, 1994-2012	75
Figure 11: National Institutes of Health Annual Spending 1950-2016 (Adjusted, 2016\$b)	95
Figure 12: Merck & Co. Inc. sales and net income, 1941-1961	112
Figure 13: Merck & Co. Inc. sales and net income, 1962-1985	113
Figure 14: Merck & Co. Inc. sales and net income, 1986-2016	114
Figure 15: Merck & Co. Inc. revenues and employees, 1946 -2016 (in 2016 dollars)	115
Figure 16: Changes in the revenue composition by therapy (% of total revenues).....	139
Figure 17: Major product launches by decade, first 50 years of R&D at Merck, 1933-1982	149
Figure 18: Pharmaceutical sales by major American companies, 1950-90 (US\$2016)....	159
Figure 19: Merck & Co. Inc., net income (NI), R&D, and capital expenditures (CAPEX), 1976-2016 [adjusted in 2016 dollars]	203

Figure 20: Merck & Co. Inc. R&D as percent of sales and dividends (DV) plus share repurchases (RP) to net income (NI), 1976-2016 [FC]	205
Figure 21: Comparing shareholder payouts by CEO, 1950-2016 [in 2016 \$]	206
Figure 22: Stock performance, buybacks and executive compensation, 1994-2016.....	208
Figure 23: Merck & Co. Inc. dividends and stock repurchases, 1974-2016 [in 2016 \$]...	211
Figure 24: Internally vs. externally-sourced innovation at Merck & Co., 1996-2016	216
Figure 25: Relative importance of Merck & Co.'s different products as a percentage of total sales, 2007-16	217
Figure 26: Total revenues, by country of product origin, all years	223
Figure 27: Total revenues, by country of product origin and decades in products launched	224
Figure 28: AstraZeneca (AZ)	225
Figure 29: GlaxoSmithKline (GSK).....	226
Figure 30: Bayer	226
Figure 31: Merck KgAA (Merck-Serono).....	227
Figure 32: Sanofi-Aventis	227
Figure 33: Novartis	228
Figure 34: Roche Holding AG (Hoffmann-La Roche).....	228
Figure 35: Europe top 7 product candidates in pipeline, by clinical phase	229
Figure 36: Changes in labor turnover by region at Roche during the post-merger restructuring period, 2007-2013	271
Figure 37: Changes in employment at Roche by region, 1986-2016	272
Figure 38: Changes in market capitalization and average compensation of top executives at Roche vs Genentech, 2000-2016	275
Figure 39: Roche's capital expenditure and net income, 1984-2016	277
Figure 40: Genentech Inc. net income, R&D, and payouts to shareholders.....	282
Figure 41: Roche Holding net income, R&D, and payouts to shareholders	284
Figure 42: Growth index in employment (EE), R&D, revenues (REV), net income (NI), capital expenditure (CAPEX), and total shareholder payout (TSP)	285
Figure 43: Comparing the shareholder payouts of top 7 pharmaceutical companies, % change from 1997-2006 to 2007-2016	300

LIST OF TABLES

Table 1: Comparing the characteristics of old economy and new economy business models	23
Table 2: Company rankings by drug sales, 1993 and 2013-15 average	58
Table 3: Percentage share of ethical drug in total sales of top US pharmaceutical companies, decade average, 1950s-90s	131
Table 4: Employment at Major American Pharmaceutical companies, 1950-2016.....	180
Table 5: Merck & Co. Inc. gains from exercising stock options, 1994-2016, top five executives and average gains of all other employees	195
Table 6: Research and Development Investments of Major American Pharmaceutical Companies as a percentage of total sales by decade	202
Table 7: Profitability* of major American pharmaceutical companies, by decade.....	204
Table 8: Stock repurchases (RP), cash dividends (DIV), R&D (RD), and profits (NI), top 5 US firms, 1977-2016	209
Table 9: Biopharmaceutical product revenues and % share in total revenues by the Top 7	221
Table 10: Comparison of Merck and Roche's business models.....	288
Table 11: Productivity and economic performance of R&D at Roche, 1993.....	296

LIST OF APPENDICES

Appendix 1: Summary in Slovenian language / Daljši povzetek disertacije v slovenskem jeziku.....	1
Appendix 2: Timeline of major policy changes affecting pharmaceutical industry in the US	14
Appendix 3: Comparing the Theory of Innovative Enterprise (TIE) and the “innovating firm” vs. the Theory of Market Economy (TME) and the “optimizing firm”.....	15
Appendix 4: Conceptual framework for analyzing the evolution and influence of the social conditions of innovative enterprise in a national context	17

LIST OF ABBREVIATIONS AND ACRONYMS

CRA	Cooperative Research Center
CRADA	Cooperative Research and Development Agreement

FDA	Food and Drug Administration
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IND	Investigational New Drug
M&A	Merger and Acquisition
MSV	Maximizing Shareholder Value
NDA	New Drug Approval
NEBM	New Economy Business Model
NHE	National Healthcare Expenditure
NIH	National Institutes of Health
NME	New Molecular Entity
NSAID	Non-Steroid Anti-Inflammatory Drug
OEBM	Old Economy Business Model
OTC	Over-The-Counter
PhRMA	Pharmaceutical Research and Manufacturers of America
PLIPO	Product-less initial public offering
Rx	Prescription drug
SCIE	Social Conditions of Innovative Enterprise
TIE	Theory of Innovative Enterprise
TME	Theory of Market Economy
USPTO	United States Patent and Trademark Office

INTRODUCTION

The US institutional environment provides unique advantages for the development and commercialization of biopharmaceutical drugs. Through the National Institutes of Health (NIH), the US government provides in excess of \$30 billion per year to support life sciences research, implemented through a well-established network of government, nonprofit, university, and hospital research labs. Scientific talent is drawn from around the world to study in American universities and pursue research careers in US government, civil society, and corporate settings. The US legal system facilitates the transfer of federally-funded research to business enterprises, and then grants these firms 20-year patents on drug discoveries.

In addition, under the Orphan Drug Act of 1983, biopharmaceutical companies can receive seven-year market exclusivity from the time that the Food and Drug Administration approves a drug for rare and genetic diseases. These companies can also benefit from many different types of research subsidies at federal, state, and local levels. In addition to these advantages for funding biopharmaceutical drug innovation, the United States is the only major nation that does not regulate biopharmaceutical drug prices, which are generally at least double in the United States as in other advanced nations (Lazonick et al., 2017). And the US market for biopharmaceutical drugs is the largest in the world, with government agencies paying for in excess of 40 percent of these expenditures.

High biopharmaceutical profits are made possible by high unregulated drug prices. Data collected by the UK Pharmaceutical Price Regulation Scheme for 2004 through 2010 shows that US prices were about two and a half times those of most other advanced economies, and that the disparity was increasing over time. With the UK price index at 100 in 2010, the US index was 254, while the French index was 95, the Italian 103, and the German 142 (UK Department of Health 2012, p. 30).

High drug prices and economies of scale provide biopharmaceutical companies with ample profits that can be allocated to new drug discovery. Indeed, the largest US biopharmaceutical companies that are included in the S&P 500 Index spend about 16 percent of revenues on research and development (R&D). Yet despite a national system so highly conducive to innovation, there are widespread claims that a crisis of productivity afflicts the US biopharmaceutical industry (Garnier, 2008; Munos, 2009; Paul et al., 2010; Pammolli et al., 2011; Scannell et al., 2012; Rafols et al., 2014; Gleadle et al., 2014; Scannell & Bosley, 2016; Kinch, 2016).

Although there is widespread consensus that a productivity crisis exists in the biopharmaceutical industry, there are numerous, often competing, theories seeking to explain the origins of the problem. Initially perceived as a temporary decline in the industrial performance of launching new drugs after enjoying a productivity boom in the

1980s and 1990s, the decline on the industry's innovative performance turned out to be rather a systematic issue, which, this thesis argues, could be solved neither by eliminating regulatory hurdles to increase the pace of the clinical approval process and reduce the cost of drug R&D nor by pouring more money into the drug R&D to boost industrial productivity. As I discuss in the next chapter, such market-based solutions are often proposed by economic analysis following a traditional line of inquiry rooted in the neoclassical theory of the market economy.

Driven by the ideology of maximizing shareholder value, Lazonick and Tulum (2011) argue, that the US biopharmaceutical industry has adopted a highly-financialized business model. Its key performance metrics are stock-price yield and dividend yield, supported by distributions to shareholders in the forms of large-scale stock buybacks in addition to ample dividends. With this financial behavior incentivized by stock-based executive pay, value extraction from corporations for the sake of distributions to shareholders can be at the expense of productivity in drug innovation. Lazonick et al. (2017) identify changes in the financial behavior of the US biopharmaceutical companies and reveal the escalation of value extraction from those companies for the sake of distributions to shareholders.

Based on the compelling evidence adduced by Lazonick and Tulum (2011) and Lazonick et al. (2017), this thesis posits that the US pharma's transition from innovation to "financialization" is the real culprit behind the productivity crisis of this industry. This research also contends that to explain the US pharma industry's productivity problem one needs understand how, why, and to what extent operating under a system of corporate governance that supports financialization rather than innovation impacts the innovative productivity of the US biopharmaceutical companies. A broad objective of this research is to gain an understanding of the mechanisms linking "financialization-hypothesis" to the industry's "productivity paradox".

In *Shaping the Industrial Century* (2005), Alfred Chandler offers one of the most extensive account on the evolution of the chemical and pharmaceutical industries in the post-World War II decades based on comparative business histories of large industrial corporations in the United States and Europe that Chandler compiled. In the subtitle of his book, Chandler describes the evolution of the pharmaceutical industry as a "remarkable story". But Chandler's perspective on this remarkable story reflects the period leading up the 1990s when Chandler ended his analysis to start writing the book.

At the time when Chandler was writing *Shaping the Industrial Century* in the 1990s, small biotech companies that began to emerge in the late 1970s and 1980s increasingly placed competitive pressure on long-established US pharmaceutical companies that were struggling to incorporate new technologies emerging in the field of biology into their already existing organizational capabilities. During the same period, *maximizing shareholder value* (MSV) ideology began to transform the long-established corporate

governance norms that prevailed at the US companies and supported innovation until the 1970s, into a dominant corporate governance regime that supports financialization.

In the 1990s and early 2000s the US pharmaceutical industry experienced a period of productivity growth because of the new biologics that were previously acquired from, or co-developed with, pioneering US biotech companies such as Genentech, Amgen, Biogen, and Genzyme. Lazonick and Tulum (2001) argue that the “biotech boom,” a popular narrative that refers to a brief period of productivity growth that the US pharmaceutical industry enjoyed in the 1990s and 2000s, was a cautionary tale. This research explains that this cautionary tale in fact captures the evolution of the US pharmaceutical industry in the period following the remarkable industrial development story documented by Chandler that ended in the 1990s.

According to Chandler an analysis of the operations and performance of such large industrial enterprises as long-established pharmaceutical companies is key to gaining insight into the evolution of an industry such as pharmaceuticals. The analysis on the strategy and structure of the most competitive players is key to understand the dynamics of industrial development to which they contribute, given that such core companies (a) are the first movers into new markets that they explore through their integrated learning bases; (b) extend the periphery of the industry in which they operate by innovating new markets; (c) determine market structure as they redefine their own strategic boundaries; (d) determine the industrial composition by creating barriers to entry; and (e) ultimately determine the rate of growth in the industry in which they operate.

Given this theoretical perspective that Chandler (2005) applied to his analysis on the evolution of the modern chemical and pharmaceutical industries, this research in this dissertation is based on the proposition that the pursuit of comparative-historical analysis on the operation and performance of the core companies in the pharmaceutical industry producing drugs that are on chemical (small molecule) and biological (large molecule) basis is the most logical approach to develop more in-depth understanding of the industry’ productivity paradox. As stated previously, a broad purpose of this research is to gain an understanding of the mechanisms linking financialization to an ongoing productivity crisis that afflicts the US biopharmaceutical industry.

Besides the comparative-historical work of the historian Chandler, the research in this dissertation builds on the work of Edith Penrose in her now-classic book *The Theory of the Growth of the Firm* (1959). William Lazonick has in turn integrated the work of Chandler and Penrose in his theory of innovative enterprise (Lazoncik, 2001, 2010 & 2013b). As Penrose, Chandler, and Lazonick argue, the growth of an industry relies upon a unique set of organizational skills and capabilities that modern industrial enterprises accumulate over time. Therefore, the only way to gain insight into the mechanisms linking financialization to industrial productivity is through analyzing the operation and performance of the particular firms in their historical contexts. In the first part of the analysis, the research in

this dissertation evaluates the firm-level evidence to explain why and how adopting a financialized business model can result in a productivity crisis such as the US biopharmaceutical companies currently face. In the second part of the analysis, the research evaluates the validity of the argument that, the US biopharmaceutical industry, under a system of corporate governance that supports innovation rather than financialization, could be much more innovative than has been the case since the 1990s. The thesis then evaluates the firm-level evidence to explain why and how less-financialized European biopharmaceutical companies are making use of the US innovation system, characterized by government funding and subsidies as well as high product prices in an expansive national market, to outcompete the US companies in the US market.

To explain the impact of financialization on the operation and performance the firm, however, one needs to understand, first, the processes through which value is created within the firm. This thesis adopts *the theory of innovative enterprise* (TIE) framework to analyze the activities and assess the performance of the business enterprise through examining the social conditions of innovation that enhance or inhibit the growth of the firm (Lazonick, 2002). Through the TIE framework, Lazonick focuses on the social conditions of innovative enterprise (SCIE)—strategic control, financial commitment, and organizational integration—as well as the economic institutions pertaining to governance, employment, and investment that may, alternatively, enable or proscribe innovative enterprise. Through comparative-historical study of two company cases, this research explains how the social conditions of innovation that prevail at those companies come into tension with financialization to enable or proscribe innovation.

The productivity paradox and the financialization of the US biopharmaceutical industry

As the analysis in the following chapters shows, the United States is an ideal environment for drug companies that are focused on developing effective new drug therapies that can potentially disrupt the market and lead to generating significant financial gains in return. The United States can also be an ideal environment, however, for those interested in making investments in drug development programs that can lead to higher and quicker yields even without developing highly innovative new drug therapies, or developing no drug at all. If the number of major companies in the latter group exceeds the number in the former, the industrial trajectory can change in a way that begins to reward shareholders at the expense of other stakeholders such as patients, taxpayers, and the employees of such companies. Such a change in the industrial trajectory has been the source of the tension between innovation and financialization that prevails at the US biopharmaceutical companies since the 1980s.

The tension between innovation and financialization becomes vastly more problematic when the company is governed for the sake of financial interests who have the power to

extract far more value for themselves than they have contributed to the value-creation process. And, indeed, in an institutional environment dominated by the ideology that a company should be run to “maximize shareholder value” that is precisely what has occurred in the United States (Lazonick and O’Sullivan, 2000; Lazonick, 2017; Lazonick, 2018; Lazonick and Shin, 2018). Corporate executives, Wall Street bankers, and hedge-fund managers have been the beneficiaries of massive distributions of corporate cash to shareholders in the forms of stock repurchases and cash dividends, with their financial gains being out of all proportion to contributions that they have made to the corporations’ value-creation processes.

The US biopharmaceutical industry is an extreme case of the financialization that afflicts US business corporations more generally. As Lazonick et al. (2017) reveal, the 459 companies in the S&P 500 Index that were publicly listed from 2006 through 2015 distributed 90 percent of their profits to shareholders. Lazonick (2017) has called this financial behavior the “largely legalized looting of the US business corporation.” The financialization of the US biopharmaceutical industry is even more egregious when, as outlined in Lazonick and Tulum (2011), one considers all the government-funded benefits that the industry receives including massive government spending on life sciences research; world-leading investments by governments and households in educating the science and engineering labor force; patent privileges and other product-market protections; numerous federal, state, and local financial subsidies; and government-financed demand for its product.

The US biopharmaceutical industry is also a prime example where the distinction between innovation and financialization can be found in business practice. Through comparative historical case analyses, this research explains how the long-established US company Merck has transformed from innovation to financialization since the 1980s, and how the Swiss company Roche, in part through its acquisition of the “New Economy” US company Genentech (founded in 1976), has over the same decades augmented its innovative capabilities within the US market.

At the end of 2016, Merck and Roche, the two companies that are central to this study of the tension between innovation and financialization, employed 68,000 and 94,000 people, respectively. Hence, in and of themselves these companies are complex social organizations in which the relation between value creation and value extraction is not simply the sum of individual choices. Given the uncertain, collective, and cumulative character of the work in which these tens of thousands of people engage, one needs the theory of innovative enterprise to conduct a systematic analysis of the evolution of the tension between innovation and financialization in these enormous, and hugely consequential companies.

Transition from innovation to financialization

According to Lazonick (2009) an innovative enterprise becomes financialized if and when managerial decisions to allocate productive resources are driven to create gains for a group of people, including the senior executives themselves, that is well in excess of their contribution to the value-creation process. The prime means of what can be called “predatory value extraction” are distributions to shareholders in the forms of not only dividends but also, and more importantly, stock buybacks. Lazonick argues that such a predatory mode of resource allocation emanates from the dominant corporate governance ideology, maximizing shareholder value (MSV), rooted in the neoclassical theory of the market economy. According to MSV, shareholders are the only economic actors who take risks and hence are the only actors who have the incentive to allocate resources to their most efficient alternative uses.

Lazonick critiques this position by arguing that when workers supply their skills and efforts to enable the firm to generate the products that result in future revenues, they take the risk that the future employment and pay that they expect as returns will not be forthcoming, either because the innovative strategy is unsuccessful or because a corporate predator extracts the value that the workers helped to create. Similarly, when, through government agencies, households as taxpayers supply the firm with physical infrastructure and human knowledge, they take risks because the corporate profits out of which the firm pays taxes back to households may not be forthcoming or because the corporations may convince politicians to lower the tax rate. At the same time, the public shareholders, for whom MSV says the firm should be run, take very little risk because they simply buy and sell shares on the liquid stock market, and can sell their shares at any time they choose at a low transaction cost. Moreover, rooted as it is in the neoclassical theory of the market economy, MSV has no theory of how “the most efficient alternative uses” are created. That is, as a theory that legitimizes value extraction by those who contribute the least to the value-creation process, MSV lacks a theory of value creation.

Building on Lazonick and O’Sullivan (2000), Lazonick (2015) summarizes the mode of resource allocation that is necessary for innovation as “retain-and-reinvest”: the company retains its money and people and reinvests in productive capabilities, particularly those of the labor force. But at some point in its history, the company’s mode of resource allocation may shift from “retain-and-reinvest” to “downsize-and-distribute”; the business enterprise downsizes the labor force (through layoffs, pay cuts, and outsourcing) and distributes corporate cash to shareholders. The transformation from retain-and-reinvest to downsize-and-distribute is the transformation from innovation to financialization.

Analyzing the tension between innovation and financialization

What is the most fundamental driver that motivates a business enterprise to pursue economic growth? Is it profits or products? The conventional neoclassical view of the

world sees the pursuit of profit maximization as the firm's objective, with the production and sale of products as simply means to this end. But, as Lazonick (1991; 2002; 2017) has shown, the neoclassical perspective, with its constrained-optimization methodology, lacks a theory of innovative enterprise. The objective of the innovative enterprise is to transform technologies and access markets to generate goods and services that are higher quality and lower cost than those previously available.

From this perspective, profits result from the firm's success in generating innovative products, and the investment of profits to augment the company's innovative capabilities provides the financial foundation for the continued growth of the firm. Indeed, from the perspective of innovative enterprise, the pursuit of profits for their own sake is likely to undermine the social conditions of innovative enterprise, elevating value extraction over value innovation, and giving rise to the productivity disease known as financialization across different industries, including biopharmaceuticals (Lazonick, 2013a & 2017; see also Baldwin & Clark, 1992; Froud et al., 2006; Hopkins et al., 2007; Christensen et al., 2008; Andersson et al., 2010; Kessel 2011; Lazonick & Tulum, 2011; Montalban & Sakinç, 2013; Haslam et al., 2013; Gleadle et al., 2014).

All business corporations confront a tension between innovation and financialization. The enterprise must invest in value creation in order develop the high-quality, low-cost goods and services that enable it to generate revenues on product markets that will yield sufficient profits for a company to emerge and survive as an innovative enterprise. But once a company has been successful as an innovative enterprise, participants in the enterprise, including workers, taxpayers, and financiers, who have contributed to the value-creation process will want to extract some or all of the increased value that innovation has made possible. This value extraction will reward those workers, taxpayers, and financiers for their contributions to value creation, but if they extract too much value from the enterprise, they may undermine the financial viability of the company as a going concern—including the financial capacity of the company to renew its investments in the next generation of innovative products.

The theory of innovative enterprise

To examine how some actors within the economy can extract value without contributing to the innovation process through which value is created, one needs an economic theory that explains the processes through which value is created. Only then can one understand the relation among those actors who contribute to value creation and those actors who exercise power over value extraction. In research carried out since the late 1980s, Lazonick (1991, 2002, 2013b, 2017) has constructed the theory of innovative enterprise (TIE) framework to analyze the activities and assess the performance of the business enterprise through examining the central social conditions that enhance or inhibit the innovation process and the consequent growth of the firm.

Innovation—the process of creating value—drives the growth of the firm, and with it the growth of the economy, but it also opens up the possibility for financialization—the extraction of the value that has been created by parties whose labor and capital played little if any role in the value-creation process. Even for an individual working on his or her own, there would be a tension between value creation and value extraction. Should the individual who reaps profits through value creation devote those profits to further value creation, or should he or she benefit from some or all of those profits through value extraction? Once, through the application of the individual's labor effort in combination with the individual's financial investment, the firm has transitioned from a new venture to a going concern, should he or she maintain the prior intensity of effort, or should he or she reduce the amount of time and energy devoted to the value-creation process? At what point and to what extent should the individual turn from value creation to value extraction? These questions become vastly more complicated when it is recognized that a modern business corporation is a highly complex social organization, operating in a highly complex institutional environment, in which the types of individuals who have the power to extract value may not be the types of individuals who have devoted their skills, efforts, and savings to the process of creating value.

How does the work of people, collectively at a point in time and cumulatively over time, contribute to the value-creation process and growth of the firm? In an innovative enterprise, Lazonick argues that strategy, organization, and finance, have to be formulated and implemented carefully to confront the uncertain, collective, and cumulative characteristics of innovation. Innovation is uncertain: no return is guaranteed when investing in the innovation process, and hence strategy is needed to allocate resources to innovative investment projects. Innovation is collective: innovation cannot be done all alone, but rather requires organizational learning efforts among individuals from different capabilities and responsibilities. Innovation is cumulative: innovation cannot be done all at once, but requires sustained learning, and hence committed finance, to accumulate the knowledge to generate a high-quality product and then capture a large extent of the market to reap economies of scale (Lazonick, 2013b).

Lazonick offers the social conditions of innovative enterprise (SCIE) framework to analyze the operation and performance of the firm. Strategic control is a set of social relations that determine the abilities and incentives of those who allocate the firm's resources to invest in inherently uncertain innovation processes. Organizational integration is a set of social relations that mobilizes the skills and efforts of individuals with different capabilities and responsibilities to engage in collective learning. Financial commitment is a set of social relations that sustains the collective learning processes so that learning cumulates from the time at which investments in the innovation processes are made until, through the sale of innovative products, financial returns are generated (Lazonick, 2013b).

Thesis outline

Chapter 1 lays out the research strategy developed based on Lazonick (2002) historical-transformation methodology guided by the TIE framework. As the social relations inside the major US biopharmaceutical companies change from innovation to financialization, managerial priorities change in ways that ultimately make the downsize-and-distribute resource allocation strategy a managerial goal to attain, carried out in the name of maximizing shareholder value. The most explicit indicator to measure whether, or to what extent, a public company is financialized is the level of resources the company allocates to repurchase its own shares, also known as stock buybacks, which in some extreme cases it can exceed net income by eating into cash reserves, taking on debt, shedding employees, and selling assets.

Given that the transition from innovation to financialization is to some extent company-specific, there is a need to research leading companies in the US biopharmaceutical industry to identify when the companies made such a transition from innovation to financialization. The research has chosen case-based comparative business history analysis as the most appropriate research approach based on the following theoretical assumptions. According to the TIE perspective, even within the same industry innovative companies are inherently distinctive in the ways in which they transform technologies and access markets. Furthermore, even within the same institutional environment, the strategy, structure, and performance that characterizes different companies can vary significantly. As explained in Chapter 2, this research utilizes the *historical-transformation* methodology, an analytical approach Lazonick (2002) proposes for multidirectional analysis of organizations that integrates theory and history.

From this perspective, the empirical analysis in Chapter 3 pursues a rigorous historical study examining the changes in the institutional change in which the biopharmaceutical companies are embedded. The resulting historical account derived from documenting the evolution of the major US economic institutions related to governance, employment, and investment verifies the relevance of the theory employed in this thesis to explain the social phenomenon investigated. Chapter 3 also documents the evolution of the US innovation system for biopharmaceutical drug development since the 1980s, emphasizing the ways in which it has sought to support innovation, even as major US biopharmaceutical companies have in fact undermined innovation through the financialized corporate resource-allocation behavior that is documented in Chapter 4.

Chapter 3 explains that the availability of speculative markets in the United States gave rise to the New Economy biotech companies in the 1980s and 1990s. It is the speculative nature of the US stock market that often enables biotech start-ups, even the most risky companies without any products on the market to generate steady streams of product revenues, to raise large sums of capital from stock traders through initial public offerings (IPOs) of corporate stocks. Having dubbed such New Economy biotech companies as “product-less initial

public offerings” (or PLIPOs), Lazonick and Tulum (2011) explain how the existence of speculative markets gave rise to the PLIPO phenomenon starting with iconic biotech IPOs such as Genentech and Cetus in the early 1980s, creating precedents for many other biotech start-ups to follow a similar path to access capital in the speculative markets.

Arguing that the financialization of the US biopharmaceutical business model is the real culprit behind the diminishing productivity of the US biopharmaceutical companies, Chapter 4 explains in great detail why and how Merck & Co made the transition from innovation to financialization. The analysis in this chapter reveals the underlying causes of Merck’s decision to abandon an innovation-driven growth path in the last half of the 1990s and the consequences that these managerial actions had on the company, which had bolstered its productivity and enjoyed substantial economic growth in the previous decade.

Incentivizing research personnel with the lure of gains from stock options rather than career employment security, the use of broad-based stock options as a mode of compensating research employees contributed to a breakdown in the Old Economy “career-with-one-company” norm, as the increase in labor mobility resulted in an outflow of R&D workers from Big Pharma to PLIPOs. As Big Pharma failed to innovate, in part because of the breakdown in organizational learning due to increased labor turnover, it sought to maintain revenues through M&A activity that could give these established companies control over proven drugs that typically had years of patent life left. This strategy of consolidation generally resulted in massive layoffs, which had the effect of further undermining, and perhaps destroying, organizational integration.

Chapter 5 assesses the evidence that the less-financialized European biopharmaceutical companies, which are subject to price regulation in their home markets, augment their innovative capabilities by tapping into the immense US knowledge base and selling their products in the United States at high, unregulated, prices. Recognizing that all business corporations confront a tension between innovation and financialization, the theory of the innovative enterprise provides a framework for analyzing the evolution of the tension between innovation and financialization for US and European pharma companies operating in the same institutional environment.

Examining the unique ownership structure Roche has maintained during the past century, Chapter 6 explains how the abilities and incentives of strategic managers remained somewhat unchanged, allowing the organization to keep strategic focus on improving innovative productivity, even as the US industrial economy, where the company’s R&D operations were concentrated, became increasingly financialized. More specifically, chapter 6 explains that, by undermining the social conditions of innovative enterprise, the value-extraction efforts of financial interests in the United States enabled an outsider, Roche, to gain access to valuable US-based knowledge flows that would have otherwise been far more difficult for it to obtain.

Chapter 7 offers a comparative summary of the finding of the case analyses. In the comparative analysis of two biopharmaceutical company cases sampled, the research first illustrated how the social conditions adapted to overcome the challenges that emerge during the innovation process. The research also explains how the dynamics of financialization become established within productive organizations and how financialization practices develop to such an extent that they begin to undermine industrial productivity, or drug innovation, and to interfere with the social conditione of innovation within innovative biopharmaceutical enterprises.

The final chapter of this thesis explains the policy implications of this research, discussing how, under a system of corporate governance that supports innovation rather than financialization, the US innovation system could result in a much more innovative biopharmaceutical industry that would focus on treating medical problems at affordable costs rather than on boosting stock yields to increase the financial gains of senior executives and financial interests. The dissertation concludes with a discussion on the need for future research using the comparative-historical case-based approach to analyzing the evolution of the tension between innovation and financialization in the global economy.

1 THEORY AND CONCEPTUAL FRAMEWORK

In this chapter, I conduct a survey of the current literature on the drug innovation crisis in the US biopharmaceutical industry to provide a theoretical perspective on the industry's diminishing R&D productivity and failure to meet the market demand for effective and affordable medicinal products. The literature review focuses on the innovation crisis in the context of the industry's prevailing business model rooted in a financialized corporate governance ideology widely known as *maximizing shareholder value* (MSV).

The financialization-hypothesis argues that the influence of finance over corporate governance grows and incentivizes top executives to engage in a destructive mode of resource allocation that entails downsizing productive assets and distributing available cash flow to the shareholders as opposed to retaining earnings and reinvesting in the acquisition or development of productive resources. MSV provides the intellectual basis for this strategy of resource allocation that enhances shareholder value at the expense of other stakeholders such as sick patients or employees.

This chapter reviews the key concepts of the neoclassical theory of the market economy (TME) because the basic tenets of MSV are deeply entrenched in such market-based theory. The chapter then details *the theory of the innovative enterprise* (TIE) and argues that the TIE offers more appropriate analytical tools to explain how the drug industry's increasingly financial business model plays a key role in its ongoing innovation crisis. The literature review outlines the need for a more effective methodological approach to explain the mechanism through which financialization undermines drug innovation in the United States. Based on the premise that business organizations are the drivers of industrial

productivity, this chapter finally argues that analyzing the changes in the social conditions of innovative enterprise provides an effective research approach to understanding how financialization undermines industrial productivity.

1.1 The theory of market economy and varieties of resource allocation modes

Lazonick (2013b) argues that the neoclassical “optimizing-firm” is not innovative and that the market-based neoclassical account of economic growth often contradicts the historical narrative or the real-time evidence. Neoclassical theory perceives a market as an effective means for allocating the productive resources of an economy in efficient ways, depending on the competitive structure of the market. Neoclassical theory is also based on the assumption that a market can allocate resources most efficiently when the market is perfectly competitive. In this market-based model, deductive reasoning is used to identify the factors that cause a suboptimal state of market equilibrium. Such analysis, however, does not seek to explain the process through which the firm transforms the productive capability of input factors to result in more efficient outcomes—that is, higher-quality, lower-cost products.

The baseline for such analysis is the “pareto-optimum”—the most efficient state of market equilibrium. This implies that no other combination of price and quantity exists that would make the market exchange more efficient. In the neo-classical model, any transition from a suboptimal state to the “pareto-optimum” optimal one is regulated by the market mechanism consisting of the competing forces of supply and demand. In such a model, the market price is considered as the prime mechanism for the market to enter into a self-correction phase. This continues until the current price brings the market to “pareto-optimum”, a specific state of the market that is unlike any other combination of price and quantity in which the exchange of product could be more efficient. This optimal combination of quantity and price will vary depending on whether the market structure corresponds to conditions of perfect or imperfect competition.

According to general equilibrium theory, perfect competition results in the ideal, even if unattainable, rate of efficiency. Because barriers to market entry and exit have been removed in a perfectly competitive market, an increasing number of new market actors participate in the voluntary exchange of products and services and ultimately the marginal power of each individual actor diminishes to the point where no single actor can exercise power over market forces in order to set prices. In this competitive state, the market is considered efficient “allocatively” but not necessarily “productively.” In this interpretation of how the economy works, firms are operating as profit-maximizing supply agents who can only adapt to market signals (changing price levels) in search of opportunities for profit while engaging in a series of on-going operational adjustments to adjust their levels of output marginally in response to the forces of supply and demand.

In work published since his pathbreaking book, *Business Organization and the Myth of the Market Economy* (1990), Lazonick (2016), following Schumpeter (1942) has challenged this neoclassical theory of the firm and the ideal of perfect competition on the grounds that it fails to analyze how, through strategy, organization, and finance, the innovating business enterprise can transform the technological and market conditions that the “optimizing” firm takes as given constraints, and differentiate itself from these competitors by generating higher-quality, lower-cost products than previously were available. There are high fixed cost to developing a higher quality product that in and of themselves place the innovating firm at a competitive disadvantage. But as the innovating firm captures a larger extent of the market, it spreads out these fixed costs to achieve lower unit costs through economies of scale, driving the growth and profitability of the firm. As a result, the innovating firm creates new standards of efficiency, while the optimizing firms of neoclassical theory seek to maximize profits subject to technological and market conditions that have become inefficient. It is for this reason that Lazonick invokes Schumpeter’s argument that “perfect competition is not only impossible but inferior, and has no title to being set up as a model of ideal efficiency” (Schumpeter, 1942, p. 106).

Accepting technological and market conditions as give constraints on firm decision-making, neoclassical economics in effect idealizes an inefficient economy precisely because it lacks a theory of innovative enterprise. Neoclassical growth theory aggregates all the productive agents in an economy to analyze them as a single market construct. By doing so, Lazonick argues that such a theory conceals the productive contributions of innovative actors within an economy and fails to consider the sources of productivity gains that permit firms to generate profits from innovation and contribute to the growth of the economy in which they operate. He proposes an alternative, the TIE framework, which essentially deconstructs the “market-based” argument into its productive elements and highlights the “innovating-firm” as the true medium for the distribution of an economy’s productive resources as well as its engine for growth.

In failing to offer a sound theoretical argument to explain successful transformation of productive resources by the “innovating firm” yields economic growth, TME cannot begin to understand how the value that the innovation process generates is shared among participants in that process and how certain economic actors who make little if any contribution to the process of value creation might gain strategic control over the allocation of a firm’s resources to extract far more value than they create—which is the firm-level definition of “financialization”. Lazonick (2002) argues that the inadequacy of the neoclassical “optimizing-firm” to explain innovation and growth means that TME’s “constrained-optimization” methodology cannot be used to analyze the process of innovation and growth. Instead, he argues, one needs a “historical transformation” methodology in which one uses history (or facts) as a means of constructing theory (or logic), and the resultant theory as a guide to analyzing history as it unfolds over time.

1.2 Transition from managerial-capitalism to shareholder-capitalism

Lazonick's TIE approach places "corporate governance" at the center of economic analysis. In their extensive literature survey, Shleifer and Vishny (1997) refer to *corporate governance* as the ways in which investors exert power over executives to control the resource allocative decisions of the companies in order to protect and enrich the return on their investments. Lazonick (2009) identifies two particular periods in the evolution of the modern corporation in the US economy with distinct corporate governance characteristics. The dynamics of governance among shareholder (principles) and top business executives (agents) in US public corporations are different enough in terms of governance mechanisms and economic performance for Lazonick (2009) to distinguish between the periods of the *Old Economy Business Model (OEBM)* and that of the *New Economy Business Model (NEBM)*. The first period of OEBM is one of *managerial capitalism* during which corporate executives had power to control the allocation of productive resources within their firms or across the industries in which the firms were embedded. Because of the importance of the prospect of a quick initial public offering (IPO) on the speculative NADSAQ stock exchange in inducing venture capital and human resources to join startups under the NEBM, there is pressure on firms that do an IPO and grow large in the era of the NEBM to distribute cash to shareholders in the forms of dividends and stock repurchases (also known as stock buybacks) rather than investing in new productive capabilities to sustain the firm as an innovative enterprise. Cash distributed through stock buybacks, often in addition to dividends, deplete retained earnings that are the financial foundations for investing in the next generation of innovative products.

As Jensen (1989) argue "management was loyal to corporation, not to the shareholders" during the Old Economy Business era. Shareholding was fragmented among household (or retail) savers, leaving management to invest in the growth of the firm. Content with collecting quarterly dividend payments when and if the firm could afford to pay them, these households as savers exerted little if any influence over the allocation of corporate resources. The future value of the shares that they held were bound up with the abilities and incentives of management to make investments in productive capabilities that could yield innovative outcomes (Lazonick, 2014a). The viability of managerial capitalism changed significantly as certain corporations known as conglomerates pursued major diversification campaigns in the 1960s that resulted in lower profits and growth in the 1970s and 1980s. According to Jensen (1989), this period represents the "eclipse of the public corporation" as this form of business enterprise came to the end of its life cycle and no longer served the economy. This changing face of the public enterprise, however, had also been preceded by the emergence of the NEBM and the spread of the ideology of *maximizing shareholder value* (MSV), of which Jensen was the leading proponent.

Jensen argues that some major corporate and industrial restructuring effort witnessed in the US economy in the 1980s had sobered up the corporate executives, who had initially hoped to discover new sources of growth with shareholder's support but came to recognize that a

major overhaul on the governance of the US public corporations was inevitable. Drawing from his earlier work Jensen (1989), argues such an outcome was necessary as the rapid decline of the public corporations in the 1970s had emerged as a byproduct of the “conglomerate movement” of the 1960s. The *agency problem* that this created subsequently required the introduction of operational efficiencies. Lazonick (2003) argues, on the other hand, that the conglomerate movement emerged mainly as an overextension of the idea that the new multidivisional structure of the modern corporation could combine new economies and scope to build competitive strength both nationally and internationally. For Lazonick, the problem of conglomeration was that under this form of firm growth in which those who exercised strategic control became disconnected from the firm’s innovation processes, shareholders exercised too much, not too little control, over the allocation of corporate resources.

1.2.1 Capital markets emerging as corporate locksmiths that “unlock” value for shareholders

Jensen & Meckling, (1976), Jensen (1989) and Homlstrom and Kaplan (2001), as proponents of what is known as agency theory”, explain how changes observed in the capital markets paved the way for some activist shareholders to pursue leveraged takeovers of companies with control over the allocation of significant productive assets waiting to be “unlocked” for shareholders. Holmstrom and Kaplan (2001) argue that two particular impacts of the capital markets on the industrial economy ultimately resulted in the “return” of greater value to the shareholder. On the one hand, during the 1980s, the capital markets “reversed the ill-advised corporation diversification” decisions and, on the other hand, they “disciplined managers who had ignored shareholders” in order to maximize the value returned to other stakeholders. Along with hostile takeovers as a tool for taming managerial power, agency theorists also advocated more “shareholder-friendly” tactics such as increasing the proportion of stock-based pay in compensation packages so that managers as *agents* would be more incentivized in to enhance stock-price performance and shareholder value for the sake of shareholders as principals (Jensen & Murphy, 1990).

Claiming that shareholders are the only risk bearers in business corporations, MSV challenged the stakeholder perspective and argued that shareholders are the only claimants of residual value, or profits, generated by a firm. With a fundamental belief in the market-driven resource allocation regime, MSV argued that, by “returning” the corporation’s *free cash flow* to the only *residual claimant*, shareholder value would be maximized and the market would find more efficient ways to invest the economy’s productive resources (Fama & Jensen, 1983; Jensen, 1986; Holmstrom & Kaplan, 2001). I place “returning” in quotation marks because, as Lazonick (2016) has shown, public shareholders do not invest in the productive capabilities of companies; they only invest in outstanding shares. So how can value be “returned” to them?

As we shall see in this research, the MSV claim that shareholders are the only risk-bearers in the business corporation has problematic implications in the context of biopharmaceutical industry, in which both taxpayers and workers who contribute to the innovation process take risks of whether gains from innovation will be forthcoming and whether they will share in these gains. For the shareholders in biopharmaceutical companies, *value-extraction* is possible without making the necessary contributions to the *value-creation* process for three reasons: (i) the far-reaching knowledge-base upon which biopharmaceutical companies depend has been developed through strategic government programs funded generously by US taxpayers; (ii) it takes teams of scientists years if not decades to develop an effective drug, and (iii) there is a drug market largely financed by the government that can absorb innovative new therapies.

1.2.2 Capital markets vs corporate management for allocating resource

Rooted in the neoclassical theory of the market, MSV ideology assumes than an economy's resources can be allocated most efficiently through markets. As capital can be best allocated among productive actors by the market, MSV then goes on to argue that the top executives of a business enterprise should restrain themselves from engaging in *retain-and-reinvest* resource allocation strategy in favor of a *downsize-and-distribute* mode of resource allocation. There are three pillars of corporate governance system: product markets, the internal control mechanism that is at the discretion of the Board of Directors and the capital market. Jensen argues that the capital market appears to be the most efficient to ensure that business executives deliver higher investment yield and enhance shareholder value.

Jensen (1989) argues that product markets played no "disciplining role" by explaining that the domestic product market for US corporations had expanded to such an extent since the Great Depression that retained corporate earning never weakened enough to affect the financial health of corporations. As regards the internal control mechanism, Jensen argues that the growing emphasis on increasing the number of independent directors would not change the effectiveness of a board of directors to impose discipline and monitor executive performance, as executives exercise significant power over the process of selecting and appointing independent directors. Lipton (2015), however, challenges this view and argues that the function of the Board has changed from one of "strategy and advice" to one of "investigation and compliance". As a result, executives are discouraged from sharing concerns with directors who are too "investigative and defensive". In addition, as the disciplining and monitoring function of the directors increased, so too did the demand for professionals such as lawyers, accountants and consultants to act as consultants to management. Lipton (2015) argues that this overreliance on consultants raises the question of whether external consultants exercise more control than directors who represent public shareholders.

The proponents of MSV argue that “for a company to operate efficiently and maximize value, free cash flow must be distributed to shareholders rather than “retained”. Chandler argues, however, that retained earnings can often be “one of the cheapest sources of long-term capital for investment in commercializing new products.” (Jensen, 1989, p. 8; Chandler, 2005, p. 8). Chandler’s extensive historical analysis of the development of the modern chemical and biopharmaceutical industries in the United States, stands in stark contrast to Jensen’s claim that retained earnings are better-off in the hands of the shareholders. Chandler (1990) argued that retained earnings “provided industrial managers with most of the funding needed to finance continuing growth” and were vital to US industrial development (p. 597).

For Jensen (1989), the premiums of 50 percent above market price that were paid on average by firms to go private during the corporate takeover movement are an indication of how much value could had been destroyed by the executives of these firms before they were taken over by private investors. The same indicator could be used, however, to question how these executives managed to build assets valued at 50 percent over market price. As private investors were interested in extracting such value, it is worth considering what role the shareholders played in creating this value during the process leading up to leveraged buyouts (LBOs) or corporate takeovers. Jensen (1989) explains that such transactions were conducted in the 1980s by “activist shareholders” who were frustrated by the lack of an effective monitoring mechanism to control the inefficient management practices of executives by shareholders. Yet a comparative analysis of the investment decisions of public and private corporations by Asker, Farre-Mensa, and Ljungqvist (2015) finds evidence of distorted investment decisions on the part of public firms due to increasing short-term shareholder pressure, in particular among those firms whose stocks are “most sensitive to earning news”.

In addition, not all investors or legal experts who counsel CEOs on shareholder relations share the MSV sentiment on the value “shareholder-friendly” ways to “return” excess cash flow. In his Annual Letter to CEOs on January 24, 2017, Larry Fink, co-founder and CEO of BlackRock, one of the worlds’ largest private equity firm, urged his investors and employees not to indulge the idea of “shareholder-friendly” practices given that certain types of capital can reduce value for long-term shareholders such as BlackRock in favor of shareholders with a short-term investment perspective (Fink, 2017). Warren Buffett is another example of an investor who is known to focus on creating long-term value for shareholders. He warned his shareholders against the perils of running a corporation with the primary objective of meeting short-term financial goals:

...If management makes bad decisions in order to hit short-term earnings targets, and consequently gets behind the eight-ball..., no amount of subsequent brilliance will overcome the damage that has been inflicted.

Berkshire Hathaway Company Annual Report 2005

Jack Welch, the legendary Chairman and CEO of General Electric (GE) led the company during the period when MSV rose to become the dominant corporate governance ideology among US corporations. However, he termed MSV the “dumbest idea in the world” (Guerrera, 2009). Denning (2015) cites other CEOs who share Welch’s view of MSV. These include Vinci Group Chairman and CEO who called MSV “totally idiotic,” and Tim Cook, CEO of Apple, who also denounced MSV ideology and claimed that senior managers in Apple “don’t consider the bloody ROI,” when making customer-oriented decisions.

The investment phenomenon that became popularly known as “quarterly-capitalism” was considered to have such socio-economic risks that it was among the major themes of the 2016 US presidential election. One of the candidates, Hillary Clinton, even suggested ending the practice of corporate reporting on quarterly-basis to avoid the short-term pressure that executives felt to meet the corporate targets on earnings in anticipation of shareholder expectations (Long 2015). While such regulatory changes may not suffice to eradicate short-termism entirely, such proposals are evidence of a growing desire to limit potentially unsound allocative decisions to meet such earning targets. By reducing layoffs, excess liquidations, or, in extreme cases, manipulation of figures in financial statements to conceal any negative information, it is expected that corporations will instead focus on long-term investment programs and prefer measures that preserve long-term growth prospects.

1.3 The theory of innovative enterprise (TIE) and the social conditions of innovative enterprise (SCIE)

Lazonick (2002 & 2013) proposed a theory of the firm that is based on the assumption that it is innovative by nature because the growth of the firm depends on its ability to transform industrial conditions into competitive advantage. In doing so, the “innovating-firm” functions as an allocative and transformative agent and acts as the primer and catalyst for economic growth. As already indicated, such a view of the firm is in sharp contrast to that of the “optimizing-firm” proposed by the neoclassical theory of the market economy (TME). The following section surveys the literature on *the theory of innovative enterprise* (TIE) and compares it to alternative theories in which the MSV ideology, the dominant governance doctrine widely accepted among the US industrial organizations, is rooted. While an in-depth discussion of neoclassical *market theory* is beyond the scope of this thesis, the current review constitutes a basis for comparison of TIE with the dominant contemporary approach to corporate governance theory, that of *maximizing shareholder value*.

MSV provides the intellectual basis for the corporate governance structure that is widely accepted by US corporations and it has become more prevalent among the biopharmaceutical companies in the United States. Such a governance ideology, along with its theoretical and methodological roots in neoclassical economics, stands in sharp contrast

against Lazonick's TIE framework and historical-transformation methodology. As a theoretical tool for understanding the growth and performance of the firm, TIE provides a relevant and rigorous account of how business organizations create value and improve their economic performance in the real economy. Through TIE, Lazonick conceptualizes a theory for the firm that achieves growth through productive transformation and explains how an innovating firm obtains resources and transforms them into revenue generating goods and services that are higher in quality and lower in cost than what was previously available. Unlike the neoclassical "optimizing" firm whose economic growth is constrained by the productive capability of the resources available to the firm, the "innovating" firm uses organizational learning to overcome the challenges that stem from constraints on resources in order to create competitive advantage and build a path to sustainable growth.

In order to capitalize on a market opportunity, or to explore and conceptualize new opportunities, an innovative entrepreneur or manager needs to engage in three fundamental activities:

1. conceiving, designing and executing an innovative strategy and engaging in organizational learning to develop and utilize resources and to coordinate innovation efforts;
2. forming an organization where the process is embedded and facilitated;
3. acquiring finance to procure, develop or utilize resources and to sustain the innovation process until it delivers the intended outcome.

The process of productive transformation is important because it ultimately leads to innovation, which, in Lazonick's terms, is defined as the generation of "higher quality products at lower costs than had previously been available". In an innovative enterprise, Lazonick (2015) argues that *strategy*, *organization*, and *finance* have to be formulated and implemented carefully to confront the challenging characteristics of innovation which is:

- *uncertain* (no return is guaranteed when investing in the innovation process);
- *collective* (innovation cannot be done alone, but requires collective learning efforts among individuals with varying skill-sets);
- *cumulative* (innovation takes time to accumulate the necessary skills and knowledge).

The social and complex nature of the innovation process requires the conceptualization of a new theoretical framework that can capture such complexity with the use of tangible concepts and measure innovation performance based on the evidence manifested in socio-business indicators. As a response to this theoretical challenge, Lazonick offers three concepts, termed the *social condition of innovative enterprise* (SCIE) as a theoretical

framework for the assessment of the economic performance of business organizations. The three social conditions, *strategic control* (SC), *organizational integration* (OI) and *financial commitment* (FC) allow the systematic analysis of organizational performance. SCIE implies a set of relations (Lazonick 2015), which:

- empowers managers to make resource allocation decisions that support the innovation process (SC);
- incentivizes people from different functions and capabilities to dedicate their skills and efforts in achieving strategic objectives (OI);
- ensures that the necessary funding is committed to the innovation process until the intended financial returns are generated through sales of an innovative product (FI).

The adoption of a financialized business model inhibits innovation, and in so doing negatively impact on the economic performance of an innovating enterprise and the entire productive economy. As *value-extracting* activities increase, the social conditions of innovative enterprise change to such an extent that they no longer effectively support innovative strategies, organizational learning efforts, and sustained committed finance.

1.3.1 Schumpeterian, Penrosioan, and Chandlerian Antecedents to TIE

Schumpeter's focus (1939) on "cyclical instability" highlighted technological change in industries and led to the emergence of an alternative perspective on the role of large industrial organizations as the engine of innovation and economic growth. The increasing number of scholars interested in Schumpeterian growth theory meant that large business establishments became a subject of intense research in an attempt to analyze the impact of the growth of large business establishments on industrial change and economic growth. And, as previously mentioned, in his 1942 book *Capitalism, Socialism, and Democracy*, Schumpeter called for a theory of the innovative enterprise that, in the process of growing large, drives the process of economic development.

The extensive studies of the prominent business historian, Alfred D. Chandler Jr., are the most influential publications on the history of the large industrial corporations in the United States. Chandler (1962) initially documented the evolution of the large US corporation into a multi-divisional structure that allowed it to explore new growth opportunities across product or geographic market segments in from the 1920s to the 1950s. In another influential piece of work, Chandler (1977) examined the rise of the managerial class within the corporation in the late 19th and the early 20th century, as well as the early efforts among industrial corporations to establish a new managerial structure to sustain the efficiency of fast-growing business operations. By mastering this new managerial structure, US corporations were transformed into the new multi-divisional structure that allowed them to enjoy economies of scale and scope from extending

operations into new markets. Chandler went on to compare US corporations with the large industrial corporations in Great Britain and Germany, the major industrial powers of the same time period.

Through this comparative analysis, Chandler (1990) revealed the importance of the unique capabilities for organizational learning that constitute the basis for a corporation's competitive strength. The ability to benefit from economies of scale and scope depends on how successfully corporations build an "integrated learning basis" from which to develop superior products and processes and move into new markets for further growth. From this theoretical lens, Chandler (2005) examined the growth of the modern chemical and pharmaceutical industry and, to some extent, attempted to explain how Merck & Co. and Hoffmann-La Roche managed to make their historical transitions from industrial chemical firms to the ethical drugs business in the first half of the 20th century.

The important work of the economist Edith Penrose reflects Chandler's belief that large industrial corporations played a key role during the massive expansion of the US economy in the 20th century. Penrose (1959) recognized that modern industrial corporations function as social entities and that their unique capabilities are embodied within a pool of knowledge and skills that are accumulated by the individuals employed in these firms. Penrose contends that the collective actions of individuals can only lead to productivity growth for US corporations if their efforts are effectively coordinated by management. Citing the Penrosian theoretical perspective on the growth of the firm, the resource-based view (RBV) of the firm seeks to explain why we observe different levels of economic performance among firms that are operating within the same industry and implementing similar strategies (Teece, 1982; Wernerfelt, 1984; Barney, 1986a & 1986b; Amit & Schoemaker, 1993).

Pisano (2017) argues that explaining the ways in which firms accumulate capabilities goes beyond the scope of theoretical realm of resource-based view (RBV) of the firm. Putting forth a dynamic capabilities perspective, he contends that the RBV fails to explain why and how some firms outperform others in creating and developing capabilities that lie at the heart of their competitive advantage. The dynamic capabilities perspective, most fully developed by Teece (2009) postulates that it is a distinct set of capabilities embedded within firms, as opposed to markets through pricing system, enables the creation of "private wealth" in a market-based economy. In their original essay on dynamic capabilities, Teece, Pisano, and Shuen (1997) highlight such a set of firm-specific capabilities that allow a firm to achieve competitive advantage over its rivals resulting in disparity in terms of economic performance among the firms competing in any given industrial sector.

Although rooted in the work of Chandler and Penrose, Lazonick's theory of innovative enterprise (TIE) framework extends beyond the theories of these two influential management scholars. Chandler and Penrose's theoretical perspective on the growth of the

modern corporation diminished in relevance as the realities of innovation, competition, and growth changed drastically in the decades from the 1980s. Having adopted the same core principles of the growth of the Chandlerian and Penrosian modern corporation, TIE offers a more dynamic theoretical perspective that can capture the dynamics of the growth of the firm regardless of time, institutional setting, or industrial conditions.

Lazonick (2002) argues that while Chandler's theory of the growth of the firm accounts for the mechanism that links productive transformation with economic growth, but his abstract view of the corporation fails to capture the underlying social process that allows such a transformation to occur (Lazonick 2002). Chandler's account of the growth of the firm thus lacks an explanation of the socio-organizational roots of the ongoing productivity crisis as his growth theory offers no operational understanding of how the forces of financialization could undermine the development of "integrated learning basis (ILB)" within an organization and ultimately damage the potential for industrial growth in the long-term. In this respect, The TIE framework is compatible with the dynamic capabilities framework, but considers the analysis of the growth of the firm in particular institutional environments, with social power rooted in both collective action and access to finance playing central roles.

1.3.2 From innovation to financialization: the shift from the Old Economy business model (OEBM) to the New Economy business model (NEBM)

Lazonick (2009) compares the key characteristics of the Old Economy Business Model (OEBM) and the New Economy Business Model (NEBM) based on the key components of the three core activities of firms: strategy, organization, and finance. Regardless of their size, all businesses need strategy, organization and finance to transform the industrial conditions, namely *technology*, *market*, and *competition*, in order to produce innovative (high-quality and low-price) output for economic growth. In the context of the biopharmaceutical industry these two distinct business models correspond to different levels of economic performances. The first is observed during the period of significant growth of the OEBM, which took place primarily during the post-World War II decades. The era of the NEBM began to emerge in the 1970s but mostly grew during the 1980s and the 1990s, along with the change in the dominant business practices in the US. Table 1 identifies the key characteristics of OEBM and NEBM that biopharmaceutical firms share with the firms in the other industries that Lazonick (2009) has studied.

Different industries, characterized by different technologies, markets, and competitors, respond differently to the same institutional settings, while the transformation of business models in leading sectors such as information-and-communication technology (ICT) and biopharmaceuticals influence the reshaping of those institutional settings over time. Lazonick (2014b) argues that the transformation from the OEBM to the NEBM was accompanied by the rise of maximizing shareholder value (MSV) ideology. For ICT and biopharmaceutical firms, this was partly linked to their reliance on the speculative

NASDAQ stock market to attract venture capital (VC) and knowledge workers. VCs firms were attracted to the exit strategy that a quick IPO on NASDAQ offered. In addition, high-tech labor was induced to leave secure employment at Old Economy companies through the use of attractive stock options as a form of remuneration at the New Economy companies.

Examining the evolution of the modern pharmaceutical industry in the United States, Chandler (2005) explains that both domestic and foreign drug companies received the significant boosts from three major productivity-enhancing events in the second half of the 20th century. The first event took place in the first decade after the end of World War II when drug companies began to leverage newly-acquired skills and knowledge and quickly introduced new antibiotics, steroid-based anti-inflammatories, and diuretics (blood-pressure medications) to the drug market.

Table 1: Comparing the characteristics of Old and New Economy business models¹

	Old Economy Business Model (OEBM)	New Economy Business Model (NEBM)
<i>Strategy (product)</i>	<i>Growth by building on internal capabilities;</i> <i>Business expansion into new product markets based on related technologies;</i> <i>Geographic expansion to access national product markets.</i>	<i>New firm entry into specialized markets;</i> <i>Sale of branded components to system integrators;</i> <i>Accumulation of new capabilities by acquiring young research-intensive firms.</i> <i>Acquisition of branded components by system integrators;</i>
<i>Strategy (process)</i>	<i>Corporate R&D labs;</i> <i>Development and patenting of proprietary technologies;</i> <i>Vertical integration of the value chain, at home & abroad</i>	<i>Corporate R&D labs (decentralized many)</i> <i>Cross-licensing of technology based on open systems;</i> <i>Vertical specialization of the value chain;</i> <i>Outsourcing and offshoring (to some extent).</i>
<i>Finance</i>	<i>Venture finance from personal savings, family, & business associates;</i> <i>NYSE listing;</i> <i>Payment of steady dividends;</i> <i>Growth finance from retentions leveraged with bond issues.</i>	<i>Organized venture capital;</i> <i>Initial public offering on NASDAQ;</i> <i>Low or no dividends;</i> <i>Growth finance from retentions plus stock as acquisition currency;</i> <i>Stock repurchases to support stock price.</i>
<i>Organization</i>	<i>Secure employment: career with one company;</i> <i>Salaried and hourly employees; unions;</i> <i>Defined-benefit pensions;</i> <i>Employer-funded medical insurance in employment & retirement.</i>	<i>Insecure employment: inter-firm mobility of labor;</i> <i>Broad-based stock options;</i> <i>Nonunion;</i> <i>Defined-contribution pensions;</i> <i>Employee bears greater burden of medical insurance</i>

Source: Reprinted from Lazonick (2009, p. 17). Sustainable prosperity in the new economy? Business organization and high-tech employment in the United States.” WE Upjohn Institute.

¹ See the table in appendix 3 that compares the characteristics of Old Economy pharmaceutical and New Economy biotechnology companies.

The second event was observed in the 1980s when new learning in biochemistry and enzymology coupled with the rational [drug] design approach to drug discovery led to the development of a new generation of anti-hypertensives and statins (cholesterol medications). The third event occurred in the late-1990s and early-2000s as advancements in molecular biology and *recombinantDNA* technology were combined with new information on the genetics of organisms (genomics) from the Human Genome Project (HGP) to pave the way for the discovery and development of new generation biologicals. This final event benefited further from parallel advances in the information and communication technologies (ICT).

The latter two events unfolded from the 1980s to the 2000s, which also corresponds to a period when leading research-based industrial organizations in the US were going through a fundamental change in their “business model”. These changes were characteristic of a new high-tech economy that was growing in importance in the US (Carpenter et al., 2003; Lazonick, 2009; Carpenter & Lazonick, 2017). The fledgling field of biotechnology in particular experienced rapid growth as an increasing number of “New Economy” companies began to emerge in the west coast of the US which was traditionally the home of ICT firms.

A group of highly-specialized investors with experience of supplying capital to high-risk technology VCs were seeking new technology fields in which to diversify their investment portfolios outside of high-tech start-ups in the ICT industries. VCs began to test the suitability of the NEBM in the emerging biotechnology field in the 1970s and 1980s. In biopharmaceuticals, this process began with Cetus in 1971 and then gathered pace with Genentech in 1976, Biogen in 1978, Amgen and DNAX in 1980 and Chiron in 1981. Cetus and Genentech raised significant capital from their initial stock offerings at NASDAQ, although they remained many years away from putting their first products in the market. As a result, the biotechnology industry quickly expanded through what Lazonick and Tulum (2011) and Lazonick and Sakinç (2010) have termed “product-less initial public offerings” or “PLIPOs”. The rise of the PLIPO phenomenon between the 1980s and the 2000s underlies the importance of the speculative nature of NASDAQ in the growth of the NEBM in the biotechnology sector. Despite having no product-revenue stream to secure funding through conventional finance sources, high-risk biotech ventures became the new darlings of speculative stock traders (Schrage & Henderson, 1984). This source of funding has subsequently contributed to the financialization of the US biopharmaceutical business model since the 1980s (Lazonick & Tulum, 2011)

Innovative new drug therapies were thus beginning to emerge within New Economy companies in the budding field of biotechnology with financing from the VC industry based on the west coast of the United States. Meanwhile, the incumbents of the pharmaceutical market were located on the East Coast, mainly in the “Pharma Belt”, a region extending from Pennsylvania to New York but mostly centered on New Jersey. The large pharmaceutical firms began to have interactions with the New Economy

biotechnology companies in the 1990s and they slowly transformed themselves to take advantage of the looming biotechnology revolution. Along with the productivity boost from the earlier decade and the transition to NEBM, pharmaceutical firms also began to engage in significant distribution of cash to shareholders and increased executive pay, in accordance with the practices promoted by the emerging new corporate governance ideology of MSV.

With the rise of the “new economy” biotechnology companies, the transition of “Old Economy” pharma into NEBM guided by the principles of MSV quickly changed the dynamics of the pharmaceutical business model. The borders between biotechnology and pharmaceutical companies began to blur. On the one hand, the research-productive biotechnology firms began to inspire conventional pharmaceuticals to imitate their capabilities. On the other hand, smaller biotechnology companies sought opportunities to develop their skills and become fully-integrated pharmaceutical companies in order to fight off big pharmaceutical firms that had already started acquiring smaller firms to capture their productive capabilities. The interdependence of the two types of drug companies meant that the emergence of a new form of company was inevitable. Big pharma depended on the innovative capabilities of biotech and biotech relied on the vast resources and commercial skills of big pharma. This ultimately led to the birth of “biopharmaceutical”, embodying both the characteristics of “Old Economy” pharma and “New Economy” biotechnology in its early development phases. However, these new biopharmaceutical firms were also characterized as NEBM companies, as the industry had concluded that it was their nature as NEBM firms that explained the success of biotechnology start-ups.

This belief is mistaken. There had been a brief and temporary surge of productivity as the pioneers in the new biotechnology field picked the “low-hanging fruit” in the 1990s and benefited from new drug discovery and development instruments. However, the discovery of more complex therapies obliged pharmaceutical companies to engage in further learning in biology, and as a result pharmaceutical faced a growing productivity challenge. This is the point in the 1990s and 2000s when industrial restructuring occurred. At this point, under the influence of MSV, financialized biopharmaceutical began to pursue more “efficient” capital allocation strategies that would allow organizations to capture economic opportunities in the drug market without necessarily making substantial commitments to organizational learning.

The adverse implications of such an ideology can be observed in the US biopharmaceutical industry today. The organizations committed to this profit-driven ideology engage in value-extracting efforts having adopted a *downsize-and-distribute* resource allocation regime. During this period, the dominant business model employed by the large biopharmaceutical companies began to manifest the key characteristics of the NEBM such as vertical specialization in the value chain; cross-licensing and corporate acquisition to build patent portfolios and new product platforms. Some long-established pharmaceutical companies such as Merck began to downsize their global operations and distribute large sums of cash

in the name of enhancing shareholder value. The growth in the value of stock buybacks and the increase in executive pay among what is known as Big Pharma are indicators of the financialization process that has come to characterize the US biopharmaceutical industry. This thesis will examine the implications of such a process from the perspective of corporate governance, in comparison to the alternative framework of the TIE developed by Lazonick (2014b).

1.3.3 Analyzing the “innovative enterprise”

As will be discussed in more detail in chapter three, this thesis adopts the *historical-transformation* methodology Lazonick (2002) proposes as an effective methodological tool that “seeks to integrate theory and history.” Lazonick devised such a methodological tool as an alternative to of the shortcomings of the neoclassical “constrained-optimization” methodology discussed previously. Two empirical attributes characterize the “innovative-enterprise” (IE) for Lazonick and they explain why the IE as the most strategic unit of analysis to explores the process through which productive resources are transformed into innovative outputs and economic growth. Researchers thus perceive the innovative enterprise as,

1. A “distinct unit of strategic control” to analyze at the micro-level;
2. An element of an “allied network of firms that undertakes this transformation process” to analyze at the macro-level.

Such attributes are key elements of an economic analysis that seeks to link productive efforts of the innovative enterprise to the overall economic performance of the economy in which it is embedded.

A second set of methodological assumptions are key to such an economic analysis relate to the three characteristics of organizational learning that is engaged through the innovation process and that is a necessary condition of the *productive transformation* of the innovative enterprise. The innovation process is inherently uncertain, as it is pursued to resolve challenges that stand in the way of an organization competing in the productive transformation process. At the onset of the process, the challenges are still unknown, as the innovative enterprise does not yet know what unidentified issues remain to be resolve or, even if the remaining challenges are known, no solution is available as yet and the learning process needs to be initiated to find out what still needs to be known to resolve these issues.

In an innovative enterprise, Lazonick argues that strategy, organization, and finance, have to be formulated and implemented carefully to confront the three challenging characteristics of innovation which is *uncertain*, *collective*, and *cumulative* (Lazonick, 2013b). Innovation is *uncertain* because there is no guaranteed return on investment in the

innovation process for as long as the process cannot overcome three types of uncertainties: *technological*, *market*, and *competitive* (Lazonick & O’Sullivan, 2000):

1. *Technological uncertainty* refers to issues concerning the firm’s ability to generate the intended innovative output, including whether or not it will have the necessary knowledge, skills and instruments to develop the required product or service.
2. *Market uncertainty* refers to the firm’s ability to verify the availability of a profitable market to be exploited in the event that the innovation process successfully delivers an innovative output.
3. *Competitive uncertainty* refers to the challenges of predicting the competitive structure of the future market at the onset of the innovation process.

Economic analysis must also address innovation as a *social process*. Innovation is not conducted by individuals within business organizations and it requires a group of individuals to engage in *collective learning* through which the innovative-enterprise overcomes the challenges of the transformation process. In addition, the analysis must recognize the innovation process as a *dynamic process* through which the firm accrues technical, functional and managerial knowledge through collective efforts across functions and units over time.

Recognizing innovative enterprise as the critical agent for change in economic theory, Lazonick explains how industrial transformation leads to economic development via the innovative enterprise that transforms changing industrial conditions –technological, market and competitive – into innovative output with greater economic value through the process of social learning – collective and cumulative – that takes place within and across a number of innovating firms embedded within the same industrial setting. In such analysis, Lazonick’s *social conditions of innovative enterprise* (SCIE) framework is employed to identify how the key characteristics of the prevailing business model in the United States have changed over time and how such changes contribute to economic performance.

1.4 Financialization and the drug innovation crisis

The Oxford dictionary (2017) defines *financialization* as “the process by which financial institutions, markets, etc., increase in size and influence”, thus linking economic activity that may generate productivity gains to the financial sector. Finance has become a force that has altered the dynamics of modern industrial production and, in the last decades of the 20th century, the locus of the distribution function of the economy’s productive resources has shifted from business enterprises to outside interests exerting their influence through financial markets. Such a shift has re-defined the distribution of productive resources as well as the economic surplus generated through productivity improvement among the productive actors of the capitalist economy.

Magdoff and Sweezy (1987) define financialization as the “increasing role of the financial sector in the capitalist market operations,” while others see it as the “financialization of capital accumulation,” (Krippner, 2005; Foster, 2008; Aalbers, 2008) which recognizes the growing influence of the “financial sector” over the “real sector” as “financial interest” captures more financial gains from “productivity improvement” than any other “non-financial actors.” Lazonick (2013a) relates *financialization* as the changes in metrics and indicators used to evaluate the performance of a business enterprise. These have been shifting away from operational measures that are derived from elements such as the size, process, outcome or growth potential of business operations and include, for example, the number of workers employed, the number of innovative new products offered or new markets served and the sales growth. In their place, new metrics are more commonly identified in financial terms such as earnings per share (EPS), the price-earnings ratio (P/E) and the return on equity (ROE).

Traditionally, retained earnings generated through productivity improvements achieved in the real economy provided the main source of capital that was invested in the growth of production that, in turn, led to further accumulation of capital surplus and a sharing of the gains with households as taxpayers, workers, and savers that raised standards of living (Chandler, 1977; Lazonick, 2014a; Aalbers, 2008; Krippner, 2005). However, the neoclassical *theory of the market economy* and the new corporate governance ideology promoted by Jensen (1986 & 2000) as “*Maximizing Shareholder Value*” (MSV) in the 1980s have allowed financial interests to capture such the economic surplus from productivity gains in the non-financial sector, with the help of top business executives who have been incentivized to distribute corporate cash to shareholders.

The neoclassical *efficient market hypothesis* legitimized policy changes that deregulated financial institutions and stimulated financial innovation with a view to increasing the depth and liquidity of financial markets so that the financial sector could support the expansion of industrial production (Palley, 2007; Dore, 2008; Lazonick, 2015). During the same period, innovative financial instruments such as “securitization” were, in theory, designed to help the “real economy” by alleviating the risks of production stemming from market uncertainties concerning industrial production (Dore, 2008). Dore (2008) also argues that such financial innovations contributed greatly to the expansion of the financial sector in the real economy in the United States. Lazonick (2009) details the changes in financial institutions since the 1970s that explain the “Great American Transformation” from an economy based on corporate capitalism to one based on shareholder capitalism. Milberg (2008) explains how the macroeconomic outlook of the US economy simultaneously created favorable conditions for the financial sector as interest rates rose and challenges for the industrial sector due to price instability in product and factor markets. Expansion of the financial sector has also been “crowding-out” the labor market and attracting highly skilled and educated workers across disciplines into employment in the financial sector (Freeman, 2010). In addition to depriving the real economy of talent, Lazonick et. al. (2014) argue that the growing financialization of the corporate economy of

the US has led to a sharp decline in the availability of *collective and cumulative careers* (CCCs).

Financialization can also exacerbate the depth and extend of cyclical changes in the productive economy as specific events or patterns of events can generate “irrational exuberance” among investors and over-stimulate investment activities in certain sectors or technologies. Such an economy is prone to experience “market bubbles” in these speculative periods, followed by a recovery period as markets wait for investors to regain confidence in the sector. Janeway (2012) argues that such “market bubbles” can be beneficial for society. Even though they give rise to numerous failed business, speculative periods occasionally produce American icons such as *Amazon.com*.²

Lazonick (2009) argues that the success of a small number of technology companies has been an impetus for the diffusion of the New Economy business model to the wider economy since the 1980s. The innovative performance of the first generation of New Economy companies such as Apple Computer, Genentech and Amazon began to disrupt large markets for computer and electronics, pharmaceuticals and retail respectively. As these markets had been dominated by Old Economy companies, it was increasingly argued, that New Economy companies with disruptive technologies could enter and capture such markets and replicate what had happened in other sectors. Aalbers (2008) believes that a productive economy focused on *maximizing shareholder value* is a byproduct of financialization. As large investors increase their equity position, Stockhammer (2010) argues that shareholders have increased their influence over top business executive in the non-financial sector and, as a result, can demand greater returns in the name of MSV. Mukunda (2014) concludes that any productivity loss that is the result of *financialization* is “the price of Wall Street’s power” that the real economy has been paying for decades.

This study identifies “financialization” as the emergence of a set of new organizational governance objectives and values in which the goal of achieving capital efficiency exclusively for maximizing shareholder value (MSV) supersedes other objectives and values that benefit the wider stakeholder-base. In the context of the US biopharmaceutical industry this thesis explains how financialization gave shareholders greater returns on the financial gains generated from productivity improvement in the “real economy,” legitimized shareholders’ requests to “disgorge” corporate cash, allowed MSV to become a norm in corporate management, and contributed to the ongoing innovation crisis.

² *Amazon.com* is a corporate icon that emerged from the “dot.com” bubble. The “dot.com” era refers to a speculative period in the US stock market in the late 1990s when demand for the shares of technology companies, including online retailers, was excessive. Numerous start-ups such as “pet.com” copied Amazon and entered the online retail industry but many failed miserably and the capital investments made in such firms did not generate productive returns.

1.4.1 Financialization in the context of biopharmaceutical industry

In the 1990s, the value of capital invested in the US biotechnology industry grew significantly and this stimulated further entrepreneurial activities within the industry. Pisano (2006) showed that only a small number of dedicated biotechnology companies enjoyed profitable growth during this period, illustrating that the “reality” of the fledgling science-based business proved to be different than what it appeared to “promise”. Nightingale and Martin (2004) also questioned the extent and sustainability of the productivity growth the US biotechnology industry achieved in the 1990s. Similar to Hopkins et al. (2007), Nightingale and Martin (2004) question the “myth” of a productivity boost in medicinal innovation driven by the “biotech revolution.”

Pisano (2006) concluded from his analysis of growth that the biotech “boom” was unsustainable given the complexity of the research and development process in the “Science Business”. Lazonick and Tulum (2011) argue, however, that Pisano’s assessment of industrial growth is incomplete as it fails to explain the basis for a remarkable interest shown by financial interest in such risky, product-less biotechnology startups with no proven track record for profitability. Lazonick and Tulum (2011) examined the prevailing BP industry business model to reveal the missing piece in what the authors termed the *Pisano Puzzle*³. Their analysis revealed a unique industrial setting that allowed financial interests to generate financial returns from emerging, novel technologies without having contributed to the value creation process, corresponding to what Lazonick (2013a) defines as the *financialization* process. Such industrial settings are discussed in more detail in chapter four of this thesis.

While profitable growth may be a viable scenario for a small number of product-less startups at some point in time, most of these firms remain profit-less over sustained periods of time. Such “start-ups” have often made substantial investments in productive resources and engage in intensive learning, lasting at least a decade or two before generating a stream of product revenues from innovative new therapies. However, despite the length of the process for developing innovative new drug therapies and the significant amount of time needed before profitability, financial investors’ interest in risky biotechnology startups has not been dampened.

Andersson, Gleadle, Haslam and Tsitsianis (2010) highlight the role that speculative markets played in sustaining such interest on the part of financial investors in highly risky biotech. Based on the analysis of R&D announcements issued by public biopharmaceutical companies, Mc Namara and Baden-Fuller (2007) revealed that investors in stock markets respond positively to news that announced the initiation of new R&D activities, particularly among small startups. Lazonick and Tulum (2011) explained that such announcements are the basis for speculation and manipulation by short-term traders to

³ By *Pisano Puzzle*, the authors refer to the funding/performance paradox identified in Pisano (2006)

generate financial gains that are only possible in volatile markets with fluctuating stock prices. Control over firms within the biotechnology industry is thus increasingly dominated by financial interests who are more interested in extracting the gains from past innovation than in mobilizing labor and capital to generate new innovation. Moreover, hundreds of younger biotechnology firms that are listed on the stock market can be termed “product-less IPOs” (PLIPOs).

Through speculation in and manipulation of the stock price of such firms, financial interests can reap tens, or even hundreds, of millions of dollars, even without a commercial product (Lazonick & Sakinç, 2010; Lazonick & Tulum, 2011; Sakinç & Tulum, 2012; Lazonick et al., 2017). Lazonick et al. (2017) have documented how the scale of executive compensation in US biopharmaceutical grows hand in hand with the level of stock buyback programs executed by companies in the sector. A financialized business model offers greater incentives for top pharma executives to engage in price-gouging (Hemphill, 2010; Pollack, 2015; Kantarjian & Rajkumar, 2015; Hopkins & Lazonick, 2016). Montalban and Sakinç (2013) explains that such a pricing strategy is a key component of Big Pharma’s blockbuster-driven, financialized business model, allowing the top executives to increase profits quickly and enhance shareholder returns.

Top management within the financialized US biopharmaceutical sector often pursues such pricing strategies to maintain a sizable profit margin in order to boost stock buybacks in the name of maximizing shareholder “returns”. Although many BP executives often justify high drug prices as necessary to cover the increasing cost of drug innovation, recent firm-level analyses by Roy and King (2016) has highlighted the strong links between the excessive pricing of specialty therapies and massive stock buyback programs implemented by the developers of such products in the US biopharmaceutical market. A number of studies have examined the changing innovative performance of the biopharmaceutical industry in relation to the financialization of biopharmaceutical in an international context. Hopkins et al. (2013) analyze the evolution of the UK biotechnology industry and notes the growing importance of financial interests. In the context of Canadian healthcare technology startups, Lehoux et al. (2014) examine the ways in which business models affect the process of healthcare technology innovation, and Lehoux et al. (2015) explains how financial interest, namely venture capitalists, influence the innovation process to shape the trajectory of healthcare technology development within Canadian healthcare technology start-ups.

Based on the spatial analysis of biopharmaceutical publication developed by the US and European Big Pharma, Rafols et al. (2014) reveal that there is a growing trend towards externalizing risks associated with innovating new drug therapies and a growing number of R&D activities concerning early exploratory research and new target discovery are being outsourced. Using the locations of pharma publications as a geographical proxy for the intensity of R&D activities, Rafols et al. (2014) also indicate a growing trend towards publications developed through R&D operations that are located away from the

headquarters of Big Pharma and within emerging markets in developing economies. Rafols and his co-authors reveal a radical shift in Big Pharma's growth strategy as they become "network integrators" for the purpose of shrinking the drug development cost. To some extent, they are thus eliminating the risks associated with the innovation process, by investing less in value-enhancing drug development capabilities internally and more in building inter-organizational networks of drug R&D globally. The study of pharma publication trends provides empirical evidence of a causal relationship between the efforts to downsize internal research operations for new drug discovery and the ongoing productivity crisis within Big Pharma.

Nightingale (2000) explains that the economies of scale developed over time by Big Pharma allows the companies to conduct biopharmaceutical experimentations efficiently by utilizing a growing body of new knowledge across a broad array of sub-disciplines within biomedical science as well as employing new computer-aided drug screening, design and data analytics tools. Nightingale (2000) argues that Big Pharma possesses the necessary resources to acquire such tools and screen large compound libraries effectively and that this can potentially lead to the discovery of new therapeutic applications for the existing compounds in such libraries that have yet to be pursued commercially.

Rafols et al. (2014) consider, however, that such a decline in the investment in early research undermines the productivity of the innovation process within Big Pharma and their competitive advantage when such companies fail to leverage productive resources more efficiently than smaller biotech rivals despite the economies of scale that Nightingale (2000) argues they possess. Supporting the findings of Rafols et al. (2014), Gleadle et al. (2014) argue that the financialization of the BP business model is the culprit behind Big Pharma's recent strategic overhaul to restructure global R&D operations. An earlier study by Froud et al. (2006) discusses the transition of GSK's business model from OEBM to NEBM in relation to the company's decision to expand into the US drug market. This was done with a view to ensuring more profitable growth in the world's most unregulated drug market where there is no powerful price controlling mechanism. In the context of French Big Pharma, Leaver and Montalban (2010) reveal that Sanofi-Aventis pursued a similar growth pattern through the US drug market to that observed by Froud et al. (2006) for GSK.

From the perspectives of the TIE framework and MSV ideology, Gerbin and Drnovsek (2013) compare and contrast the US and European biotechnology industries in three particular contexts:

- (a) the critical role universities play as gatekeepers managing the flow of new technology from the non-profit to the for-profit domain;
- (b) the crucial role public investments play in building a competitive knowledge-base and a productive science and technology research infrastructure;

- (c) the ways in which innovation in biotech is financed in ways that can either augment or undermine the productivity of the innovation process.

Building on existing research documenting the evolution of biotechnology industry, Gerbin and Drnovsek's (2013) empirical analysis in a comparative context reveals some major flaws that are inherent to the financialized US business model. Based on the supposed efficiency of US-based BP companies, many activist shareholders are building alliances with top business executives to lobby for institutional reforms that would allow European companies to adopt the financialized US biopharmaceutical business model (Tagliabue, 2001; The Economist, 2002). Gerbin and Drnovsek (2013) conclude with a call for caution in adopting policies for institutional reforms that would allow European biopharmaceutical companies to emulate the financialized US business model.

The theoretical framework and analytical methods employed in this thesis overlap with some of the current literature summarized in this section. Gleadle et al. (2014), for instance, examine the vertical disintegration of R&D operations in Big Pharma and question whether outsourcing certain R&D functions and activities to biotech is a viable business strategy to improve both innovative productivity and capital efficiency. They argue that neither *transaction-cost theory* nor the *resource-based-view* can justify the rationale for vertical disintegration that virtually implies “distancing the capability for innovation from the resources for innovation” to improve R&D productivity.

Gleadle et al. (2014) consider the *financialization* argument as a more appropriate theoretical perspective to investigate the impact of financialization on the productivity of Big Pharma through the case analysis of UK-based GSK, one of the world's largest biopharmaceutical companies. The authors of this study provide insight into how the changes observed in GSK's allocative strategies were made by top management at GSK in response to external factors. The study however fails to provide answers to two key questions of “why” and “how” *financialization* influences innovative productivity. What changes were observed in the abilities and incentives of top business executives at GSK that stimulated such strategic actions? How did the restructuring affect the *social conditions of innovation* within GSK? The analysis in this research proposes a more in-depth and comprehensive account of how financialization of the biopharmaceutical business model can contribute to a productivity crisis by employing Lazonick's TIE framework to overcome such theoretical constraints.

Unlike Gleadle et al. (2014), Gerbin and Drnovsek (2013) draw heavily on Lazonick's theoretical framework to compare and contrast the innovative performance of the US and European biotechnology industries. In the TIE framework Lazonick argues that economic institutions are key components of a complex innovation network supporting the process of *productive transformation*. These institutions are broadly categorized as *governance*, *employment* and *investment institutions*. According to Lazonick (2013b) these institutions often “enable” or “proscribe” the *social conditions of innovative enterprise* to the extent

that such institutions can potentially enhance or undermine the innovative productivity of business enterprises, and subsequently the economic performance of industrial sectors, in any given economy.

Gerbin and Drnovsek (2013)'s comparative analysis seeks to explain the variation of the innovative performance in the US and Europe biotechnology industries by comparing and contrasting economic intuitions in these regions to identify major difference between them and explain whether such institutions support or undermine the process of *productive transformation*. Through an extensive survey of the current literature, they find that what distinguishes the institutional environments within the biotechnology industry in the US and Europe is the governance and finance of innovation in each region. Gerbin and Drnovsek highlight how the intellectual property regime (IPR) shaped by specific US public policies ultimately determines the mechanism through which knowledge generation and diffusion occurs within the US biotechnology industry. They also recognize the importance of public investment, particularly through the National Institutes of Health (NIH) in the establishment of a competitive science and technology (S&T) infrastructure in addition to a productive knowledge-base. It is this knowledge base that enabled the development of the world's most innovative biotechnology industry in the US.

Gerbin and Drnovsek also outline the distinctive financing for biotech R&D that relies on speculative markets in the "highly monetized" US business model. Lazonick (2009) argues that such a financialized business model began to emerge in the high-tech industries such as biotechnology in the 1980s and 1990s when economic institutions in the US went through major transformation and began to adopt the principles of the *maximizing shareholder value ideology*. Gerbin and Drnovsek's analysis mobilizes the *theory of innovative enterprise* framework and fails to confirm the neoclassical argument that the financialized US biotech business model can deliver higher innovative productivity. On the contrary, Gerbin and Drnovsek argue that such a financialized business model relies heavily on speculative markets driven by short-term financial gains and companies adopting such a business model are merely engaging in value extracting efforts to comply with the sole corporate objective of *maximizing shareholders value*.

Gerbin and Drnovsek's (2013) comparative analysis employs both a macro-level approach to understand the differences observed in the innovative productivity of the US and European biotechnology industries, and a more longitudinal, in-depth, and firm-level comparative analysis to explain how the changing relations between biopharmaceutical business enterprises and economic institutions in the US ultimately determines the innovative productivity of the US biopharmaceutical industry. As proposed by the TIE framework, this research recognizes the *social conditions of innovative enterprise* as the focal point for any economic analysis regardless of its analytical scope. A series of firm-specific analyses can thus be aggregated to conduct broader economic analysis to assess the economic performance of sectors or regions. This research adopts a similar research perspective to provide an economic assessment of the US biopharmaceutical industry

through the comparative case analysis of two purposefully sampled BP companies that are representative of the population from which the samples are selected. The next section provides the summary of the theoretical discussion as well as the empirical evidence to confirm that the US biopharmaceutical industry is suffering from an innovation crisis.

1.4.2 Identifying the innovation crisis in the biopharmaceutical industry

Based on the perspective of TIE framework, this thesis adopts a contextual definition of innovation as transforming technologies and markets for (A) generating higher quality and (B) lower cost drug therapies (C) to meet the medicinal needs of consumers in the biopharmaceutical product market. This is not the definition that is used by the competing theoretical perspective, which is that of the “optimizing-enterprise” proposed by TME. From the TME perspective, innovation is viewed as transforming factors of production to an optimal level under certain technological conditions. In other words, market-induced constraints generate new drug therapies and the cost and quality of such therapies depends on the market structure under which the profit-optimizing firm is competing.

The competitive structure of the prescription drug market is one of monopolistic competition. Drug companies are allowed to exercise temporary legal monopolies in the market and, by design, they are free to sell their products at the price level deemed most profitable. With monopolistic power, drug companies can charge, in theory, the maximum price maximum that payers can bear. However, discriminative incentives exist in this profit-optimizing pricing strategy and they produce inequitable distribution of benefits which are skewed largely toward the most affluent members of the global community.

A profit-optimizing firm should invest in drugs for diseases that afflict the most affluent patient groups in the most profitable segments of the global drug market. The markets with affluent customer bases are in the world’s most industrialized regions and they already possess significant drug development capabilities. Based on the positive correlation between the profitability of product markets and the innovative capabilities in the regions in which those markets are embedded, the profit-oriented business model proposed by TME theoretically leads to an output in which innovation is skewed. It is biased against markets with less-affluent customer bases in underdeveloped regions with few drug development capabilities. As a result, patients in the world’s most under-served regions suffer from illnesses that have no effective treatment, while markets for drugs to address illnesses afflicting wealthy patients can be flooded with “me-too” drugs. This term was coined by Angell (2005) to refer to drugs that are not clinically superior to existing drugs.

From the TME perspective, profit-optimizing firms pursue a resource-allocation strategy based on the ideology of maximizing shareholder value (MSV) which is viewed as the sole fiduciary responsibility of corporate executives. Stock-based compensation packages serve to align the personal interests of corporate executives with the interests of those shareholders who are seeking relatively fast financial gains through the appreciation of the

company's stock price in a short time frame. The converging interests of principal and agent to boost corporate earnings in the short- or medium-term is often accompanied by the "downsize-and-distribute" mode of resource allocation, thus burdening other stakeholders with the costs of MSV.

Large business establishments are integral to the development, utilization and distribution of an economy's productive resources. As a result, increasing distributional inequality among stakeholders within large businesses contributes to increasing inequality in the wider economy in which those firms are embedded. Given its theoretical scope, however, this thesis will only evaluate the managerial and business strategy implications from an economics perspective. The following section discusses the perils of MSV ideology in connection to the biopharmaceutical industry's ongoing innovation challenge.

Diminishing productivity of industrial R&D

Although there is widespread consensus that an innovation crisis exists in the biopharmaceutical industry, there are numerous, often competing, theories seeking to explain the origins of the problem. Such theories are categorized as being one of three themes: (1) those which focus on issues stemming from the limitations of science and technologies (S&T); (2) those concerned with the role of regulations and government interventions; and (3) those which address issues related to the governance of innovation.

Within the first group, there are arguments that focus on the discrepancy between knowledge in S&T and drug discovery. Some commentators have focused on the limitations of devising and utilizing effective drug screening strategies, for example, (Booth & Zemmel, 2004; Lindsay, 2003; Swinney & Anthony, 2011; Sidders et. al., 2014) while others have highlighted efforts to overcome the complexity of systems biology (Hood & Perlmutter, 2004) and the need to process the information overflow emanating from a "genomic bubble" (Pollack, 2010; Evans et al., 2011). Baker (2004) argues that in the profit-driven drug business, the discovery of "patent mines" that allow firms to gain monopolist power in a competitive market is the most important incentive for companies to identify new learning opportunities.

In a drug firm that wishes to optimize value for shareholders by engaging in a *downsize-and-distribute* form of resource allocation, top executives can delay investment in transformative research ideas that require long-term learning initiatives. These require strategic control, organizational integration, and financial commitment and, as a result, they are harder to sell to short-term investors who expect reductions on R&D programs to improve earnings.

Given that the body of knowledge can only accumulate over time through collective learning efforts within organizations, such studies provide no perspective on how the industry's prevailing business model incentivizes top biopharmaceutical executives to

undermine such learning efforts as they continue to downsize organizational R&D spending in order to improve capital efficiency and optimize profit in the name of enhancing shareholder value.

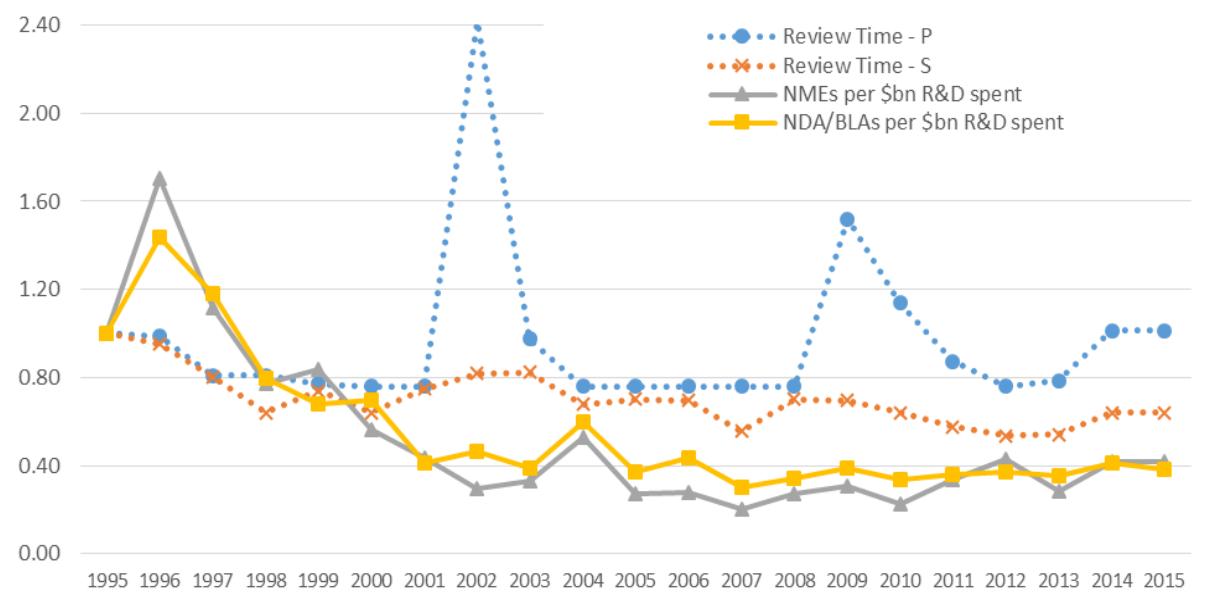
Lazonick et al. (2014) discuss the disappearance of collective and cumulative careers (CCCs) as an explanation for diminishing organizational ability to acquire new knowledge and transform productive resources into products and services. According to a recent nation-wide biannual employee engagement survey conducted by a major human resources management organization, slightly over one-third of the workforce in the US biopharmaceutical industry is seeking to change employer. The reasons cited mainly concerned (1) lack of flexibility and consideration of the structure/size of workhours/workload; (3) performance-based bonuses entrenched in the current mode of compensation; (2) investments in employee skills and careers.

The second group of explanations of the productivity crisis link declining R&D efficiency with the regulatory approach of the Food and Drug Administration (FDA) during the drug approval process, as it is believed to have extended the length of clinical trials (Dickson & Gagnon, 2004; Miller & Henderson, 2007; Kaitin & DiMasi, 2011). According to this body of literature, the growth in R&D spending reflects the increasing level of stringency in FDA approvals. This occurred in the aftermath of product withdrawals linked to safety issues in the early 2000s and it is argued that the more cautious approach adopted by the FDA since then has been impeding BP innovation (Kaitin, 2010; Roy, 2012).

The FDA data that is reported annually on the average drug review time (Figure 1) indicates no significant increases in the FDA drug review process over the past two decades with review times – both for priority (P) and standard (S) drugs – unchanged in the past 20-year period, apart from sporadic surges caused by major policy revision for NDA filings. These are discussed further in the next chapter. Nonetheless, R&D productivity fell significantly in the late-1990s. R&D productivity is measured in two ways. One is by the number of new molecular entities (NMEs) – recognized by the FDA as innovative new therapies. The second is the number of new drug/biological licensing applications (NDAs/BLAs) per billion dollar spent by the industry. R&D productivity, measured in terms of both NMEs and NDAs/BLAs, has not grown since the 2000s and it has not recovered to the significantly-higher productivity level of the index year, 1995.

Studies that have attempted to measure the cost of drug innovation have revealed a dramatically increasing trend since the 1990s (DiMasi, Hansen & Grabowski, 2003; DiMasi & Grabowski, 2007; Adams & Brantner, 2010). Based on these cost estimates, Cockburn (2006) argues that the industry's productivity problem is overstated as changes in corporate R&D investment have been more significant than changes in the number of new drug approvals, and investments have not been adjusted to cover the rising cost of drug development.

Figure 1: Changes in the FDA Review time (standard vs priority) and R&D productivity, between 1995 (index year) and 2015.



Source: Own illustration based on data from Center for Drug Evaluation and Research [CDER], New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products

The argument that increasing costs explain drug pricing strategies have also been challenged on several other bases:

1. It has been argued that is the exacerbated cost structure of companies that leads to excessive cost-estimates (Public Citizen, 1991);
2. The widely-cited cost-estimate studies have been accused of lacking clear evidence (Light & Warburton, 2005a & 2005b);
3. It has been pointed out that the argument of industry lobbyists that premium prices are justified by innovation is not supported by the amounts being reinvested for the discovery and development of NMEs (Angell, 2005). In their study of biopharmaceutical prices in relation to underlying costs, Yu, Helms, and Bach (2017) also concluded that the high drug prices in the US market cannot be explained by the cost of drug development alone given the disparity between the prices occur in the US and other markets.

Yu, Helms, and Bach (2017) suggest that there is potentially a premium built into the US market prices to compensate for losses accrued in foreign markets where regulatory price pressures have been growing over time. Light (2017), however, disputes this “foreign-free-rider myth” and argues that such logic may simply serve to shift political pressure in the direction of the price-conscious foreign governments, and away from the biopharmaceutical manufacturers.

Former CEO and Chairman of Merck & Co. Roy Vagelos (1991) initially defended the industry's pricing policies and argued that such practices are necessary to keep up with ever-increasing drug innovation costs and bring innovative new therapies to patients. Toward the end of his tenure as CEO, however, Vagelos (2006) argued that the industry-wide practice of increasing drug prices on a regular-basis above the rate of inflation could no longer be justified. He also argued that such a strategy had damaged the industry's reputation and instigated government scrutiny into general business practices and he pledged that Merck would change its pricing strategies in favor of a more transparent method that linked any price adjustment to changes in the consumer price index.

Other companies made similar pledges but Figure 2 shows that this campaign failed to achieve its intended outcome and pharmaceutical product prices have been rising often faster than the overall consumer price in the US since the 1970s (Figure 3). While the general consumer price index in the US eventually leveled off at a more predictable growth pattern, the pharmaceutical index continued to rise as a result of periodic price increases and it began to surpass the general index in the early-2000s.

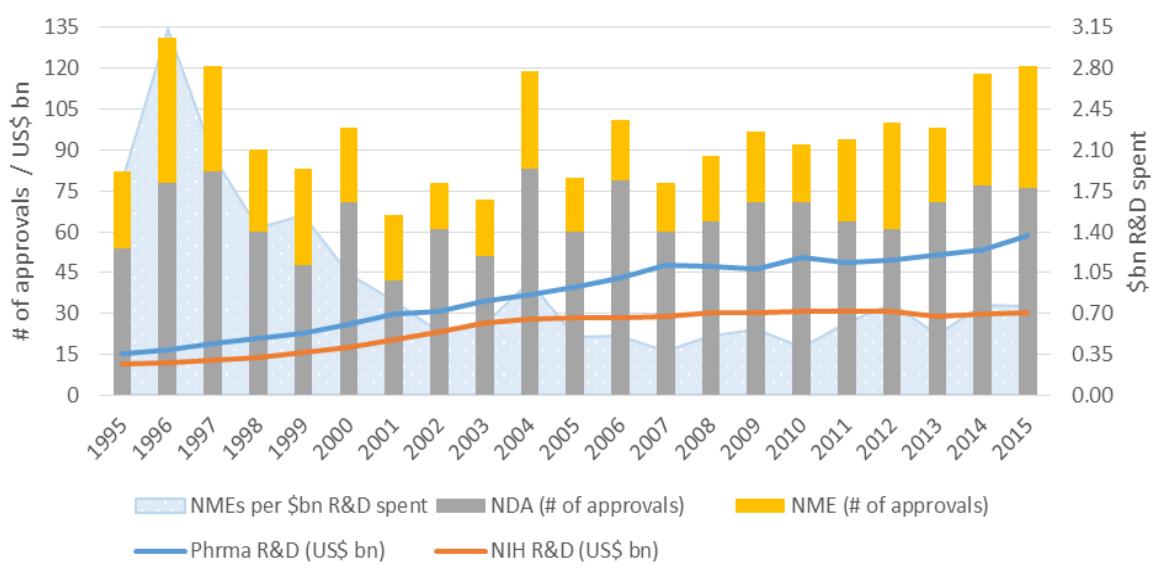
Supporters of such a pricing strategy claim that current prices include a premium for investing in innovation to develop future products. If this were, in fact, the case, the higher premiums being charged in the early-2000s could be expected to greater industrial productivity today, as measured in terms of innovative output (number of approved New Molecular Entities – NMEs) yielded by billion US dollars invested on R&D by the industry. As Figure 2 shows, however, industrial funding for R&D⁴ has been outgrowing government funding provided through the National Institutes of Health (NIH) since 1995⁵. During the period when the pharmaceutical price index surpassed the general index, the output of industry innovation (NMEs per \$bn R&D spent) remained relatively stagnant.

The number of approvals in NMEs and NDAs was highly volatile in the second-half of the 1990s and the early 2000s. The number of approved NMEs, and subsequently NDAs, was historically high in 1996 (131 NDAs approved including 53 NMEs) as was the number of new approvals per billion dollars spent (R&D productivity). R&D for drugs experienced this exceptionally productive year in 1996 as the industry launched some of the best-selling drugs of recent history, including Lipitor, which was the world's leading cholesterol medication. Pfizer's Lipitor quickly took over the market for statins and the company achieved a dominant position in the market.

⁴ Based on data provided by PhRMA, the main industrial trade group

⁵ During the period of analysis the data suggests a flat-line indicating stagnant government support on biomedical R&D below the industrial investments however, based on the R&D figures gathered for a sample of company, Cockburn and Henderson (2001) documented that the US government had been consistently outspent the industry from the early-1960s until the early-1990s in the support for biomedical research. Also see: Hopkins and Lazonick (2014) also discusses extensively the government investments in the high-tech knowledge base in the US and the productivity growth such investments yielded.

Figure 2: Industry (PhRMA) and government (NIH) funding for R&D, New Drug Application (NDA), New Molecular Entity (NME) approvals and the productivity of R&D, per \$B spent, 1995-20



Source: Own illustration based on data from FDA (n.d.) & PhRMA (2016)

LaMattina, former president of Pfizer global R&D, explained that during the productivity surge in 1996, 21 out 53 NMEs brought to the market by small- to mid-sized biopharmaceutical companies were all acquired by a few big biopharmaceuticals companies, with Pfizer particularly present as an acquiring firm (LaMattina, 2015). The launch of some of those blockbuster drugs led to an industrial consolidation in the late-1990s and early 2000s and these drugs drove the industry's overall growth over the next decade. Pfizer's director of R&D, LaMattina (2011) considered that the long-term implications of industrial consolidation could potentially undo short-term gains realized through post-merger restructuring and have a negative impact on industrial productivity.

The third group of arguments about the innovation dilemma in the sector focus on the governance of pharma firms and investment of productive resources in R&D. It is argued, for example that a more strategic approach to the management of R&D within big pharma could have resulted in more efficient outcomes by tapping into external networks of innovation (Munos, 2009; Pisano, 2015). The post-genomics era of R&D efforts concentrated on the uncharted territories of complex therapies such as oncology and neurodegenerative diseases. These efforts were geared towards pursuing high-reward targets but in the process accrued significant losses, given the complexity of underlying biological systems (Munos, 2009; Pammolli et al., 2011; Swinney & Anthony, 2011; Scannell et. al, 2012).

Profits result from the firm's success in generating innovative products, and the investment of profits to augment the company's innovative capabilities provides the financial foundation for the continued growth of the firm. Indeed, from the perspective of innovative enterprise, the pursuit of profits for their own sake is likely to undermine the social

conditions of innovative enterprise, elevating value extraction over value innovation, and giving rise to the productivity disease known as financialization across different industries, including biopharmaceuticals (Lazonick, 2013a & 2017; see also Baldwin & Clark, 1992; Froud et al., 2006; Hopkins et al., 2007; Christensen et al., 2008; Andersson et al., (2010); Kessel, 2011; Lazonick & Tulum, 2011; Montalban & Sakinç, 2013; Haslam et al., 2013; Gleadle et al., 2014).

There is also a growing body of literature that offers compelling evidence of the role that financialization of the US biopharmaceutical business model has played in the ongoing efficiency crises. The industry's overreliance on a blockbuster-driven model to sustain profitability has incentivized strategic managers to make unsubstantiated bets on fledging new technologies without building the necessary knowledge bases to leverage such investments and generate successful products (Nightingale & Martin, 2004; Pisano, 2006; Andersson et al., 2010; Lazonick & Sakinç, 2010; Lazonick & Tulum, 2011; Kessel, 2011; Hopkins et al., 2007; Montalban & Sakinç, 2013; Froud et al., 2006; Haslam et al., 2013; Gleadle et al., 2014).

Unhappy that such bets have led to higher failure rates and inefficiency, shareholders demand more managerial action to increase product prices and reduce R&D spending in the name of maximizing shareholder value (Scannell et al., 2012, p. 193). Recent studies provide evidence to support such trends and indicate that increased profits generated through price hikes are deployed in other areas such as a) financing M&A activities to rejuvenate aging product portfolios or drying pipelines (Higgins & Rodriguez, 2006; LaMattina, 2011; Lazonick & Tulum, 2015); b) compensating for financial losses resulting from the loss of patent protection on legacy products; or, c) from distributions to shareholders through stock repurchases and dividend payouts (Lazonick & Tulum, 2015; Kantarjian & Rajkumar, 2015; Guatam, 2016; Roy & King, 2016; Lazonick et al., 2017).

From a financialization perspective, this thesis challenges the cost-centered arguments that perceive the cause of inefficiency in biopharmaceutical innovation as external to the governance and organization of the biopharmaceutical industry. Using TIE framework, this thesis will explore whether the efficiency crisis is induced by external factors or is deeply rooted in biopharmaceutical organizations. With the social conditions of innovative enterprise (SCIE) framework, this thesis will examine how an innovative enterprise can challenge such “constraints” that are said to be imposed by technology and markets to transform technologies and access markets to their own advantage.

Market-driven innovation, inequitable access to biopharmaceuticals and distribution of health

Investment decisions related to innovation in the biopharmaceutical industry have implications for the well-being of society. Public concern about accessing innovative therapies has thus grown during with the period when the financial performance of

biopharmaceutical firms was taking precedence over innovation. Biopharma executives, industry leaders and other lobbyist increasingly have had to defend themselves and, to do so, they often estimate drug costs development that are periodically published by the Center for the Study of the Drug Development (CSDD) at TUFTS University. The studies published between 2001 and 2014 indicate an increase in the cost of drug development that is more than three-fold (DiMasi, 2001 & 2014). The study published in 2001 estimated drug costs at approximately \$800 million (or approximately \$1 billion when adjusted for 2013 dollars, the last year of the analysis) and the revised figure for 2014 was \$2.6 billion. While this estimate provides the basis for much debate and policy discussion, however, the validity or credibility of the data used in this study has not been independently verified.

In addition to the policy implications which are outside of the scope of this thesis, the question of the cost of drug development has implications for the research issues under investigation. The estimates of growing drug development costs produced regularly by reputable academic institutions such as Tufts University legitimize the argument that price increases are a prerequisite for drug innovation. Despite the lack of further validation of such estimates of the cost of drug development, however, drug prices continue to grow and the economic wellbeing of those who need the drugs involved is reduced as a result.

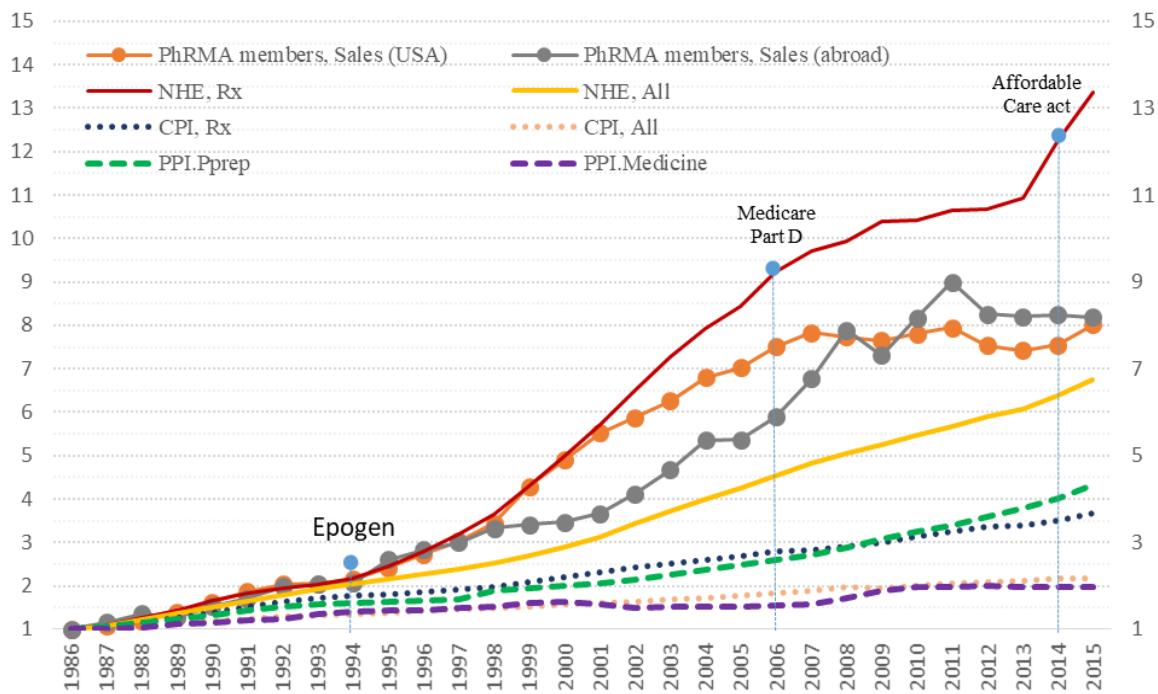
Figure 3 highlights the existence of such a pricing strategy, which is a key driver of the outstanding performance of biopharmaceutical companies who then reward shareholders with a level of returns that is the envy of investors in most other industries. Based on the 2015 PhRMA company survey data collected from 31 of its members including some of the world's top pharmaceutical and biotechnology companies, Figure 3 places the changes in the industry's domestic US sales in perspective in the light of changes in the consumer price index as well as the national healthcare expenditures on prescription drugs.

In Figure 3 consumer price index for prescription drugs (CPI, Rx) illustrates the changes in the drug prices consumers pay at the pharmacies in the US since 1986. CPI, Rx appears to be increasing faster than the prices of all other consumer products (CPI, All) especially after the mid-1990s. Such a soaring drug prices in the US since the mid-1990s appears to have impacted already increasing US national health expenditures given that the rate of increase of the national expenditures on prescription drugs (NHE, Rx) has been greater than for the national health spending on all healthcare items (NHE, All) since the mid-1990s.

It appears that PhRMA member companies' drug sales in the US accelerated in the mid-1990s, particularly following the launch of first generation biologics such as epogen in 1994, which was above the CPI Rx but it followed a similar trendline along with NHE Rx (Figure 3). Although the Figure doesn't imply that such increases on domestic sales can be exclusively explained by the rising drug prices however it indicates an explicit correlation between the two indicators. Given that the industry trade group data doesn't specify the number of units sold to accompany those dollar-based sales figures, it is hard to infer from

the data whether such a rising annual sales has to do with net changes in the number of units the drug companies sold or the rising domestic sales are merely the byproduct of soaring drug price. A strong evidence for price-led increases is that while the companies' drug sales abroad were slowing the domestic sales took a sharp turn upwards particularly between 1998 and 2008.

Figure 3: Changes in the PhRMA members annual sales (domestic and abroad), National Health Expenditures (Total vs prescription drugs), and Consumer Price Index (All city vs. prescription drugs), 1986-2015



Pharmaceutical Research and Manufacturers of America [PhRMA], member company annual sales in USA and all other countries [abroad]; national health expenditures [NHE] for prescription drugs [Rx] and overall [All]; consumer price index [CPI] for prescription drugs [Rx] and overall [All]; producer price index [PPI] for pharmaceutical preparations [Pprep] (pharmaceutical products ready for consumption in dose forms by drug manufacturer) as well as medicinal and botanical manufacturing [Medicine] (uncompounded chemicals ready for processing into pharmaceutical preparations).

Many of the first generation biologics began following Epopen to the US market after Amgen received the FDA approval to launch one of the first biologics in the market in 1994; Medicare Part D went into effect in 2006 to expand the prescription drug coverage to all Medicare enrollees; the Affordable Care Act mandate for purchasing health insurance purchase went into effect in 2014.

Source: Own illustration based on data from PhRMA (2016), CMS (n.d.), BLS (n.d.)

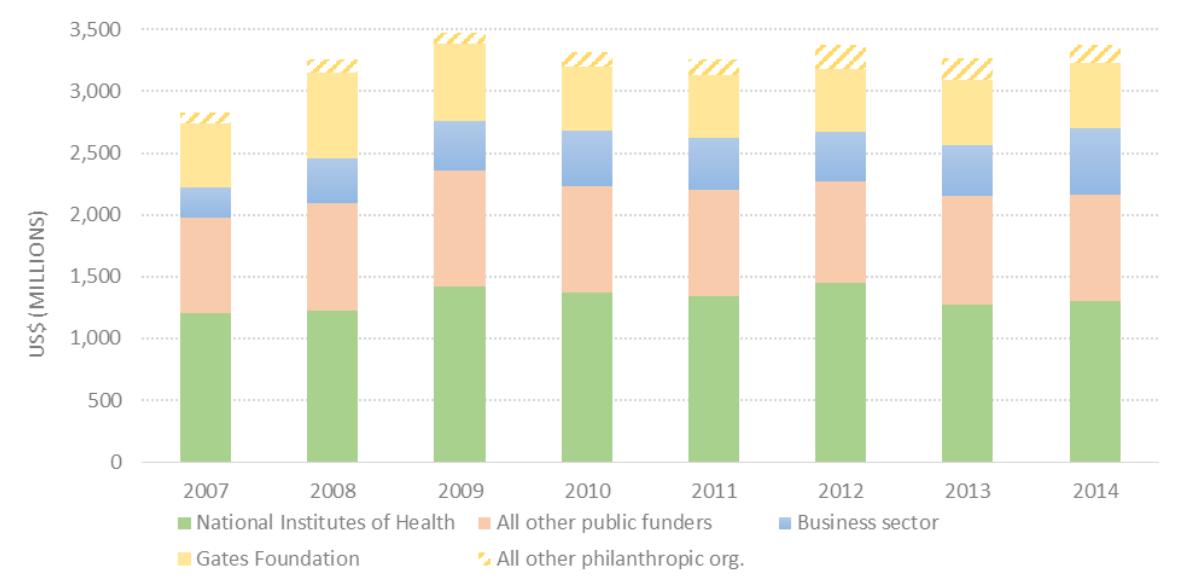
Although the gap between CPI-Rx and CPI-All began to close during the 1980s, the growth rate of CPI-Rx begins to exceed the growth of overall price index by the 1990s, leading to a public outcry about the rising cost of pharmaceutical prices. The CPI-Rx index continued to outgrow the CPI during the 1990s. Calls for regulatory inquiries into the business practices of the pharmaceutical industry were grew during William [Bill]

Clinton's election campaign for the White House and lasted throughout his presidency. In the 1990s and during the dot-com era expansion at the end of this decade, the CPI did not increase significantly, while the CPI-Rx did, as emerging therapies from new biotechnology companies began to hit the market in the 1990s. By the end of 1990s, the CPI-Rx caught up with the CPI, and began to "outperform" it in the early-2000s. Since then, the prices of prescription drugs have continued to rise and the CRP-RX has grown faster than the CPI.

Declining R&D in neglected diseases

A Sydney-based non-profit organization, Policy Cures, has been keeping track of global biopharmaceutical R&D efforts in neglected diseases. This data base is built on continuous, detailed monitoring of a powerful data source known as G-FINDER through which researchers can examine the state of R&D and monitor any further development, or lack thereof, in drug therapies to address neglected diseases. In 2014, Policy Cures surveyed 190 organizations with regard to products to address 35 neglected disease groups, as well as the clinical pipeline of new therapies being developed for such diseases at the time of the survey. These neglected diseases include HIV/AIDS, malaria, Tuberculosis, Ebola and the hepatitis C virus (HCV).

Figure 4: R&D Funding for [poverty-related] neglected diseases by institution, 2007-2014



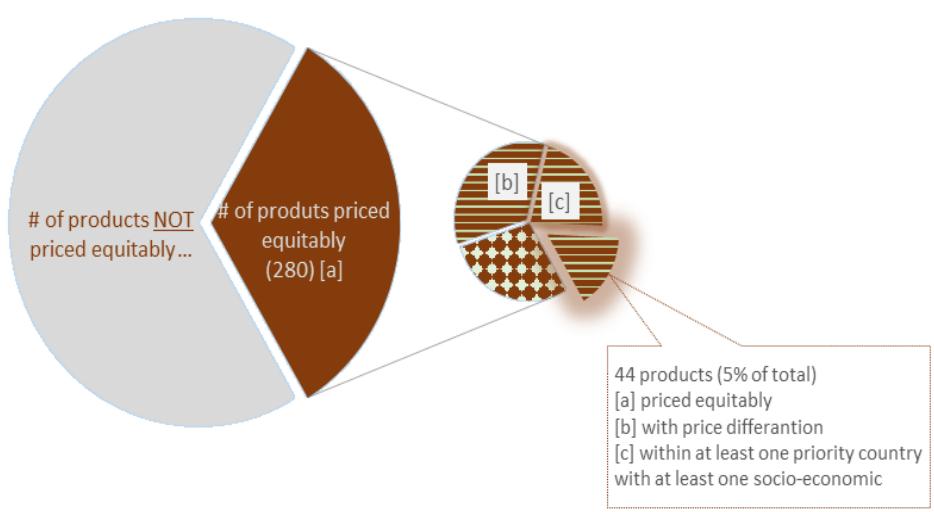
Source: Adapted from Policy Cures (2015)

According to G-FINDER (2015), the National Institutes of Health (NIH), the leading US government agency in biomedical research as well as the Bill & Melinda Gates Foundation were the top two supporters of the R&D programs for these neglected disease groups. Figure 4 reveals that these two agencies alone accounted for nearly 54 percent of the entire \$3.4 billion invested globally on developing therapies in neglected diseases that disproportionately affect the part of the world's population that is concentrated in

underdeveloped regions. On the one hand, Moses et al. (2015) forecast greater biopharmaceutical company involvements in the R&D for neglected diseases. On the other, Baker (2004) argues that, without the prospect of a strong patent portfolio to control competition in a lucrative market, Big Pharma neglects rare or tropical diseases.

Figure 5 reveals two striking facts about the state of R&D in neglected diseases that confirm Baker's argument. First, despite steady growth in the total funding for R&D in neglected diseases, investment by biopharmaceutical companies amounts to less than two percent of their overall investment in R&D, reported as slightly over \$140 billion level in 2014 (IFPMA, 2017). Secondly, although Figure 4 shows a doubling in funding from "aggregate industry", this \$534 million invested in neglected diseases accounts for less than one percent of the total amount spent by members of the Pharmaceutical Research and Manufacturers of America (PhRMA) on R&D in 2014. It can be argued that such a funding disparity reveals the consequences of a drug industry operating on the premise of profit-optimization in the name of enhancing shareholder value that finds no incentive in the business of innovating new therapies for the vast majority of the patients concentrated in the most underdeveloped regions of the world.

Figure 5: Accessibility of innovative therapies in high-burden disease areas, 2015



Source: Own illustration based on data from Access to Medicine Foundation [AMF], 2016 Access to Medicine Index

In addition to the lack of innovation in neglected diseases, another problematic issue concerns limitations on patient access to existing therapies. The Access to Medicine Foundation (AMF) assesses how well the industry serves public health needs and it judges the biopharmaceutical industry as poorly on this basis as it does on other indicators. AMF (2016) conducted a comprehensive analysis of 850 products identified as being in "high-burden" disease areas, which means that they affect a large portion of the world population. The study did not include specialty oncology drugs for cancer. It investigated how manufacturers of those products performed in terms of implementing a global pricing

policy to ensure that patients in various different income groups in the world, particularly in low-income groups, have the access to such medicine.

The AMF (2016) analysis revealed that only one-third of the products identified for the analysis were products with equitable prices. Only 9.4 percent of the products examined were priced differently across countries and only 7.2 percent of those products with differentiated pricing policy were actually available in at least one priority (low-income) country. More importantly, in cases when prices were set differently across countries and when one of these countries was a high priority country, only five percent of the drugs studied were priced on the basis of socio-economic factors by the drug manufacturers,

The AMF (2016) found that Gilead Pharmaceuticals and GlaxoSmithKline (GSK) were the most prominent firms in the practice of not differentiating prices although drugs for HIV/AIDS, hepatitis C virus (HCV), and other major antivirals account for a large portion of those companies' global sales. In the absence of a differentiated pricing policy in different markets, such drugs could find no customers in low-income countries with state-sponsored social healthcare programs who could not afford the excessive prices that had been set originally in the US drug market. It is argued that Gilead's multi-faceted pricing strategy has devastated national health budgets in various other countries around the world (Roy & King, 2016)

At the same time, such companies are among those ranked as the most successful in terms of creating shareholder value based on their stock price performances that are mainly driven by massive stock repurchases. Other US-based companies also boost their stock performance through massive stock buyback programs while pushing the drug prices higher arguably to keep up with (a) the growing cost of drug R&D in the US as well as (b) the rising market pressure across the global that forced the companies to reduce soaring drug prices.

Arguments rooted in neoclassical market theory consider such shortages of new therapies or price hikes to be the result of market failure that may need to be addressed by government interventions to incentivize further innovation efforts to develop therapies with a steep learning curve that require substantial R&D investments. They propose government intervention that is limited to the supply of market incentives such as R&D tax credits, SBIR grants and further extending the scope of federal laws such as the Orphan Drug Act. These arguments are further discussed in the next chapter of this thesis.

TME-based arguments propose a variety of market-based solutions to overcome the innovation challenge. One group of solutions centers on a reward-based funding system that encourages drug companies to engage in a long-term drug discovery and development programs and bring innovation new therapies to market by assuring a significant financial payout (Love & Hubbard, 2007). In recent years a group of scholars from MIT's Sloan School has been promoting the idea of creating large investment pools that would provide

the source of financial stability many small biopharmaceutical startups are seeking to fund their complex and highly risky long-term innovation programs (Fagnan et al., 2014).

Such a fund would pursue financial returns with significantly longer investment horizon than other funding sources and offer a sizable reward program in the form of a large lump-sum payment to companies who bring an efficient new drug to market in specific disease groups. (Fagnan et al., 2014). Such investment vehicles, however, introduce elements of complexity that resemble the “innovative” financial tools generated in the 1990s by prominent members of the finance program at Sloan had generated. These tools include the mortgage-backed financial securities that brought the entire US financial system to its knees (Ugolik, 2015).

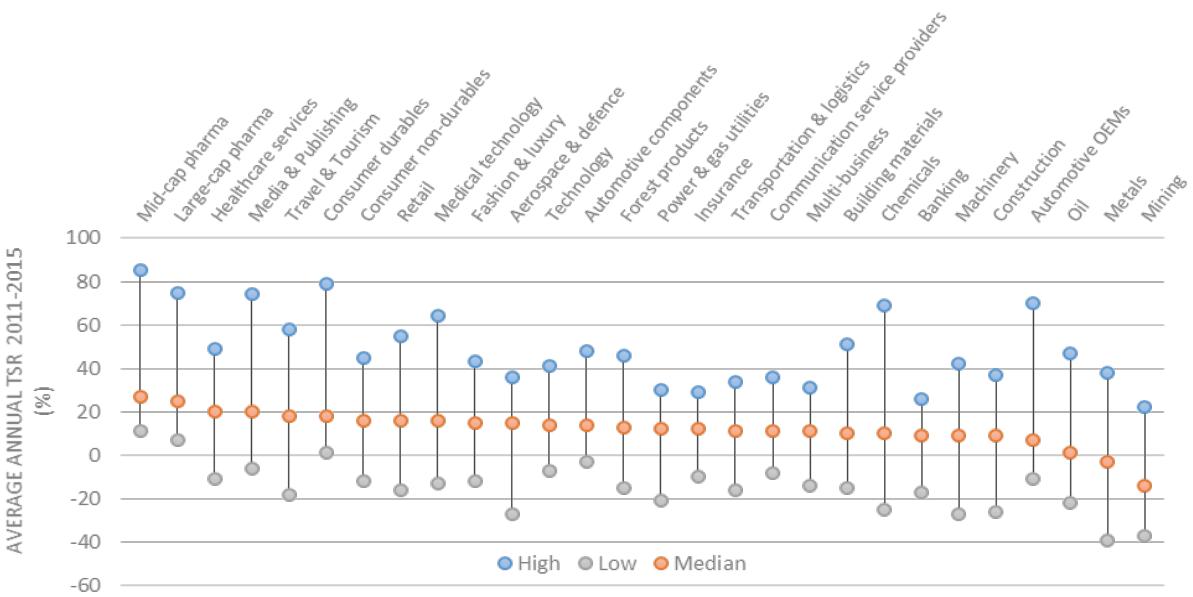
The proposed \$30 billion fund would be geared towards generating a long-term funding alternative to support ambitious research initiatives in complex fields such as cancer as these are areas that the debt market is unwilling to fund. The proposal for such a fund implicitly confirms that a lack of patient capital is the source of the industry’s innovation crisis in risky areas of research such as oncology. However, it is still uncertain how the proposed financial engineering experiment would alter the industry’s current business model in order to support the social conditions of innovation within biopharmaceutical organizations.

1.4.3 Maximizing shareholder value (MSV) ideology and the transition into Blockbuster-driven New Economy Business Model in the US biopharmaceutical sector

Analysis conducted by the Boston Consulting Group [BCG] (2016) provides empirical evidence of the existence of financialization. The scale at which it is observed in the biopharmaceutical industry compared to other sectors is particularly striking. The performance of biopharmaceutical companies attracts extensive interest from a variety of investors with a wide spectrum of time horizons from speculative short-term stock traders to large institutional investors with patient capital indicating that it is possible to continue to support efforts to promote innovation as there will be capital available to support organizational learning efforts.

BCG (2016) presents data on shareholder “value creation” in different sectors and allows for comparison of the biopharmaceutical industry with others based on total shareholder returns (TSR). The performance of the sector is further evidence that MSV ideology has spread across the industry to become a prevalent corporate governance regime. In addition, four latecomers to the biopharmaceutical industry: Regeneron (#1), Allergan (#2), Gilead Sciences (#3) and Biogen (#6), are listed by BCG among the top ten creators of total shareholder value in the “2016 Value Creators Ranking”.

Figure 6: Top shareholder value creators in 2016, ranked by major industry groups, average annual TSR 2011-2015 (%)



Source: Adapted from Boston Consulting Group, 2016 Value Creators Rankings

Out of approximately two thousand companies within 25 different industry groups that are ranked based on the annual percentage average of total shareholder return (TSR⁶) between 2011 and 2015, mid- and large-size biopharmaceutical companies in terms of company market value are the top performers in MSV in the world. The details of such a ranking reveal striking results about the shareholder “returns” that biopharmaceutical companies generate. Shareholders of mid- and large-size biopharmaceutical companies can obtain yields that are much greater than the yields that shareholders can obtain from the allocation of their financial portfolios to the securities on other industries. Furthermore, the shareholders of Regeneron have obtained yields that are more than six time higher than the average yields of the other industries.

1.5 Research implication and contributions

Among the anticipated theoretical contributions of this thesis is to fill a gap in the current literature, which only offers very limited insight into the mechanisms linking financialization and an ongoing productivity crisis afflicting the US biopharmaceutical industry. Both theoretical and methodological issues concerning the economic analysis of industrial organization diminish scholarly interest in exploring such mechanisms. The conceptual diversity that characterizes the social factors enabling innovative productivity makes it difficult to operationalize the innovation process (Marcoulides and Heck, 1993).

⁶ *TSR is a financial metric calculated for each company based on five major financial ratios (sales growth, margin change, multiple change, dividend yield, and change in the number of shares outstanding as well as change in net debt. See BCG (2016) http://image-src.bcg.com/Images/BCG-Appendix_Creating-Value-Through-Active-Portfolio-Management-Oct-2016_tcm9-123159.pdf for more information on the methodology.*

In addition, mainstream market-based economic theories lack the analytical depth and breadth to capture this conceptual diversity, thus restricting earlier scholarly efforts to develop more in-depth empirical knowledge on how financialization affects innovation within organizations (Lazonick, 2013b).

As already indicted, in a recent study examining the impact of financialization on Big Pharma's decision to restructure R&D operations, for instance, Gleadle et al. (2014) argue that the market-based economic theories such as the *resource-based view* (RBV) of the firm or the *transaction cost framework* are inadequate to explain the basis for such decisions. With a case-based analysis, the study explains the impact of financialization on the business model of Big Pharma and the governance of productive resources that ultimately led to the “vertical disintegration” of R&D operations. The study however offers no insight into the ways in which such vertical disintegration impacts on the innovative performance of the economy but concludes that such an in-depth analysis is needed to “gain a better understanding of the dynamics of financialization.”

According to Chandler, a high-tech industry such as pharmaceuticals is the byproduct of profit-seeking interests seeking new learning in science and engineering that often leads to new opportunities to commercialize. Once the economies of the large industrial enterprises reach to certain scale, they begin to seek diversification into new markets. While the growth of the firm comes from successful expansion into new markets, industrial growth and economic development occurs when a number of industrial enterprises completes their expansion.

From the perspective of TIE, the disappearance of the Chandlerian corporation can be explained in three stages. In the first stage, *strategic control* was weakened by activist shareholders who built conglomerates from the 1960s that sought to run businesses in a wide range of unrelated industries in which those who exercised strategic control had scant if any knowledge of the productive capabilities in the constituent businesses. In the second stage from the 1980s *organizational integration* in US mass-production enterprises was compromised by Japanese competition that rendered obsolete the efficiency of the US-style “mass-production”. In the third stage, *financial commitment* as a social condition of innovative enterprise was decimated within the Chandlerian corporation as the *maximizing shareholder value* (MSV) ideology began to dominate the large corporations in the United States in the 1990s, resulting in massive distributions of corporate cash to shareholders.

Industrial, organizational, and institutional conditions, which had previously enabled the modern industrial enterprises to grow, have been changing since the 1970s such that the theoretical argument Chandler postulated for the modern industrial enterprise no longer applies in the era when corporations operate under what Lazonick (2009) calls the US “New Economy business model” (NEBM). In fact, “in the 2000s,” Lazonick argues, “the Chandlerian corporation has ceased to exist,” as NEBM displaces the US “Old Economy business model” (OEBM) that characterized the Chandlerian modern industrial enterprise. In the context of Merck, one of the core US pharmaceutical companies highlighted by

Chandler (2005) in his analysis of the evolution of modern pharmaceuticals in the United States, this research assesses the evidence to the disappearance of the Chandlerian firm in the US biopharmaceutical industry, as this industry transitioned from innovation to financialization in the 1990s, contributing to its ongoing productivity crisis.

There is generally a lack of empirical data on how financialization influences the *social conditions of innovative enterprise* and undermines the productivity of the innovation process within the innovative enterprise. Employing the most appropriate theoretical framework and methodology are critical to generating the relevant data and drawing its logical implications. The digital revolution has now made it possible to access electronically highly detailed and useful data from a vast array of sources available. By employing the TIE framework and the *historical-transformation* methodology the Lazonick proposes, the research in this dissertation seeks to make better use of data in qualitative and quantitative forms gathered from both primary and secondary sources.

Finally, although one of the most extensive historical studies of the pharmaceutical and chemical industry, published by Chandler (2005), covered the period of financialization, it ignored MSV and its impact on productivity. Chandler's techno-historical evaluation of modern pharmaceuticals is a highly significant contribution to understanding of the dynamics of the sector, and it can be further developed to analyze the impact of financialization. The ambition of this thesis is to build on this seminal work with a specific focus on the role of financialization of the biopharmaceutical industry and the implementation of the MSV agenda, in order to analyze and understand in more depth importance of the social conditions of innovative enterprise for attaining higher levels of economic performance by generating high-quality, low-cost products,

2 RESEARCH DESIGN AND METHODOLOGY

The purpose of this thesis is to understand how the adoption of a financialized business model ultimately inhibits innovation, and thus the economic performance of an innovating enterprise and the productive economy. This study identifies “financialization” as the emergence of a set of new organizational governance objectives and values in which the goal of allocating corporate resources for maximizing shareholder value (MSV) supersedes all the other objectives and values to which a firm might aspire.

Enterprises that operate according to a financialized business model seek to continuously improve profitability and cash flow to generate financial gains that can increasingly be “returned” to shareholders through dividends and stock repurchases. The top managers of such business enterprises immersed in such a business model develop an inherent shareholder-bias over time as their incentives are aligned with practices that maximize shareholder value. Those incentives are conditioned to meeting certain financial goals and such goals often determine the degree to which the top managers pursue activities to extract value for shareholder and themselves.

As value-extracting activities increase throughout the financialization process, the social conditions of innovative enterprise change in such a way that they no longer effectively support innovative strategies, organizational learning efforts, and sustained committed finance. In support of this “financialization hypothesis”, this research highlights growing engagement in value-extraction efforts by managers who engage in downsizing-and-distributing productive assets particularly through stock repurchases. In doing so, they are substituting an organization’s prospects for sustainable long-term growth and reducing productivity in the long term. In other words, the prospect of achieving strong growth in the future is foregone, along with the opportunity to make the productive investments presently as the top executives distribute corporate cash to maximize shareholder value and their own gains.

The transition of business enterprises from innovation to financialization has major implication on their productivity. A traditional line of inquiry that bases its analysis on neoclassical economics cannot adequately address the question of why, how, and to what extent, the transition of a previously innovative enterprise into financialization impacts its productivity (Lazonick, 2012). Inquiries that rely on aggregate data for an industry or an economy systematically fail to capture company-specific differences in the transition from innovation to financialization at a particular point in time and over a period time (Lazonick, 2002). In the context of this research studying the innovative productivity of the pharmaceutical companies in the United States, a macro-level analysis relying on data aggregated to the industry-level would not reveal an inter-organizational performance variance such as the one this thesis observed between Merck and Roche.

Such a macro-level analysis is not suitable for the purposes of this research given that aggregated data would fail to capture the organizational underpinnings of performance variance among the companies operating in the same industry or institutional environment. An analysis based on time-series data cannot explain why and how the productivity growth of companies such as Merck and Roche that have access to same industrial support in the US biopharmaceutical industry diverge significantly over time.

This research aims to integrate theory (how changes impact the innovation process) with history (how these changes occur over time), an approach that deviates from the more commonly pursued application of constrained-optimization methodology in neoclassical economics. As explained by Lazonick (2002), the utilization of such a methodology is key to explaining why economic performance varies from firm to firm over time even as those firms continue to operate within the same institutional environment and macroeconomic conditions and face similar technological and market challenges. Building on earlier work (Lazonick and Tulum, 2011) that gives a broad perspective on the role of financialization in the R&D crisis of the biopharmaceutical industry in the United States, this thesis focuses on developing an in-depth understanding of the mechanisms that link financialization to the innovation crisis. Such links are illustrated in this thesis through historical and in-depth case analysis of two pharmaceutical companies of significant importance.

There have been different streams of scholarly efforts in understanding the growth of the large industrial corporations since Schumpeter (1942) first proposed the idea of considering large industrial organizations as the unit of analysis for the growth of the economy. A particular stream in those research efforts developed a methodology based on the Schumpeterian idea that any sound economic theory that is relevant to empirical evidence should be constructed upon the “historical experience” of those large corporations. Alfred D. Chandler, Jr. pioneered the scholarly efforts to build an extensive case catalogue of large industrial corporations that were accumulated through in-depth business history research. Chandler’s contribution in the fields of management and strategy through influential books such as *Strategy and Structure* (1962), *The Visible Hand* (1977), and *Scale and Scope* (1990) is monumental because of the methodology he championed that aspired to integrate theory with history.

Lazonick’s *historical-transformation* methodology in part is rooted in the business history approach extensively employed by Chandler and Penrose in their analysis on the operations and performances of the modern corporation. Like Chandler and Penrose, Lazonick argues that the most appropriate way to analyze the operations and performance of business enterprises is through pursuing comparative business history research. Only through the accumulation of company cases, Lazonick argues, can one develop a broader understanding of how, why, and to what extent transitions from innovation to financialization occur, and the implications of these transitions for the economic performance of industries and regions.

Unlike Chandler and Penrose, however, Lazonick argues that such business histories cannot be analyzed without identifying the broader industrial setting in which business enterprises are embedded. Lazonick’s “social conditions of innovative enterprise” framework integrates the institutional environment and industrial conditions in the analysis to assess the economic performance of business enterprises. In order to analyze the strategic, organizational, and financial conditions that support or undermine drug innovation efforts within the biopharmaceutical industry, this thesis adopts the “theory of innovative enterprise”, an effective theoretical perspective to carry such analyses (Lazonick & O’Sullivan, 2000; Lazonick, 2010). This research identified the *social condition of innovative enterprise* (SCIE) as the most appropriate analytical framework to guide the qualitative analysis and draws extensively from Lazonick (1991, 2002, 2013b, 2017). Such a framework is a compelling theoretical aid that enables researchers to analyze the structure, organization, and performance of business enterprises based on the systematic analysis of three key organizational concepts identified as “social conditions of innovation.”

Innovation requires constant learning about how to transform new technologies or to access new markets. Learning, as a process enabling and facilitating innovation within organizations, is a social activity that is dynamic in essence and the efforts can be characterized as uncertain, collective, and cumulative. An innovative enterprise utilizes strategy, finance and organization to address respectively these three challenges of the

learning process: that it is uncertain, that it can be carried out collectively and that it occurs over time or cumulatively.

SCIE implies a set of relations that guide managers who are committed to the innovation process in their resource allocation decisions; incentivizes people from different functions and capabilities to dedicate their skills and efforts in achieving strategic objectives; and ensures that the necessary funding is committed to the innovation process until the intended financial returns are generated through sales of an innovative product (Lazonick, 2015).

Many prominent academics in business, economics and other related disciplines who study business history and the environment in which businesses operate are associated with the Business History Conference, an international organization that supports scholarly efforts in the advancement of business history research. William Lazonick and Mary O'Sullivan, who have been presidents of the Business History Conference in 1990-1991 and 2017-2018 respectively, are the most prominent academics whose researches have been integral to the development of business history approach as a sound research methodology for economic analysis. There is a growing body of literature using this approach including Carpenter, Lazonick, and O'Sullivan (2003) on the study of major competitors of in the global optical networking industry; Lazonick and Prencipe (2005) on the study of Rolls-Royce; Lazonick and March (2011) on Lucent Technologies; Lazonick, Mazzucato, and Tulum (2013) on the analysis of Apple, Inc.; Carpenter, Bell, Glimstedt and Lazonick (2014) on the global leaders of the information and communication technology (ICT) industries; Sakinç (2016) on Airbus and Boeing; and Carpenter and Lazonick (2017) on the global communications technology companies are among the studies that employed the comparative business history approach to analyze innovative enterprise.

2.1 Historical-transformation and case study methods

The analytical applications of cases vary depending on the research objective. Cases can be employed for the purpose of contrasting, iterating or extending the baseline argument (Yin, 2005). In fact, the case-study method can be the most appropriate research strategy for comparative organizational analysis (Maxwell, 1996; Yin, 2003; Fiss, 2009). Using an analogy from natural science Eisenhardt (2007) compares a case study to a laboratory experiment. The case study's relevance to theory can be reinforced through building multiple cases to "replicate logic" in the same way as natural scientists conduct a series of experiments to build the necessary body of evidence (p. 25).

Cases can be developed to explore complex organizational issues systematically by compiling empirical evidence that is often qualitative in nature (Creswell, 2007). Unlike many quantitative alternatives, a case-based analysis can provide the "real-world context" for a theory to offer a compelling argument (Yin, 2005; Lazonick, 2002). Case-based research inquiry thus seeks to develop theories based on the "real-world" evidence. Given the inherently dynamic nature of the SCIE framework, Lazonick (2002) proposes

comparative case analysis as the most appropriate research method for such an extensive economic analysis.

Case analysis can be an effective methodological tool for theory building (Eisenhardt, 1989). Eisenhardt and Graebner (2007) indicate some major contributions to literature in organizational studies in fact employ case-based analysis. Although the theories constructed based on cases can be construed as “subjective”, such theories can be “surprisingly objective,” Eisenhardt and Graebner (2007) argue, given that researchers have to remain “honest” in theory building since they cannot fall too far from what is empirically evident in the data subject to analysis.

Further stipulating on the “honesty” of researchers in the building of new theories from cases, Eisenhardt and Graebner (2007) argue that “the data provide the discipline that mathematics does in formal analytic modeling.” But, unlike research in natural sciences such biology that can “isolate the phenomena occur,” Eisenhardt and Graebner (2007) argue, “case studies emphasize the rich, real-world context in which the phenomena occur.” In other words, a theoretical postulate that is built through a static and context-free intellectual approach cannot find itself a use in real-world context, hence, such a theory serves no utility to researchers as context-matter changes. Lazonick’s *historical-transformation* methodology fulfills the need for a methodology to study organizations that integrates theory and history.

As discussed extensively in the previous chapter, the current literature on the innovative performance of the US biopharmaceutical industry documents an ongoing productivity crisis that is prevalent in this industry. Also discussed in the previous chapter is a growing body of literature, in line with Lazonick and Tulum (2011), Lazonick et al. (2017), that reveals the financialization of previously innovative enterprises as the real culprit behind this ongoing productivity crisis. Supported by the analysis of a large set of qualitative and quantitative data, this thesis research links the ongoing productivity crisis with the transition of the US pharmaceutical industry from innovation to financialization.

Having departed from a traditional line of inquiry and adopted a highly robust analytical framework to utilize a significant amount of data available electronically, this thesis overcomes major theoretical and methodological challenges to analyze the innovative performance of an industry in connection with the financialization of companies operating in the same industry. Through historical and comparative case analysis of two companies, Merck & Co. and Roche Holding AG, this research examines in detail how the allocative decisions made by top executives at Merck and Roche corresponds to choices to ignore or pursue investment opportunities in new learning. On the basis of the opportunities available to each firm based on its specific technological and market trajectories, the economic outcomes for the two companies will be shown to differ significantly.

Chapter four studies the rise and fall of Merck & Co., an iconic American drug maker that had transformed the US pharmaceutical industry during the second half of the 20th century.

Merck's iconic growth of the late-1980s and early-1990s turned into a corporate collapse of epic proportion as early as late-1990s. In chapter six, Swiss-based Hoffmann-La Roche is studied as the second case for comparative-historical analysis. Having survived a multitude of crises stemming from issues or events concerning the economic, political, technological, and market environment of the period, Roche's innovative performance transcends today's industrial standards. The historical transformation of Roche is a remarkable illustration of why and how the social conditions come into play when the innovation process in a business enterprise faces challenges that stem from changes in the market and technology.

2.2 Sampling and data collection

Without gaining direct access to those who are in the position of making allocative decision in the upper echelons of management at a business organization, it is almost impossible to gather the data that is required to conduct meaningful quantitative analysis that could measure the impact of financialization-driven allocative decision on the company's economic performance. Even in the event of accessing such data from surveys of senior management, its reliability would be questionable; as such allocative decisions have direct repercussions on the annual compensation of such executives given that a large proportion of executive pay in the US is tied to the market performance of company stocks.

The equity-based executive performance incentive scheme that has grown to prominence in the US means compensation for senior management is determined by the extent to which executives meet specific financial performance targets that financial terms (i.e. earnings-per-share, etc.). Such a compensation strategy has the potential to distort the investment horizon of top executives, particularly in the pharmaceutical industry, where the concept of "long-term" in the context of "return-on-investment" implies different time-horizons for different executives depending on their career planning. Given the complexity of the issue, a survey aimed at identifying the determinants of allocative decisions of top executives could clearly be influenced by issues of personal interest on the part of respondents.

Rather than risk conducting a biased or unreliable quantitative survey, a qualitative research strategy was thus adopted in this thesis to gain insight into the growing symbiosis of financial and industrial actors in the US economy. The research is investigative in nature and was conducted by compiling both quantitative and qualitative empirical evidence, in order to conduct a qualitative analysis based on the TIE theoretical framework. Significant qualitative and quantitative data were gathered from secondary sources. Given the descriptive nature of the research questions, the case study method is employed in order to analyze the extensive empirical evidence in a systematic way in order to investigate the innovation challenge of the pharmaceutical industry from the perspective of the "financialization hypothesis".

2.3 Purposeful sampling

Chandler (2005) argues that many pharmaceutical companies failed to remain competitive because of a lack of investment in building integrated learning bases throughout their evolutionary path and, as a result, many pharmaceutical companies disappeared through industrial consolidations in the second part of the 20th century. The top twenty global companies listed below (Table 2) are the byproducts of major industrial consolidation efforts in the past decades. From a series of merger and acquisition (M&A) transactions, these twenty companies have emerged to control a significant portion of the world's drug market. In addition to M&A activities, these large pharmaceutical companies also control a significant portion of the new drug market as they partner with the vast majority of biotechnology start-up companies to license innovative therapies and commercialize them globally.

Financialization manifests itself in different ways and with varying influence on economic performance. However, there are certain characteristics of financialization that are observed across the organizations adopting a financialized business model. Lazonick (2009) coined the term New Economy Business Model (NEBM) as a general term to refer those companies adopting a financialized model. Since the 1980s, NEBM has been replacing the Old Economy Business Model (OEBM) that had constituted the basis for the great expansion of the US economy for most of the 20th century. Based on the TIE theoretical framework adopted, this study categorizes the major pharmaceutical companies into these two distinct groups from which the samples are drawn.

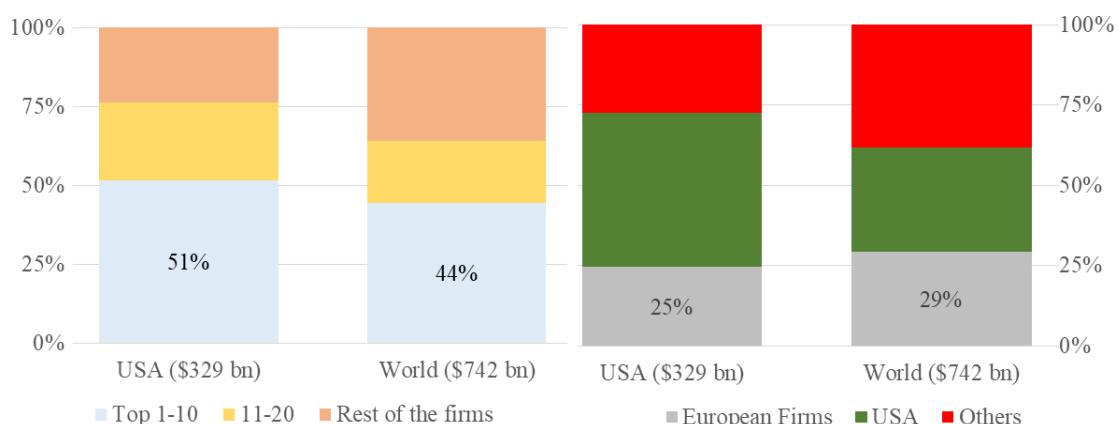
A purposeful sampling method is employed to identify the established BP companies that are representative of companies in two categorical groups adopting distinctly different business models (Eisenhardt, 1989): Old Economy Business Model (OEBM) and New Economy Business Model (NEBM) (Lazonick, 2005). For the case analysis of small samples, Seawright & Gerring (2008) identify seven common purposive sampling methods: typical, diverse, extreme, deviant, influential, most similar and most different. Each method has distinct strengths and weaknesses to serve various different research needs and objectives depending on the relationships being investigated among the key variables. For the purposes of this research to contribute to the *financialization hypothesis*, two companies were selected from among the top twenty pharmaceutical firms as representing typical, deviant, and extreme cases. Each case is analyzed contextually in relation to the relevant period studied in its evolutionary path.

In the case of pharmaceuticals, it is feasible to analyze the global industry as a whole through the accumulation of company cases. Figure 7 shows that a nearly half of the US and worldwide prescription drug markets in 2015 were in fact controlled by 10 global pharmaceutical companies (51 percent vs 44 percent). The sales of those top 20 companies together accounted for 76 percent of the US prescription drug market while dominating 66 percent of the worldwide prescription drug market. Figure 7 shows the distribution of total

US and worldwide prescription drug sales in 2015, grouped by the regions of the companies based on the location of their headquarters. While the top seven European biopharmaceutical companies accounted for one-quarter of US prescription drug sales, 12 US-based pharmaceuticals companies accounted for 48 percent of the US market. While the 12 companies on average generated nearly \$13.1 billion revenues in 2015, the seven European companies averaged \$11.6 billion in the same year. Figure 7 clearly show that European Big Pharma is quickly catching up with US Big Pharma in marketing competitive products.

Such a finding confirms the findings of Light (2009), who argues that European began to boost their innovative productivity ahead of American firms. The analysis of Light (2009) shows that European biopharmaceutical companies increased their innovative productivity, measured in terms of new chemical entities (NCEs)—that is, novel new therapies with no competing alternatives—from 1982-2003 period to the 1993-2002 period. This improved performance allowed European companies to outperform their US opponents in the race to bring novel therapies (products with “first-in-class” designation), biotech and orphan drug products to market (Light, 2009, p. w972; Gambardella et al., 2007)

Figure 7: Concentration of prescription drug sales in the US (left) and worldwide markets (right), % shares in market total by companies grouped in sales



Source: Own illustration based on data from EvaluatePharma World Preview 2016, Outlook to 2022

The US pharmaceutical industry company population size is relatively small when the sales value of each company is taken into consideration. A large proportion the \$330 billion prescription drug market in the US is dominated by a relatively small number of pharmaceutical companies of both US and European origins. The top fifteen companies accounted for nearly three-quarters of the total drug sales in the US in 2015 while the rest of the population responsible for the remaining drug sales (EvaluatePharma, 2016). The pharmaceuticals sales of the top five companies, including only Roche from Europe, accounted for 29 percent of US sales. The top 10 included Merck & Co., Novartis and Sanofi-Aventis from Europe as well as Roche, accounted for 51 percent. The top fifteen firms included GSK and AstraZeneca from Europe and accounted for 66 percent of sale.

The top twenty companies accounted for 76 percent of the total US drug sales in 2015. Roche and Merck & Co. together account for nearly 10 percent of the total drug sales in the US.

Table 2: Company rankings by drug sales, 1993 and 2013-15 average

Rank, US Rx market				US Rx Sales (\$bn)		
1993	2015	2013-15	Company	Country	2015	2013-15, ave.
9	4	1	Roche	SWISS	18.3	17.3
6	2	2	Pfizer	USA	18.8	17.2
11	3	3	J&J	USA	18.3	16.5
-	1	4	Gilead	USA	21.2	15.4
10/12 [a]	8	5	Novartis	SWISS	15.5	15.3
1	7	6	Merck	USA	16.2	15.1
-	6	7	Amgen	USA	16.5	15.1
-	5	8	Allergan	USA	17	14.7
4/14/19 [b]	9	9	Sanofi	FRA	13.6	13.5
	10	10	AbbVie	USA	13.5	11.5
-	11	11	Teva	ISR	11.2	10.8
2/5/21 [c]	12	12	GSK	UK	10.4	10.1
18/20 [d]	13	13	AstraZeneca	UK	9.5	9.8
8	14	14	Eli Lilly	USA	8.6	9.4
3	16	15	BMS	USA	8.2	8.1
-	15	16	Novo Nordisk	DEN	8.5	7.7
-	20	17	Boehringer Ing.	GER	5.4	5.5
-	18	18	Biogen	USA	6.5	5.2
-	17	19	Valeant	USA	7.1	4.9
-	19	20	Celgene	USA	5.6	4.7
Top 20, Total US Rx Sales				250	227.6	
CMS, Total US Rx Sales				328.4	301.5	

[a]Sandoz/Ciba-Geigy; [b] Hoechst/Rhone-Poulenc Rorer/Marion Dow (Merrell);[c] Glaxo/SmithKline Beckman/Wellcome; [d] Astra/Zeneca. J&J: Johnson&Johnson; AbbVie: Abbott Pharmaceuticals; GlaxoSmithKline; BMS: BristolMyersSquibb. Rx: Prescription-only drugs; CMS: The Centers for Medicare & Medicaid Services

Source: Companies' annual reports, EvaluatePharma World Preview 2016, Outlook to 2022 and The Centers for Medicare & Medicaid Services (CMS) data

A year in the early 1990s was chosen as an appropriate benchmark as innovative new biotechnology products had begun to enter the drug market during this period. Newly emerging biotechnology companies such as Biogen, Amgen, Genentech had begun to challenge big pharma companies in the drug market and were forcing them to consider overhauling their research operations and, potentially, consolidation. In 1993, for instance, Merck ranked top in the list of pharmaceutical revenues and generated nearly 1.74 and two times greater revenues than Roche and Pfizer respectively. Merck was thus in a far more

competitive position in 1993 in relation to the firms that ended up being the top two pharmaceutical firms based on the average revenues for three-year between 2012 and 2015.

Merck & Co. vs Hoffmann-La Roche

Given the high concentration of BP industrial output produced by approximately a dozen firms, a sample size of two was considered adequate number for purposeful sampling of this sector. All top 20 companies have a significant presence in the major global drug R&D centers, access to the same pool of scientists in the labor market, the same access to academic research centers, etc. Given the technologies, markets, and competitors that characterize the industry, the differences in market performance among the top pharmaceutical companies are the result of their distinctive prior investments in innovation.

For the purpose of this study, Merck and Roche are thus the two companies selected as sample firms for the case analysis. The market analysis in chapter 6 examined competition in the US drug market and highlighted that market size is even smaller in disease-specific segments of the drug market. GlaxoSmithKline, for example, is a leader in the vaccines market but has no major presence in the oncology field. Merck and Roche compete within all the major segments of the prescription drug market against a small number of other big pharmaceutical companies and these two companies are considered to be suitable representatives of the true population for a number of reasons.

First, Merck and Roche occasionally stood out as *influential* market leaders. At times, they steered the industrial R&D efforts as their innovative new therapies instigated a competitive rush to develop follow-on therapies based on the knowledge they had developed. Products developed in the US by Merck and Roche include vitamin B12, vitamin C, streptomycin, valium, cortisone, diuretics and statins and they were pioneers in their fields. These products often emerged at critical turning points in the sector's industrial history as a result of significant investment in basic research at state-of-the-art industrial labs in Merck's Rahway site and Roche's Nutley site, both in New Jersey, USA.

The two companies had transformed new knowledge from the emerging field of organic-synthetic chemistry in the early-20th century and the areas of antibiotic and steroids more recently. Despite being a European firm, Roche, for example, managed to outperform US-based companies in their home-base to capture significant market share in the competitive US drug market. Roche has made a significant leap forward ahead of its competitors over the last two decades, despite the fact that some of the rivals from the 1993 list have completed mega-mergers. Pfizer, for example, acquired American Home Products [AHP]; Glaxo merged with SmithKline Beecham; Bristol-Myers acquired Squibb and Hoechst eventually merged into Sanofi.

Merck, the first sample firm chosen, experienced a sharp decline in the 2000s and the company decided to acquire Schering-Plough in 2009 to bolster its ailing product portfolio.

Over the past two decades, Merck has made numerous acquisitions to bolster innovation and has conducted significant stock buyback programs to maximize shareholder return. During the same period, the company downsized its global R&D operations and laid-off employees through a series of corporate restructuring programs. In doing so, Merck lost both its place on the list of America's "Most Admired Companies" and its role as the champion of industrial productivity and stakeholder interest that it represented in the late-1980s and early-1990s. This makes the company an ideal candidate for the *most similar* case of a financialized company suffering from the impact of the productivity crisis that is a result of the changes in the social conditions of innovation.

Swiss-based Hoffman-La Roche, on the other hand, has grown to a position of leadership in the global prescription drug market during a period when the industry overall is suffering from a productivity crisis. This makes Roche an *influential* case within the establishment of large pharmaceutical firms. In addition to global revenues, profitability and market capitalization, the firm has the one of the most successful product portfolios as well as a pipeline of clinical candidates (see chapter 6 for analysis), adding to the company's influence. Roche had experienced similar economic success in the 1960s, in the midst of an industrial productivity crisis, after launching a popular tranquilizer, Valium. This drug was arguably the first drug to generate such a significant level of sales that it was referred to as a "blockbuster".

Roche is also selected as the *most similar* case for an "innovating-firm" as the company's business model closely resembles that of the OEBM. The company's current economic performance is, therefore, not the only criteria used for its selection as the second case for the proposed comparative analysis. Roche's presence in the US has developed significantly since establishing the Nutley, NJ campus in 1929 and it grew even further in the early-2000s with the acquisition of Genentech. Despite its global operational focus, however, Roche is still a Swiss company controlled by the executives based in Basel.

Roche is also the *most different* case given its unique ownership structure such that the company is arguably the only pharmaceutical company still to be controlled by members of the founder's family. Although a large portion of the company stocks are traded in the public markets, the Hoffmann-Oeri family, who are descendants of the company's founder Fritz Hoffman, continues to retain majority control through a unique ownership structure. Seeking to maintain Roche as an independent specialty drug company, the family has retained strategic control throughout the company's history as ownership passed from one generation to the next. The stability in governance ultimately became an essential part of the firm's corporate identify and has helped it to recruit and retain productive scientists who have mostly remained employed at Roche throughout their careers.

2.4 Data for market analysis

Chapter 6 analyzes the recent innovative performance of the top seven European drug makers to analyze whether the drug R&D network in the US plays an important role for the leading European drug developers as they seek to build a competitive portfolio and pipeline of products from which to generate significant profits. The purpose of the analysis is to identify the most European drug maker that utilizes the productive resources of the US pharmaceutical industry most effectively and to evaluate if a European firm is making better use of the American science and technology (S&T) infrastructure than a financialized US pharmaceutical company.

The product portfolio and pipeline data are mostly compiled from the Form 20-Fs filed by the subjects of this study. As foreign companies whose stocks are traded on the US market, the companies are required by the SEC to submit Form 20-F annually and these documents provide extensive discussions of the state of product portfolios and pipelines. For the purposes of this thesis, all product candidates that are still in the preclinical discovery phase have been excluded from the analysis in chapter 6. The latest year for which the data were available at the time the analysis was conducted was 2015. An extensive review of annual reports from this year revealed 159 biopharmaceutical products generating significant revenues for the seven European companies, and 527 product candidates currently being tested for safety and efficacy through clinical trials in anticipation of regulatory approval for marketing in the near future.

The company annual reports reveal only very limited information on the origin of drugs presented in their product portfolios or pipelines. Country of origin and other basic information on the products examined were thus gathered from Springer's *AdisInsight*, a comprehensive database of drugs that have been approved or that are under development. In addition, the publication "Approved Drug Products with Therapeutic Equivalence Evaluations", commonly known as the "Orange Book", were accessed frequently during the data-gathering process, as was the database for Acronyms & Abbreviations, a comprehensive data source made available by the Food and Drug Administration (FDA).

The country of origin of a pharmaceutical drug is determined by the location of the institution at which the key component in a product was discovered by an individual or team of scientists. Given that a significant portion of products were either developed through external collaborations or acquired, the origin of a drug may or may not be the same as the company marketing the drug. The product launch date is the official marketing date of the drug granted by the FDA in the US market. In the case of a drug being discovered through inter-institutional collaboration (i.e. company-company or university-company) the country of origin was considered to be the country in which the initial patent application was made. In such cases, the data for the applicant of the key patents were gathered from the Google Patents website.

Various other resources such as medical journals, industry reports, biographies of inventors, and miscellaneous news and on-line content were also used during the data collection process. The current sponsor of a drug registered with the regulatory agency, the FDA, may not necessarily be the original source of discovery and the ownership of a key molecule in a prescription drug may have been transferred through mergers and acquisitions, a thorough investigation of various types of historical transactions was necessary to identify the origin of certain drugs.

2.5 Data for case analysis

Qualitative data for the case analysis was compiled from searches of news archives, historical documents, corporate legal filings, and field observations. Online resources such as oral history archives at the University of California Berkeley and the Chemical Heritage Foundation proved to be an invaluable source for accessing an extensive archive of in-depth interviews with key current or historical figures in the field of pharmaceuticals. The interview transcripts obtained from oral history archives have been instrumental not only in gathering qualitative data for the case analysis but also cross-checking facts in the interviews obtained from different informants.

Historical data: Oral history achieves; official company history published by corporate achieves

The study reviewed qualitative data from the individual accounts of almost sixty people who were involved with Merck, Roche, Genentech or Cetus (Chiron) in various capacities. Such qualitative data were published in oral history interviews, autobiographies, personal essays, and biographical memoirs dating from 1971 until 2015, with a concentration of sources appearing around the 2000s. Most of the people interviewed were key scientists, research leaders and the top R&D directors but the list also includes start-up founders such as Robert Swanson and Herb Boyer, chief executive officers such as Roy Vagelos, Kirk Raab and George Rathmann, as well as chief finance officers, legal counsels, directors, venture capitalists such as Moshe Alafi and Thomas Perkins, marketing managers and science or business consultants.

The data gathered through oral histories interviews with key science and business managers provided rich insight based on first-hand knowledge from key informants in relation to strategic, organizational, and financial matters. Such interviews were available from institutions who maintain extensive oral history achieves (OHA), including the Oral History Center at the Bancroft Library of the University of California; Oral History Collections at the Chemical Heritage Foundation; the National Cancer Institute Oral History Programs as well as institutions such as the American Association of Immunologists Oral History Project, and the Lyndon Baines Johnson Library Oral History Achieve.

Fifty-four key informants were interviewed by leading historians as part of the oral history programs of those institutions. The information gathered covers intimate personal accounts of the matters concerning the development of biomedical science and pharmaceutical business. Analysis of this information involved reviewing the records of more than 50 different interviews that lasted on average three hours, but some of whom took up to ten-hours. The total transcriptions amounted to approximately 4,800 pages of interviews. The record-keeping institutions mostly made such records accessible to the public free of charge but in some instances a small donation was requested by these not-for-profit institutions.

Those oral history interviews are invaluable to scholars with varying research interests. Interviews are often conducted by narrators with sufficient knowledge, experience or insight into events to ensure that narrators engaged with the key informants and extracted as much insightful information as key informants were willing to share. The main objective of those interviews was to build a collective memory bank of the evolution of biochemistry and biotechnology both within industry and academia. In addition to the objectivity of these interviews, they also provide the industrial context for scholarly use. Their historical accuracy can be ensured by cross-checking the data gathered from a key informant with the data from other informants, as well as with the historical records that the narrators gathered on the individuals and the events discussed during the interviews.

Using Lazonick's SCIE framework, the qualitative data extracted from the transcriptions of those interview was systematically scanned for details about the three key socio-economic constructs: strategic control, organizational integration, and financial commitment in order to consider what changes within an organization may be related to an observed change in economic performance. The first stage of searching the record sough to identify tangible evidence by scanning the records for any us of a single term or combination of terms such as stock, shares, market, buybacks, repurchases, turnover, commitment, integration, funding, security, employment, shareholder, maximizing shareholder value, etc.

The data analysis then concentrated on examining certain key events such as the launch of a new product, the completion of a key milestone, the ending a research program, a product failure, a leadership change, a merger or acquisition, growing rivalry among different research teams within an organization or across different institutions to complete a project first, etc. This exercise proved critical in developing different narratives within the case analyses that are outlined in chapter five and chapter seven to illustrate the ways in which changes occur in the social conditions of innovation in the context of financialization.

The following chapter analyzes the governance, labor and investment institutions that facilitated the transformation of the large established companies in the US economy from innovation to financialization Through a historical case analysis of Merck, chapter five first explains how the institutional environment supported the organizational efforts to develop highly innovative new drugs until the 1990s by enabling the social conditions of

innovation. It then goes on to show how such an environment in the US has, since then, been undermining these social conditions that support organizational innovation.

2.6 Methodological contributions and future implications

This research makes a major contribution to the current literature on financialization by offering a comprehensive understanding of mechanisms linking the financialization of the US biopharmaceutical companies and the productivity crisis in the industry in which those companies are operating. The complexity of the organizational issues involved poses a significant research challenge that centers on the identification of relevant empirical evidence for systemic analysis that is based on the TIE theoretical framework. The SCIE framework examines the socio-organizational implications of basic business concepts such as *strategy, organization, finance (SOF)* as the basic units of observation in the dynamic analysis of socio-organizational conditions. Any changes observed in the ways in which a business enterprise makes use of strategy, organization, finance is thus examined in relation to the changes observed in relation to the economic performance of the enterprise.

In the *historical-transformation* methodology, “theory” refers to a simple explanation of complex real-world context, and “history” refers to a change in the real-world context that is “ongoing” or that continues to “unfold.” So, Lazonick’s “iterative intellectual approach” allows one to keep theory relevant so the scholar of organizational change can “catch up with history.” Such a dynamic methodology also allows the researcher to identify highly relevant quantitative or qualitative data from massive resources available electronically and utilize these data in the analysis of complex organizational matters that are rooted in social constructs such as *strategic control, organizational integration, and financial commitment*.

Such complexity of the data in fact allows researchers to triangulate sources that can otherwise be challenging. This thesis, for instance, made great use of a number of oral history interviews with key informants who were involved with Merck and Roche that were instrumental in corroborating conflicting testimonial on critical organizational matters from various different accounts. Information gathered from a wide array of sources allowed this research to develop cases that are highly rich in content, permitting further theoretical arguments to be drawn from these cases and tested through qualitative and quantitative inquiries. As I continue to pursue the same line of inquiry and accumulate company cases, the analysis of this research will be further leveraged to develop a much broader understanding of this industry across different institutional environments.

3 AN OVERVIEW OF THE CHANGES IN THE INSTITUTIONAL ENVIRONMENT AND THE CONDITIONS OF THE PHARMACEUTICAL INDUSTRY IN THE UNITED STATES

Aspirin has been the standard to which other anti-inflammatory drugs have been compared for over a century. This pioneering non-steroid anti-inflammatory drug (NSAID) had

brought fame and wealth to Bayer, but 100 years later a callous attempt to overtake its competitors in the NSAID market nearly destroyed Merck. Merck's Cox-2 inhibitor, Vioxx, marketed briefly as a "super-Aspirin," had been developed as a therapy presumed "safer" than the competing NSAIDs for the treatment of the chronic ailment rheumatoid arthritis (RA). Unlike the competing products the 'super' Aspirin, Vioxx, did not cause stomach problems as other NSAIDs did, but it began to cause serious heart problems and killed many patients before it was withdrawn from the market. Ironically, this event unfolded around the time when Bayer was getting ready to celebrate Aspirin's 100th year of success in the market (BAYER, 1997).

Emanating from the industry's prevalent business model, the social, economic, and legal issues that dominate the current healthcare debate have historical roots. Recently documented issues such as collusion among a small number of producers within an oligopolistic market, soaring drug prices, and failure to comply with ethical and legal guidelines in the development and marketing of medicinal products have also been observed at other points during the evolution of the modern pharmaceutical industry in the US. Vioxx offers one of the most recent and notable examples of how can a pharmaceutical company may disregard ethical and legal obligations to cut corners and launch an unsafe product with the aim of overcoming a long-lasting productivity problem. Chapter 5 will explain the rise and demise of the world's most, and perhaps sole, respected pharmaceutical company, Merck & Co.

In his Theory of Innovative Enterprise (TIE), Lazonick (2013b) postulates a reciprocal relationship between the *social conditions of innovative enterprise* (SCIE)—*strategic control, organizational integration, and financial commitment*—and economic institutions—*governance, employment, and investment institutions*—that “enable” or “proscribe” those conditions—in any given economy. According to Lazonick (2013b), *governance institutions* regulate the process of the resource-value cycle, which comprises the development, utilization, and distribution of productive resources within an economic unit (i.e., an enterprise, nation, or industrial sector.) *Employment institutions* mediate the ways in which workers, as productive actors within the economic unit, develop skills and capabilities as well as collectively engage in production activities to generate and enhance productivity. Moreover, economic institutions also determine the ways in which the economic unit ensures the future supply of productive actors throughout the resource-value cycle. *Investment institutions* determine the supply of capital that enables the resource-value cycle to complete its process.

Depending on this relationship, economic performances across business enterprises or industrial sectors vary among nations and over time (Lazonick, 2013b). These economic institutions often enable or proscribe strategic, organizational, and financial activities in which a business enterprise engages, and influence the social conditions of innovation within the enterprise that determine economic performance. SCIE can alter the dynamics of

those economic institutions over time and determine the direction and the rate of change in the economic performance of business enterprises and industrial sectors.

This chapter explores how, as US business enterprises transitioned from the Old Economic Business Model (OEBM) to the New Economic Business Model (NEBM), changes in economic institutions that "enable" or "proscribe" the *social conditions of innovative enterprise*, and how they resulted in the current economic performance of the US biopharmaceutical industry. In the context of the US biopharmaceutical industry, changes in governance, employment, and finance institutions are evaluated in the following sections. Changes in the regulatory environment are examined as a subset of changes in governance institutions, after which changes in the employment and investment institutions are examined separately.

3.1 Governance institutions

In the aftermath of the Vioxx scandal, for instance, the public in general came to know about a major flaw in recent amendments to two major drug regulations, the *Prescription Drug Use Fee Act* (PDUFA) of 1992 and the *US Food and Drug Administration (FDA) Modernization Act*, the latter adopted in 1997, two years before Vioxx was approved for market. As will be discussed below, since the PDUFA provided that fees collected from the applicants, it can reasonably assumed that big pharma's influence over the FDA increased following its enactment. In fact, these laws were passed in the aftermath of the thalidomide tragedy of the early 1960s, which had caused hundreds of babies to be born with defects in Europe; their goal was to prevent a major crisis from taking place in the US, but they failed to achieve it in the case of Vioxx.

Lazonick (2013b) argues that governance, employment, and finance are three pertinent economic institutions that come into play with business enterprises –through “enabling or “proscribing” social condition of innovation within these enterprises-- to support the productive transformation process and mediate the economic performance of industrial sectors. The three institutions may vary across nations given that the social conditions of innovative enterprise within a nation may transform those economic institutions via their business activities (strategy, organization, and finance) that also vary across nations. A new form of corporate-governance ideology rooted in the market-based economic theory most commonly referred to as “maximizing shareholder value” (MSV) began to emerge in the 1980s and transformed a distinctly “managerial capitalism” into “shareholder capitalism.”

As the US companies fast adopted the NEBM, as it emanated from the MSV ideology, a distinctly unique US-style capitalism emerged in the last decades of the 20th century that viewed markets as having replaced industrial organizations as the main distributor of an economy’s productive resources among the competing actors. MSV perceives shareholders as efficient agents who perform the function of monitoring the management performance on the utilization of scarce resources within public companies to ensure market efficiency.

MSV also postulates that when the value-creation process is completed within a business enterprise its managers are obliged to return the excess value to markets via shareholders.

According to Michael Jensen, MSV ideology has been spread through investor activism, which has roots early in the 20th century. Jensen (1989) argues that iconic figures in the world of finance -- such as John Pierpont Morgan, who founded one of the most influential banks in the world, -- had engaged in investor activism as they closely involved themselves in the strategy and governance of business enterprises to ensure safe and profitable returns on their investments. Jensen and other agency theorists attribute the rapid expansion of the US economy in the late 19th and early 20th century to what they see as an allocative efficiency of the stock markets fostered by a J.P. Morgan-style investor activism that induced efficiency in managerial organizations.

Lazonick (2015), although agreeing on the existence of a causal relationship between Wall Street financiers and managerial organizations, disputes the direction of the causality. J.P. Morgan and other leading Wall Street financiers heavily involved in the financing of managerial business enterprises pursued profitability and growth for the long term. It was the productivity boost that US managerial corporations achieved at the turn of the century from whose growth Wall Street profited, first by financing mergers in the capital-intensive industries to build economies of scale, and later by transforming traditional owner-operated business organizations with “superior managerial capabilities” into public corporations whose stocks were traded among a large number of shareholders on the stock market (Chandler, 2005; Lazonick, 2007).

Such events at the turn of the 20th century allowed the separation of control from ownership, which came to be distributed among public investors as the stock market -- namely, the New York Stock Exchange (NYSE) -- grew rapidly with the initial public offerings (IPOs) of these new managerial organization. These IPOs transformed some traditional entrepreneurial establishments into public companies that later developed the necessary managerial capabilities that enabled them to excel in enhancing productivity amid rapid expansion of operations and to contribute to industrial growth. It is clear that the development of the stock market was the byproduct of rapid economic growth; the case for growth’s being a result of stock market activity cannot be confirmed by the historical evidence (Chandler, 2005; Lazonick, 2007; O’Sullivan, 2000).

Jensen (1989) also argues that Morgan-style investor activism dissipated due to certain policy events that occurred during the period leading up to the start of the Great Depression in 1929. Jensen argues not only that top managers’ dominance of corporate strategy and governance, which was reinforced as policy measures of the post-depression era restricted activist investors’ involvement with public corporations, increased the challenge of monitoring corporate activities, but also that investors’ limited involvement with corporate strategy and governance increased “the cost of being an active investor” overall (Jensen, 1989, p. 8).

While the Glass-Steagall Banking Act of 1933 and The Banking Act of 1935 divorced the investment and commercial banking activities of large banking institutions, limiting their activities to issuing loans as debtors as opposed to acquiring corporate stocks as equity investors, while cutting investment banks' direct access to federal deposits. The Securities Act of 1933 changed the nature of public corporations' disclosures to investors, while the Securities Exchange Act 1934 brought more regulation to the exchange of securities. The Bankruptcy Act of 1938, known also as the "Chandler Act," made it difficult for shareholders to influence the post-bankruptcy reorganization process and empowered debtors to access the bankruptcy system.

The new regulation introduced with the Investment Company Act of 1940 paved the way for mutual funds to emerge as institutional investors. Despite the capital invested in the growth of public corporations, Jensen (1989) argues the involvement of institutional investors had become less than adequate, if any, with corporate strategy and governance. Chandler (1977) explained the transformation of the US traditional business enterprise into a modern, multi-unit business whose growth relied on the efficient functioning of managerial hierarchy within it. This transition gave rise to the managerial capitalism at a time when active investors were left without the power to monitor public corporations (Jensen, 1989.)

Effective governance in the modern managerial corporations entailed investing in productive resources and transforming them into innovative product and services. Retained earnings supplied the capital for corporations making the productive investments and sustaining growth (Lazonick, 2007; Lazonick & O'Sullivan, 2002). In this modern corporation, economic growth had ultimately become a self-propelling process of productive transformation through retaining and reinvesting corporate earnings (Chandler, 1977; Lazonick, 2009). This corporate-governance ideology was enhanced in the two decades following the Second World War as the multi-unit, modern US corporations decided (i) to take on the challenge the conquer international markets and (ii) to take advantage of looming growth in the war-ridden European and Asian markets, which were recovering quickly in the post-war period, in order to further capitalize on wartime technological advancements. When growth opportunities overseas leveled off as competition rose in international markets in the 1960s, the large US managerial corporations decided to enhance their economies of scope by diversifying the markets in which they operated. Having failed to attain the growth that had been anticipated, many public corporations that had expanded during conglomerate movement began, in the 1970s and 1980s, to incur the wrath of activist investors -- namely, corporate raiders -- and to experience the perils of their unruly intervention in the stock market.

Jensen (1989) argues that this activism, even in its most brutal forms, such as the hostile takeover, is justifiable as the result of action by a large number of shareholders disenfranchised by corporate executives. During what Jensen calls the "eclipse of public corporation" in the 1980s, corporate executives were forced to ally themselves with rising

shareholder activism because of the leveraged-buyout (LBO) movement driven by corporate raiders. In fact, the alliance between executives and raiders quickly became institutionalized as a new form of incentive-driven corporate-governance ideology that, in Jensen's view, rescued waste-ridden public corporations from the reign of inefficient management to enhance market efficiency and economic growth via maximizing shareholder value (Jensen, 2000).

Lazonick (2011) disputes in a starkly contrasting MSV that Jensen and other agency theorists have been touting for decades as the most efficient form of corporate governance regime that can enable greater economic growth while generating superior "returns" for shareholders. First, according to Lazonick, a corporate-governance strategy that excels in delivering shareholder value often entails downsizing productive assets, in the name of reducing wasteful investments and enhancing capital efficiency, in order to increase the amount of "free cash" available for distribution to shareholders.

This *downsize-and-distribute* mode of resource-allocation appears to be the main enabler of what Lazonick (2009) calls the "New Economy Business Model" (NEBM), which has gained traction among the fledgling computer, electronics, and biotechnology companies clustered in and around Silicon Valley. MSV ideology has grown in prominence in the corporate-governance practice as the high-tech economy has expanded in the US, to the extent that the New Economy companies have been able to challenge industrial incumbents which, operating under the Old Economy Business Model (OEBM), employed a distinctly different corporate-governance regime based upon a *retain-and-reinvest* mode of resource allocation.

This growth in prominence of the *downsize-and-distribute* mode of resource-allocation among US corporations since the 1980s stands in sharp contrast to the *retain-and-reinvest* mode of resource-allocation that had held sway in managerial thought as US corporations gained dominance in global markets and had driven industrial growth in the US. MSV has profoundly changed executive incentives: It has led to a shareholder bias on the part of US corporate executives that has imbued them with an ever more constricted, and ultimately myopic, management view.

This view is rooted in a performance-based executive-reward system that is disproportionately linked to the market performance of corporate stocks. Given this incentive scheme, Lazonick argues, top business executives with greater shareholder bias often show less willingness to engage in "value creation" through innovation because they are more focused on pursuing "value extraction" through artificially bolstering corporate financial performance. This thesis argues managerial view that results from the *downsize-and-distribute* mode is the culprit behind the innovation crisis of the US pharmaceutical companies. The following section examines changes in the US regulatory environment in relation to changes in US governance institutions.

3.2 Employment institutions

Since the NIH budget is the major funding source of biomedical research in the US, if not globally in the world, its doubling between 1998 and 2003 was an important policy milestone. Initially, the ambitious idea of doubling NIH's appropriation within five years was conceived as a way of offsetting the growing cost of medical research and supporting efforts to build a new science and technology infrastructure that would enable the research community to advance scientifically and technologically in a new era of medical research.

The early years of the doubling period coincided with significant growth in other high-tech areas, such as information and communication technology, and with major scientific breakthroughs in the medical field (human DNA mapping, stem-cell therapy, etc.). As expectations grew that scientific achievements would yield significant results, universities attracted more funding from non-government sources. This support, in combination with the doubling effort, created a significant incentive for the research community to rapidly expand the physical infrastructure that would support the new age of research (Teitelbaum, 2014; Stephan, 2012).

This physical expansion was achieved through leveraging the steady flow of government money, which not only covered the direct cost of doing medical research but also allowed research institutions to include facility use and other costs associated with the improvement of certain facilities and equipment, such as debt service, in the project budget as permitted under OMB Circular A-21 budget guidelines⁷. The growth in facilities increased the pressure to fill the new spaces being created and to recover their cost rapidly by maximal utilization of space through augmented research and training activities (Alberts, 2010).

Ambiguity around cost-accounting mandates and the failure of attempts to regulate accounting practices caused an expansion of indirect costs associated with NIH-funded medical research that ultimately contributed to the build-up of facility and administrative staff within academic organizations (Teitelbaum, 2014). The increase in research activities also increased the demand for science "laborers," particularly postdoctoral researchers and research assistants, who were often engaged on a contract basis and so lacked employment security (Teitelbaum, 2008). This supply surge for biomedical scientists, which some contented was driven by periodic surges in government funding, as experienced in other high-tech fields, rather than by changing demand factors in the labor market (Nature, 2011; Taylor, 2011). For instance, a policy effort supported by the biomedical research community in the late 1990s was geared toward increasing the number of physician-scientist and clinical researchers who play critical roles at the clinical phase of the drug development process (Ley & Rosenberg, 2005).

⁷ See OMB A-21 Circular in Cost Principles for Educational Institutions available at http://www.whitehouse.gov/omb/circulars_a021_2004

The Public Health Improvement Act of 2000, popularly known as The Clinical Research Enhancement Act, included various provisions to increase NIH involvement in clinical research such as launching the Extramural Clinical Research Loan Repayment Program to repay the loans that scientists who engage in clinical research previously accrued through their undergraduate and graduate education (GAO, 2002). The basis for this new policy was concern about the declining amount of translational research pushing scientific progress achieved in laboratories into clinical research. Academic experts argued that the decline in clinical progress was partially caused by a slowing of funding support for clinical research and a decrease in the supply of clinical scientists who were key to translating scientific achievements in laboratories into viable drug candidates. NIH Director Varmus responded to this concern in 1995 by requesting that the Director's Panel on Clinical Research (CRV) evaluate the NIH programs and provide policy recommendations to address the issue (Varmus, 2009).

The panel, made up of research scientists both from academia and industry, indicated that external funding for NIH's clinical research was adequate but should be closely monitored going forward. The panel went further to "strongly endorse" the lobbying effort to increase the overall NIH budget, as doing so would increase the funding for clinical research given the growing opportunities in medical research (Smaglik, 1997; Check, 2002; Relman & Angell, 2002). The panel also made policy recommendations for addressing the waning pipeline of medical scientists that included increasing funding for training programs for medical scientists and enacting a loan repayment program to support the education of future medical scientists.

The biomedical lobby played a crucial role in the passage of the American Competitiveness in the 21st Century Act of 2000, which ultimately paid off in the exemption of H1-B visa holders working at non-profits and universities from being counted toward the annual limit on the number of H-1B visas the government can issue – meaning that these institutions could employ this category of non-immigrant visa holders virtually without restriction. This apparent victory for industry was in reality a compromise, as changes in the legislation affecting visa approval and school admission standards could have been expected to reduce the number of foreign students available to the universities based in the US. Along with changes in the rules concerning the length of Optional Practical Training that essentially allowed longer stays for foreign students to complete the full period of time they were allowed under H-1B rules as well as the removal of the cap on H-1B visas for universities was expected to increase the number of foreign candidates pursuing studies in STEM fields who might join the US STEM workforce if subject to fewer restrictions thanks to recent changes in immigration legislations.

Growth in the supply of foreign STEM workers would continue to suppress the wages of those employed in STEM fields in the US, which would potentially continue to divert the pipeline of native workers to more lucrative, non-STEM fields such as finance and banking. (Matloff, 2013). Despite the growing basis for research funding, the scientific

productivity of federally funded research exhibited a slowing trend similar to that seen in the business sector in the post-doubling period. Frederic Sachs' (2007) study on the scientific outcome of the doubling the NIH budget, which used publications as one measure of productivity, indicated a parallel trend in the number of publications. As the scale of the NIH budget grew, so did the range of the research it supported.

Not only is NIH responsible for supporting basic science, it is also expected to play a varied role in medical research, from encouraging entrepreneurship through the SBIR program and conducting clinical trials to training physician-scientists and supporting the commercialization of medical technology. And, most important, the agency is responsible for the education and training of a growing pool of scientists who have greatly suffered from the uncertainty that has reigned in the aftermath of the NIH budget increase.⁸ From 1938 through 2016, the US National Institutes of Health expended slightly over \$1 trillion, measured in 2016 dollars, funding life sciences research (Figure 8). Its 2016 budget was \$32.2 billion (NIH). The US system of higher education produces a world-leading STEM labor force that is available to US pharma and pharmaceutical firms. More generally, US governments at the national, state, and local levels provide financial subsidies and tax breaks to firms in the biopharmaceutical industry.

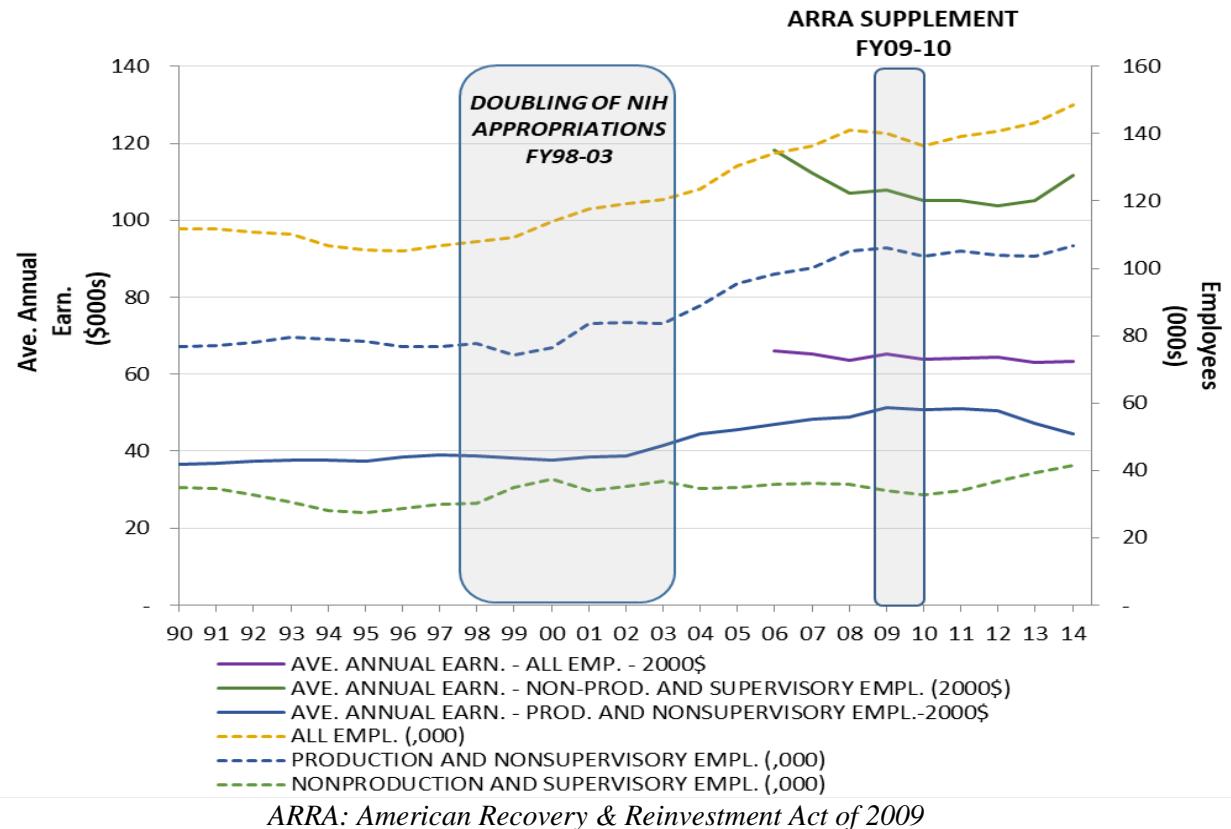
Given that organizational flexibility is one of the core competencies of firms in the field of pharmaceuticals, the ability to quickly up- or downsize operations to take on the market makes career prospects in the STEM occupations offered by biotech companies highly questionable. Since the STEM workforce makes up a significant portion of PLIPOs' labor cost, acquisitions by big pharma, major setbacks in clinical trials, or attempts to avert speculative attacks in the stock market are often followed by major layoffs that particularly affect the R&D workforce.

The growing trend in "hire and fire" markets for STEM workers pose a threat against the sustainability of STEM jobs and organizational capabilities that depend heavily on the productivity of STEM workers. For this reason, the impact of pharmaceutical's changing business model on the career prospects of STEM workers deserves closer attention and further analysis. As the cost of acquisitions grew big pharma firms were forced to pay a premium for those companies with potential candidates for blockbuster status. One way to offset this cash drain is through cutting unproductive R&D units, something often accomplished by laying off R&D workers, as has often been documented in the media in

⁸ According to National Institutes of Health (NIH) Biomedical Research Workforce Working Group Report published in 2012 tenure-track faculty among biomedical scientist has declined from 34 percent in 1993 to 26 percent in 2012; starting salary for biomedical assistant professor was \$68,000 in 2011 when compared to \$79,000 for clinical and health fields and over \$100,000 for economist; NIH research project grant award success rate went from 32 percent during the time doubling down to 17 percent in 2013; close to 18 percent of all principle investigators (PIs) who were awarded with R01 grants in 1980 were age 36 and the figure for this age group went down to 3 percent in 2010.

the aftermath of major pharmaceutical mergers and acquisitions (M&As), which ultimately became a norm for carving quick cash for M&As (Herper, 2011).

Figure 8: Employment and Average Annual Earnings in NAICS 54171 Biotechnology Research (2000\$)



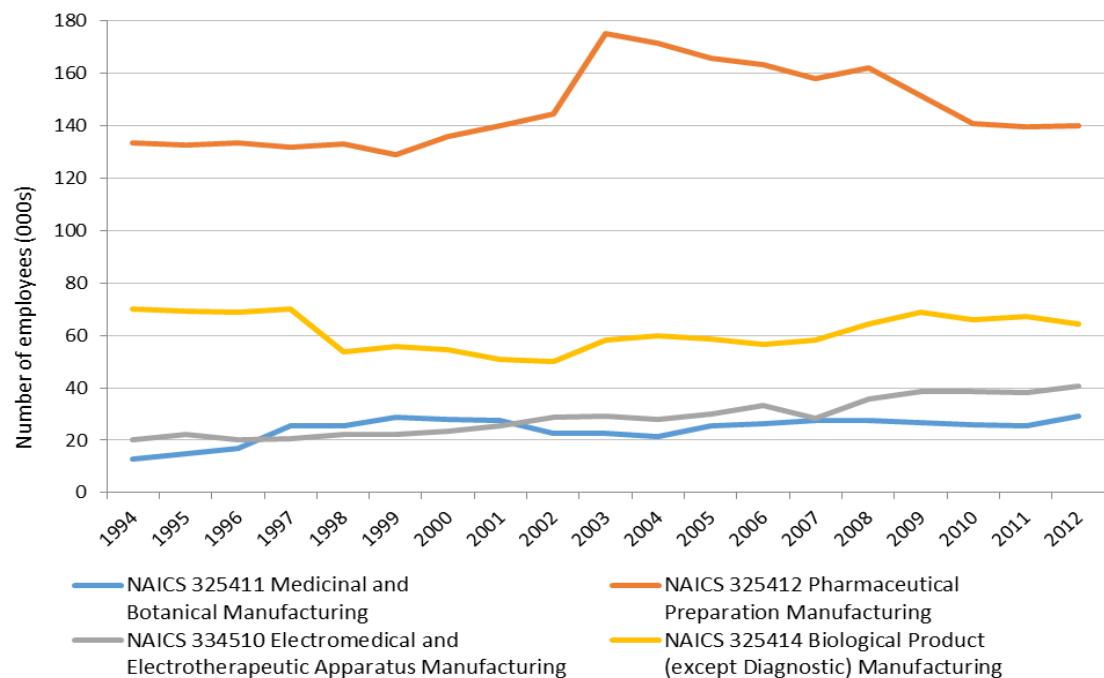
Source: Own illustration based on data from Bureau of Labor Statistics

How long excess supply of pharmaceutical scientists can be absorbed by the companies is highly uncertain given the industry's gloomy innovation outlook. As illustrated in Figure 9, which analyzes Current Employment Statistics (CES) from monthly establishment surveys between 1990 and 2014, there has been no significant employment expansion in biotechnology research except during the period between 1998 and 2003, when NIH increased its funding for national medical innovation efforts. And even if employment increased significantly during the doubling of NIH funding, the growth in annual earnings within the NAICS 54171 biotechnology research subcategory was slow, particularly among production and nonsupervisory employees (P&NS).

For the period between 1998 and 2014, the data reveal a 33 percent increase in all employees, a 39 percent increase in P&NS, and a 25 percent increase in nonproduction and supervisory employees (NP&S); these increases were observed mainly between 1998 and 2008, with employment remaining flat since then. During the period between 1990 and 2010, annual employment among NP&S remained in the range of 27,000-37,000 employees, with occasional declines in the mid-'90s. Real wages increased by 22 percent for P&NS in the period 1998-2013 but peaked in 2009, when they were 33 percent above

real wages in 1998. Although NP&S made up only 27 percent of all employees on average, their earnings were considerably above the industry average.

Figure 9: Employment in Major Life Sciences Manufacturing Industries



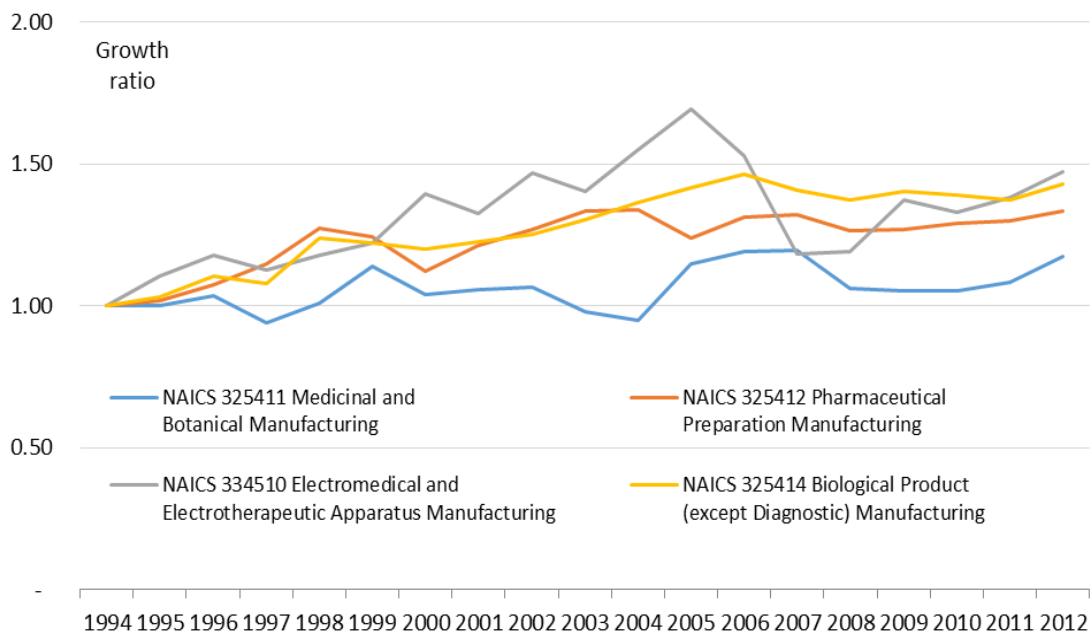
Source: Own illustration based on data from Bureau of Labor Statistics

Aggregate annual payrolls for NP&S made up almost 50 percent of the aggregate annual payrolls for all employees, and the real wages of NP&S were almost double those of P&NS in the same subcategory for the years earnings data was available between 2006 and 2014.

The earnings gap separating NP&S and P&NS has been increasing in recent years. Although these data address the quantity of the jobs in biotechnology research, they address neither the quality of those jobs, which are scarce, nor the career prospects attached to jobs offered by organizations in the life sciences fields. As further discussed in the following section, this concern can be addressed through company-level studies that aim to collect organizational data through surveying companies' HR and R&D managers, and the STEM workers employed.

Employment levels in major life sciences manufacturing industries reveal similar trends to that in the NAICS 54171 biotechnology research sub-industry category. As illustrated in Figure 10, NAICS 325411 medicinal and botanical manufacturing (MBM) and NAICS 334510 electrometrical and electrotherapeutic apparatus manufacturing (EEAM) experienced employment growth of 130 percent and 100 percent, respectively, in the period 1994-2012, during which employment in NAICS 325412 pharmaceutical preparation manufacturing (PPM) increased only 5 percent, and employment in NAICS 325414 biological product manufacturing (BPM) declined by 8 percent.

Figure 10: Wage Growth Index in Major Life Sciences Manufacturing Industries, 1994-2012



Source: Own illustration based on data from Bureau of Labor Statistics

Despite the 130 percent employment increase in MBM between 1994 and 2012, the growth in real wages was only 17 percent in this category in the same period. EEAM experienced a 47 percent increase in real wages as employment doubled. PPM showed the least employment growth but experienced a 34 percent increase in real wages, while the increase in real wages in the BMP category was 43 percent. Figure 11 also indicates that greater wage fluctuations were observed in the MBM and EEAM categories, which also registered the largest growth in employment. In 2007, the peak year of real wages, annual average wages in the BMP category were up by 20 percent and in 1997 went 6 percent below the level of 1994, the series start date. Real wages were up by 69 percent in EEAM's peak year of 2005 but then began a decline that lasted until 2009.

3.3 Investment institutions

Special forms of financial intermediaries exist to fund the entrepreneurial activities of high-technology firms. These specialized financiers -- namely, business angels, venture capitalists (VCs), and specialty investment funds such as growth capital, mezzanine, and distress -- emerged in the US during the computer and information technology (ICT) revolution of the 1970s for the particular purpose of addressing the capital needs of high-technology ventures. VCs were integral to the growth of many major ICT firms, such as Apple Inc., CISCO, and Google, and have played an important role in the development of this industry both nationally and globally. Having honed their investment skills on ICT firms, VCs were quick to recognize the market potential that could be captured through the

newly emerging biotechnology firms and immediately extended their investment horizon to BP ventures in the 1970s and 1980s

Lazonick's study highlights the institutional reform efforts of the 1970s, which began with the launch of the National Association of Securities Dealers Automated Quotations (NASDAQ) in 1971. With the establishment of NASDAQ, a major obstacle to accessing the public market was removed for entrepreneurs and VCs. The Securities and Exchange Commission's (SEC) decision in 1975 to bar exchanges from charging a fixed fee on stock trades, another important reform, was effective in reducing the cost of stock transactions. In another major reform actively supported by the industry, the tax rate on capital gains was reduced to 20 percent, initially, from 40 percent in 1978, and eventually, from 28 percent in 1981 (Lazonick, 2009; Gompers and Lerner, 1999). An important milestone in the history of the venture capital industry was the 1979 amendment to the Employee Retirement Income Security Act (ERISA) Act of 1974. The VC industry experienced a significant influx of capital after the change in the ERISA "prudent man" rule that allowed pension funds to invest in VC funds (Gompers, 1994; Kotum and Lerner, 2000; Lazonick, 2009).

As discussed above, the reform efforts in the 1970s were critical in establishing a new institutional environment that was ultimately geared toward encouraging and fostering entrepreneurship and innovation. Increasing entrepreneurial efforts resulted in a rapid economic expansion in the late 1980s and throughout the 1990s. This entrepreneurship-driven growth was path-breaking in that it instigated the transformation of "Old Economy" businesses, which embraced the norms of the rising "New Economy" era. Lazonick and O'Sullivan (2004) argue that in this New Economy era, the function of the stock market has evolved beyond merely providing a place to exchange stock and now performs five distinct roles: creation, control, combination, compensation, and cash. The control function refers to the stock market's ability to alter the capital structure of public companies and to influence the exercise of strategic control over allocating resources as the ownership of corporate assets changes hands in the stock exchange.

The combination function involves that the stock market facilitates corporate merger and acquisition (M&A) activities by converting corporate stock into exchange currency so that such transactions can take place. The compensation function involves that, as an exchange currency, corporate stock in more liquid forms enables corporations to recruit and retain highly skilled and productive employees while incentivizing value-creation efforts among managers. As to the creation function, Lazonick and O'Sullivan (2004) argues a strong correlation between entrepreneurship and the stock market in R&D-intensive industries, in which entrepreneurship has been promoted through the establishment of a well-functioning stock market.

Without pointing to the stock market specifically, Lerner (2010) describes certain key aspects of the creation function of the financial markets to foster innovation through

entrepreneurship. Financial instability, experienced during a downturn in the market cycle, often hampers innovation, as the availability of funding to sustain entrepreneurial activities declines. Furthermore, Lerner (2012) argues, accessing capital to sustain entrepreneurial efforts is a challenge even during an upturn in the market cycle, given that only few targeted industries enjoy generous funding from public and private markets. Therefore, entrepreneurship and innovation appear to be highly susceptible to the cyclical changes in financial markets on which entrepreneurial finance in high-technology ventures depends.

Aside from the creation function, Chemmanur and Fulghieri (2013) argue, the source of finance matters for maintaining the integrity of organizational learning and innovation efforts for two particular reasons. First, the extent and nature of innovative projects undertaken by a firm can be affected by ways of funding innovation because, (i) the availability of funding at various points in the firm's life, and (ii) the cost of capital incurred by the firm are determined by the type of financing event and the source of capital. Second, certain provisions included in the contract with the funder may undermine innovation by diminishing the effects of incentives for employees who participate in the innovative process or the managers who supervise them.

3.3.1 The rise of product-less IPOs (PLIPOS) as New Economy pharmaceutical businesses

As from the 1980s this remarkable national innovation system was being put in place, the largest pharma companies reaped the gains from past innovation, augmented by price-gouging. In 2015 the US prescription drug market amounted to \$324.5 billion, representing over 10 percent of national health expenditures (Centers for Medicare & Medicaid Services [CMS], 2015), and accounting for nearly half of the world's \$742 billion spent on prescription drug sales in that year. Based on the aggregate spending figures for the decade 2007-2016, 17 percent of total US prescription drug expenditures were paid out of pocket by US patients, with health insurance programs funding the remainder (CMS, 2015). During this period, 44 percent of all prescription drugs sold were accessed through a private health insurance program, and 38 percent through a government healthcare program coordinated by the U.S. Department of Health and Human Services (Medicare, Medicaid), Department of Defense, and Department of Veteran Affairs as well as other subsidized federal and state insurance programs.

The lion's share of the industry's profits has gone to the largest companies. In 2015, the top 10 global pharmaceutical companies accounted for slightly over 50 percent of the prescription drug market in the United States. As US pharmaceutical companies secured more advantages that could increase their profits—ostensibly for the sake of faster, better, and cheaper research into drug development—many of the leading companies also moved sharply from innovation to financialization, as explained in detail in Chapter 2. The US pharmaceutical business model became focused on jacking up drug prices for the sake of jacking up stock prices rather than taking advantage of the manifold benefits for drug

innovation that, with the encouragement of PhRMA's lobbying efforts, the US institutional environment bestowed upon the drug manufacturers.

Over the same decades, however, thousands of new drug companies emerged in the United States, using the new technologies of the biotech revolution. Backing these new companies were venture capital firms, themselves representing a new industry devoted to new-firm creation and growth to which the microelectronics revolution had given birth (Lazonick, 2009, c. 2). The first wave of successful biopharmaceutical companies, such as Genentech, Amgen, Biogen, and Genzyme, in the early 1980s were able to pick "the low-hanging fruit" of drug discoveries made possible by decades of prior NIH funding (Lazonick & Tulum, 2011). With the Bayh-Dole Act, the Stevenson-Wydler Act, the Orphan Drug Act, and the Diamond v. Chakrabarty ruling at their disposal, venture capitalists teamed up with academic scientists to plumb the fledgling new fields in biochemistry such as molecular biology and genetic engineering for potential commercial opportunities. Major US pharmaceutical companies in the United States were reluctant to invest in the new organizational learning that the biotechnology revolution required.

The first-generation of biopharmaceutical companies had already harvested most of the low-hanging-fruit by the mid-1980s, so that the second-generation of biopharmaceutical companies could only tackle more challenging diseases such as cancer (Alafi, 2013). The greater complexity of the learning processes required increased the length of the drug development process from discovery to market. The "New Economy" biotech companies had to attract, retain, and reward teams of scientists and engineers who, in the 1980s, could find secure career employment in the research labs of not only government agencies and civil-society organizations but also "Old Economy" pharmaceutical companies (Lazonick et al., 2014).

As startups, the New Economy companies could not realistically hold out the offer of a career with one company that, in the 1980s was still the norm in the research labs of the Old Economy companies. Starting with the initial public offering (IPO) of Genentech in 1980, a company that had been founded only four years previously, New Economy startups were able to attract venture capital by the prospect of a relatively quick IPO on the highly speculative NASDAQ stock exchange. So too, these New Economy startups used the offer of stock options to lure science, engineering, and management talent to work for them. The shares in these options could become very valuable if and when the New Economy company would do an IPO. And indeed, the experience of the 1980s and 1990s was that hundreds upon hundreds of young biopharmaceutical companies were able to go public on NASDAQ within a few years after founding, lacking a commercial product. Rather they functioned as research entities in search of an approved drug. We have dubbed these publicly-listed New Economy pharmaceutical companies "product-less initial public offerings" or PLIPOs (Lazonick & Tulum, 2011), by which we mean both private companies seeking a listing on NASDAQ even without a product and those that had already secured a listing, still without a product.

Established pharmaceutical companies have acquired many young biopharmaceutical firms, providing the young firm's shareholders with an alternative "exit strategy" prior to an IPO or, typically, a substantial premium over the price of a listed stock when acquired. From 1988 to 2000, Danzon, Epstein & Nicholson (2007) identified 2,808 M&A pharmaceutical and biotech deals, of which only 165 deals were considered to be "transforming mergers", defined as a deal size of either \$500 million or 20 percent or more of the company's stock changing ownership. Measured in 1999 dollars, the Danzon et al., study revealed that the total value of the 165 "transforming mergers" was \$514 billion, which was nearly 4.4 percent of the value of the M&A deals that had taken place during that period. They argue that looming patent expirations represented the primary motivation behind the large M&A deals. The study also shows that among these young companies, it was those that had achieved steady streams of product revenues that were more likely to be acquired.

In 2016, the US biotech industry (which is largely pharmaceuticals) generated \$112.2 billion revenues, with profit margins of 8.2 percent (Ernst & Young, 2017). There were 449 public biotech companies in 2016 (Ernst & Young, 2017). In an important study, Pisano (2006) argued that only a small number of biotech companies are in fact profitable and have products to generate a steady stream of revenues. The ability of PLIPOs to raise cash for operations on the speculative stock market sustains these companies—until the stock market crashes, as happened in 2001 and 2008 (Lazonick & Tulum, 2011). Ernst & Young surveys have shown that of all small and mid-size human therapeutics companies in operation, the proportion that had sufficient cash on hand to keep them solvent for two years or less was 54 percent in 1995, 42 percent in 2005, and 45 percent in 2015. In 2016, the proportion of companies with less than two years of cash reserves had risen to 55 percent. Funds secured through establishing R&D partnerships with major US pharmaceutical companies often provide the smaller companies with financial stability, although at the cost of loss of strategic control over some of the company's marketing rights. For its part, Big Pharma has become dependent on PLIPOs for discovering and developing innovative therapies, while PLIPOs depend on Big Pharma to commercialize their products (Kneller, 2005; Kneller, 2010 Schuhmacher et al., 2016).

Relying on the combination of NIH funding and speculative PLIPOs for drug discovery and development, the established pharmaceutical companies have let their own in-house R&D capabilities decline (Higgins & Rodriguez, 2006; Hirschler & Kelland, 2010; LaMattina 2011; Mirowski, 2011, c. 5). Indeed, Big Pharma has become even bigger as established companies such as Merck and Pfizer have acquired other established companies to gain access to proven blockbusters with patent life remaining. Then, in the name of MSV, the acquirer pumps out cash to shareholders from the merged enterprise rather than building in-house capabilities for drug discovery (Montalban & Sakinç, 2013; Lazonick & Tulum, 2015; Lazonick et al., 2017). Indeed, since the late 1990s, Big Pharma's attempts to engage in in-house learning have been undermined by the exit of technical and managerial personnel to try their luck in the PLIPO segment of the industry,

further bolstering those within Big Pharma who argue that its own success depends on boosting stock prices as a way of using stock options to compete in the market for talent.

3.3.2 Big pharma's financialized "blockbuster" model

High unregulated drug prices support this process of industrial concentration among established drug companies. Of particular importance in these M&A deals is control over blockbuster drugs—those with at least \$1 billion in sales in one year—that have a significant number of years of patent life left (Montalban & Sakinç, 2013). The acquiring companies then use the increased profits from the blockbusters that they now control to boost stock prices, with the degradation of Big Pharma organizational learning as the result. Yet, the industry's trade association PhRMA argues that high drug prices fund the growth of the industry's R&D spending, thus benefiting the public. For example, in its 2016 annual meeting, PhRMA president Stephen Ubl argued that prescription drugs are "a relatively small and stable share of overall health care spending" that improves the quality of life in a cost-effective way (Norman & Karlin-Smith, 2016). PhRMA has consistently used this argument to counter public discussion over the rising cost of healthcare that might result in new legislative attempts to regulate drug prices.

Besides enormous government funding of drug development, the US government is a major procurer of pharmaceutical drugs. The prescription drugs that the US government procures through various different health insurance programs such as Medicare Part D make up a significant portion of product revenues that major drug companies generate. In some cases, the gains of a pharmaceutical company from price-gouging the public is extreme. One such case, which Congress has investigated, is Gilead Sciences (Wyden, Grassley, & Hatch, 2015, p. 117; Roy & King, 2016; Lazonick et al., 2017).

As Lazonick et al. (2017) revealed, Gilead executives have topped the list of highest-paid executives in the US biopharmaceutical industry. Harvoni and Sovaldi, two top selling Gilead products, ranked 1st and 15th in the list of top biopharmaceutical products that the US government purchased through Medicare Part D program in 2015. Medicare paid \$8.4 billion (before rebates, the amount of which is unknown) for the two products, which accounted for nearly 40 percent of the \$21.2 billion in revenues Gilead generated from these two drugs in the United States and 26 percent of the company's \$32.6 billion in global net sales in 2015. Analysis based on the 2015 Medicare drug spending data reveals that 21 prescription drugs, almost half of them belonging to European drug companies and each costing the US government over one billion dollars, generated a total of \$42.8 billion in revenues for 15 different drug companies. The amount spent on those 21 products in fact accounted for nearly 31 percent of \$137.4 billion that the US government spent through the Medicare Part D program.

National health expenditures for prescription drugs have been on the rise in the past decade despite the fact that the US Congress has passed two major landmark policies to tackle the

national crisis of soaring healthcare costs. First, in 2009 it passed the Patient Protection and Affordable Care Act, which enabled many uninsured citizens to obtain affordable healthcare. Before the ACA, however, the Bush Administration enacted a new bill in 2003 to go into effect in 2006, the Medicare Prescription Drug, Improvement, and Modernization (MPDIM) Act that included a provision extending prescription drug benefit coverage to include outpatient drug costs for Medicare enrollees through Medicare Part D. Although the Act was celebrated among US retirees, with the new law the Department of Health and Human Services (HHS) signed away its rights to negotiate drug prices with the drug companies. Unlike the Department of Veteran Affairs (VA) that negotiates drug prices, the HHS is banned from negotiating drug prices, assigning the rights to business-sector insurers that implement the Medicare Part D program.

Ironically, many US pharmaceutical companies have been spending more on R&D as the companies have dismantled their early research programs, closed many R&D operations across the globe that came into their possession through M&A activities, and downsized R&D labor forces. Very little is known about the details of R&D data reported by the pharmaceutical companies, But one can safely deduce from all the financial information publically available that the money that the drug companies say that they spend on R&D may be used for other purposes, namely for marketing activities.

For instance, R&D expenditures include post-marketing, or Phase IV, clinical trials, which have become standard procedures in the past decade, extending the length of clinical studies to monitor drug safety and efficacy even after a product has gained regulatory market approval. According to PhRMA, in 2014 Phase IV trials represented 16.6 percent (\$8.8 billion) of total US pharmaceutical R&D, while “uncategorized” R&D expenditures were 8.9 percent (\$4.8 billion) (PhRMA 2016). After analyzing the results of these types of post-marketing studies in Germany, Spelsberg et al., (2017) revealed that none of the 558 trials analyzed, which were all sponsored by drug companies, reported a single adverse drug reaction. The authors of the German study could verify that less than one percent of the results from the trials were actually published in scientific journals. It has been argued that, in doing the Phase IV trials, a company seeks to compile clinical evidence to prove a drug’s superiority against its many “me-too” competitors (van Thiel & van Delden, 2008). That is, these so-called R&D expenditures are merely marketing research (Malerba & Vonortas, 2009, p. 89; see also Scherer, 2011; Gale, 2012).

It may be that US pharmaceutical companies deliberately inflate their R&D figures to justify the high prices that they charge for drugs in the United States. Perhaps these companies manipulate their R&D numbers to send a signal to the stock market that, even though they are distributing vast amounts of corporate profits to shareholders, they still have drugs in development in the pipeline that will generate the revenues to drive future profits. Inflated R&D figures may help start-ups justify large sums of funds raised through stock issues raised in initial public offerings and secondary issues. In fact, there is little public information on how US business corporations, including pharmaceutical companies,

compile their R&D figures (Hopkins & Lazonick, 2014). A growing body of empirical evidence, however, indicates that, despite all of the support for innovation by the US institutional environment, major US pharmaceutical companies have ceased to function as innovative enterprises (Lazonick & Tulum, 2011; Kessel, 2011; Hopkins et al., 2007; Montalban & Sakinc, 2013; Froud et al., 2006; Haslam et. al., 2013; Gleadle et al., 2014).

3.4 Creating the national innovation system

Several existing studies analyze the evolution of both science and technology and healthcare policy in great depth to explain how changes induced by policy measures have led to the establishment of a competitive, high-tech knowledge base in the US (Hopkins & Lazonick, 2014) and to the development of the modern pharmaceutical industry (Temin, 1979; Chandler, 2005; Cockburn & Henderson, 2001; Tobbell, 2011; Teitelbaum, 2014). Through historical analysis of certain drug policies in the US, Tobbell (2012) documents in great detail how the biopharmaceutical industry gained an extensive political power in the extent to which key players in the industry began influencing the national policy agenda and shaping the institutional environment in the US. Tobbell explains such a power has been gained as the US government began adopting major policy reforms in the cold war era to transform this industry into a global leader in innovative productivity. As they benefited extensively from certain policy reforms, which had laid the institutional foundation to turn the industrial environment in the US to become highly supportive of drug innovation, the biopharmaceutical industry and the medical research community in the US has colluded to gain political power and begun resisting against other policy reforms to constrain their financial gains.

This section focuses exclusively on examining the changes observed on major public policies that had enabled the US pharmaceutical companies to acquire and develop innovative skills and capabilities during the evolution of the market for prescription drugs in the US. The changes identified in this section are examined in relation to the innovation crisis of the large US pharmaceutical companies. Chapter two provides an extensive analysis of, and discussions on, such a crisis. The policies identified in this section are examined because they caused uncertainties, which Lazonick (2013b) identifies them as market, technology, and competitive, led to are the source of changes occur in certain industrial conditions that challenge the pharmaceutical companies in the process of transforming productive resources into innovative drugs. In the *social conditions of innovative enterprise* (SCIE) framework Lazonick (2013b) identifies such industrial conditions as “market”, “technological”, and “competitive” uncertainties. As top pharma executives invest in new products and processes to confront rising market, technological, and competitive uncertainties, “the innovating firm” begins to enhance its innovative capabilities, through engaging in collective and cumulative learning, so that the firm transforms such uncertainties into competitive advantage.

In an innovative enterprise, strategy, organization, and finance, the generic activities of any firm, confront the uncertain, collective, and cumulative characteristics of the innovation process (see Table 11 and Appendix 3). Uncertainty is inherent characteristics of the innovation process in the sense there is no guarantee that the innovation process will generate the higher-quality, lower-cost products that bring economic success, and hence strategy is needed to allocate resources to innovative investment projects (Lazonick, 2013b). At some point in time the policies examined in this section constituted the basis for an uncertainty (*technological, market or competitive*) that challenge top pharma executives when making allocative decisions to pursue an innovation strategy.

Depending on the intended outcome of each policy – that is, whether it was introduced to (a) affect the overall safety and efficacy of biopharmaceutical products being pursued by drug companies; (b) improve existing national drug R&D capabilities; or (c) create and maintain a profitable market – an innovative strategy may face an uncertainty, --that is, whether (a) the firm possess the necessary capabilities to attain effective drug development processes and innovative therapies through implementing an innovation strategy (*technological uncertainty*); (b) a profitable market still exists to generate the anticipated returns long after making the innovative investments (*market uncertainty*); and whether an competitors can outperform the firm in the race to bring more innovative therapies (higher-quality and lower-cost) to capture the targeted market.

Policies governing drug safety and efficacy

The government-led wartime research efforts led to the discovery in the United States and Europe of new drugs, among them penicillin and other “wonder drugs,” for treatment of many infectious diseases that were claiming millions of lives. However, the makers of those drugs knew very little about their pharmacodynamics (the ways in which a drug affects an organism) and pharmacokinetics (the ways in which a drug progresses through the organism from intake to discharge), and very few laws were in effect that allowed the US government to oversee the market for the purpose of assuring their safety.

In the years following the Great Depression and the Second World War, policy efforts were generally geared toward achieving a fast recovery from economic devastation, which had resulted in great social and economic disparity. As part of the New Deal program, a major policy reform was introduced by Franklin Delano Roosevelt (FDR) that authorized the government to regulate the market for ethical drugs for the first time. The “Elixir Tragedy” of 1937 had urged the legislative efforts to propose a major policy overhaul to address the public uproar concerned over the safety of marketed drug therapies. Without any investigation into its safety, a liquid form of sulfanilamide, ‘Elixir Sulfanilamide,’ had in 1937 been introduced nationwide for the treatment of streptococcal infections only to claim the lives of 100 people in more than fifteen states within weeks. Proposals for a major policy overhaul had already gotten under way during the height of the “Elixir

Tragedy” before the Federal Food, Drug and Cosmetic Act (FDCA) was signed into law by FDR in 1938.

Among many other important measures, the FDCA was particularly significant because it marked the first time a government agency was assigned to evaluate the safety of medicinal products prior to their launch onto the market. Adopted in 1951, a major amendment to the FDCA, ‘Durham-Humphrey Amendment’, required the dispensing of certain pharmaceutical products with the risk of drug addiction or harmful side effects through prescriptions obtained from physicians. The reforms of the 1960s and 1970s were intended to set an institutional framework for the ways in which medicinal products were developed and marketed. The intention of these policies was that pharmaceutical companies conduct their business in a more orderly way by following a set of safety standards. Some current pharmaceutical safety standards can be traced back to the regulations enacted by the US government in those decades.

Although the 1951 Amendment required that patients obtain prescriptions from medical doctors to access certain drugs, there were still no laws in effect that required pharmaceutical manufacturers to extensively assess and evaluate the safety of their products or to obtain approvals from FDA before bringing them to market. A widely prescribed drug used to treat sleeplessness among the insomnia patients in the post-war era, Thalidomide, had turned out to cause side-effects in the newborns of pregnant women who had taken it. The drug, launched initially in Germany and later in 46 other countries, was advertised as “completely safe” for everyone -- “even for pregnant women” -- upon the completion of the manufacturer’s toxicity and safety trials on animals, which had proven inconclusive for adverse effects (Fintel, Samaras & Carias, 2009). The birth of 161 children in Europe with serious birth defects in the form *phocomelia*, the shortening or absence of limbs in children, quickly alarmed the US authorities in 1961 and instigated a series of policy actions in the years that followed (*ibid*).

The refusal by an FDA inspector, Frances Kelsey, to grant approval for this drug may have prevented many children from being born with this birth defect, but, more important, her action also strengthened the hand of critics who were asking sufficient regulatory power for FDA to enable the agency to carefully assess the safety of new medications before their approval. Amid growing public concern over the safety of prescription drugs, in October 1962 John F. Kennedy signed an important legislative change into law, the Drug Efficacy (or Kefauver-Harris) Amendment to the Federal Food, Drug and Cosmetic Act of 1938.

This policy marked an important turning point in the history of the biopharmaceutical industry, as the amendment further heightened the regulatory power of FDA to oversee drug safety. The new FDA regulations required for the first time that a prescription drug maker provide a “proof-of-efficacy,” which is a report the FDA asks from drug manufacturers to submit along with other documents required for new drug application (NDA) seeking regulatory approval for marketing. Prior to attaining final market approval manufacturers in

such a report have to show the regulators that a sufficient amount of reliable medical evidence has been gathered on an NDA to prove that such a drug effectively delivers the intended health outcome. This new requirement commenced a new period in the evolution of the drug-development process, which now had to include extensive clinical trials on animal and human subjects. The law also required drug makers to be more transparent in advertising their products so that the user of prescription drugs would be adequately informed of their benefits and side-effect.

Several major changes subsequently occurred in the US policies governing the safety and efficacy of pharmaceutical products. A change in the FDA guidelines in 1987, for instance, permitted the “treatment use” of investigational new drugs (INDs) among people suffering from life-threatening conditions if and when there were “no alternatives while the data to support marketing [were] being collected” (FDA, n.d.). This need had emerged as the length of the FDA review process increased, with the industry intensifying its lobbying efforts to resolve the issue of heavy “regulations,” which it often held up as the major inhibitor of the pace of drug discovery and driver of the cost of drug development.

Growing industry lobbying of lawmakers on “regulations” led to the approval of the Prescription Drug User Fee Act in 1992. With the enactment of this legislation the Administration was authorized to collect fees from companies when they filed applications to clinically pursue INDs. Under the new law, pharmaceutical companies paid a fee upon gaining regulatory approval to begin clinical trials. After collecting these fees, the FDA could expand the size of staff dealing with the review of new drug applications at the Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER) by 60 percent.

In the same year the FDA also launched a new program called “accelerated approval,” which essential entails prioritizing the review process for a condition that the manufacturer can provide no “actual evidence of improved survival” with the use of the drug under accelerated approval. In order to benefit from the accelerate approval program the FDA allows the manufacturer to demonstrate an “encouraging effect” on the treatment of such a condition and “verify the actual clinical benefit” of the drug candidate (FDA, n.d.).⁹ In the 1990s there were more changes to be observed in the FDA’s regulatory guidelines concerning patient safety. The National Institutes of Health Revitalization Act of 1993 eliminated any restrictions in the FDA guidelines issued in 1977 and required the inclusion of women (of “childbearing potential”) and minorities in clinical trials. The same act

⁹ An example for such a condition would be elevated blood-cholesterol, and for such a drug candidate seeking accelerated approval would be a cholesterol-lowering medication. Although the clinical evidence links the elevated cholesterol in the bloodstream and increasing risk of heart disease such as heart attack – recorded as the leading cause of death in the US according to CDC (2016) -- the manufacturer of a cholesterol-lowering drug cannot prove that such a drug can prevent heart attacks and improve survival. The manufacturer however demonstrate encouraging effects, such as lowering the cholesterol level in the bloodstream, and verify the actual health benefit showing that managing blood-cholesterol can lead to healthy and well-functioning heart.

permitted research on human fetal tissue regardless of its source -- that is, whether or not it came from a voluntary abortion.

Another important policy change introduced with the Food and Drug Administration Modernization Act (FDAMA) of 1997, and its reauthorizations in 2002 and 2007 (Best Pharmaceuticals for Children Act), encouraged pharmaceutical companies to develop drug therapies for pediatric use by offering them six months' marketing exclusivity for any drug with a proven pediatric application. The Pediatric Research Equity Act of 2003 mandates that the drug companies produce clinical evidence to obtain this exclusivity, which would require a company to invest in clinical pediatric research in order to confirm the efficacy of the drug candidate.

Policies governing drug research and development

By the end of 1960s, growth in the healthcare market, along with the supply of innovative new therapies, was beginning to slow down. A 1969 amendment to the Military Authorization Act (popularly known the Mansfield Amendment) is the leading cause of the funding draught for R&D experienced in various different science, technology and engineering (ST&E) fields in the US during the 1970s. At a time when academic scientists in the US from varying disciplines struggled to secure funding for sustaining their research programs, Nixon's "War on Cancer" came into effect, reinvigorating research efforts in the fledgling fields of biochemistry, particularly molecular biology, in their most formative years (Teitelbaum, 2014).

In December 1971, Nixon signed the *National Cancer Act*, which would mark the beginning of an extensive and prolonged R&D campaign, often referred to as the "War against Cancer," primarily stemming from civilian needs. Nixon overcame his initial reluctance to sustain federal support in biomedical research in the face of growing public concern over declining federal support for cancer research and the dimming prospect that an effective cure for cancer would soon be found. Robinson [Judith] (2001) explains that prominent philanthropist and influential public figure, Mary Lesker, with the support of leading lobbying organizations such as the American Cancer Society, coordinated a media campaign and other public efforts to obtain more federal support for national cancer research efforts.

Lesker's efforts to engage the general public in the healthcare policy debate were instrumental in persuading Nixon to change his policy on federal support for cancer research (Robinson [Judith], 2001). In contrast to Lyndon Johnson's approach of instituting regional centers to coordinate research efforts on various healthcare challenges – among them, heart disease, cancer, and stroke -- what Nixon proposed was a broader strategy aimed at building a national research infrastructure substantially funded by the federal government that would target a specific healthcare challenge: finding a cure for Cancer.

This federal boost to the national science and technology (S&T) infrastructure stimulated the national R&D efforts to expand the knowledge-base in the US that was necessary for the advancement of cancer research. As they were eyeing the grand prize, a silver bullet that would cure the disease, major pharmaceutical manufacturers were struggling to revitalize their drying revenue streams and product pipelines. As part of an effort to quickly pump up their sales, which had been slowing due to aging product portfolios and increasing competition, and their profit margins, which had been decreasing due to growing drug-development costs, pharmaceutical companies increased their efforts to push FDA to change its rules on switching drugs from prescription-only to over-the-counter (OTC) sales. With the introduction of a new mechanism for Rx-to-OTC switch in May 1972, industry efforts to increase sales and re-energize marketing operations accelerated. Using brand recognition and advertising campaigns, big pharma tried the expansion of products in the OTC category to prop up their revenues.

The Era of Technology Liberalization and Deregulation

In the two decades following the end of WWII, the US government had been the single largest supporter of biomedical R&D, funding nearly half of the research performed in the US (Cockburn & Henderson, 2001; Hopkins & Lazonick, 2014). Post-war period growth in R&D leveled off somewhat in the 1960s and 1970s, before funding, particularly through NIH, began to skyrocket in the mid-1980s. Following the sharp increase in federal funding for biomedical research was a series of policy changes implemented by the US government in the 1980s aimed at reforming the rules and regulations covering the transfer of government-funded technologies to the private domain.

A small number of economic concerns were among the major drivers of the legislative changes that occurred in the 1980s. First, US companies were facing an increasingly stiff challenge from foreign competitors in international markets. The US government adopted a series of policy measures aimed at rejuvenating the competitiveness of American companies as concern over their declining ability to compete in international markets grew in the 1980s. Second, as competitors in fast-growing regions such as Japan continued to develop their innovative capabilities, the cutting-edge technologies emerging through public investment in the US were increasingly being absorbed by those foreign competitors. American know-how was being transformed so rapidly into innovative goods and services at the hands of foreign competitors that those innovative products were later to be imported by the US and to contribute to the growth of its trade deficit (Rahm, 1989).

Another economic concern was the US's inefficient transition of its military-oriented technologies to civilian use. Very few of the inventions that the federal government had supported through their discovery phases were filed with the US patent and trademark office (USPTO) and licensed for commercial use (NRC, 1987). The government was reluctant to invest further in the development of those underutilized technologies. Unless commercial interest sufficient to push those technologies into product markets could be

raises, the return on taxpayer investments in R&D would remain suboptimal. In this context the US government developed a series of policy regimens to address these economic concerns, starting with the implementation of a major policy overhaul focused on the commercialization of federally funded technologies.

Bayh-Dole, Stevenson-Wydler Technology Innovation, The Federal Technology Transfer Act and CRADA agreements

The Bayh-Dole (or Patent and Trademark Law Amendments) Act of 1980 explicitly permits research institutes, including the nation's leading research universities, to transfer the results of federally-funded research to commercial entities (Mowery et al., 1999). Until the Carter administration, issues concerning the transfer of federally funded research to the private domain for commercialization purposes were handled under state-level regulations. After his election Carter asked the Senate, then under the control of the Democrats, to propose new legislation that would regulate the transfer of technology at the federal level (Stevens, 2004). NIH had put a program in place under which it was transferring ownership of patents whose development it had funded to the universities to which they had been granted, but judging the program to be outside its policy objectives, the Carter Administration ended it.

In response, Norman Latker, the program's chief architect and NIH's patent counsel at the time, took on the Carter Administration (Bremer, Allen & Latker, 2009). A legal framework similar to that implemented at NIH for technology licensing was adopted in the early versions of the Bayh-Dole Act of 1980, and it later influenced the 1986 Federal Technology Transfer Act, which extended the jurisdiction of the Bayh-Dole Act to other federal laboratories (Allen, 2009). After Latker had joined the Office of Federal Procurement Policy (OFPP), the sponsors of the new technology transfer bill, Senator Birch Bayh of Indiana and Robert Dole of Kansas, proposed that OFPP act as the regulator authority for the implementation of the Bayh-Dole Act. Although the legislation was welcomed by the industry and the universities, President Carter vetoed the bill at first but ultimately signed it as the 10-day limit approached in response to unprecedented pressure from stakeholders (Allen, 2009).

The Bayh-Dole Act was initially designed to give small businesses easier access to tax-payer funded technologies carried out in university labs, however, the bill later expanded beyond "universities" to include all "non-profit" research organizations first, and later to include the technologies that are carried out in federal laboratories (Allen, 2009; Whalen, 2015). Before the Act was signed into law, large defense contractors intensified their lobbying efforts to include a new provision in the later version of the bill ensuring that the new act wouldn't impact the technology licensing arrangements between federal agencies and big corporations such as large defense contractors when it comes to assigning ownership rights to tax-payer funded technologies invented by those large for-profit research organizations, (Allen, 2009).

Despite its success in getting through Congress, Bayh-Dole was not an effective law as first implemented owing to two measures the original bill contained. The foremost issue was the inclusion of a “march-in” clause, which is a legal right permitting the US government to revoke licenses granted under the act in the event that licensees fail to “use their best effort” to commercialize such technologies (Whalen, 2015, p. 1087). Under such a provision individual the US government left the decision to exercise march-in right in the discretion of individual in the case that a licensee failed to produce the evidence that the products resulting from tax-payer funded research are ‘brought to market under “reasonable terms” (Whalen, 2015, p. 1011). In various petitions previously filed by patient advocacy groups raising concerns over high prices of innovative new drugs, to which the public had limited access, the proponents of march-in clause argued that the regulatory requirement to bring products to market under “reasonable terms” should also mandate companies to determine a “reasonable” price for those products emanating from tax-payer funded research (Whalen, 2015; Arno & Davis, 2001). Such argument however has yet to be taken into consideration by government agencies to act upon after the public or Congress filed those petitions and no major action has yet to be taken against a drug company under the Bayh-Dole act (Whalen, 2015; Arno & Davis, 2001).

A clause of this kind has been controversial at various times given that it was considered to be the major deterrent of business interests that might otherwise explore the commercial opportunities offered by federally funded technologies. It was also controversial because the NIH leadership at the time had refused to consider exercising its rights under the “march-in” clause to intervene in the market when drugs developed from federally funded research were sold at prices significantly higher than might have been viewed as “reasonable.” The second issue was the inclusion of the “exceptional circumstances” clause, which would leave the decision as to whether to transfer a technology at the discretion of the federal agency where it had been developed. Under this clause the Department of Energy (DoE) refused to transfer any technologies to which export controls applied. The list of these technologies was long, and their transfer from agencies such as DoE that dealt with highly security-sensitive technologies was almost impossible.

Once DoE had made clear that it would not engage in technology-transfer activity under the “exceptional circumstances” clause, the Bayh-Dole Act became completely impracticable; other agencies, following in DoE’s footsteps, decided they would not cooperate either. President Reagan then asked a panel of experts, headed by David Packard, the co-founder, CEO, and chairman of Hewlett-Packard, to review and report back on the federal laboratory system in 1983¹⁰. The Packard report pointed to a mismatch between the values of federal, university, and industrial research laboratories but argued that the federal laboratories had to collaborate with the other labs to deliver the greatest benefit possible to the public (Boffey, 1983). Upon the submission of this report, President

¹⁰At the time Packard was mentoring Robert Swanson, the co-founder and CEO of Genentech, and serving on Genentech’s board of directors.

Reagan issued a memo instructing federal laboratories to obey the new federal law; this executive memo failed to mobilize federal research laboratories to engage in technology transfer, however.

The Federal Technology Transfer Act (FTTA) of 1986 and the Cooperative Research and Development Agreement (CRADA)

In the meantime, a separate bill authored by Adlai Stevenson of Illinois and John Wydler of New York came before the Senate Commerce and House Science and Technology committees. What came to be known as the Stevenson-Wydler Technology Innovation Act of 1980 was approved in the last sessions of the same Congress that had passed the Bayh-Dole Act. The Stevenson-Wydler Technology Innovation Act of 1980 authorized the establishment of “Cooperative Research Centers” (CRCs) to encourage industry-university collaboration and mandated that each federal laboratory establish an “Office of Research and Technology Applications” to actively engage in technology transfer from the labs to commercial enterprises. When Ronald Reagan became US President, he declined to fund the CRCs on the grounds that the provisions of the Bayh-Dole Act offered more autonomy to universities to use their own discretion in the licensing of federally-funded research.

President Reagan later signed the 1986 Federal Technology Transfer Act (FTTA) to eliminate weaknesses of the Bayh-Dole Act and Stevenson-Wydler Act in the transfer of federally-funded research to industry. The FTTA created the “cooperative research and development agreement” (CRADA) to foster the interaction of government and business research efforts, quicken the transfer of technology to business enterprises, and make it easier for businesses to file patents based on this cooperative research. Through CRADAs, FTTA eliminated any resistance on the part of federal laboratories to actively seeking partnerships with industry. In particular, this Act facilitated the transfer of military-sponsored research to civilian uses (Allen, 2009).

CRADA agreements could become a regulatory tool for the federal government to monitor the cost and effectiveness of many drug therapies in the market, and to intervene in the drug market, if and when deemed necessary. Such an intervention could be done by requiring technologies, which for-profit or non-profit institutions license through CRADAs to develop new drugs, serve the public health and safety needs that are also “reasonably priced” (Arno & Davis, 2001). Many in industry considered this clause an implicit way of enforcing drug price restrictions for the following reason: in the event that the price of a product derived from the licensed technology subject to CRADA is deemed excessive, the licensee of such a technology may decide to exercise the “march-in” clause by claiming that such a price making the product unaffordable fails to meet the health and safety needs of the public (Rabitschek & Latker, 2005). The likelihood of such a scenario occurring had constituted the basis for the concerns over entering into CRADA because the price of a drug then becomes an arbitrary measure of the health and safety standard. Not surprisingly, the “reasonable pricing” clause was removed with the National Technology Transfer and

Advancement Act (NTTAA) of 1996, which amended the Stevenson-Wydler Act to make CRADAs more attractive to drug companies. NTTAA also capped the royalty payments federal researchers could receive from their inventions.

CRADAs became opaque and ineffective instruments of price regulation that undercut demands for the open and direct regulation of drug prices. The “reasonably priced” clause persisted when the federal technology transfer program was reauthorized under the National Competitiveness Technology Transfer Act of 1989. But it was removed with the National Technology Transfer and Advancement Act (NTTAA) of 1996 that amended the Stevenson-Wydler Act to make it more attractive for drug companies to enter into CRADAs. NTTAA placed a cap on the amount of royalties that federal researchers could receive on their inventions. After the removal of “reasonable” pricing clause, the number of CRADA applications increased significantly. The new amended version of the Stevenson-Wydler Act allowed more exclusivity to licensees under a CRADA agreement (Allen, 2009).

Among the most notable examples of products developed through CRADAs are Burroughs-Wellcome's popular drug, azidothymidine (AZT) for Human Immunodeficiency Virus (HIV) infection, and Bristol-Myers' Taxol (Robinson [Jeffrey], 2001). Most of the benefits of the Bayh-Dole Act, the Stevenson-Wydler Act, and FTTA (CRADAs) have gone to small biotechnology start-ups and the nation's leading research universities. In 2010, on the occasion of the 30th anniversary of the Bayh-Dole Act, it was revealed that 154 FDA-approved drugs had been discovered, partly or wholly, by public sector research institutions, with an estimated sales volume of \$103 billion (Loise & Stevens, 2010).

Supreme Court ruling and the orphan drug act

Patent protection has been fundamental to the US innovation system. The biopharmaceutical industry has benefited from general patent laws, including the 17 years of protection against competition from the time of filing a successful patent that prevailed from 1861 through 1994 and the 20 years of protection in existence since 1995. In addition, there have been special protections applicable to the medical drug industry. In the wake of the recombinant DNA revolution of the 1970s, in 1980, in *Diamond v. Chakrabarty*, the US Supreme Court ruled that a genetically modified bacterium could be patented (Eisenberg, 1992).

Ananda Mohan Chakrabarty, an engineer at General Electric, filed a patent application after developing for a genetically-modified bacterium that was intended to support efforts to clean water after an oil spill or similar catastrophe involving contamination of water caused by crude oil or its byproducts. Chakrabarty's application met with automatic rejection under the Patent Law of 1793: because living organisms currently exist in nature, no patents could be granted on them (Kevles, 1998, p. 65-79). Chakrabarty appealed USPTO's decision to the Court of Customs and Patent Appeals, which ruled in his favor.

The Commissioner of Patents and Trademarks, Sidney Diamond, brought the case to the US Supreme Court, capturing the attention of the entire US biotech community (Kevles, 1998). The biotech community played an active role in supporting Chakrabarty during the entire litigation of the case. Many scientists at the nation's leading universities as well as industrial research laboratories began to offer their expert opinions on the case, drafted letters in support of Chakrabarty's arguments, and urged the Supreme Court in an amicus curiae brief to remove what they regarded as a legal obstacle blocking the growth of the fledgling molecular biology and DNA engineering industries. On June 16, 1980, the Court ruled in favor of the industry.

In light of the Court's decision and industry's policy victories regarding federal technology transfer programs, it is evident that the 1980s was to become the most transformative period of the modern biopharmaceutical industry. Another in industry's long list of policy accomplishments came with the 1983 passage of the Orphan Drug Act (ODA) of 1983. ODA provided financial subsidies and market protection for pharmaceutical companies to develop drugs for rare and genetic diseases. Lazonick and Tulum (2011) have shown that these so-called orphan drugs were the foundation for pharmaceutical revenue growth in the 1990s and 2000s. From 1983 through 2017, there 4,437 ODA designations and 670 approvals (Food and Drug Administration [FDA], 2017).

ODA also offers R&D tax credits as well as FDA assistance in ensuring the rapid transformation of a promising therapy into an approved marketable drug. Most importantly, ODA incentives include seven-year marketing exclusivity for a specific therapeutic application. Unlike patent protection, which begins at the outset of the drug discovery process, ODA exclusivity begins once the drug has been approved by the FDA for sale. Moreover, the company that has obtained ODA approval does not necessarily require patent protection to have market exclusivity in selling the drug. Orphan drugs, which have typically come with very high price tags, were central to the growth of the leading companies in the biopharmaceutical drug industry, including Amgen, Genentech, Genzyme, Biogen IDEC, Cephalon, and Allergan (Lazonick & Tulum, 2011). Large pharmaceutical companies have also benefited from orphan drugs, either by acquiring smaller biotech companies or by entering into co-marketing deals with them that entail both equity investments and research contracts critical to funding the quest to develop an approved orphan drug (Daniel et al., 2016; Tribble & Lupkin, 2017)

Building the National Institutes of Health (NIH) and the science and technology infrastructure for biomedical research in the US

NIH funding forms a foundation for the elaborate sets of laws and institutions that define the US system of drug innovation. Since the republic was established, the US government has been an active player -- and often the sole or most important player -- in the building of an infrastructure to address the nation's ever-growing public health needs. The establishment of a nationwide public health program traces its origin back to the

establishment of the Marine Hospital Service for merchant seaman signed into law by John Adams in July 1798 through “an act for the relief of sick and disabled seamen” (NIH, 2017a). This act enabled the 5th Congress to establish Marine Hospital in New York, which was initially for merchant seaman but later extended its services to the members of the US Navy. A network of marine hospitals emerged as new hospitals were established in different parts of the country. The services of those hospitals were partially funded by moneys deducted from the pay of seamen and Navy officers, making the system the nation’s first prepaid medical care plan (NIH, 2017a).

In parallel to the growth observed in the scale of this network, the scope of services offered through marine hospitals were widened extensively as the nation experienced public health crises, mainly the consequence of wars in which the country had fought. As part of these expansion efforts, the “Hygienic Laboratory” was established in 1877 at the Marine Hospital in New York to cope with the growing danger of infectious diseases by increasing the nation’s healthcare research and vaccine development capabilities. This effort would ultimately lead to the establishment of the National Institutes of Health (NIH) and the building of one of the world’s most sophisticated and advanced innovation systems in the life sciences.

During Theodore Roosevelt’s presidency the nation’s public health program underwent a structural transformation in which a highly progressive policy agenda prevailed. In 1902, the name of the network of marine hospitals was changed to the Public Health and Marine Hospital Service to reflect the growing scale and scope of the health services offered. The Pure Food and Drug Act, signed by Roosevelt in June 1906 as part of a pro-consumer policy agenda, was meant to ensure the safety of medicinal products through a new federal entity formed within the US Department of Agriculture (USDA), the Food, Drug, and Insecticide organization, which shortly thereafter was renamed the Food and Drug Administration (FDA). The Act is considered a significant policy milestone for the pharmaceutical (BP) industry, since it represented the first government attempt to regulate the production and marketing of medicinal products in the US.

In the years following Roosevelt’s presidency, the public health system went through some further structural changes. In 1912, the Public Health and Marine Hospital Service was renamed the Public Health Service (PHS) as some old marine hospitals were decommissioned and more health service coverage was extended to the general public. As part of the efforts to centralize activities concerning public health, the Hygiene Institute became a part of Public Health Service (1922). Growing concerns about infectious diseases prompted the government to launch more research initiatives and to play a more active role in coordinating and supporting research efforts, which were being carried on mainly by major government institutions, the army in particular, and by leading academic institutions. As part of this effort the Ransdell Act, signed by Herbert Hoover in May 1930, reorganized the Hygienic Laboratory and re-established its authority as the nation’s the leading government agency for medical research under a new name, National Institutes of Health.

The US government “doubles” the bet on improving healthcare in the age of genomics

As their desperation for more government funding escalated, the research community began to question for the legitimacy of NIH's intramural activities (Varmus, 2009). The research community claimed that the merits of allocating resources to the NIH intramural program were dubious, as US universities, their facilities and researchers supported by NIH funding and headed by former NIH personnel, were better equipped than NIH itself to conduct clinical investigations (Varmus, 2009, p. 158).

To address these claims and evaluate the intramural research program (IRP), the newly appointed director of NIH, Harold Varmus, assembled the External Advisory Committee in 1994 whose members included Merck CEO Roy Vagelos and future Eli Lilly Vice-President of Scientific Affairs Gail Cassell as co-chairs, along with current and former leaders of various medical research organizations, some of whom had worked at NIH and joined venture capital firms later in their careers. Varmus summarized the committee's report thus:

... It stressed the need for a more rigorous review process. It acknowledged that the intramural research could not be different in all aspects from research at other places, such as academic medical centers, but ought to be different in some ways because of [NIH's] size, its capacity to respond more quickly to public health emergencies, its ability to recruit patients from around the world for clinical research, its emphasis on experimental work rather than classroom teaching, its budgetary stability, and the diversity of its technical capabilities. But the report also noted that the intramural research program was less competitive than many academic organizations in recruiting outstanding scientists because of the relatively low government salaries, limited opportunities to consult for industry or perform other “outside activities,” several aging laboratory buildings, and a declining reputation. (p. 159)

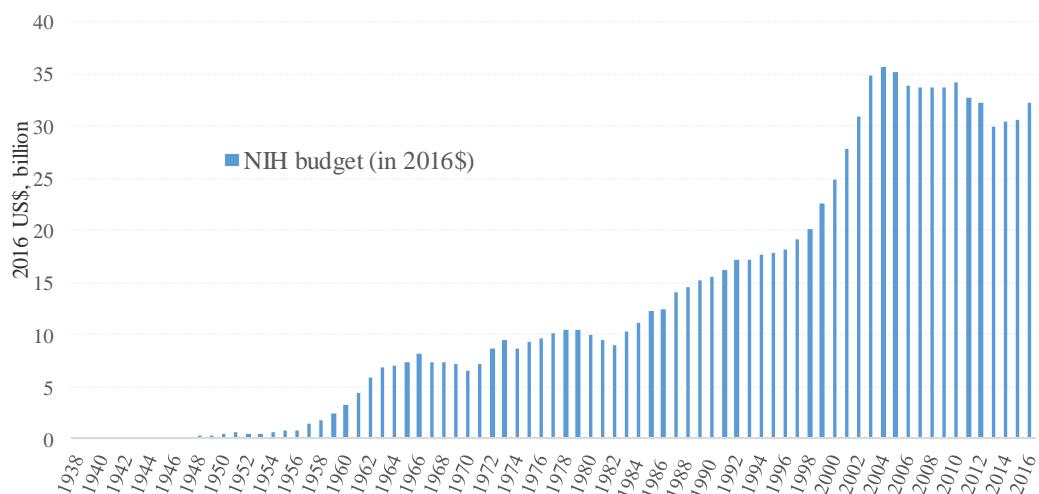
PhRMA is one of more than 500 members of Research!America (R!A), formed in 1989 for the purpose of advocating public support for biomedical research. R!A quickly became the umbrella organization for all the stakeholders of NIH funding including major research universities and academic institutes, Big Pharma and other drug companies, disease advocacy groups, professional societies, etc. (Research!America [R!A], n.d.; Slaughter & Rhoades, 1996). In 1992 R!A was in the forefront in lobbying for the Prescription User Drug Fee Act, under which the FDA could charge drug companies fees for reviewing drugs for approval in exchange for faster review times (Goozner, 2004, p. 240-241). Along with R!A, PhRMA played a key role in the successful lobbying efforts to double NIH funding in the late 1990s and early 2000s (Smaglik, 1997; Check, 2002; Relman & Angell, 2002).

This expansion of the NIH along with the growing support for life-sciences research from non-governmental sources resulted in the rapid expansion of physical infrastructure to

support research to develop innovative therapies (Teitelbaum, 2014; Stephan, 2012). Subsequent to the doubling of the NIH budget in the early 2000s, the 21st Century Cures Act of 2016 was the first major legislative effort to increase funding for the NIH, and included \$1.8 billion in new funding over seven years to the National Cancer Institute for the Cancer Moonshot, sponsored by Vice President Joe Biden.

Without the funding that the NIH have expended on life-sciences research, there would be no possibility of pharmaceutical innovation in the United States. The 2017 NIH budget was \$33.1 billion, up from \$32.3 billion in 2016. Figure 1 shows NIH spending, measured in 2016 dollars, on life-sciences research for 1938 through 2016, for a cumulative total of just over \$1 trillion over these 79 years. Note the virtual doubling of the NIH budget in real terms between 1996 and 2004. The NIH contends that, on average, every one dollar that they have spent since the US government begun funding its biomedical research in 1938 has translated into \$2.13 in US pharmaceutical sales (NIH, 2017b). The centrality of NIH funding to US pharmaceutical drug innovation in and of itself justifies government regulation of the prices of the drugs that result from it.

Figure 11: National Institutes of Health Annual Spending 1950-2016 (Adjusted, 2016\$b)



Source: National Institutes of Health (NIH) Budget, at <https://www.nih.gov/about-nih/what-we-do/budget>

Despite the critical role that the government played in building a biotechnology industry in the US through providing substantial funding for basic research via the National Institutes of Health, government has always been portrayed as creating barriers to innovation, either through a lack of interest in funding cutting-edge technologies or through adding to regulatory obstacles that hinder the innovation process (Lazonick & Tulum, 2011).

Further policy initiatives to impact biomedical R&D in the US

The US biotechnology entrepreneurs' excitement over corporate tax incentives stimulating industrial R&D had been peaked in the early 1980s before it mostly receded by the mid-

1980s Among notable tax incentives resulted such an excitement among the biotechnology entrepreneurs were: the Economic Recovery Tax Act of 1981, which included a special tax credit for R&D carried out in the US; and the Small Business Innovation Development Act of 1982, which first established the Small Business Innovation Research (SBIR) program to fund the R&D efforts of small, research-based organizations.

The Tax Reform Act of 1986 however lowered the marginal tax rate of the R&D deduction and prohibited the passing of any accrued R&D expenses to investors to claim as a legitimate investment expense. The implications of the 1986 Tax Reform Act was particularly important for start-ups such as Genentech, whose ability to raise large sums of cash through R&D partnership deals to fund research was severely damaged by it, as investors in R&D partnerships could no longer reduce their tax liabilities by claiming a deduction on the R&D expenses accrued. Chapter seven provides more detailed discussions on how the changes introduced with the 1986 Act proscribing the transfer of R&D tax benefits to investors disabled Genentech's entrepreneurial financing strategies leveraging such tax incentives to raise capital in speculative markets.

With the creation of the National Human Genome Research Institute in 1988, NIH was officially assigned to oversee US participation in international research efforts on the mapping of the human genome. This was important milestone for the industry, as the international genomic research alliance revamped its efforts, whom the Institute was assigned to coordinate the research efforts within the US, would begin to unravel certain organisms hidden in the genetic codes although such secrets were not revealed to the greatest extend until the end of the 20th century.

Toward the end of his tenure, President Obama signed a series of healthcare bills, one being the Food and Drug Administration Safety and Innovation Act; this law extended the Prescription Drug User Fee Act of 1992, which allows FDA to collect fees on applications for approval to market drugs, and contained a new provision encouraging the development of new products for pediatric use. The Generating Antibiotic Incentives Now Act (GAIN) of 2012 was intended to incentivize the development of a new generation of antibiotics as antibiotic resistance became an alarming public health issue. The 21st Century Cures Act of 2016, among the last major policy initiatives of the Obama Administration, boosted funding for NIH by \$6.3 billion annually to support efforts in cancer research, part of the Beau Biden Cancer Moonshot initiative. While the funding was geared toward brain research, also provided was funding to support various mental health initiatives.

Creating markets for innovative therapies

Through historical analysis of the enactment of certain drug policies in the United States, Tobbell (2012) documents how the biopharmaceutical industry gained political power that enabled it to shape the national innovation system in which it operates in the United States. This innovation system enabled the US biopharmaceutical industry to become the global leader. At the same time, however, the US biopharmaceutical industry and the US medical

research community used their political power to resist policy reforms that would constrain, regulate or appropriate their financial gains.

The enactment of the Federal Food, Drug and Cosmetic Act (FDCA) in 1938 established the world's foremost regulatory agency—now known as the Food and Drug Administration (FDA)—to monitor drug safety. With a major change in the FDCA in 1951, the Durham-Humphrey Amendment created the legal basis for what is known as the “prescription drug market”, which ultimately required the dispensing of pharmaceutical products with the risk of drug addiction or harmful side effects through prescriptions obtained from physicians. Another major change in the FDCA came with the Kefauver-Harris Amendment of 1962, which for the first time required the pharmaceutical companies to provide the regulators with clinical evidence of the efficacy of drugs prior to being sold on the market.

Another major policy effort was reforming the US healthcare system with the introduction of the Public Health Service, created in legislation signed in July 1944 by President Roosevelt. The importance of this legislation stems from its being the first attempt to consolidate and revise all the existing laws concerning the Public Health Service. Under this act, the governance of public health services was assigned to four major public entities: the Office of the Surgeon General, the Bureau of Medical Services, the Bureau of State Services, and the National Institutes of Health. The act was particularly important in that it empowered agencies to conduct and support medical research that would ultimately contribute to the building of a highly advanced national innovation system that has led or enabled discoveries in pharmaceutical drugs up to today.

As Lyndon Johnson began his second term as president and Hubert Humphrey, a former pharmacist who was the co-sponsor of the Durham-Humphrey Amendment of 1951 –an important legislative change to the Food Drug Cosmetic Act of 1938 introduced the federal mandate on dispensing certain drug through prescriptions obtained from physicians– entered the office of vice president, the Johnson administration was pursuing a progressive social policy reform agenda known as the Great Society.” The passage within months of the Social Security Amendments of 1965 brought part of Truman’s Universal Public Health Insurance scheme alive by building on the landmark legislative victory of New Deal era, the Social Security Act of 1935. Provisions of the 1965 Amendments resulted in the launch of new social insurance programs: Medicare, for retirees, and Medicaid, for families and individuals who could not afford to meet their healthcare needs.

Separate amendment of the Public Health Service Act allowed the Johnson administration to introduce what a presidential commission called a “National Program to Conquer Heart Disease, Cancer, and Stroke” by instituting Regional Medical Programs (RMPs) designed to generate and foster cooperative innovation efforts among medical research organizations. The Heart Disease, Cancer, and Stroke Amendments of 1965 would be instrumental not only to the development of drug therapies for heart disease but also to

understanding the mechanism through which the leading risk factors, such as hypertension and elevated cholesterol, were linked to cardiovascular problems (Tobbell, 2011, p. 146).

The Health Maintenance Organization (HMO) Act of 1973 (also known as the Federal HMO Act) was among the first market-based policies intended to rein in the soaring cost of healthcare in the United States. The HMO Act restricts consumer choice in healthcare providers by setting up healthcare units—the HMOs—that households on less expensive health insurance plans would have to use. This model of healthcare provision assumes that the HMOs can be managed to lower the costs of healthcare delivery. According to Starr (1983, p. 403), the HMO Act was the most market-friendly solution that the political conservatives could engineer to curb the growing appetite of progressives for “socialized medicine” in the age of medical inflation.

After the passing of the HMO Act, the federal policy efforts to control healthcare costs continued in the 1970s, in the face of anti-regulation resistance that included pharmaceutical manufacturers (Starr, 1983; Brown, 2010). The biopharmaceutical industry lobbying efforts in the 1970s through 1980s focused on maintaining the status quo, which essentially meant preventing the federal government from regulating drug prices. Industry rhetoric portrayed government interference in the pharmaceutical market as a major obstacle to innovation—particularly whenever the federal government considered legislation to rein in soaring drug prices. And US legislators have accepted this free-market (i.e., neoclassical) view of the world.

Yet, dating back to the Morrill Land Grant Act of 1862 which created the national system of public universities, the US government has put in place the most formidable national system of innovation in history (Ferleger & Lazonick, 1993; Ferleger & Lazonick, 1994; Hopkins & Lazonick, 2014). With the launching of the National Institutes of Health (NIH) in the 1930s, this national innovation system included a focus on pharmaceutical drug development. Lazonick and Tulum (2011) underline the critical role that the US government has played for decades in making the investments in scientific and engineering personnel and life-sciences and computer-sciences research that have underpinned pharmaceutical drug innovation in the United States.

Although the patent system exists to stimulate innovation, a legal system of this sort may constrain an innovative enterprise from induce competitive pressure on the other productive actors to improve industrial productivity through further innovation. As value-extraction efforts among the pharmaceutical oligopolists emerged or increased in the 1980s and 1990s, their lobbying effort intensified significantly to persuade policy makers to extend the length of patent protection. Ironically, the industry was petitioning for further patent protection at the very time that the anti-competitive measures it supported were stimulating further price increases as opposed to further innovation.

For instance, after US policy makers reacted to the public outcry over the price increases of medicinal products in the 1980s and introduced generic-drug solution to bring the drug prices down, the drug industry walked away with additional protection against competition in the drug market. The Drug Price Competition and Patent Restoration Act of 1984 (popularly referred as the *Hatch-Waxman Act of 1984*) was an attempt to control the soaring drug prices of the 1980s by allowing generic drug makers to introduce exact equivalents of patented drugs in the market. Because those generic new drugs were permitted to avoid replicating the costly clinical trials that had to be run with investigational new drugs (INDs) to comply with regulations on acquiring the FDA approval for market, the prices of generic drugs could be kept significantly lower than those of drugs under patent, at least in theory¹¹.

According to Grabowski and Vernon (1995), the Patent Restoration Act was the first major revision of the terms of US patent law since 1861. The act's passage led to major courtroom battles between the brand-name and generic drug makers in the next decade as the attempts of the latter to file Abbreviated New Drug Applications (ANDAs) were blocked by patent holders using legal injunctions to delay the process. The Democratic bill Greater Access to Affordable Pharmaceuticals (GAAP) Act of 2002 was intended to further strengthen the Hatch-Waxman Act by closing loopholes in it that often seriously delayed generics' reaching the market.

The bill also included a provision to permit importing low-cost alternatives to pharmaceuticals priced excessively high in the US market. The GAAP Act failed to generate the necessary support to become law and was replaced by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. The 2003 Act extended Medicare coverage to outpatient drug costs, a measure that industry influence had prevented from becoming law as part of several legislative proposals in the 1980s; in return, certain provisions of the Hatch-Waxman Act were amended in favor of the pharmaceutical producers.

When the Act was first proposed in the early 1980s, the major US drug makers counterattacked with full force and were subsequently presented with certain incentives -- such as extension of market protection for brand drugs facing patent expiration-- to calling off their fight to lobby against such a new law. First, a developer of a new molecular entity (NME) or new biological entity (NBE) was granted five years of "data exclusivity," allowing them to market the NME or NBE without facing competition from the generic versions even if the molecular or biological entity in question was not be protected by a patent.

¹¹ *Nearly two decades after the generic drug bill signed into effect in 1984, the major generic drug makers in the US were scrutinized by a group of US lawmakers and petitioned for the basis for pricing generic products such high prices (Lazarus, 2014).*

The second takeaway was an extension of the length of a product's patent life for the amount of time it had spent under regulatory review. This essentially meant that the longer the FDA took to finalize its review of a new drug, the more time the drug would enjoy patent protection in the market after gaining regulatory approval. The policy debate between the political conservatives and progressives became more heated as the cost of pharmaceutical products, along with the overall cost of healthcare in the US, rose in the 1980s. As conservatives devised more market-friendly solutions, addressing the problem of the growing cost of healthcare through incremental changes in existing policies, progressives pushed for more fundamental change in national healthcare policy. Since earlier attempts at passing new legislation creating a federally-sponsored universal healthcare program had failed, the policy efforts of the late 1980s were geared more toward extending Medicare coverage to a larger portion of the US population.

Under the Consolidated Omnibus Budget Reconciliation Act (COBRA) of 1985, health insurance coverage was extended to those who had left employment but still needed insurance during the post-employment period. Adopted in 1988 despite some heavy opposition, the *Medicare Catastrophic Care Coverage Act* was an attempt to extend prescription drug coverage to all Medicare patients, but the bill was repealed in 1989, ending prescription drug coverage under the Medicare program. Another bill, the Omnibus Budget Reconciliation Act, became a law in 1990 aimed at reining in soaring drug prices by mandating the establishment of a "Drug Utilization Review" board to devise and implement new drug purchasing guidelines and an official formulary through state-level health insurance programs, including Medicaid.

The new formulary, essentially a list of preferred drugs, was intended to eliminate the discrepancy in the cost of pharmaceutical products that existed among government-sponsored insurance programs. Through the list of drugs, the Board recommended that state insurance programs consider purchasing biopharmaceutical products prioritized according to the overall value they offered. This formulary was instrumental in getting state programs to consider substituting branded products with their generic equivalents if and when possible, since the list often preferred the cheaper generic equivalent over the more expensive branded product. The bill also mandated that the drug companies offer biopharmaceutical products to Medicaid programs at as low a price as the Veterans Administration paid at the time.

The Federal Veterans Health Care Act of 1992 represented another attempt to use government purchasing power to lower drug prices in the nation. Amending the Public Health Service Act of 1965, the new act mandated extending purchasing agreements between the Health and Human Services (HHS) secretary and the drug companies to purchases for the Veteran Administration. This essentially meant that drug companies had to offer their products at the same rate that the federal government had to pay for them through the Medicare and Medicaid programs.

After the Hatch-Waxman Act, the second major revision to patent law came in the mid-1990s. In 1944, as the drug industry battled to defeat the Clinton healthcare plan, it was getting ready to receive another handout in the form of greater patent protection. That year, the parties to the General Agreement on Tariffs and Trade (GATT) institutionalized the legal framework they had agreed upon for international trade under the intergovernmental World Trade Organization (WTO), which became the governing body for global trade. Enacting the Uruguay Round Agreements Act of 1994, the US government adopted a series of changes aligning the national laws with this new international trade accord, including the extension of patent protection from 17 to 20 years -- a benefit demanded by, and of immense importance to, the biopharmaceutical industry.

The market incentives for pharmaceutical innovation were not limited to generous patent protections; they varied across different therapeutic areas. The US's supply of vaccines, for instance, had been very unstable, as some of its big pharma companies -- even those like Merck whose core capabilities were rooted in vaccine production -- considered opting out of the vaccines market in the 1980s and 1990s. The National Childhood Vaccines Injury Act of 1986 essentially provided vaccine producers with legal immunity against financial liability stemming from injury claims linked to the use of childhood vaccines covered by the law. With the establishment of the National Vaccine Injury Compensation Program (VICP), the US government released the vaccine makers from financial liability by settling relevant injury claims with the funds raised through the Program. The Omnibus Budget Reconciliation Act of 1993 also included a provision to create the Vaccines for Children Program to subsidize the cost of vaccines for kids who have no access to them or are uninsured.

Marketing pharmaceuticals

Marketing new biopharmaceutical products in mass markets using media -- starting with radio and newspapers and, later, through television and the Internet -- has been among the strengths of US pharmaceutical companies since the early days of the industry. Chandler 2005 explains the leading US pharmaceutical companies of the early 20th century such as Bristol-Myers, Warner (of Warner-Lambert now part of Pfizer), Plough (of Schering-Plough now part of Merck & Co.), and American Home Products (later renamed as Wyeth now part of Pfizer), were all heavily involved in the advertising-driven drug sales and distribution activities nationwide to capture the fast growing medicinal drug market in US market.

As drug makers sought to improve their sales and marketing capabilities in order to expand into new markets and to increase their revenues more policy actions were required to regulate their aggressive marketing campaigns. The Federal Trade Commission (FTC) was authorized under the Wheeler-Lea Act of 1938 to oversee the business practices of pharmaceutical and other US manufacturers and to ensure that businesses were not engaged in the "unfair or deceptive acts or practices" prohibited under the same law. The

Lanham (Trademark) Act, signed into law in July 1947 by President Truman, allowed the FTC to deny any trademark claim that might inhibit the marketing of generic products under generally accepted common therapeutic names. A complaint lodged by Bayer provides a great illustration of the legal objectives and scope of this law. “Aspirin,” the brand name for acetylsalicylic acid, is registered as a Bayer trademark, and the company complained that it was being violated by manufacturers of generics who marketed products containing acetylsalicylic acid under the name “Aspirin.” The claim was denied under the Lanham Act on the grounds that “Aspirin” had become a household name for a medicinal product containing a chemical substance with a complex generic name.

Through Fair Deal programs of his presidency, Harry Truman generally aimed at sustaining or extending the social and economic objectives of the New Deal. Truman administration attempts to launch a national health insurance program failed due to the strong opposition of the American Medical Association and other major industry and professional associations. In October 1951, however, Truman signed the Durham-Humphrey Amendment to the Federal Food, Drug and Cosmetic Act, which required any potentially harmful or habit-forming drug that was deemed unsafe for self-medication to be prescribed by medical doctors. The law provided FDA with legal authority to classify certain drugs as requiring a prescription from a physician based on their safety profiles. Prior to the law’s enactment, US pharmaceutical companies had been marketing directly to consumers through a wide network of media outlets and enjoying increasing sales. But owing to the new law the utility of that marketing strategy diminished, as physicians became the gatekeepers in the process of distributing products in the drug market.

With all of the government funding and market protection of the biopharmaceutical industry, one might assume that the US government would regulate drug prices. But, with the help of neoclassical economics, the industry made the argument that it should be the market, not the government, which regulates drug prices. They argued that the market mechanism could kick in when a drug went off patent, with generic producers entering the commercial fray to compete for market share.

This market-directed “regulatory” approach was put into force by the Drug Price Competition and Patent Term Restoration Act of 1984, often referred as the Hatch-Waxman Act. Generic competition works in some cases and to some extent, although even then it takes 20 years from the filing of a patent before open generic competition can take place. Although the market entry of generic makers has induced some downward pressure on drug prices first, the patented drug producers later began using some of their monopoly profits to bribe generic producers not to enter the market when a drug goes off-patent, and they continued charging high prices (I-MAK, 2017).

When threats of drug-price regulation arose in the 1990s, the established pharmaceutical companies, known as “Big Pharma”, and the rapidly growing New Economy biopharma companies joined forces to defeat this interference with so-called “market forces.” As

already mentioned, in 1994, in the wake of renewed Congressional attention to high drug prices, the Pharmaceutical Manufacturers Association changed its name to the Pharmaceutical Research and Manufacturers of America, or PhRMA, to emphasize that its members were engaged in research activities for the benefit of the United States. One year after this name change, PhRMA helped to persuade US lawmakers to extend patent protection from 17 years, which had prevailed since 1861, to 20 years, which was in line with changes in intellectual property rights advocated by the World Trade Organization. Focused on securing every possible advantage of government support for the industry while avoiding price regulation, PhRMA has become one of the most powerful lobbies in Washington D.C (Tobbell, 2012). After becoming the new CEO and Chairman of Merck in 1994, Raymond Gilmartin had begun serve as the chairman of PhRMA until he was asked to serve in the Bush administration as a member of the transition team for the Department of Health and Human Services (DHHS) in 2000.

Besides defeating proposals to regulate drug prices in the 1980s and 1990s, the industry worked successfully for the adoption of new regulations that would seal the US drug market against the intrusion of cheap alternative products. Amending the 1938 Federal Food, Drug, and Cosmetic Act, the Prescription Drug Marketing Act of 1987 blocked the re-importation of previously exported products in addition to restricting the distribution of any biopharmaceutical product through authorized channel. While the 1987 act ensured that the safety of biopharmaceutical products was not compromised as they proceeded from drug warehouses to customers' medicine cabinets, it also ensured that drugs sold at lower prices in foreign markets would not return to the US, where the prices charged for the same products were much higher. A major policy coup of PhRMA was the Food and Drug Administration (FDA) Act of 1997, which removed any regulatory restriction on television broadcasting of drug information, allowed the drug companies to provide medical professionals with some information in peer-reviewed academic journals on the off-label use of any prescription drug; and granted drug companies an additional six months of data exclusivity on biopharmaceutical products developed for children. With the passing of this legislation, direct-to-consumer pharmaceutical advertising went from \$360 million in 1995 to \$1.3 billion in 1998 and then \$5.0 billion in 2006 (Donohue, 2006).

The FDA Modernization Act of 1997 not only allowed companies to conduct clinical trials on children, who had previously been excluded from clinical studies, to explore potential pediatric applications, but it also provided the drug companies with a six-month extension of patent life for products with pediatric applications. The Best Pharmaceuticals for Children Act (BPCA) of 2002 extended that six-month pediatric exclusivity for another five-year period, and with the enactment of the Food and Drug Administration Amendments Act of 2007, BPCA along with the six-month pediatric exclusivity clause

was reauthorized once again.¹² Also, although the 1962 Kefauver-Harris Amendment had allowed FDA to regulate the labeling and marketing of prescription drugs, it was not until the 1997 FDA Modernization Act its regulations were applied to direct-to-consumer marketing via the mass media.

The clarification of this regulation came after large pharmaceutical companies had drastically shifted their marketing strategies in the 1990s to employ direct-to-consumer efforts aimed at establishing strong brand loyalty around market leaders. This type of product-placement strategy was particularly visible in hyper-competitive markets overcrowded by “me-too” drugs: drugs with therapeutic benefits that are not significantly greater than those provided by the market leader (Goozner, 2004). In the age of “me-too” drugs, concern over the common marketing practices of pharmaceutical companies in the US grew to such an extent that the industry felt the need to adopt a set of rules -- before the federal government did so -- requiring drug makers to abstain voluntarily from unethical marketing practices. In 2002, the Pharmaceutical Research and Manufacturers Association (PhRMA), the lobbying arm of the industry, adopted a code of conduct outlining industry standards for the marketing of biopharmaceutical products to physicians.

In the aftermath of September 11 attacks and amid the perceived threat of further terror attacks, a series of new measures concerning biopharmaceutical industry took effect. Executive Order 13329, titled “Encouraging Innovation in Manufacturing” and signed by President Bush in 2004, targeted national manufacturing efforts for medicinal products deemed critical to national security. Amending the Public Health Service Act of 1944, the Project Bioshield Act of 2004 authorized stockpiling \$5 billion worth of vaccines for use in the event of a potential terror attack involving biological weapons, while the Pandemic and All-Hazards Preparedness Act of 2006 established a Biomedical Advanced Research and Development Authority to oversee federal efforts to prepare for public emergencies through developing and procuring medicinal products deemed critical to public health in the event of such attacks.

In 2010, President Obama signed landmark legislation officially named the Patient Protection and Affordable Care Act but popularly known as the “Affordable Care Act,” the “ACA,” or “Obamacare.” Among its key components is the Biologics Price Competition and Innovation Act, which amended the Public Health Service Act of 1944, the keystone of the US healthcare legal infrastructure, to clarify the regulatory process by which biosimilars (generic versions of biological therapeutics) enter the drug market. The second component of the ACA is the Health Care and Education Reconciliation Act, which includes provisions offering new tax credits for purchasing insurance plans; closing the Medicare Part D “donut hole,” a portion of the cost covered by Medicare patients when purchasing prescription drugs; and various other regulatory mandates and subsidies. Since

¹²*The new rule also applied to any other therapeutic benefit of a drug that has yet to be approved by FDA for the marketing of products in such therapeutic areas. The 1997 Act also allowed drug companies to utilize peer-reviewed journal articles that discussed the off-label use of products.*

the ACA became law in 2010, the biopharmaceutical products market has been going through changes that are re-defining reimbursement policies and payment systems.

The drug industry's prevailing innovation and marketing strategies appear to be subject to further changes in light of the continuous political attack that has threatened ACA's existence. In recent years, big pharma companies have been painstakingly maneuvering in the direction of more specialized markets while ending their dependence on mass markets and what is commonly known as the "blockbuster" model. Hoffman-La Roche, discussed in chapter 6, is among the top companies to develop a product portfolio centered on specialty drugs that face less competitive pressure on prices.

Other large BP companies also have been attempting to conquer price pressure by shifting their focus to capturing niche segments of the drug market through products with higher profit margins. The popularity of orphan drugs is on the rise as more firms, regardless of their size, have been seeking ways to increase the number of products for rare diseases in their product portfolios and pipelines (Lazonick & Tulum, 2011). Orphan drugs are often more cost-effective and can access and penetrate the markets far more quickly than mass-market drugs due to the priority reviews and regulatory assistance offered by FDA (Lazonick & Tulum, 2011). ODA also provides monopolistic market power to the makers of orphan-designated products by exempting them from market competition. As the only available therapies for long-neglected conditions, orphan products are seen as entitled to protection from some regulatory and pricing pressures.

Additionally, the industry has been, and will continue to be, prone to sharp revenue drops as the patent lives of blockbuster drugs expire and generic drug makers to enter the market at significantly lower price points. Pharmaceutical companies are searching for new marketing strategies as competitive and regulatory pressures compromise existing marketing strategies for their highly sophisticated and advanced products. While stepping up efforts to expand within the premium products markets, big pharma has also targeted the over-the-counter personal care product markets in order to shore-up its position in various segments of the healthcare product market (i.e. antacids, vitamin, eye care products) that big pharma historically had legacy in pioneering and dominating such markets. Additionally, acquisition of major generic drug makers not only allows big pharma companies to defend their market share in particular disease segments, but it also enables them to seek growth in emerging markets overseas..

The key business strategy makers of brand-name drugs have been following of late to protect their market share against generic drugs appears to be filing legal claims in an attempt to delay the entry of generics producers into the market. Making large "reverse payments" (also known as "pay-for-delay" agreements) through confidential arrangement to delay the entry of generic makers is another business strategy, and the U.S. Congress has failed to pass such a new law that specifically prohibits reverse payments as the Preserve

Access to Affordable Generics Act since it was first introduced in 2007 (Backus, 2007; Bagherian, 2007; Kesselheim et al., 2011).

The productivity of the biopharmaceutical industry can be paramount to the future of healthcare. Pharmaceutical costs do not constitute a significant portion of the nation's overall healthcare budget -- on the contrary, they are often considered the silver bullet for bringing down overall healthcare costs, since they can potentially help patients avoid long-term surgical or hospitalization risks. An increase in the number of citizens with healthcare coverage will potentially increase demand for pharmaceuticals.

Additionally, increase in the use of prescription drugs may be adopted as a quality and efficient care measure that might prevent the hospitalizations and invasive surgeries constituting a significant portion of overall healthcare spending. If so, the new legislative changes may be important incentives for big pharma to further innovate products that will substitute traditional therapies. This appears to be a viable marketing strategy for big pharma to follow, as market and policy changes do much to cloud the prospect for growth.

This chapter examined major policy events that have played roles to some extent in shaping the institutional environment in the US. A more extensive list of policies concerning the US biopharmaceutical industry can be found in Appendix I at the end of this thesis. As shown in the analysis in this chapter, the US is an ideal environment for some drug companies focused developing effective new drug therapies that can potentially disrupt the market and lead to generating significant financial gains in return.

The US can also be an ideal environment for those interested making investments on drug development programs that can lead to higher and quicker yield even without developing highly innovative new drug therapies, or developing no drug at all. In the event when the number of companies in the latter group exceeds the number in the former, the industrial trajectory changes in a way that it begins to reward shareholders at the expense of other stakeholders such as patients or employees of such companies.

Examining the changes in the social conditions of innovative enterprise in a major American pharmaceutical company, the following chapter will explain how a previously innovative company such as Merck had benefited from such an institutional environment, which has been conducive to innovation, to become a global leader in the biopharmaceutical industry, by making investments on drug development program, until the 1990s. Having played a major role in the national lobbying efforts to influence policy decisions, the following chapter will document Merck's transformation from being an innovative enterprise to pursuing a financialized business model.

4 AN ANALYSIS OF THE TRANSITION FROM INNOVATION TO FINANCIALIZATION: MERCK & CO., INC.

“We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we have remembered it, the larger they have been.”

George W. Merck,
President (1925-1950) and Chairman (1949-1957) of Merck & Co., Inc.

“...[M]edicine is for the people., It is not for the profit,” in the words of George W. Merck, a leading figure in the biopharmaceutical industry in the mid-20th century. Merck’s statement revealed the essence of the strategy that his company, Merck & Co., adamantly pursued for the greater part of the 20th century. After having inherited the company from his father, George Merck, Sr., in the mid-1920s, George W. Merck had transformed Merck & Co. from a leading producer of bulk and fine chemicals to a research-based, fully integrated, global pharmaceutical company by the time he retired from active leadership in the early 1950s.

George W. Merck initiated this ambitious strategy in the early 1930s as part of an organizational overhaul aimed at allowing the company to compete against industry incumbents in the fast-growing international market. His vision was realized through prolonged engagement in basic research, which led to Merck’s recognition as the beacon of industrial research for medicine. The successful execution of this research-driven growth strategy ultimately paid off financially, as Merck & Co. became the nation’s most admired company, its market capitalization surpassing those of such prominent American companies as IBM and GE in the late-1980s and early-1990s.

It is the introduction of innovative new products that brought celebrity status to Merck in the last decades of the 20th century. In 1987 Merck was selected the Best Managed Company by Business Month magazine, and it was declared the Most Innovative Company of 1988 by Forbes magazine. Forbes also named Merck & Co. America’s Most Admired Company for seven consequent years, 1987 and 1994. During the company’s golden year of 1987, one of its innovative products as well as its sales force were selected as Product of the Year by Fortune magazine and Best Sales Force by Sales and Marketing Management magazine.

In addition to its business merits, the company’s social impact was praised during a period of explosive productivity growth. In 1987 Working Mother magazine selected Merck & Co. as the Best Company to Work For because it availed working mothers one of the most supportive work environments in the nation. After donating millions of dollars’ worth of Mectizan to treat river blindness, a disease affecting the world’s poorest communities, Merck was selected Best Company in Public Service by BusinessWeek magazine in 1988.

The productivity growth that brought the company fame and fortune lasted a relatively brief period of time, mainly overlapping with the tenure of the highly respected CEO P. Roy Vagelos and ending shortly after his retirement in 1994. Struck by a series of clinical, legal, and financial disasters in the following decade, Merck & Co. shifted in the public's perception from being widely recognized as the most admired organization of the early-1990s to suffering from serious public-image, innovation, and productivity problems beginning in the early 2000s.

While its reputation was a century in the making, Merck's demise was quite rapid, and the company has yet to recover fully from the events that took place at the turn of the 21st century. Despite being recognized as the beacon of productivity in drug development until as recently as the mid-1990s (Reingold, 1995; The Economist, 1997; Hawthorne, 2006), Merck is today seeking a new path to repossessing the valuable asset it has lost: the corporate image that was once a symbol of strength and stability. But even as it has attempted this, the company has been engaging in business activities that run contradictory to the founding principles that had brought the fame and success the company once enjoyed.

As the company's productivity steadily declined in the second half of the 1990s, Merck became more susceptible to attacks from shareholders accusing the company of being inefficient in the allocation of resources and demanding the distribution of excess cash it had accrued over time. Such shareholder attacks slowly undermined the organization's founding principles: Merck began to pursue innovation for the sake of *profit* – that is, to maximize shareholder value – at the expense of the company's efficiency and its products' affordability. This in turn undermined the welfare of the *people* whose lives depended on them.

The patient-oriented drug-innovation strategy with a long-term view of value creation for stakeholders that prevailed at Merck until the end of 1980s was slowly replaced by a short-term business strategy mainly geared toward extracting value in the name of maximizing shareholder value (MSV). The acquisition of Medco Health Solutions, Inc. (MEDCO) –one of the leading Pharmacy Benefits Management (PBM) in the US-- marked the beginning of a new era at Merck in which the marketers captured strategic control of organizational resources from the scientists, the ruling class within the organization since the 1940s.

Research operations within Merck, already in a weakened state, were permanently paralyzed by the fatal crash of Vioxx, the company's new cox-2 inhibitor envisioned upon its launch in the late 1990s as a “super-aspirin” that would rule the multi-billion-dollar rheumatoid arthritis market. In addition to claiming the lives of many patients who took it as a supposedly “safe” alternative to the nonsteroidal anti-inflammatory drugs (NSAIDs) commonly used at the time, Vioxx brought the company itself to the brink of death in the early 2000s. Merck was obliged to wage a prolonged legal battle following allegations that

it had knowingly misrepresented as “safe” a drug that turned out to induce heart attacks in patients with cardiovascular problems.

The leadership at Merck was alleged to have ignored clinical evidence provided by the biomedical experts within and outside of the company that had pointed to a potential safety issue with the drug. Locked in fierce competition for a highly profitable market with Pfizer, which was also pursuing a cox-2-inhibiting compound, Merck’s leadership had crossed ethical boundaries, damaging the reputation that the company had maintained throughout the long period when patient safety had been its primary concern. Prior to Vioxx, no Merck product had ever been recalled by the FDA, and the company was recognized as the industry’s most conservative when it came to drug safety.

Financial troubles stemming from the acquisition of MEDCO and the Vioxx scandal profoundly affected the company’s strategic control and organizational integration. Vagelos’s replacement as Merck CEO, Raymond V. Gilmartin, failed to overcome the leadership vacuum created by the departure of his predecessor, so that an already bleeding research organization continued to lose scientific talent to biotechnology start-ups. These fledgling companies not only promised an exciting new career offering an opportunity to contribute to human welfare, but also held out the prospect that riches might flow from the stock options in which employees were paid. Many Merck scientists had felt betrayed by their employer when the news of the mishandling of the highly toxic Vioxx became public, and they had begun to leave the organization simply because the company was no longer perceived as an exemplar of innovation in the pharmaceutical field and a standard bearer for business ethics.

Having failed to produce greater financial returns, the company’s ailing in-house research operations were cut back in favor of new organizational capabilities aimed at looking beyond Merck’s labs in seeking and acquiring new-product opportunities. This new vision for drug innovation, which shifted company focus from intramural R&D efforts to sourcing innovative new products externally, largely through merger and acquisition (M&A) activities, has persisted. The strategy based on it is in accord with the shareholder-primacy perspective in allowing the company to avoid the risks associated with the drug-innovation process and thereby to maximize capital efficiency. Having successfully defeated government attempts to control drug prices in the past, Merck and other drug producers managed, by hiking the market prices of their drugs, to offset the cost increase associated with paying a premium price to acquire novel therapies already fast approaching the market from the smaller biotechnology start-ups that had developed them.

This innovation strategy was already established as an industry trend when Merck finally joined the cohort of big pharma companies purchasing novel therapies from others rather than developing them. As a common side effect of this innovation model’s being widely embraced by pharmaceutical companies, the market prices of biopharmaceutical products, as well as the labor turnover within the biopharmaceutical industry, have been on the rise

since 1990s. Since the 1990s the US pharmaceutical companies have drastically shifted their focus from developing innovative drug therapies to enhance the quality of life for people who suffer from diseases, to enhance the scale of financial “returns” for financial investors in speculative markets who demand greater shareholders value. Such a shift in focus can be attributed to the finalization of the pharmaceutical business model that is explained further in chapter two of this thesis.

During the period of financialization the leading US BP companies vertical disintegrated their operations in drug research and development and begun to outsource large portions of the activities on the research-side, particularly the activities involving basic research and early discovery, in favor of the activities on the development-side. As discussed earlier in chapters two and four, the downsizing of R&D within large US BP is directly linked to the rise of the product-less IPOs (PLIPOs). Those highly specialized research-intensive PLIPOs often possess highly productive capabilities to discover and develop new drug therapies, but they lack the productive resources, mostly financial, necessary for bringing those such innovative therapies to market.

Trading their innovative capabilities for cash, resource-constrained PLIPOs essentially enable the cash-rich large pharmaceutical not only to downsize their investments on R&D and free more cash from funding current operations, but also to externalize the risk concerning drug innovation and ensure a profitable growth in the future. For this reason, core competencies of the large US pharmaceutical companies have become less distinguishable, and the large BP companies have begun to rely for competitive advantage more on sales and marketing skills and less on innovative capabilities. A prominent player in the fast-changing institutional environment of the biopharmaceutical industry, Merck has been susceptible to changes that have diminished its own capacity for innovation.

How did Merck achieve the exalted market position it had enjoyed prior to adopting a new corporate-governance ideology oriented toward maximizing shareholder value? What does Merck’s changing business model mean for the future of R&D in the biopharmaceutical industry? For the role of the state in supporting, and even initiating, investment in new technologies? And for the relation between corporate resource-allocation decisions and the performance of the economy in which the company grew and in which, as a corporate entity, it still resides?

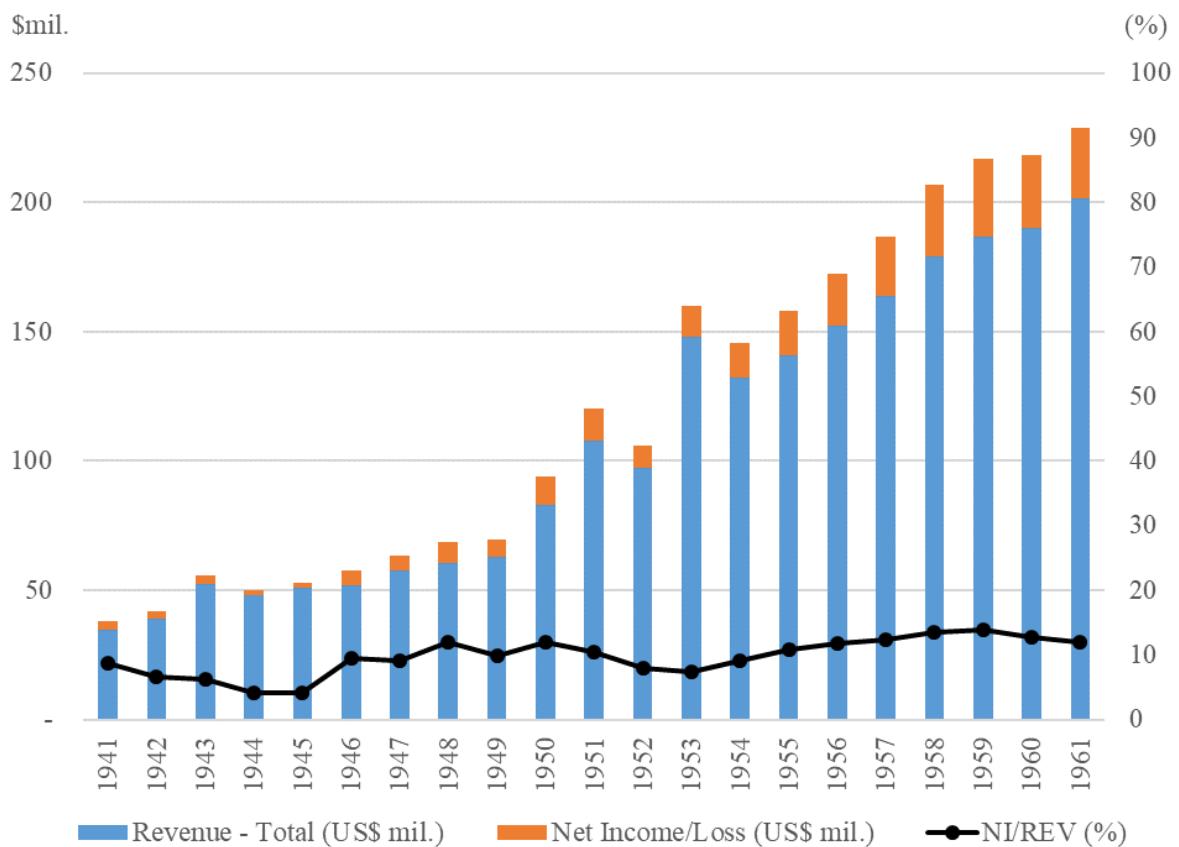
These issues will be explored through a systematic analysis of Merck & Co.’s economic performance in light of its changing business model from the perspective of the “Theory of Innovative Enterprise”. This case study will elucidate how business-model changes affected the “social conditions of innovation” – *strategic control (SC), organizational integration (OI), and financial commitment (FC)* - within an innovative business enterprise and ultimately contributed to a decline in the company’s economic performance. A number of the questions to be raised can be answered only by analyzing how strategic control,

organizational integration, and financial commitment interact to determine the firm's economic performance. Among these questions are:

- How important was George W. Merck as a strategic decision-maker, and how important to his company's success were the new roles he assigned to business and to research? How did strategic decision-making vary during the next three-decade period, when George W. Merck was absent from the company but his vision remained? How was strategic decision-making different during the 10 years when Vagelos was the head of research and during his next 10 years as the company's CEO and chairman of the board? And how is it different now under CEO Kenneth Frazier, whom Vagelos both hired and mentored during his early career at Merck?
- What types of organizational capabilities enabled Merck to generate innovative products, first in the period following the Second World War and then, more important, at a time when the company began to dominate the US drug market in the 1980s? What key scientific progress did Merck achieve within the company, and what did it acquire from outside? What was the role of organizational integration in Merck's learning processes, and how, in the post-Vagelos era, might this condition of innovative enterprise be breaking down?
- What, during different phases in its history, were the sources of finance that enabled Merck to grow? Given the growing shareholder focus on Merck's stock-price performance in the last three decades, what has been the role of the stock market in financing the company's growth? What are the implications for Merck's future of its decision to dole out as much as \$139 billion to shareholders since the company began to accelerate the repurchases of its own stocks from 1995 to 2016? The rapid increase of stock repurchases marks an important turning point in the company history. From 1995 to 2016 Merck distributed nearly 9 percent more than the total net income the company generated in this period. More importantly, Merck's shareholder payout was nearly 30 percent more than how much the company had spent on R&D in total from 1995 to 2016.

Merck's transition from a chemical manufacturer to a prominent company in the biopharmaceutical industry was achieved through its development of a series of antibiotics and steroid drugs in the 1950s. As Figure 12 shows, both Merck's revenues and profitability increase with the launch of the company's own branded ethical drugs in the period following the end of the Second World War. As Figure 12 shows in addition, Merck nearly tripled its annual revenues after the acquisition of Sharp & Dohme (S&D) in 1953. Philadelphia-based S&D was more advanced in biopharmaceutical production and marketing skills, of which Merck was in dire need if it was to leverage its productive research operations and profit from newly launched innovative products in the competitive pharmaceutical market.

Figure 12: Merck & Co. Inc. sales and net income, 1941-1961



Source: Own illustration based on data from company annual reports

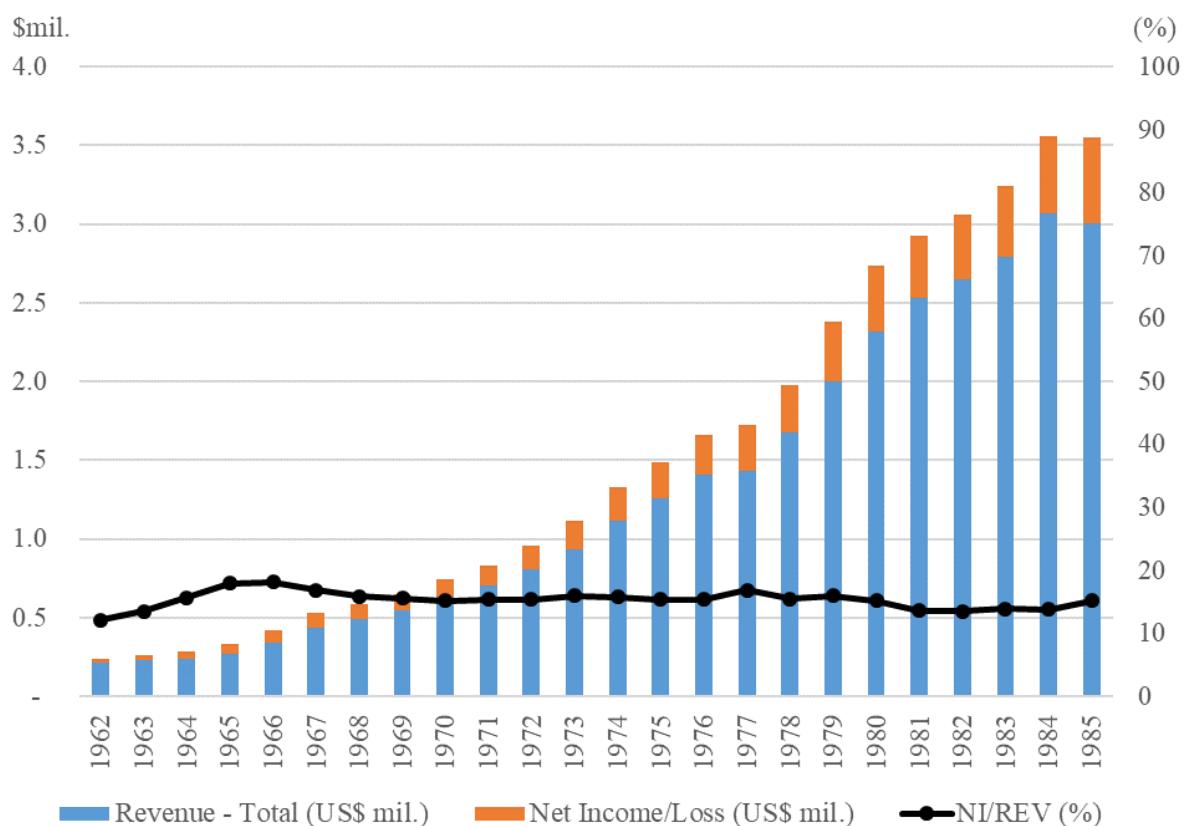
The pharmaceutical companies saw such regulation as likely to increase the complexity and risk associated with the development of new drugs, thereby inhibiting innovation and destroying perspectives for growth. Concerned by recent developments, the management at Merck decided to pursue alternative paths to growth by diversifying the company's product portfolio into markets requiring lower research intensity.

Figure 13 illustrates the revenue growth achieved by Merck's acquisition spree of the late 1960s and the early 1970s. In 1973 the company's annual sales had hit the \$1 billion mark for the first time, and they went on to grow by more than three times in the next 10-year period. Merck's sales and net income from 1976 to 1986 make clear the success in improving R&D productivity achieved under Vagelos, but also the fact that the company had not yet embarked on the stratospheric growth that was to come. Merck's domination of the biopharmaceutical industry in the last decade of the 20th century can be attributed to a series of innovative new drugs, particularly in the area of cardiovascular diseases, introduced in late 1980s and the early 1990s.

After hiring Vagelos as the head of basic research in 1975, the company began to increase its investment in R&D. In the following decade, it nearly doubled its R&D spending, from \$575 million in 1976 to \$1.1 billion in 1986, when it began the launch of a series of new-

generation cholesterol and blood-pressure medications. Vagelos, having become president of Merck Research Laboratories (MRL) in 1976, was promoted to executive vice president in 1985, by which time Merck had managed to double its revenues to \$3.6 billion from nearly \$1.6 billion in 1976. This growth had been driven mainly by incremental improvements that extended the life cycles of the company's existing products. During Vagelos's tenure as CEO and board chairman between 1986 and 1994, Merck's revenue grew nearly threefold, from \$3.6 billion at the end of 1985 to \$10.5 billion at the end of 1993. Overall, during his 18-year tenure as head of research and CEO, Merck's annual revenues increased sevenfold, from \$1.5 billion to \$10.5 billion.

Figure 13: Merck & Co. Inc. sales and net income, 1962-1985



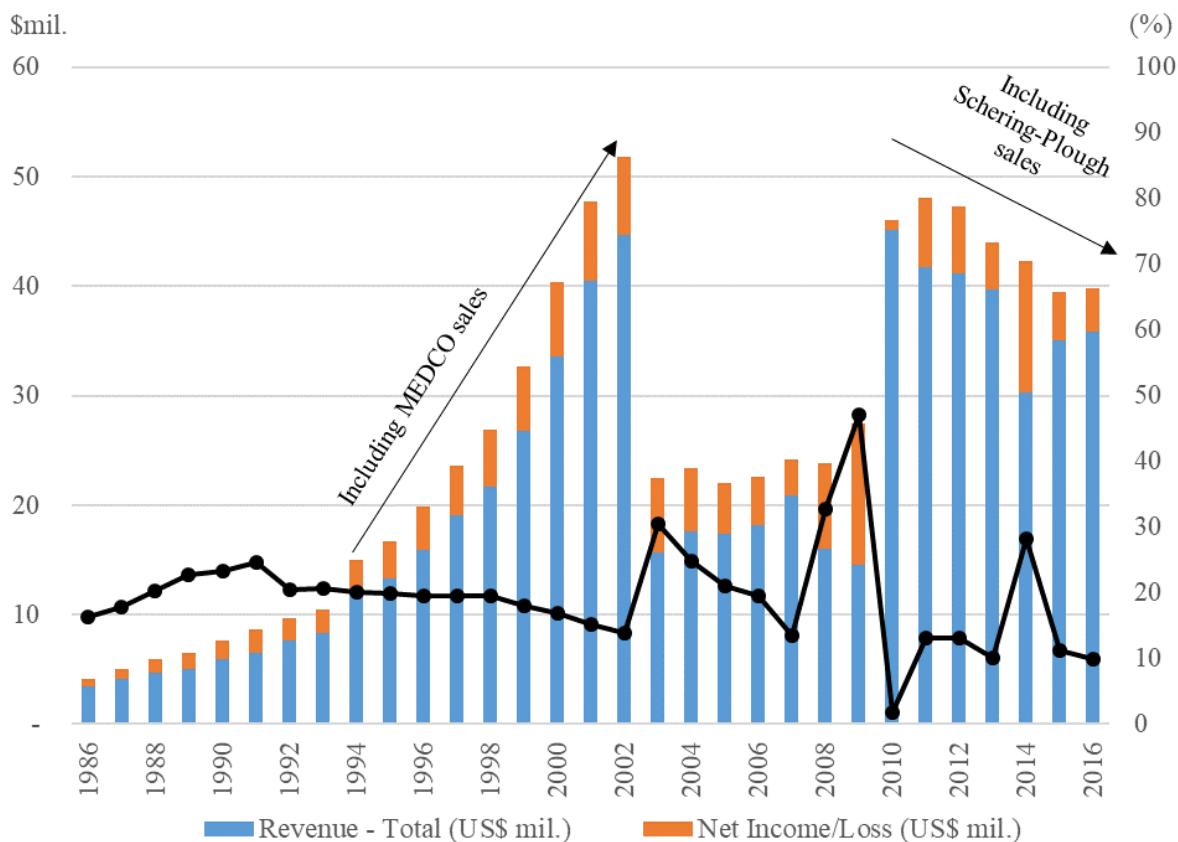
Source: Own illustration based on data from company annual reports

Figure 14 shows that Merck's annual revenues grew only 1.8 times between 1994, the year Gilmartin succeeded Vagelos as CEO, and 2005, the year Richard T. Clark in turn succeeded Gilmartin, who had decided to take retirement earlier than previously planned. In his first year, Clark decided to acquire Schering-Plough in an attempt to rejuvenate Merck's ailing product portfolio. The Vagelos-era products still accounted for nearly half of Merck's pharmaceutical-product sales in 2009, and the company's three blockbuster drugs were to reach patent cliffs in the early 2010s.

It is also evident from Figure 14 that the company's level of profitability declined after the acquisition of MEDCO, from nearly 20.6 percent in 1993 to 13.8 percent in 2002, when

Merck decided to spin MEDCO off. Profitability jumped to 30.4 percent in 2003, but following the withdrawal of Vioxx the company's profit margin declined, falling to the 13.5 percent level in 2007, the year it agreed to pay \$4.9 billion to settle the legal cases arising from the Vioxx scandal. The company's profit margin then jumped again, to 32.7 percent in 2008 and 47 percent in 2009.¹³

Figure 14: Merck & Co. Inc. sales and net income, 1986-2016



Source: Own illustration based on data from company annual reports

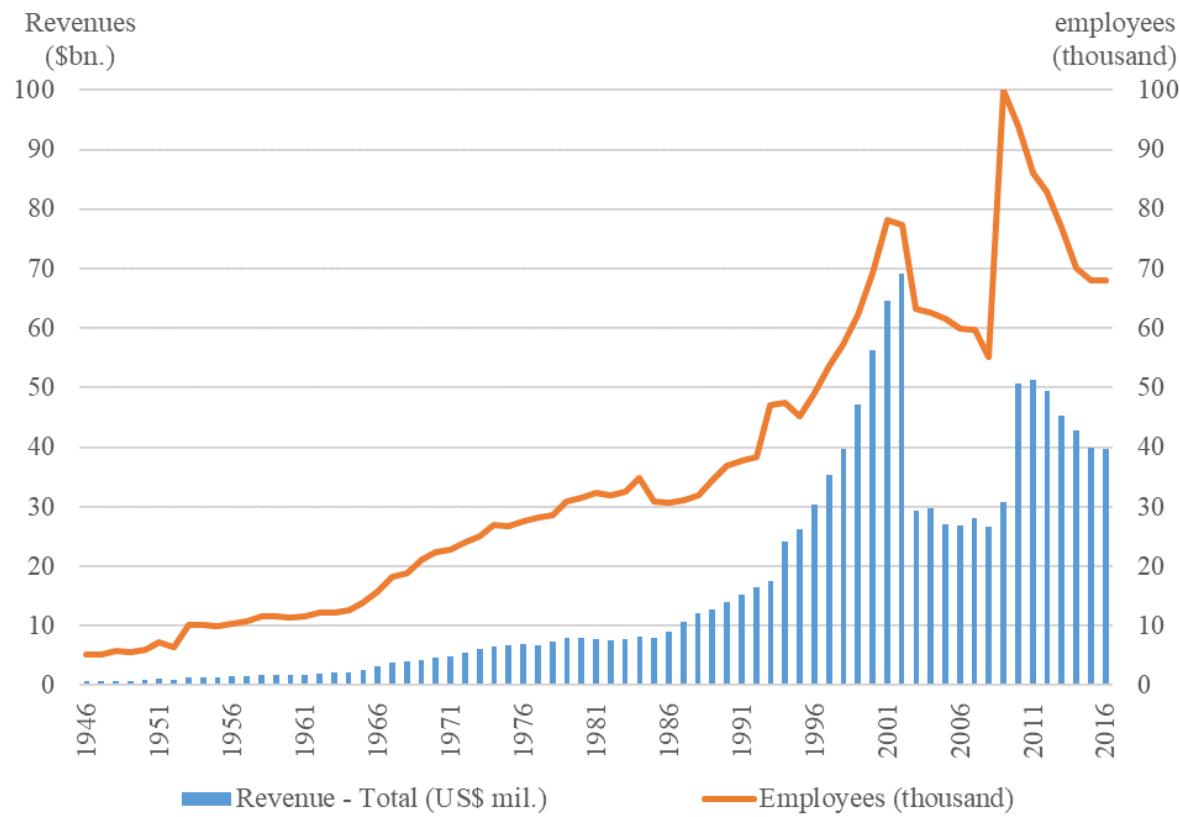
As Figure 14 further illustrates, Merck recorded its highest level of sales in 2011, although this excludes a revenue peak in 2002, when sales from MEDCO went toward the total. Its 1991 profits were its largest recorded, with the exception of those booked in 2003, 2008, 2009, and 2014, which included net gains from the sale of assets or from savings yielded by corporate restructuring programs (namely, the layoffs). While Merck's sales increased by 4.6 times between 1991 and 2016, however, its profits declined by nearly 60 percent.

As shown in Figure 15, employment at Merck increased by 22.6 percent upon the 1993 acquisition of MEDCO. In the following 10-year period, which ended with MEDCO's

¹³ The surge in net income Merck reported in 2009 occurred as a result of the 2008 Corporate Restructuring Program. Through such a program Merck had reduced its workforce by 12.6 percent. After selling its equity in the joint-venture with AstraZeneca \$4.8 billion cash Merck generated had also contributed into the surge in net income the company reported in 2009.

spin-off, the size of Merck's global workforce nearly doubled, from 384,000 employees in 1992 to 773,000 in 2002. Due to declining R&D productivity and rising legal costs associated with the Vioxx case, Merck, wishing to improve its fast-declining profit margin (see Figure 14), initiated various corporate-restructuring programs that reduced its global workforce by 12.6 percent between 2003 and 2008.

Figure 15: Merck & Co. Inc. revenues and employees, 1946 -2016 (in 2016 dollars)



Source: Own illustration based on data from company annual reports

Meanwhile, Merck engaged in efforts to improve capital efficiency through liquidating assets and decreasing spending on CAPEX and R&D, as well as by consolidating global operations to reduce employment. At the same time, the company was increasing its stock repurchases under the \$10 billion buyback program it had announced in June 2002. This stock-repurchase program was completed prior to Merck's 2009 acquisition of Schering-Plough.

As shown in Figure 15, employment nearly doubled, from 55,200 in 2008 to 100,000 after the 2009 acquisition of Schering-Plough. In the five-year period following the acquisition, the workforce in the combined entity was reduced by 32 percent; the company employed 68,000 in 2015, a figure that remained unchanged in 2016. Even as declines in revenues, net income, and employment, along with that in R&D spending, continued in the post-acquisition period, the company's stock repurchases and dividend payments increased significantly. Nearly \$67 billion in cash was distributed to shareholders through stock

buybacks and dividend payments between 2009 and 2016, equivalent to 1.3 times the total net income accrued and 1.03 times the money spent on R&D during the period.

Since the turn of the 21st century the US biopharmaceutical industry in general has been facing a productivity crisis; this crisis has, however, been particularly severe at Merck. Since its acquisition of Schering-Plough in 2009 Merck's revenues, profitability, R&D spending, employment level, and various other performance indicators have shown a decline (see Figure 14 & 15). But, despite the gloomy performance trend, Merck has maintained a steady stream of dividend payments and has increased its buybacks.

The year 2005 had been an important turning point in the company's history. After succeeding Gilmartin, who generally avoided any major acquisitions to boost the company product portfolio and future clinical pipeline, Clark, as well as Frazier after succeeding Clark, pursued a series of acquisitions. Since 2005 Merck has generated nearly \$427 billion in revenues, of which 17 percent represent net income. During the period from 2006 to 2011 Merck spent nearly 20 percent of revenues on R&D and an additional 16 percent on the acquisition of pharmaceutical firms of various sizes, locations, and research-focus areas¹⁴.

Of the early acquisitions, mainly companies with platform technologies that had market-disruptive potential, most failed to generate returns.¹⁵ At the time Merck acquired Schering-Plough, it was one of the last remaining independent, mid-size pharmaceutical companies and had an extensive product portfolio and clinical pipeline, both in pharmaceuticals and biologics. Merck's later acquisitions, in contrast, included companies with extensive drug-development programs in fields in which Merck had possessed competence historically, such as antibiotics and infectious diseases, or in fields that Merck had recently decided to enter, such as immunology and oncology.

¹⁴ In addition to many smaller ones Merck acquired Abmaxis for \$80 million in 2006; Sirna Therapeutics for \$1.133 billion in 2006; NovaCardia for \$366 million in 2006; Schering-Plough for \$51.4 billion in 2009; Inspire Pharmaceuticals for nearly \$500 million in 2011; Idenix for \$3.849 billion in 2014; Oncoethix SA for \$375 million in 2015; Cubist Pharmaceuticals for \$9.091 billion in 2016; cCAM for \$605 million in 2016; Afferent Pharmaceuticals for \$1.260 billion in 2016; and IOmet Pharma for \$400 million in 2016.

¹⁵ For instance, Rolofylline (KW-7418), an experimental diuretic acquired through NovaCardia in 2007 for \$366.4 million failed to show any clinical significance when tested against a placebo in 2009. Merck took a \$325.1 million writedown on the program in 2009. Merck's R&D spending increased nearly 22 percent (\$1.04 billion) from previous years and Rolofylline-related expenses accounted for 34 percent of Merck's increase in annual R&D expenses from 2008 to 2009. The remaining increase in R&D spending came from upfront payments for research collaboration agreements Merck had signed with other companies. Merck had also acquired California-based Sirna Therapeutics, among the pioneers in the field of Ribonucleic Acid interference (RNAi) technology, for \$1.1 billion in 2006. Having failed to make progress in the field, Merck decided to sell Sirna to AnalyM, another biotechnology company that was a leader in RNAi technology, in exchange for cash, stocks, future milestone payments, and royalties based on products potentially to be developed through the siRNA drug-development platform. Roche is among the collaborators of Massachusetts-based AnalyM, co-founded by the founders of Biogen.

For 14 major acquisitions between 2005 and 2016, including that of Schering-Plough, Merck spent nearly \$70 billion in addition to the \$83.3 billion it spent on R&D. The payments Merck made under research-collaboration agreements with external parties often constituted its increase in R&D spending between 2005 and 2010. While Merck accelerated its R&D investment scheme as a measure intended to overcome its productivity crisis, the company also continued making dividend payments to stockholders at a rate that held steady until 2009, then increased after the Schering-Plough acquisition was completed in 2010. Except in 2009, when the company completed the largest acquisition in its history, Merck increased the purchase of its own stock every year between 2005 and 2016, with buybacks over the period totaling nearly \$34.1 billion. Combining buybacks with dividend payments, Merck's total payout to shareholders reached \$86.5 billion in the same period. The company's stock price followed an upward trend after Merck announced the acquisition of Schering-Plough on March 9, 2009, even though Merck's revenues, net income, R&D spending, and global workforce were declining steadily.

How can the rise and rapid descent of Merck & Co. be explained? One might be tempted to argue that it was the work of business leader like George W. Merck and of great research leaders such as Randolph T. Major, Max Tishler, and Roy Vagelos, all of whom had remarkable vision, talent, and drive, and, in addition, the fact that they happened to be in the right places at the right times. This "great man" theory of Merck's success seems all the more plausible not only because Merck, Major, Tishler, and Vagelos were all extraordinary, but also because, in retrospect, the company's innovative productivity suffered immensely in the mid-1960s through the mid-1970s as well as since the mid-1990s after the company had parted ways with those iconic research and business leaders. The three sections that form the body of this case study analyze the evolution of strategic control, organizational integration, and financial commitment, respectively, as conditions for innovative enterprise that ultimately determined the success and failure of Merck. The following sections examine the ways in which the social conditions of innovation have changed over time at Merck & Co. as the company has transitioned from a value-creating organization for stakeholders to a value-extracting vehicle for shareholders.

4.1 Strategic Control

As [Mort] Feinberg¹⁶ says, "*There is a big difference in the energy of different organizations.*" At Intel we found the energy disciplined and tense. At Apple it was buoyant youthful enthusiasm. At General Mills, Inc., there was a dynamic exuberance. At Merck it felt like the controlled power of a well-oiled machine..."

(Harmon and Jacobs, 1985, p. 8)

¹⁶ Mort Feinberg was a professor of industrial psychology at New York University at the time when Harmon and Jacobs published "The Vital Difference: Unleashing the Powers of Sustained Corporate Success" in 1985.

Merck & Co. was initially set up as the US subsidiary of Emanuel Merck of Darmstadt (hereafter EMD) based in Germany. The parent company had been transformed from a local apothecary, the *Engel-Apotheke* (the Angel Pharmacy), acquired by Friedrich Jacob Merck in Darmstadt, Germany, in 1668, to a major producer of fine chemicals and finished medicinal products, owing its success to the innovation efforts of Emanuel Merck, who had taken over the family business in 1816 (Gortler, 2000). Prior to establishing a new sales office, EMD had worked with a distributor to market the company's principal product, morphine, and other fine and bulk industrial chemicals in the fast-growing US market. However, due to increasing copyright-infringement concerns stemming from the unauthorized use of the Merck brand in the US in the late-1880s, EMD had decided to assign a German manager, Theodore Weicker, to set up the company's first US sales office in 1887 (Sturchio & Galambos, 2011). Having vested too much power in the hands of a manager who wasn't a member of the Merck family, Darmstadt had decided sent 24-year-old Georg Merck, grandson of Heinrich Emmanuel Merck, "as a constraint" of Weicker growing power in the fast growing sales office on New York's Wall Street (*ibid*).

Weicker and Merck later transformed EMD's New York sales office into a US subsidiary in 1891 as part of Darmstadt's strategy to further penetrate the growing US market. In 1900, Merck and Weicker acquired the company's future research and production base, a 120-acre plant site in Rahway, New Jersey; the company's modest production operations began at the site in 1903. Soon after completing his mission, Weicker decided to leave the company in 1904, who had later acquired Squibb Corporation from its founder's two sons in 1905 (Sturchio & Galambos, 2011). In the following decades Squibb and Merck would become important players in the US biopharmaceutical industry and fierce competitors of each other.

Having changed his German-sounding name, Georg, to a more Anglo-American version, in 1892 (Rosen, 2017, p. 159), George adopted his new home in New York fast since he had first arrived in the US. In the decade following his arrival in the US, George Merck had gained all the managerial power and ultimately become the junior partner after acquiring Weicker's shares and re-organizing EMD's US subsidiary as Merck & Co., whom George Merck had held a 20 percent stake in the new company while Darmstadt held the remaining (Sturchio & Galambos, 2011; Rosen 2017). As the company began to manufacture new products such as the key ingredients, bismuth, of a new antidiarrheal, Pepto-Bismol, as well as star-based chemicals such as carbolic acid, antiseptic, etc., Merck & Co. decided to move major manufacturing and auxiliary operations from New York to the previously acquired site in Rahway New Jersey (Sturchio & Galambos, 2011).

In the two decades following the establishment of EMD's auxiliary sales department for the US market in 1887, the company's annual sales grew substantially, from less than one-half million dollars in the first year of operation in 1887 to \$2.3 million in 1906. A New York-based competitor -- Charles Pfizer & Co., which had been in the chemicals market, particularly in the citric acids, for almost five decades before Merck had first arrived in

1887 -- had generated nearly \$3.4 million revenues in the same year in 1906. By 1913, Merck & Co. annual sales had grown to \$4 million, and by 1917, when the US became actively involved in the First World War, the company's annual sales had grown to the \$8 million level (Sturchio & Galambos, 2011; Sturchio, 1991).

4.1.1 Transformation of German Merck into an “Americanized” enterprise

By his death in 1926 George Merck had played the key role in transforming the company from EMD's small sales office in New York to one of the largest 100 percent US-owned producers and distributors of fine chemicals based in Rahway, New Jersey (Gortler, 2000). This transformation had become necessary during WWI, and especially once the US entered the war in 1917, soon after which the federal government required all US assets of German companies to be sequestered. In April 1918, the Office of the Alien Property Custodian seized the 80 percent of Merck & Co.'s shares that belonged to parent company in Darmstadt, Germany. George Merck decided to hand over his 20 percent stake in the company to a new Trust established by the US government in exchange for maintaining his position as the company's president. In addition to his stakes in Merck & Co. George Merck had lost his 19 percent stake in EMD after the German parent company decided to retaliate against George Merck having turned its 80 percent stake in the former US subsidiary Merck & Co to the US authorities (Godley & Hughes, 2014).

Despite returning all his equity stake in Merck & Co. to the government in order to retain managerial control in the company, a series of reports by auditors commissioned by the Alien Property Custodian (APC), Francis P. Garvan, portrayed George Merck for being secretive and suspicious to the extent that he was accused of concealing some assets, aside from the company's stock that were already seized, which were deemed to be the property of the US government (Godley & Hughes, 2014, p. 11). But despite the APC's mistrust, George Merck was serving as president of Merck & Co., EMD's US subsidiary, and he was seeking ways to regain control of the company. His opportunity arrived with APC's decision to sell the company through a public auction.

The first stock buyback at Merck & Co.!

At an auction on May 9, 1919, 80 percent of EMD's sequestered assets were sold for \$3.75 million to McKenna Corporation, a company that had been incorporated by George F. Merck with the support of Goldman Sachs and Lehman Brothers with the purpose of gathering the funding to bid for, and to reacquire control of, Merck & Co. (Gortler, 2000). Although he had become a US citizen in 1902, George F. Merck was still deemed too “German” and suspiciously loyal to his German roots such that the sale of Merck & Co. to its former owner couldn't have been in compliance with the objectives of The Trading with the Enemy Act of 1917, which mandated the sale of assets to American citizens whose loyalty to the country was proven.

Based on further investigation of this transaction by the government, the Secret Service recommended that the company's operations be monitored closely after its reacquisition by its German-American former owner. Following this recommendation, the Advisory Sales Committee of the APC obliged George Merck to accept the oversight of a trust that would monitor the activities of the new management to ensure that, as the company progressed along the path to becoming a fully "Americanized" business, no relations with its former parent company would be re-established (Godley & Hughes, 2014).

Because this condition had been attached to the sales agreement, the company's reacquisition solved only a small part of the issue that both the American and German clans of the Merck family were to face in 1919 and 1920. The US government's action had put the parent company and its US subsidiary alike in a difficult situation, as the sale in the US market of high-quality chemical products was banned to EMD even as Merck & Co.'s legal ties with its supplier were cut off. This period marks an important turning point in the story of the American Merck: What eventually became arguably the world's greatest pharmaceutical manufacturer would be built in a very unfriendly political and economic environment from a bulk industrial chemicals distributor recently deprived of its German supplier (Godley & Hughes, 2014).

Between the time he regained control of the company in 1919 until his death in 1926, George Merck managed to resolve the legal issues arising from the separation of the Americanized Merck and its mother ship in Germany, including the rights to the name "Merck" in North America and other markets¹⁷ and the financial loss that had resulted from sequestration¹⁸. And he had achieved this without raising a red flag with the authorities, as it was during a 10-year period of oversight by the trust that the new, American company was required to refrain from building ties with its former parent (Wilkins, 2009).

Merger with Powers-Weightman-Rosengarten in 1927

Having acquired a manufacturing plant in St. Louis and built a new one in Rahway, the American Merck of George Merck, now fully independent of the German Merck of Emanuel Merck, had become one of "Big Three" fine-chemicals manufacturers in the US by the time of George Merck's death on October 21, 1926 (Stuchio, 1991; Gortler, 2000). Luck would play a small part in George Merck's arrival at this destination: It was a legal decision in a case to which Merck & Co. was not a party that had opened the door to its

¹⁷ Today the American Merck operates in North America under the corporate brand "Merck & Co." and elsewhere as "Merck Sharp and Dohme" (MSD), while the German Merck operates in North America as "Emanuel Merck of Darmstadt Serono" ("E. Merck of Darmstadt Serono" or "EMD Serono") and is recognized as "Merck" elsewhere.

¹⁸ According to Godley & Hughes (2014) the enforcement oversight hadn't cut the ties between the American and the German Merck

becoming one of the Big Three. This it did by merging with one of that elite group¹⁹, all of whose members were ahead of Merck in sales (Gortler, 2000).

The cost of the company's reacquisition from the APC was quickly dwarfed by the further investments in new production plants that were needed after its ties to its former parent company in Germany had been cut. George Merck had already leveraged corporate assets significantly, since the acquisition was financed mostly through preferred shares sold previously on the condition that the company would buy them back at a later time, which had now passed. But then, when the descendants of the family that founded Powers-Weightman-Rosengarten (PWR) decided to enjoy a fine life in nature, as opposed to extracting its resources and using them to produce fine chemicals, they approached George Merck to take over their business (Gortler, 2000).

The merger allowed Merck not only to increase its market share rapidly but also to access the large stock of liquid assets PWR possessed at the time. Luck had entered into it when the Rosengarten brothers' appeal to merge with Pfizer was declined by the US attorney general, who argued that the merger would violate anti-trust regulations because the market share of the combined entity would give it control of the market (Adolph G. Rosengarten Jr. cited in Gortler 2000). As the only viable option remaining, PWR had decided to merge with Merck Corporation²⁰ on June 30, 1927, to form Merck & Co. (Gortler, 2000)

After transferring all the assets of PWR, along with large sum of cash borrowed from the Rosengarten brothers, the combined new entity, Merck & Co., was worth nearly \$9 million in assets; in 1928, it generated nearly \$13 million sales revenues. After servicing the debt from the preferred shares that were past due, the new Merck & Co. became a highly solvent entity. Although the merger resolved Merck's financial troubles and quickly boosted its market, it also made the four Rosengarten brothers the new entity's largest shareholder group.

Because the Rosengarten brothers had no interest in running the company's operations, the deal had come with the additional benefit to Merck that the latter would retain the new entity's strategic control. In exchange for assigning the new organization's day-to-day operations to George W. Merck as president, the Rosengarten brothers had taken three seats on the board of directors, one of them that of the chairman (Gotler, 2000). The merger increased Merck's scale and scope by giving it a wider product portfolio – with, however, minimal overlapping of product groups -- and greater market share to capture. With combined sales at over \$13 million, retained earnings could be reinvested heavily in building a competitive, knowledge-driven organization suited to exploiting opportunities in

¹⁹ There were four major producers in the early-1900s, all rooted in German/Swiss ancestry: Pfizer, Mallinckrodt, Powers-Weightman-Rosengarten, and Merck & Co.

²⁰ Prior to the merger in 1927 [old] Merck & Co. had changed its name to Merck Corporation.

[New] Merck & Co. was formed as the combined new entity inheriting the assets of [old] Merck & Co. and Powers-Weightman-Rosengarten after the two companies merged in 1927.

the ethical-drug business as well as to manufacturing bulk industrial or fine chemical intermediates.

4.1.2 Transformation into an innovative enterprise (building core competence)

When, in 1925, his ailing father, George Friedrich Merck, could no longer serve as president of Merck & Co., prior to the merger with PWR in 1927, George W. Merck had taken over the duties of president and brought in his brother-in-law, George Walbridge Perkins, Jr.²¹, as vice president. Perkins had played a critical role during the years following the acquisition of the company from the Alien Property Custodian in maintaining the relationship with the trust that the custodian had appointed. According to Adolph Rosengarten, Jr., the role Perkins played in the building of Merck & Co. in the interwar period has generally gone unnoticed outside the company (Gortler, 2000).

Aspiring to build a competitive drug business, at the beginning of the 1930s Merck and Perkins hired a world-renowned pharmacologist at the University of Pennsylvania, Dr. Alfred Newton Richards, as a consultant to begin recruiting the right talent for a research organization that would be comparable to that of an academic institution. Initial R&D efforts had begun in 1916, but they had in fact been modest development efforts geared toward making incremental improvements to existing manufacturing processes. The company had taken this action due to the fast-approaching threat of losing its German supplier, which, if it came to pass, would require the firm to build independent product-development and manufacturing capabilities.

According to Godley and Hughes (2014), this is the reason George Merck was eager to protect ties with the German ex-parent even under the watchful eyes of the trust, which, in the early 1920s, was ready to take the company away from him if he were caught. Seeking a settlement on the loss of the subsidiary, Carl Merck, representing the Merck family in Darmstadt, had travelled to the US and met with George W. Merck in 1921. Although the objective of this meeting had been to discuss the terms of a settlement, George Merck's interest had been establishing a new form of partnership between Merck & Co. and EMD.

Given the tariffs imposed on certain products imported from Germany in the post-WWI period, the prior distribution arrangements had made the products acquired from Darmstadt less competitive in the growing US chemicals market. Because products from Darmstadt had made up a significant portion of Merck's annual sales, wouldn't have been easy to do. Nor would it have been feasible to produce these complex products without acquiring the

²¹ Perkins was the son of former insurance executive, leader of the Progressive Movement, and top aide to J.P. Morgan George W. Perkins, Sr. The elder Perkins had been one of the most renowned advocates of large business establishments' fostering cooperation among businesses as opposed to competition, in the aim of achieving greater industrial efficiency (Garraty, 1957). Through his father's political network, Perkins, Jr., helped the Merck family build its company's image as a truly American enterprise and provided it with strong ties to the influential political elite in the nation's capital.

know-how needed to obtain quality comparable to that achieved in the company's German plants. But EMD's executives were aware of the risks associated with sharing proprietary know-how on production processes and had been hopeful they would be able to explore the US market at some point in the period following the end of WWI without taking on an external partner.

As Merck's sales performance had continued to fall, mostly due to an increase in tariffs taking place at the time, Carl Merck had declined to reply to frequent partnership requests from George Merck and shown no genuine interest in formalizing a partnership agreement during the 1920s. The possibility of structuring the working relationship that had long been maintained informally was revisited by EMD in the early 1930s, when George W. Merck undertook an ambitious growth strategy following its 1927 acquisition of PWR.

The building of Merck Research Laboratories in the 1930s

Early innovation efforts at Merck had been meant to address the company's inability to develop and manufacture high-quality, novel chemicals. When Merck hired William Engel, the company's first research director, in 1918, R&D activities merely involved making incremental improvements to ensure a modest production efficiency. The company had no product-development strategy at the time. In the early years of the 20th century, the young George W. Merck had met and spoken with Thomas A. Edison while visiting his lab in suburban New Jersey as a friend of Edison's two sons. At a tender age, he had experienced changes in the world he lived in that were driven by the industrial research pioneered by his neighbor, Mr. Edison. In 1925, when Merck & Co.'s fate rested in his hands as its founder's only son, George W. Merck was already envisioning a company whose cultural attributes would to some degree resemble those of its German ancestor (Sturchio & Galambos, 2011).

In retrospect, George W.'s strong devotion to advancement in science and technology appears to embody the wisdom offered him years before by Edison, who once told him, "You may not reach the goal you are seeking, but if you use common sense and keep your eyes open, you create your own opportunities for making worthwhile discoveries along the way" (New York Community Trust, n.d.). Such discoveries would be made only if one could "start a reasonable investigation of some kind, and make lots of experiments," Edison had advised.

When George W. took over the company's control in 1925, he was already predisposed to building an innovative enterprise driven by a team of top scientists performing research, both basic and applied, on a par with that of the world's top academic research centers. In the late 1920s, immediately following the death of his father, Merck had worked with Perkins to lay the foundations of an industrial research laboratory second to none. In 1930, Merck Research Laboratories (MRL) were established in Rahway, thanks in part to the

guidance and active lobbying efforts of Richards, the University of Pennsylvania pharmacologist they had hired as a consultant.

Before the opportunity presented by the Rosengarten family provided the resources to do so, Merck had been unable to make the necessary investment. From this perspective, the acquisition of PWR in 1927 was an important turning point on the company's path to world leadership in industrial-scale drug research, which it was to enjoy in the decades to come. The increasing market share and profits that followed the merger ultimately helped Merck to afford the acquisition of a knowledge base and to build core competence in developing and manufacturing high-quality medicinal products. The scientific talent available for industrial research in organic chemistry was in short supply in the 1930s. To attract scientists from major universities, George W. Merck hired Richards to consult with the company during an ambitious recruitment campaign. Having identified him as a talented young organic chemist at Princeton, Merck decided to hire Randolph T. Major to be the new leader of the organization's research efforts. It was the latter who in 1930 established the company's first Laboratory for Basic Research (LBR) and Laboratory for Applied Research (LAR). Spread over the two labs, the entire R&D team at Merck consisted of 16 chemists.

Pharmacologists at the time were both rare talents and critical to the drug-development process, since organic chemists weren't trained in identifying the efficacy of new chemical compounds. Pharmacologists were in short supply even in the academic institutions, so it was almost impossible to convince a pharmacologist to make the move to industry, something considered career suicide at the time. As it was a challenge to attract talented pharmacologists in the US, Richards recommended in 1932 that management hire one from Austria, Dr. Hans Molitor, as the head of the Merck Institute of Therapeutic Research (MITR).

Having recognized the progress Merck had achieved in capturing the US chemicals market as well as improving the efficiency of its production processes, Carl Merck of Darmstadt decided after paying another visit to Rahway in 1931 to initiate talks on structuring a partnership deal, which was to become known as the "Treaty Agreement." Darmstadt's primary objective was to place existing working relations with its up-and-coming former subsidiary at Rahway under the umbrella of an extensive formal agreement. Through this "treaty" Darmstadt attempted to explicitly define the scale and scope of the ongoing relationship, stipulating not only specific markets and products in which the two companies would either collaborate or compete, but also manufacturing methods and processes that the two companies would either share or reserve for themselves²² (Godley & Hughes, 2014). George W. Merck's interest in ratifying the treaty differed from that of Darmstadt. While the Germans envisioned a formal partnership beneficial to both sides, their

²² Godley & Hughes (2014) explain that at the time of signing the treaty in 1932 the list had consisted of approximately 250 products that the treaty had covered; and such number had gone up to 432 by 1939 (p. 20)

American counterpart was primarily looking to sustain the informal exchange of information that had improved the efficiency of its manufacturing processes at Rahway. It was because Darmstadt was threatened by the very informality of those exchanges that it had made a more extensive working relationship conditional on a formal structure anchored in a legal outline (Godlet & Hughes, 2014).

In the years following the signing of the Treaty, which took place in 1932, Merck & Co. designated Engel and Molitor as the agents for technology transfer, and the two made repeated visits to Darmstadt during the remainder of the decade to acquire the latest German methods of high-quality production. The American organization's research operations grew significantly and became scattered at a number of locations in and around Rahway. Having recognized the importance of coordinating the efforts of its fast-growing research team across different research units, functions, and scientific disciplines, in 1933 the company built a Central Research Laboratory in Rahway to consolidate all the research units (except MITR²³) (Gortler, 2000).

The increasing visibility of the research program at Rahway, facilitated by relations forged with leading academic scientists through consultancy contracts, propelled the recruitment campaign, which continued throughout the 1930s. Among the most notable recruits of the period were Karl Folkers in 1934 and Tishler in 1937. Folkers, a postdoc researcher at Yale, was hired to support the company's early product-development efforts, particularly in its vitamin and penicillin businesses. Tishler, at the time as a postdoctoral researcher at Harvard, was hired to oversee the product-development process from the discovery stage to production, with a special concentration on the development of steroid and penicillin products, as well as to find alternative routes to synthesizing vitamin B2 (riboflavin).

Under the leadership of Randolph T. Major, head of Merck research, Merck had quickly become a top competitor in the vitamin markets, which had been dominated by the German and Swiss producers earlier in the 1930s²⁴. Major championed organizational-learning efforts in the vitamin business, and it was under his supervision that the company developed Merck & Co.'s industrial manufacturing process for vitamin B1 (*thiamine*), which became a significant revenue-generating product soon after it was launched in 1937²⁵. By 1940 a significant portion of revenues were being generated by the sales of

²³ MITR had been established as an independent research entity because the laws in New Jersey at the time had prohibited industrial companies from conducting animal experiments (Gortler, 2000)

²⁴ See Achilladelis (1999, p. 65) and Sheehan (1982, p. 82): as was the case in penicillin a similar challenge was faced when manufacturing vitamins at industrial scale. If succeeded, the cost of producing synthetic vitamins could be significantly lower than the conventional fermentation methods. Major envisioned a future in vitamins market but a significant in-house capabilities had to be developed given that the experts at the time was in Europe, particularly in Germany, who were working with the competitors.

²⁵ In 1934, Robert R. Williams from Bell Lab had approached to Major for the support in to develop industrial manufacturing process. Merck had developed the process by 1935 and acquired the license in 1937 (Williams had already isolated and synthesized B1

vitamins, as the research groups overseen by Folkers and Tishler had developed vitamins B12, B6, B5, B2 within a few years after they were recruited (Gortler, 2000).

Starting with penicillin and continuing with antivirals, the role Major, Folkers, and Tishler played was critical in shaping innovation policies and strategies during their service at Merck, which in all three cases lasted nearly four decades. The research trio was also influential in building a research network within and outside the organization that was key to one of the most successful recruitment campaign of the time. Illustrating the impact of Merck's masterly recruiting on its innovation performance is the hiring of Lewis Sarett from Princeton in the early 1940s. Sarett had played a major role in the company's successful transition to steroid and fermentation chemistry, a new chapter in the field of chemistry that opened in the wake of WWII.

The rise of Merck & Co., 1940s-1960s (new learning in microbiology and virology)

A triad of entrepreneurship was emerging within Merck, as Major, Tishler and Folkers quickly settled into their leadership roles and their complementary skill sets created a unique managerial synergy. That synergy was central to the creation of an innovative organization highly motivated to explore opportunities in the fields of chemistry and biology, which were gaining importance in the 1940s and 1950. The triad had played a key role in identifying new market opportunities and in successfully coordinating the efforts of Merck's expanding research community to explore those opportunities.

The emergence of the triad's managerial synergy owed much to the fact that George W. Merck had established an institutional platform designed to provide the research community "the utmost freedom to follow leads promising scientific results no matter how unrelated to what one would call practical terms" and "the greatest possible latitude and scope in pursuing their investigations" (George W. Merck cited in New York Community Trust, n.d.). The leadership ensured that this institutional platform would evolve to fulfill the founding mission envisioned by George W. Merck:

We have faith that in this new laboratory science will be advanced, knowledge increased, and human life will win a great freedom from suffering and disease.

(George W. Merck cited in New York Community Trust, n.d.).

In sharp contrast to the treatment they had received during the First World War, in the 1930s George W. Merck and his company were welcomed into what Dwight Eisenhower was later to call the United States' "military-industrial complex," and they played a critical role in meeting the country's demand for medical products during WWII. As the wartime demand for antibacterial and anti-infectious medicines increased, Merck was presented with new opportunities to test the innovative capabilities of its fledgling research operations at Rahway.

Entering the fields of microbiology (bacteriology), fermentation chemistry, and mass-production of penicillin

It had been over a decade since 1928, when Sir Alexander Fleming first published about the discovery of penicillin. During the period leading up to WWII no significant progress had been made on penicillin, owing to the scientific challenges associated with the synthesis of this miraculous antibiotic that had been perceived as the silver bullet for fighting infectious diseases. Because the sulfa drugs of the past had had either limited or diminishing efficacy in the fight against bacterial infections, growing demand during the Second World War for a powerful antibiotic agent to use on the battlefield had moved research on penicillin to the top of the wartime medical-research agenda.

Since very little was known about the chemical structure of penicillin, in the 1930s no chemist had hit upon the design of a rational process for synthesizing penicillin. An inability to produce penicillin in larger quantities had also discouraged further research on this antibiotic at the time. As military engagement increased in the early 1940s, the US government introduced a series of wartime scientific research and development programs. In 1941 President Franklin Delano Roosevelt established the Office of Scientific Research and Development (OSRD) and appointed Vannevar Bush to head this new agency. In the same year, Alfred Newton Richards had been appointed head of OSRD's Committee on Medical Research (CMR)²⁶ to coordinate its various medical-research projects, including a project on the mass-production of penicillin to meet the surging military demand²⁷. In the following year, FDR appointed George W. Merck as the director of the newly created War Research Service (WRS). A civilian organization grouping prominent members of the US biomedical-research community, WRS had been authorized to oversee all biological warfare R&D programs in the US. Having served key positions in the wartime research programs, Merck and Richards recognized the importance of answering complex scientific questions urgently in order to meet the military's growing demand for medicines. Merck & Co., along with Pfizer and Squibb, participated in the wartime inter-organizational medical

²⁶ Sheehan (1982) explains the critical role A.N. Richards and CMR played in the national penicillin program that had started with \$8,250 budget to fund a fermentation research led by Andrew J. Moyer at the USDA Northern Regional Research Laboratory in Peoria, Illinois in 1942 to a mass network of "600 contracts at 133 universities, research foundations, and commercial laboratories" coordinated the efforts of nearly "1,500 professionals, M.D.s, Ph.Ds, and 4,000 support staff" employed throughout the program. Sheehan suspected that the total amount spent by CMR on the research programs was greater than the official amount reported which was about \$24 million before the committee was decommissioned in 1946 (p. 48). Between 1942 and 1946 Merck & Co. had spent approximately \$13.5 million on R&D, slightly over 5 percent of annual revenues. (data retrieved from Sturchio 1991 Values and Vision - A Merck Century)

²⁷ "Without Richards Americans would never have taken over production of penicillin" (Henry Harris cited in Lax (2005)

innovation challenge and dedicated significant resources to overcoming the penicillin-production challenge²⁸.

A well-documented, dramatic, and action-filled account of the penicillin challenge has been provided by Sheehan (1982); Lax (2005); Bud (2007). In the early years of 1940s pharmaceutical companies and major universities in the US received appeals from the world's two leading penicillin scientists, Dr. Howard Florey and Dr. Norman G. Heatley of Oxford University. The two were desperately seeking an industrial partner to mass produce a lifesaving mold, *penicillium notatum* (*P. notatum* for short), whose antibacterial effects had been clinically proven to treat various infections caused by gram-positive bacteria.

The US government recognized the urgent need for this medicinal product, however, ruling secrecy was mission-critical at the time when Germany was eager to develop industrial-scale production capabilities to manufacture penicillin in larger quantities. It is therefore the War Department considered involving rather a small number of mid-size manufacturers as a way of limiting the number of personnel involved in the process. The US government then decided to invite three of the leading pharmaceutical manufacturers in the US -- Merck & Co.; Pfizer, Inc.; and Squibb Corp. -- to constitute the nucleus of a research consortium (Sheehan, 1982). American Cyanamid subsidiary Lederle Laboratories, Winthrop, and Abbott joined the "big three" in a covert government-industry consortium on penicillin. These three companies, the nucleus of the national research consortium, possessed significant R&D capabilities in fermentation and other relevant technologies, stemming from their expertise in the production of sulfa drugs, vitamins, and industrial chemicals.

Having demonstrated the therapeutic properties of *penicillium notatum*, Florey and Heatley²⁹ travelled to the US in mid-1941 with the intention of sharing their new antibacterial agent in exchange for one kilogram of penicillin powder to bring back home to continue the clinical trials in Oxford, with the leading US pharmaceutical manufacturers to mass produce the agent for general use (Lax 2005). Having already cultivated a different strain of *P. notatum* at Rahway in 1940, Merck had managed to turn out 4.18 billion [Oxford³⁰] units of penicillin in 1942, the first successful attempt to manufacture antibiotics in such large quantities. Because penicillin was needed in large quantities on the battlefield, industrial efforts continued throughout the war, leading to a pair of major accomplishments: (1) the development by Pfizer in 1943 of a deep-fermentation technique

²⁸ (Sheehan, 1982) discusses the role of "nucleus" or "big three" in the early penicillin development efforts; Lax (2005) indicated that, by the end of 1943, the production of penicillin had been one of the most urgent scientific matters concerning nation's security to pursue and had come second after atom bomb (p. 207).

²⁹ Oxford team consisted of Howard Florey, Ernst Boris Chain, Edward Abraham, Arthur Duncan Gardner, Norman Heatley, M. Jennings, Orr-Ewing and G. Sanders

³⁰ An Oxford unit, also known as Florey unit, is an international measure that contains a minimum of 0.606 micrograms of crystalline compound to show antibiotic effects against bacterial infections.

that permitted ramping up production of (2) a new strain of penicillin that had been discovered the year before in a moldy cantaloupe at a government research laboratory in Peoria, Illinois (Lax, 2000). Having solved the problem with producing penicillin using biological means, the US government moved quickly to add 21 chemical producers to its list of authorized suppliers, enabling them to join the production effort.

Although smaller chemical firms indicated their interest in undertaking penicillin production, as the government had been appealing to them to do, they were falling short in raising capital to finance the acquisition of the needed tools and materials. By providing the new members of the consortium with capital, the government stimulated the production of penicillin, boosting its supply and lowering unit cost. It also required the key members of the consortium to make the production technology developed through this collaborative effort available to these smaller chemical manufacturers free of charge.

These efforts paid off: using the new strain and the deep-fermentation techniques it had developed in house, Pfizer increased its yield enough to become a world leader in penicillin production by the end of the war -- even with the drug's unit cost declining from \$20 per 100,000 units to only 20 cents as more producers came to employ the same technologies (Lombardino, 2000, p. 11).

In search of opportunities in “antibacterial chemotherapeutic agents” (the era of antibiotics)

Although Pfizer had emerged the winner of the large-scale penicillin-production challenge, as will be further discussed in the next chapter, Merck was better positioned to reap the benefits of the industrial advancements based on the knowledge newly developed in the fields of microbiology and fermentation chemistry (Galambos & Sewell, 1997). With the advancements in biology having opened the floodgates, interest in the pursuit of new antibacterial agents took off, most notably among the researchers at Merck (Achilladelis, 1999, p. 61).

Soon after the wartime penicillin program had been initiated, Merck invested heavily in its microbiology program and began to recruit the nation’s leading organic chemists, among them John C. Sheehan, who had been working on isolating and synthesizing penicillin for production that would eliminate the production risks associated with using any kind of fermentation method (Sheehan, 1982). As organic chemists recognized how difficult it might be to achieve this goal – synthesizing penicillin -- within a relatively short time frame, the members of the penicillin project, and Merck in particular, decided to pursue the conventional fermentation method in hopes of meeting the urgent need for product. Because its skill in working with the deep-tank fermentation technique was limited, Merck’s early efforts at fermentation failed to yield the production levels that had been anticipated.

To help overcome the fermentation challenge, Merck decided to recruit Selman Waksman of Rutgers University, the nation's leading soil biologist, as an external consultant. Along with his doctoral student at Rutgers, H. Boyd Woodrooff, Waksman helped Merck solve the problem of increasing its yield of high-quality penicillin. Woodrooff stayed employed at Merck and helped the company build a plant to produce another antibiotic, streptothricin, he had discovered while working with Waksman at Rutgers. But with the construction of the plant that was to produce this powerful new antibiotic already under way, the agent was revealed by further research to be highly toxic.

In response, a team of researchers at Waksman's Rutgers laboratory began screening soil cultures with the aim of identifying alternative antimicrobial agents that might be as effective as *penicillium notatum*. Through these efforts Albert Schatz, another of Waksman's graduate students, isolated two strains of *Streptomyces griseus* that produced streptomycin, which turned out to be highly effective against penicillin-resistant bacteria. Waksman approached Merck about financing the clinical development and commercialization of streptomycin, and Woodrooff, along with a team of Merck scientists, managed to bring this lifesaving new therapy to the drug market.

Merck's newly developed production skills, along with its acquisition of a new knowledge base in microbiology and fermentation chemistry, were to lead to numerous successful product launches in the decades to come. Among the new products were streptomycin, later discovered to be the most effective agent against *mycobacterium tuberculosis* or *tuberculosis*; cefoxitin, a second generation antibiotic; ivermectin, a powerful antiparasitic agent especially effective in the treatment of river blindness; and lovastatin, a cholesterol-lowering drug (Gortler, 2000).

In search of opportunities in “sterol chemistry” (the era of steroids)

Another major wartime medical-innovation mission was the isolation and synthesis of adrenal corticosteroids. As in the case of penicillin, steroid research quickly became a national-defense priority, and its urgency intensified with the United States' declaration of war on Japan in December 1941. Growing concern over the German army's use of adrenal corticosteroids to enhance its soldiers' ability to complete highly difficult missions under stressful conditions had prompted the US military to initiate another research effort in steroid medicine while the country was participating in a similar effort to produce penicillin. Merck volunteered to take part in this as well.

There were very few steroid chemists in the US at this time, and no Merck chemist had expertise in sterol chemistry. It was through another consultant, Everett Wallis, had Merck recruited Sarett from Princeton in early 1942 to pursue steroid research, working alongside Edward C. Kendall of the Mayo Clinic in Rochester, Minnesota, and reporting to Folkers at Rahway. That Sarett had been allowed to leave his doctoral program on short notice despite having completed only two years of it reflects the extraordinary circumstances of

the time. The young scientist was sent straight to the Mayo Clinic to take up his new assignment assisting Kendall, who was the nation's leading hormone researcher.

After he had spent a couple of months in Rochester observing the work of Kendall and his team on various substances isolated from the adrenal gland as potential candidates for steroid synthesis, Sarett was asked to return to Rahway and to confirm the validity of Kendall's hypothesis as to steroid molecular structure. When he proved unable to confirm Kendall's theory, Sarett began to think that his career, whether at Merck or at some other industrial-research lab, was soon to come to an end. But as he challenged the validity of Kendall's claims, he began to recognize flaws in Kendall's work.

Because scientific discoveries emerging from the work of the consortium were freely distributed among its members, Sarett had become acquainted with alternative approaches to the synthesis of steroids that had been developed by Swiss scientists (Sarett, 1990). Led by one of the world's most reputed chemists, Tadeus Reichstein, Swiss scientists were part of a working relationship between a Swiss consortium and an Allied consortium. Using the method developed by Reichstein, Sarett managed to develop a new route to deriving a synthetic cortisone by the end of 1942. This success not only rescued Sarett's career, it brought him international recognition at a very young age (Sarett, 1990).

Table 3: Percentage share of ethical drug in total sales of top US pharmaceutical companies, decade average, 1950s-90s

Company	% 1950s 1960s 1970s 1980s 1990s				
	1950s	1960s	1970s	1980s	1990s
Abbott	71.0	47.0	29.0	NA	NA
American Home Products (Wyeth)	44.0	38.0	39.0	48.0	60.5
Bristol-Myers	22.0	19.0	30.0	39.0	62.9
Johnson & Johnson	10.0	16.0	30.0	23.0	33.8
Lilly	85.0	72.0	58.0	56.0	80.3
Merck	75.0	73.0	71.0	94	63*
Parke-Davis	93.0				
Pfizer	57.0	88.0	50.0	49.0	74.6
Schering-Plough	82.0	48.0	61.0	59.0	81.9
Searle (1985)	100.0	86.0	51.0	53.0	acquired
Smith Kline & French (2000)	95.0	75.0	53.0	51.0	n.a
Squibb (merged in 1989) **	n.a.	73.0	52.0	67.0	acquired
Sterling (1988)	40.0	35.0	30.0	28.0	acquired
Upjohn (1994)	90.0	82.0	67.0	75.0	83.5
Warner-Lambert (2000)	26.0	35.0	36.0	33.0	43.2

* A significant drop from 94 percent in 1980s to 63 percent in 1990s reflects the sales of Merck-MEDCO Managed Care (MEDCO) unit sales of non-Merck prescription drug sales, which accounted for one-third of the company's total sales between 1992 and 1999.

Source: Own calculations based on data from Achilladelis (1999) & company annual reports

As illustrated in Table 3, Merck has not only become a drug company with one of the highest industrial concentration on ethical drug sales (excluding MEDCO sales) among the leading American pharmaceutical companies, but also the highest sales of ethical drugs in

the US market. While Merck generated \$11.8 billion sales revenues from pharmaceuticals, Pfizer generated \$21.4 billion and Bristol-Myers generated \$20.6 billion sales revenues from pharmaceuticals in 1990. The mid-1990s marked the era when the productivity that Merck & Co. had achieved as a product-driven, Old Economy company peaked; in the late-1990s, when its transformation into a profit-driven, New Economy company got under way, its productivity began to decline. This transformation is to be discussed extensively in the sections that follow.

Transformation into a pharma enterprise (Forward integration)

Merck took the lead in the postwar period in following up the opportunities created in the 1940s by government-industry collaboration on the development and production of antibiotics and steroids. Until he resigned from Merck & Co. to become the Assistant Secretary of State for European Affairs in 1949, George W. Perkins had been among the most influential champions of the major transformation that turned it into one of the most competitive of the research-driven drug companies in the biopharmaceutical industry.

Under George W. Merck's management the transformation efforts begun in the 1920s had been sustained into the late 1940s with the help of Vannevar Bush and Alfred Newton Richards, preeminent leaders of the US science and technology community both newly named to the company's board. The pair had worked closely during the war, Bush as head of the Office of Scientific Research and Development and Richards as head of that office's Committee on Medical Research; in addition, Richard had served as chairman of the pharmacology department at the University of Pennsylvania's School of Medicine and was, from 1947 to 1950, president of the National Academy of Sciences. With Edward Reynolds, the administrative vice president of Harvard University, also on the company's board, Merck & Co. continued its recruitment campaign throughout the 1950s with the aid of its network of its distinguished directors.

Efforts to strengthen the company's R&D leadership and its investments in basic and applied research had begun to pay off in the late 1930s and continued to do so through the 1950s. When the company was experiencing rapid growth at all its locations, both at home and abroad, and in major functions such as sales, marketing, production, and R&D, in 1950 George W. Merck, while retaining the company's chairmanship, selected a CEO, James J. Kerrigan, to whom he handed over management of some day-to-day operations. With Kerrigan's appointment, operational control of the organization was for the first time being vested in the hands of a non-Merck. With the promotion of a professional to top executive, Merck entered a new era.

But even if Kerrigan wasn't a member of the Merck family, he had been with the family long enough for it to trust him with the company's operations. In 1907 Kerrigan, at the age of only 13, had joined the company as an "order-bench boy." Later selected by George F. Merck as his apprentice, and subsequently serving the company in different managerial

capacities, including that of vice-president, Kerrigan ultimately entered the family's inner circle. Kerrigan dealt with the expansion of manufacturing operations needed to keep up with Merck's growing portfolio of medicinal products for both humans and animals -- which included vitamins, hormones, antibiotics, sulfonamides, and analgesics -- as well as other industrial chemicals and household products. George W. Merck and Perkins, Jr., meanwhile, were paving the way for the construction of a state-of-the-art industrial research center at Rahway and the recruitment of a competitive R&D workforce to staff it, helped by its prestigious directors, Bush and Richards.

Major R&D investment campaigns launched in the 1930s had resulted in significant productivity growth in the late 1940s and early 1950s, which in turn resulted in three major market- and technology-related challenges that demanded immediate management action. Having recognized the company's potential for growth and the challenges that lay ahead, Merck's management devised and implemented an ambitious strategy that began with an extensive and carefully executed organizational overhaul. As Merck was quickly taking its place among the largest producers of penicillin and antibiotic products, major pharmaceutical producers, who used to purchase bulk chemical intermediates from Merck, began to consider the company a serious competitor in the ethical drug market. Threatened by its rapid growth, such former Merck clients as Upjohn and Parke-Davis quickly devised invest plans aimed at improving their own R&D operations and in-house drug-development capabilities, thereby to alleviate their dependence on their former supplier in the decade following the end of WWII. To hedge against the risk of losing major clients and market share in the bulk-chemicals business, Merck had begun to implement an aggressive market-growth strategy by becoming a fully integrated pharmaceutical producer of brand medicines during the same period.

By the end of WWII Merck had already entered the newly discovered world of microbiology and virology. The growth achieved through organizational learning in these fledgling fields that had occasioned by the launch of novel medicines opened a new growth path to the company. Unlike the fine or bulk industrial chemicals businesses, pharma offered the potential to support the investments necessary to building a fully integrated, knowledge-based, competitive drug company. Although Merck had made significant progress toward becoming a research-driven biopharmaceutical production operation, the business growth originally anticipated was being severely limited by the absence of organizational capabilities in sales and marketing, which were preventing the organization from bringing its innovative new therapies directly to prescribing physicians and pharmacists.

At the same time that this market challenge had begun to threaten the company's future growth, however, by prompting management to enrich the organization's capabilities in the sales and marketing of branded products, it had also presented Merck with a unique opportunity to capture a larger share of the ethical-drug market, as well as to improve the return on its large-scale investments in R&D. Acquisition of skills and knowledge required

the recruitment of pharmacists, who would be able to formulate chemicals and prepare them in dosages appropriate for marketing, and sales agents, who could visit medical offices to introduce the drugs and try to convince physicians to prescribe them.

In the early 1950s Merck lacked the skill-base and knowledge-base necessary to undertaking such a market extension campaign, and especially in the growing field of biologics, even though it had begun building its R&D capabilities in that field. Sharp & Dohme, a Philadelphia-based pharmaceutical manufacturer run by a former Merck employee, John S. Zinsser, was facing market expansion challenges at the very same time. S&D possessed the competitive sales, marketing, and distribution capacity to commercialize new biological products; its challenges stemmed, rather, from its lack of the capital needed to scale up its R&D and manufacturing operations to take better advantage of the opportunities emerging in the biological-products market.

In the early 1950s Merck was competing against Roche in vitamins and steroids and against Pfizer in penicillin and antibiotics. Because Roche had not been in the penicillin consortium, it had missed the learning opportunity to move into microbiology and biological products that participation in the wartime program had afforded. Roche was, however, a fierce competitor in organic chemistry, and it was challenging Merck in the chemical synthesis of organic compounds, its success with Valium being reflective of its capabilities in organic chemistry. Though the penicillin-led microbiology revolution had passed Roche by, it was about to make a major move into molecular biology and biochemistry. Pfizer, still milking penicillin-era products, was slow to make the investments required to build a productive knowledge base. Both Roche and Pfizer had been expanding their domestic and foreign sales operations, particularly in Europe, where the post-war recovery efforts had increased the demand for vitamins and antibiotics and where American companies were in a favorable competitive position to profit from the growing market for pharmaceuticals. It was when its competitors determined to arm themselves with a robust sales force to compete in the increasingly crowded antibiotics and steroids markets that Merck's top executives identified the company's next strategic move as the acquisition of capabilities in pharmaceutical sales and marketing.

Merger with Sharp & Dohme in 1953 (Acquiring marketing skills)

To capture the value that the fledgling new fields of biology had to offer, Merck decided to modify its existing business model: It would from then promote its own novel pharmaceuticals through a newly established sales and marketing workforce. The most feasible option for pursuing this forward integration strategy had presented itself in the form of the acquisition of Sharp & Dohme. Drawn to the potential of achieving synergies by combining the two companies' resources, their chairmen, Merck and Zinsser, and their presidents, Kerrigan and William L. Dempsey, had begun to discuss the terms and conditions of a merger in 1952. In April 1953, stockholders of the both companies approved the managements' proposal to combine the assets and join the operations of

Merck & Co. and Sharp & Dohme to form Merck Sharp and Dohme³¹ (MSD), effective April 30, 1953 (Galambos & Sewell, 1997). Sharp & Dohme stockholders exchanged each S&D common share for two and a quarter Merck shares as part of the merger agreement. At the end of this merger, the number of shares outstanding had been increased by 2.49 million.

The combined entity's operations were consolidated within three divisions. A Chemical Division, which included the development, production, and marketing of medicinal, nutritional, agricultural and industrial chemicals, was established and a long time Merck director W. Johnstone was named its president. Dempsey was appointed president of the Sharp & Dohme Division, whose function was to oversee pharmaceutical and biological operations in the US and Canada. The third division, designated as Merck, Sharp and Dohme (MSD) International, was to oversee all the company's foreign operations, with the exception of those in Canada, and to be headed by another longtime Merck & Co. director, James H. Sharp³². MSD recorded \$160 million in net sales for the year in which the companies merged. Nearly two-thirds of merged companies 1953 net sales were generated by operations of the former Merck & Co., which also contributed 60 percent of its total workforce of 10,100. Upon the completion of the merger in 1953, the composition of the company's board of directors was changed, as three Merck & Co. directors by former directors of Sharp & Dohme; Charles D. Dickey, vice president of J.P. Morgan & Co. Inc.; Charles S. Garland, a partner at Alex, Brown & Sons; and Dempsey. While Zinnser was demoted from chairman at Sharp & Dohme to vice chairman of the new entity, George W. Merck and Kerrigan carried the positions of chairman of the board and president with them.

The merger with Powers-Weightman-Rosengarten (PWR) had ultimately led Merck & Co. to increase economies of scale and operational profitability. By retaining and reinvesting its profits, the company had been able to afford the investments in organizational learning that had paved the way to building a knowledge-based chemicals business; it could then realistically aspire to become a major competitor in the ethical-drug sector. Through the subsequent merger with Sharp & Dohme, Merck had leaped over an important barrier to enter the ethical-drug market and anchor itself in the fast-growing business of pharmaceuticals. Thanks to its recruitment campaign, launched in the 1930s, Merck had begun to acquire technical knowledge in drug development that was then diffused throughout the organization. Through its acquisition of PWR and merger with Sharp & Dohme, Merck had begun to engage in the organizational learning necessary to building its functional knowledge in the development; production; and sales, marketing, and distribution of pharmaceuticals and biologics. Following the 1953 merger, the company

³¹ According to Tishler (1983) Sharp & Dohme was kept in the new company's name because S&D had greater visibility in the medicinal products market at the time such that Merck & Co. could build on brand equity.

³² It was merely a coincidence that Merck had a longtime director named Sharp who had served as Financial Vice-President of Merck & Co. prior to the merger in 1953.

initiated the development of managerial skills that allowed it to complete the establishment of a fully “integrated learning basis” (ILB) in the late-1950s and the 1960s (Chandler, 2005).

As part of this managerial reform, Kerrigan resigned from president’s position in 1955, although he remained as a member of the Board until his death the following year. Upon the strong recommendation of Bush, John T. Connor was elected to replace Kerrigan. A veteran of the wartime penicillin project who served at the U.S. Office of Scientific Research and Development (OSRD), and at the Office of Naval Research, as well as having been a special assistant in the Office of the Secretary of the Navy, Connor had impressed both Bush and George W. Merck with his leadership skills.

Connor’s election came at a turning point in the company’s history. First, the recently merged company was in need of major overhaul. Lacking the leadership needed to coordinate the efforts of the Rahway and West Point groups, a research unit of Sharp & Dohme located in West Point, PA, MSD had struggled to complete the organizational-consolidation process in the post-merger period. Connor introduced a more formal managerial structure while decentralizing the operational control to empower the leaders of divisions and subsidiaries. And, most important, Connor managed to consolidate R&D leadership within a newly created division, MSD Research Laboratories, that would oversee the R&D operations in Rahway and West Point that had previously overseen by the leaders of both the Chemical and Sharp & Dohme divisions. After decades of service as the director of Merck Research Laboratories, the successor of Merck, Sharp Dohme Research Laboratories, Randolph T. Major resigned from the duties of scientific vice-president to serve as a part-time consultant and was replaced by his longtime colleague, Max Tishler.

A close friend of George W. Merck, Bush, became the chairman of the board upon Merck’s death in 1957 (Tishler 1983). Bush was the natural replacement for Merck as chairman owing to his influential role within the company, the industry, and national politics, in addition to his great interest in the advancement of medical science for public health. The election of Bush as chairman also marked the end of a period in the company’s history, as no member of the Merck family would again take a leadership role, except to serve as a director, primarily to represent the family’s interest. When Bush joined the Merck & Co. board in 1949, he was serving as president of the Carnegie Institution of Washington; when he became MSD’s chairman in 1955, he was also chairman of Massachusetts Institute of Technology’s corporation, as the school’s board of trustees is called.

In the years following the death of George W. Merck, the company’s senior managers and directors maintained the founders’ research vision. Zinnser of Sharp & Dohme had remained on the board as vice chairman, and a former vice president of Sharp & Dohme, Henry W. Gadsden, was elected as a director, while G.W. Perkins returned to the board

upon the death of George W. Merck, his brother-in-law, in 1957³³. Appointments of nationally known research leaders to its board of directors played a critical role in the company's navigating a series of political storms in the 1950s and early 1960s. The rising prices of innovative new therapies aroused public resentment against the industry, prompting lawmakers to pursue widespread investigations into its business in the 1950s. The launch by the US Justice Department of an antitrust investigation into an alleged conspiracy to fix the prices of the Salk polio vaccine was followed by several Congressional hearings focusing on the industry's pricing policies and R&D expenses. These hearings led the Senate Subcommittee on Antitrust and Monopoly, formed in 1959 and chaired by Senator Estes Kefauver, to investigate allegedly monopolistic practices in the biopharmaceutical industry in hearings that concluded in 1962 (Greene & Podolsky, 2012).

Merck's leadership took a front seat when, during these investigations, prominent members of the biomedical research community joined forces with the industry to lobby against policy efforts designed to rein in any collusive business practices that might have been affecting the safety, effectiveness, and affordability of the innovative therapies being introduced. The former government officials and high-profile leaders of the national science community among Merck's leaders -- Bush, Connor, Richards, and Perkins -- as well as many world-renowned scientists recruited by Merck as employees or consultants, the campaign that had been organized by the industry group to oppose the public outcry.

Although the policy initiative aimed at controlling the soaring prices of drugs had failed miserably, the growing public outrage unleashed in 1957 by the Thalidomide scandal³⁴ forced policy makers to take actions at least to control the safety of pharmaceuticals. Having continued through years of a wrestling match between public health activists and the industry's lobbying groups, the various committee investigations ultimately led to the enactment of the 1962 Kefauver-Harris Amendment (Drug Efficacy Amendment) to the 1938 Federal Food, Drug, and Cosmetic Act. This amendment authorized FDA to monitor the safety of newly introduced drugs by requiring pharmaceutical companies (1) to provide

³³ According to Folkers (1990), until his departure from the company in 1948, George W. Perkins had been making the "solid" decisions when George W. Merck was the company's president. Perkins' return to the company had been important for the replacement of an iconic figure such as George W. Merck to sustain the company's commitment to the Merck family vision

³⁴ Discovered by the scientists at Chemie Grünenthal, a German pharmaceutical company, Thalidomide, a powerful sedative, had been used to treat the effects of morning sickness among pregnant women in the late-1950s. Having not tested for toxic effects on humans the adverse effects of such powerful chemical agent had been only discovered after the birth (or stillbirth) of over 10 thousands children with severe physical deformities between 1957 and 1961. Unconvinced by the existing data on its safety, an F.D.A. expert, Frances Oldham Kelsey, had refused to sign-off on this medication for issuing marketing license the drug and therefore it hadn't been launched in the US market. Such tragedy occurred in Europe had stimulated the policy discussions on the monitoring of drug safety in the early-1960s.

proof of safety and effectiveness prior to the approval of any drug for marketing; (2) to disclose accurate safety information when advertising; and (3) to stop selling generic alternatives as new “breakthrough” medications.

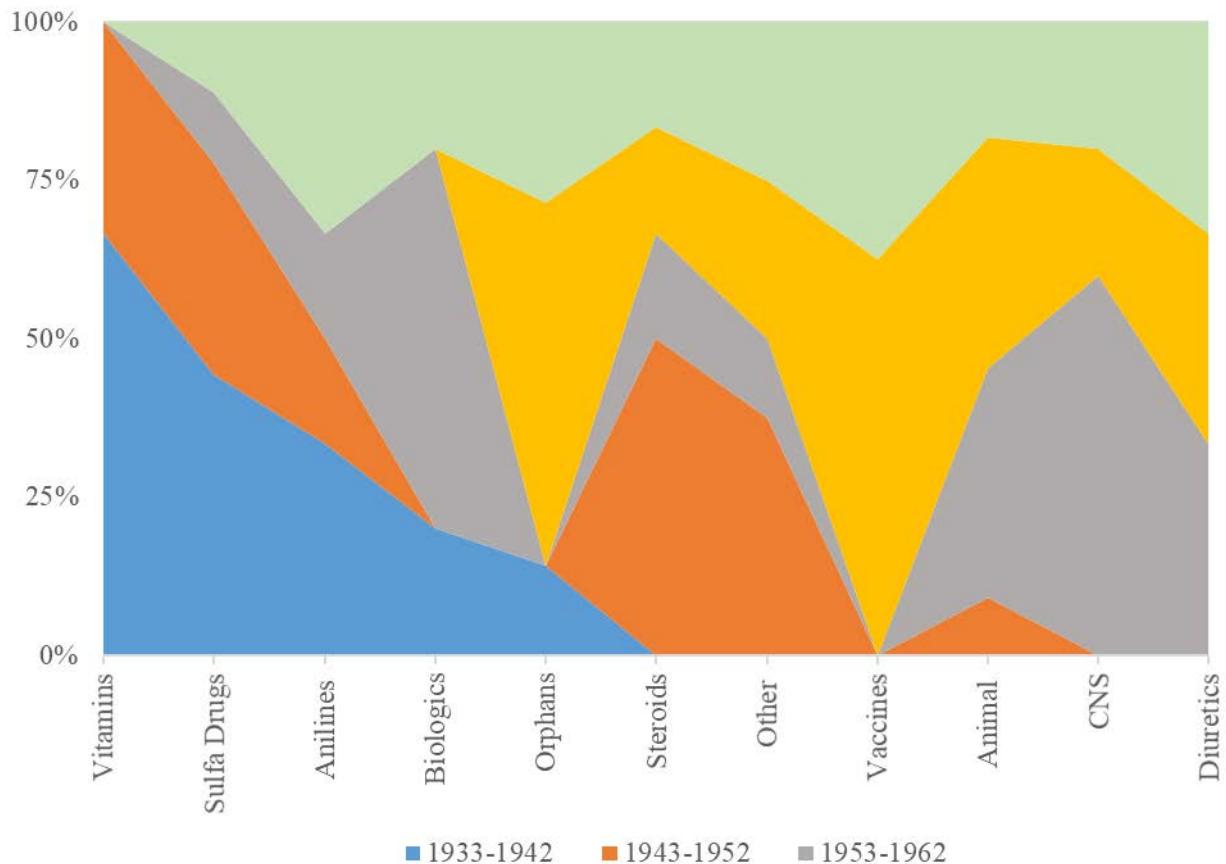
In the new era of the prescription-drug market, investment in the building of productive resources had become a prerequisite for the long-term survival of pharmaceutical companies. Having already completed its transition to a research-intensive, fully-integrated pharmaceutical establishment, Merck & Co. was among the candidates best situated to overcome the market challenge lying ahead of the industry. Proving the safety and efficacy of new products before their introduction, however, required further investment in significant organizational capabilities for drug-development research in both chemistry and biology, above all in the fields of pharmacology, to gain insight into the reaction of chemical agents within live organisms, and pathology, to gain insight into mechanisms of disease. Intimidated by this new science challenge, Merck and others in the industry decided to diversify into markets both related and unrelated markets in order to maintain their growth over the 1960s and 1970s.

Transformation into multi-business enterprise (diversification into non-pharma markets)

During Connor's tenure as president, which lasted from 1955 to 1963, Merck's R&D spending as a percentage of total sales remained at around the 7 percent level, surpassing the 5.5 percent average spending of the major American drug manufacturers (as shown in Table 6). Merck's investment in R&D paid off: In the years following George W. Merck's death, the company significantly enriched its product portfolio, adding 26 new products in 1957 alone, among them vitamins B1, C, B12 (Redifact, Redisol, Reditrin), B6, and K1; steroid hormones Cortone and Hydrocortone; and both old penicillin (Remaden) the newer antibiotics streptomycin, dihydrostreptomycin had accounted for 58 percent of the total sales (Figure 16 & 19).

Soon after Connor became its president, the company to the company introduced a new-generation penicillin (Remaden), other antibiotics (Tetrazets-antibiotic throat lozenges-Cremomycin, Cathomycin, Cathocillin and Oxymycin), steroids (Alflorone, Deltra and Hydeltra), heart-failure medications (Diuril and Inversine), and the Salk Polio Vaccine (Figure 16). In 1958, one of the most active years for product launches, saw the introduction of Diuril, a highly effective, new-generation antihypertensive which, along with its derivatives, was a significant driver of the company's growth in the following decades. Increased emphasis on the company's international manufacturing and sales operations, initiated during Kerrigan's tenure, began to pay off during Connor's, with the result that revenues from overseas operations grew 20 percent in 1957. By the end of the 1950s, international operations accounted for nearly 29 percent of Merck's overall sales.

Figure 16: Changes in the revenue composition by therapy (% of total revenues)



1933-1942: First 10 years of the Merck Research Division, vitamins, sulfa drugs (antibacterials), anilines (sedatives, analgesics), biologics (blood products), and drugs for rare diseases.

1943-1952: Post-war period; rush to commercialize penicillin, antibiotics and steroids.

1953-1962: Post-merger (Merck under Vannevar Bush & John T. Connor); biologics from Sharp & Dohme (S&D) division, animal health products (sulfas and antibiotics), Central Nervous System (CNS) drugs (mostly anilines) and diuretics.

1963-1972: Post-Kefauver-Harris Act Era; former S&D managers are no longer in power; diversification period begins; Hilleman's vaccines begin to hit the markets (high sales volume) animal health products (sulfas, antibiotics, vitamins, and steroids); CNS drugs (mostly anilines); diuretics.

1973-1982: Merck R&D under Vagelos; Merck begins to divest non-pharma assets; products for rare diseases trending (high-profits less-competitive markets); Hilleman's vaccines begin to hit the markets (high-volume sales); animal health products (sulfas, antibiotics, vitamins, and steroids); CNS products (mostly anilines); diuretics.

Source: Own illustration based on data from company annual reports, 1933-1982

In the early 1960s there were major changes at highest levels of the company. Chester S. Keefer, from 1939 to 1960 the director of clinical research at Boston University Medical Center, filled the board seat left by the death in 1960 of Perkins, a principal architect of the company who had returned to it as a director three years before. The younger son of the late George W. Merck, Albert W. Merck, was elected to the board in 1961; he would serve on it for the next three decades. Also added to the board, in 1962, was the company's top scientist and president of Merck Sharp & Dohme Research Laboratories (MSDRL), Max Tishler. Upon reaching mandatory retirement age in 1962, Bush was replaced as chairman by Garland, who had moved from Sharp & Dohme's board to Merck's at the time of the

1953 merger. Abruptly vacating MSD's presidency in 1963 was Connor, who left to serve as President Johnson's Secretary of Commerce. He was replaced the next year by Gadsden, who, like Garland, had come over from Sharp & Dohme.

Also departing for big job 1963 was Folkers, who resigned from his post as vice president for Exploratory Research to become president of Stanford Research Institute (SRI) following an interview with David Packard. During his 28-year tenure at Merck, Folkers had been involved in or overseen numerous successful product launches, notably in vitamins (B1, B6 and B12), penicillin, and other antibiotics. Another longtime Merck director, Edward H. Green, had retired from the board the year before. As George Merck's lawyer during his post-WWI negotiations to reacquire Merck & Co. from the APC, Green had provided critical advice, and he had been involved with the company since then.

Doing business in pharma after the Kefauver-Harris Amendment (Drug Efficacy Act) of 1962

These significant changes in the company leadership coincided with radical shifts in regulatory regime governing approval of prescription drugs for the US. With rare exception, one being an antidepressant launched in the late 1950s, the new product being offered in the market owed their existence to the knowledge base developed during the wartime crash programs on antibiotics and steroids. A new generation of sulfa drugs had been developed for human and animal medicine. Amprol, which was for poultry, and Thibenzole, an anti-parasitic agent for livestock, helped the company gain some market share in animal health products in the early 1960s.

Convinced that the looming Kefauver-Harris Act was being envisioned as a permanent regulatory measure, Bush and Connor had begun devising diversification strategies to establish alternative revenue sources in the healthcare field. As part of a business diversification strategy, Merck had established Quinton Company in 1962 as a marketing division for branded, over-the-counter consumer healthcare products, such as the Sharp & Dohme legacy throat lozenge Sucrets, in an advance attempt at considering new markets that might provide an alternative to ethical drugs. This diversification campaign intensified under Gadsden in the mid-1960s, as a new political storm was appeared in the offing due to the rising cost of prescription drugs in the US. American pharmaceutical companies had recognized the changing rhetorical tone of the nation's healthcare policy debate, which was becoming increasingly skeptical of their industry's business practices.

Pharma executives had grown apprehensive as to their industry's future as political assaults on their business practices escalated due to their products' soaring prices. The policy measures being proposed at the time by industry opponents favored new price-control mechanisms designed to rein in prices in Industry proponents' concerns over the direction that policy discussions were taking did now, however, reach their height until the U.K.'s 1967 Sainsbury Report recommended that that nation's government consider adopting a

strict mechanism for controlling drug prices, if not nationalizing certain segments of the industry, to bring pharmaceutical prices down.

Especially worried about the future of the prescription-drug market in the era of generic competition, major pharmaceutical companies, including Merck Sharp & Dohme, intensified their diversification efforts. In 1965 one of largest drug makers in Canada, Montreal-based Charles E. Frosst Laboratory, was acquired for \$16 million in cash, paid out of funds the company had earned and retained overseas. At the time of its acquisition, the 66-year-old Frosst Lab had exhibited a potential for steady sales growth and possessed an expert sales team, both of which were likely to allow Merck to increasing its presence in the Canadian market. Merck's legacy asthma medication, Singulair, as well as the Cox-2 inhibitor Vioxx, were to be discovered or developed at the company's research operations at the Frosst Lab in the late 1990s.

Trained in economics, Gadsden had worked as a market analyst in the early years of his professional life. Because he had spent the most formative years of his career at Sharp & Dohme, the managerial skills Gadsden developed over time were best suited to an organization with a strong sales-and-marketing orientation. In response to the major regulatory overhaul of the early 1960s Gadsden devised and implemented a new market strategy that abandoned Merck's longtime emphasis on growth in the high-value prescription-drug business in favor of an aggressive product-diversification strategy that called for entering consumer-brand, over-the-counter (OTC) medicine and other healthcare-product markets. Furthermore, the company was to pursue a growth strategy to expand industrial chemicals business by adding new product lines in industrial and commercial chemical markets. The only expansion in the pharmaceuticals sales was to be in the animal health and agricultural chemicals businesses.

The execution of Gadsden's diversification strategy began with MSD's acquisition of Metalsalts Corporation in early 1966. Based in New Jersey, Metalsalts was the developer of an industrial antifungal able to prevent the growth of mold and mildew in materials and equipment such as paints, sealants, heating and cooling systems, and paper products. Although MSD had had experience in the development of fungicides and parasiticides like tiabendazole that had animal-health and agricultural applications, with the acquisition of Metalsalts it was entering an industrial chemical field of which it had no prior knowledge or experience. Another new field MSD entered, in this case via its 1968 acquisition of Calgon Corporation through an exchange of 37.2 million shares, was that of chemicals for water purification and environmental control. The next year, Gadsden acquired 90 percent of the shares of Laboratoires Chibret in France with the objective of establishing an ophthalmic division within MSD. Besides its Consumer Products Division, which manufactured and marketed popular household items such as *Calgonite* for dishwashers, Calgon was made up of a *Water Management Division* offering both products and services for the preservation of water resources or protection against water damage; its *Pittsburgh Activated Carbon Division*, housing the world's largest granular activated carbon

production operation; a *Specialty Chemicals Division* producing a wide variety of specialty chemicals for a variety of industries; and another division producing commercial cleaning and industrial water-treatment products. This acquisition allowed the entire operations of Quinton Company, MSD's Consumer Products Division, to be merged later with Calgon's administrative operations in Pittsburgh to take advantage of the functional capabilities -- especially in the nationwide sales, marketing, and distribution of products -- that the newly acquired company had developed over previous decades.

To improve the sales performance of Calgon's Water Management Division, MSD acquired Baltimore Aircoil Company (BAC) in 1970. A supplier of products and services in water management and environmental control, BAC offered products and services that complemented those of the Water Management Division, thus strengthening its competitiveness. As the former Calgon divisions made further acquisitions to improve their market shares, BAC was allowed to expand its product line through acquisitions such as that of Pacific Pumping Co. (PPC). Both the BAC and PPC deals had been financed through exchanging 398.5 thousand and 46.2 thousand of company stock respectively.

MSD acquired Solar Laboratories in 1971, its first attempt to enter the market for medical apparatus in the field of orthopedics. Utilizing the productive capabilities it had developed through organizational learning in penicillin, antibiotics, steroids, sulfa drugs, vitamins, and industrial chemicals, MSD had been successful in the 1960s in launching new products in the animal-health and agricultural-chemicals markets, mostly in the form of fungicides, parasiticides, antibiotics, and steroids. It intensified its efforts to extend the product lines in animal health in the early 1970s, establishing experimental farms in locations throughout the world to support R&D activities in poultry diseases such as coccidiosis. As part of this market-expansion effort, MSD acquired Kelco Company in 1972 in exchange for 1,037 thousand of its shares and Hubbard Farms, Inc., in 1974 in exchange for 901.9 thousand of its shares.

The company also continued investing in the production of bulk- and specialty-chemicals manufacturing, and remained competitive in vitamins, antibiotics, sulfa drugs, and other industrial and fine chemicals throughout the 1960s. In 1963, however, MSD withdrew from the market in electronics chemicals, discontinuing production of ultra-pure silicone, which it had licensed from Germany's Siemens and, since 1957, had supplied to manufacturers of electronics equipment and components, such as rectifiers, transistors, and diodes, for both the civilian and military markets.

By the time Gadsden became the company's president in 1964, Merck had expanded the size of product portfolio and filled its pipeline with product candidates that had the potential to anchor new product lines in the ethical-drug sector. Under the direction of Tishler as president of MSD's Research Laboratories Division, the company had added new analgesics and anti-inflammatories, a new antihypertensive, and a new class of antidepressant to its existing lines of corticosteroids and diuretics. Introduced in 1962, the

antihypertensive, Aldomet, outperformed the blood-pressure-lowering medications of the previous generation. The drugs launched in the late 1950s and 1960s were the byproducts of organizational-learning efforts maintained in the maturing field of biochemistry since the late 1940s under the supervision of Major and Tishler. The diversification strategy implemented in the 1960s and 1970s affected the company's R&D operations as well. The perspective offered in an interview by Lewis Sarett, who was with MSD Research beginning in 1962 and led the division under two corporate presidents from 1969 to 1976, provides important insight into the impact of the market-diversification program on the company's allocation of productive resources.³⁵

Asked how the two top executives, Gadsden and Antonie T. Knoppers, compared with respect to management style, objectives, and vision for pharmaceutical research, described discussions he had with Knoppers and Gadsden individually and on separate occasions that especially relevant to this research. On each occasion, he said, his interlocutor revealed plans for the research division that they had carefully designed to support the company's market-growth strategies. In 1969 Gadsden, as president of MSD, had appointed Sarett both president of the MSD Research Division and senior vice president of Science and Technology. Sarett had been reporting only to Knoppers, then the vice president of MSD and second in command, from whom Sarett had been getting his directives for the Research Division. Sarett's first assignment upon his appointment as president of Research had come from Knoppers, who asked Sarett to direct his division toward getting the company back into the antibiotics business.

Considering that Merck had spent over two decades building a significant knowledge base in the discovery and development of novel antibiotics, what Knoppers was asking Sarett to do was, in essence to redeploy the company's productive but underutilized assets to the development of a new generation of antibiotics. Having been assigned this as his "number-one priority," Sarett steered his group toward developing innovative antibiotics, which led to the discovery of cefoxitin, first sold under the brand name Mefoxin. Although Sarett himself had no background in microbiology, having the relevant experts on his staff had made this discovery possible, which which led Sarett (1990) to perceive the accomplishment as "strictly a management success" (Sarett, 1990, p. 52). This broad-spectrum antibiotic, which was ready for market launch by the end of Sarett's tenure as president of the Research Division, was a major revenue source for MSD when Sarett retired in 1982.

The other research program assigned to Sarett, part of Gadsden's vision for exploring high-growth, high-profit markets, had been the development of products for people who were not actually ill, such as quick-tanning lotion and hair straightener (Hawthorne, 2004).

³⁵ Sarett, who served in two positions during the period 1962-1969, said (1990) that his promotion from director of fundamental research to vice president of basic research had been merely a change in title and a boost in rank within the hierarchy. Despite the change in title, his responsibilities had, for the most part, remained the same.

Another example of the new products Gadsden envisioned a pill that would inhibit the effect of alcohol on or render sober people who wished to drive after drinking. Although a compound was identified, it was difficult for Sarett to recruit people to engage in the developmental research. For the most part, researchers weren't enthused by the idea of developing a drug that "would induce people to drink" -- thus, in essence, "encouraging alcoholism." (Sarett, 1990, p. 41)

Despite the idea's being overwhelmingly despised, Sarett was not convinced that developing such a drug would be unethical or that the drug itself would really induce drinking and encourage alcoholism. But he was unable to sell the idea to the research community, and Gadsden's strategy of introducing lifestyle drugs failed to gain sufficient traction to move the program forward. This managerial failure to mobilize MSD's research community for the pursuit of opportunities in the lifestyle-drug market illustrates how deeply the vision implanted by George W. Merck was rooted within the organization: Its researchers had decided to sustain their commitment to developing new medicines for helping "people" rather than seeking greater "profits" at the expense of leaving life-and-death medical mysteries unattended.

Transformation into a "big pharma" enterprise (consolidation and specialization)

For over a decade, MSD was under the direction of Gadsden, the former Sharp & Dohme executive who had joined the firm through the two companies' 1953 merger. In the ten years following that merger Gadsden had risen to the top as many of Merck & Co.'s influential leaders, who had remained in power after George W. Merck's death, parted ways with the company in the late 1950s and early 1960s. Gadsden began to hand over operational control to the company's new chief operating officer and president, John J. Horan, in 1975, after engaging the company in a massive market-diversification and global-expansion experiment that spanned his entire tenure. Over the next ten years, under Horan's leadership, MSD implemented a drastically different growth strategy that returned it to Merck & Co.'s roots and core values. Horan left a prosperous law career to join the firm in 1952, since which time it had been transformed into a global pharmaceutical powerhouse employing over 26,000 and operating in numerous countries, and its annual sales had grown nearly 100 times.

After he had successfully negotiated an important trademark deal with E. Merck of Darmstadt (EMS), the former parent company, Horan's skills had been noticed by top management, and he had been assigned to oversee the development and implementation of the company's strategy for long-term growth. A longtime corporate strategist who had served the company during its most transformative years, Horan was elected as CEO and chairman of the board in 1976. While he was being groomed for the position, Horan was assigned to identify a successor to the company's chief scientist, Sarett, whose retirement was nearing at the time. Horan was aware of the changes in the science underlying drug

research and recognized that the Research Division was overdue for an organizational overhaul.

Having determined such an overhaul to be necessary, Horan began to search for a new leader for the division capable of devising a plan for such a transformation and executing it successfully. At the time attracting well-trained university scientists, especially at the most senior level, was very difficult. After the industry's years of diversification into the non-healthcare or consumer-products market, the perception of industrial research among academics had been significantly damaged. It had been quite a difficult for Horan to identify and recruit appropriate candidates for a critical post that had once been held by Major, Tishler, and Sarett, figures who had left a formidable legacy behind. Aside from having big shoes to fill, the new leader would face challenges even greater than those encountered by these legendary predecessors.

Merck Research Laboratories and the discovery of blockbusters in the late 20th century

The size of company's operations grew over time, and its operational dependence on the development of new products with greater market performance grew at the same rate. The new director of the Research Division had to meet the operational need for new products by delivering "blockbuster" market performance in the new, "big pharma" version of Merck. Given the complexity of the science underlying drug innovation, the correlation between the size of the investments in R&D operations and their innovation performance was neither exclusively positive nor linear. In the early 1970s researchers in the fledgling field of biochemistry were getting ready to revolutionize industrial research in drug discovery and development. Advances in knowledge in organic chemistry prior to the 1960s had driven industrial productivity through building large chemical libraries consisting of newly synthesized compounds. By the end of the 1960s research leadership in many major industrial laboratories had begun to recognize the importance of investing in building the knowledge base in biology that would be necessary to restoring declining innovative capabilities.

A native of Rahway, Roy Vagelos had spent his summers at MSDRL during his training in chemistry at the University of Pennsylvania in the late 1940s. After completing his medical education in the mid-1950s and spending nearly two decades in academic research at the National Institutes of Health (NIH) and the Washington University School of Medicine, Vagelos had become the world's most renowned expert in lipid biochemistry. Having kept his ties with the company in his hometown, Vagelos had been at Merck on various occasions as an external consultant to talk about his work in biochemistry. Horan had recognized the scientific and leadership skills Vagelos had to offer the company, and in 1975 he managed to recruit Vagelos, whom he saw as the successor to Sarett as president of MSDRL. In 1976, after serving one year as director of basic research, Vagelos became the president of MSDRL, with Sarett moving up to become MSD's senior vice president of science and technology. Having hired an accomplished scientist to run the research group,

Horan then focused on organizational restructuring efforts, divesting the company of all non-core business activities. Horan had invested heavily in the foreign operations to improve their sales performance, particularly in Japan during his tenure from 1976 to 1985 (Vagelos & Galambos, 2004, p. 180). John Connor, former president of MSD, had also returned to the Company Board serving as director between 1981 and 1987.

Concerned by the rise in cost associated with delays that the new regulations required drug companies to test products for drug safety and efficacy, Merck prioritized a global-expansion program aimed at capturing newly emerging drug markets overseas under Gadsden's management. Knoppers, then head of the international sales division at MSD, had successfully overseen a global-expansion campaign that had increased foreign sales from 23 percent of total sales in 1956 to 37³⁶ percent by 1966. Having boosted the range of products it could offer by acquiring new companies, most of them outside the ethical-drug business, Merck further raised its international sales, during Gadsden's tenure, which ran from 1965 to 1975.

During the period when Merck pursued a diversification strategy, which covered most of the 1960s and 1970s, the company's innovation performance, as represented by the introduction of new lines of products in human therapeutics, declined. As shown in Table 6, the company's R&D spending had increased from 6 percent of total sales in the 1950s to 9.3 percent in the 1960s. This significant increase can be attributed to the effect on product-commercialization costs of the additional safety studies that the new law required the drug companies to complete to gain market approval. To avoid lengthy clinical research, many companies had begun to carefully select product candidates to ensure a fast product launch in the US drug market.

As illustrated in Figure 16 and 17, the composition of Merck's new-product launches had changed drastically by the end of the 1950s. MSD had no new-product launches to show in vitamins, sulfa drugs (antibacterial and antibiotic products), and anilines (anesthetics, sedatives, and analgesics), categories that had constituted the basis of the company's strong growth during WWII and the decade that followed. In the 1950s the company had, however, launched an entirely new product line in biologicals (blood products and serums) after acquiring a strong product pipeline through its merger with Sharp & Dohme.

The launch of new steroid products had peaked for the most part in the 1940s, and new-product launches in this category had gradually declined in the following decades due to decreasing interest in steroid research. In an attempt to boost its slowing sales of vitamins, sulfas, anilines, and steroids, Merck engaged in new learning in hopes of developing new applications for those chemicals in the animal-health market. Medicinal products for animal health had accounted for nearly a quarter of the company's new-product launches in

³⁶ After the organizational restructuring in the early 1960s foreign operations had been consolidated under the new division of Merck, Sharp & Dohme International. 37 percent of the company revenues came from the new international division.

the 1950s. The success it had achieved in finding new applications for aging product lines had encouraged the company to invest in the animal-health and agricultural-chemicals segments in the following decades.

During the decade following the legislative overhaul of 1962, new-product launches had been concentrated on vaccines and drugs for rare diseases as well as on products in the animal-health category. The products launched in these three categories had accounted for one-third of all products launched in this period. The productivity achieved in vaccines had been the result of intensive learning efforts dating to the mid-1950s under the leadership of Dr. Maurice Hilleman, one of the world's most renowned microbiologists.

Prior to the 1962 legislation there had been no incentive for the drug companies to develop medicines for rare diseases, the limited patient population offering no significant source of revenue. But after the 1962 law, had come into effect, drug companies found themselves attracted to developing products for such small markets, since the safety studies required under the new regulations were limited in scale, given the small size of the patient populations affected. Products offered in the rare-diseases category -- examples being Cusprimine (penicillamine) for the treatment of Wilson's disease and Cosmegen (doctinomycin), an antibiotic with anti-cancer agents used to treat rare forms of cancer -- had been the byproducts of learning that had taken place under research programs in vitamins, antibiotics, analgesics, and other established drugs. (Tishler, 1983). As the company scientists occasionally discovered new chemical compounds, or new indications for existing compounds, Merck began to introduce new drug therapies for the treatment of rare diseases. Despite the small market size such products had ultimately become profit-makers (Scheinberg, 1981; Reinhold, 1981).

Extending the lifecycle of anti-hypertensives in the 1970s

Before the age of “wonder drugs” came to an end in the 1960s, Merck had initiated new learning in the area of hypertension. Driven by the idea of working “beyond the limits of knowledge,” Karl Beyer, a researcher who came to MSD through the Sharp & Dohme merger, decided to apply knowledge developed while S&D was working on sulfa drugs to the treatment of hypertension. Among the intangibles acquired through the merger had been outstanding researchers like Beyer and Dr. James Sprague. Trained in medicine and physiology, Beyer was a rare talent with a broad array of skills and expertise in such fields as chemistry, biology, physiology, pharmacology, and medicine.

At the time of the merger the scientists at both Rahway and West Point were engaged in new learning on antihypertensives. Soon after the merger Pfister’s group from Rahway and Beyer’s group from West Point had begun to exchange ideas on the potency of chemicals that each group had developed as blood-pressure-lowering agents. This effort had led to the development of a ganglionic-blocking agent called mecamylamine that was launched in 1956 as Inversine, the merged company’s first antihypertensive drug.

At the time of its market launch, the group at West Point led by Beyer and Sprague had already made significant progress in pursuing two different promising candidates. Although mecamylamine had been a better alternative to other antihypertensive compounds (quaternary ammonium ganglionic blockers) but early results of a new diuretic, chlorothiazide, had shown it to have outcompeted all the other ganglionic blockers, including mecamylamine, as an effective blood-pressure-lowering agent. The launch of Inversine had helped greatly in familiarizing the sales and marketing division with the market for antihypertensives, of which the sales people had no prior experience, and in preparing the sales force both for the use of diuretics as antihypertensives and for other innovative drugs used in managing high blood pressure and cholesterol.

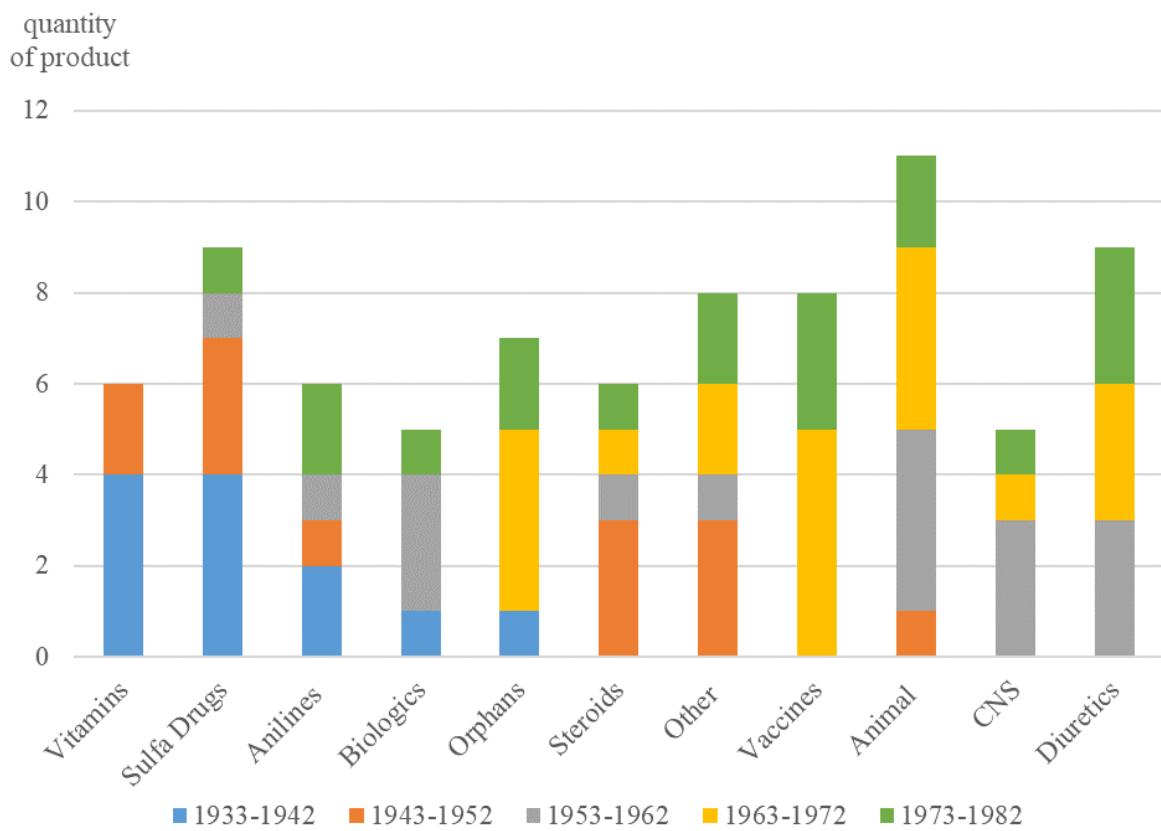
By the end of the clinical experiments conducted on hypertensive patients in 1957, chlorothiazide had been confirmed as the company's premier new medication for the management of blood pressure (diuretics), and it was launched as Diuril in 1958. Within a short time of Diuril's launch, a slightly modified, new version of chlorothiazide, Hydrodiuril (hydrochlorothiazide), was developed at MSD, and rival companies began to bring similar thiazide-based diuretics to market to compete with Diuril. The launch of Diuril also marked the beginning of a race between MSD's Rahway and West Point researchers to develop more effective antihypertensive drugs. Pfister developed methyldopa, a non-diuretic antihypertensive, which was branded as Aldomet when it was launched in 1962. The second promising lead Beyer and Sprague pursued at West Point was ethacrynic acid, a second-generation diuretic branded as Edecrin when offered in the market in 1965. Antihypertensive drugs became an important driver of sales growth in the 1960s and 1970s (Figure 16 and 17).

By the end of the clinical experiments conducted on hypertensive patients in 1957, chlorothiazide had been confirmed as the company's premier new medication for the management of blood pressure (diuretics), and it was launched as Diuril in 1958. Within a short time of Diuril's launch, a slightly modified, new version of chlorothiazide, Hydrodiuril (hydrochlorothiazide), was developed at MSD, and rival companies began to bring similar thiazide-based diuretics to market to compete with Diuril. The launch of Diuril also marked the beginning of a race between MSD's Rahway and West Point researchers to develop more effective antihypertensive drugs. Pfister developed methyldopa, a non-diuretic antihypertensive, which was branded as Aldomet when it was launched in 1962. The second promising lead Beyer and Sprague pursued at West Point was ethacrynic acid, a second-generation diuretic branded as Edecrin when offered in the market in 1965. Atihypertensive drugs became an important driver of sales growth in the 1960s and 1970s.

By the time Gadsden had stepped in as MSD's CEO in 1964, some of the major antihypertensive drugs developed by MSDRL either had been launched or were undergoing clinical tests. But Merck launched no new-generation antihypertensive drugs between the 1962 enactment of the drug-safety law and the 1970s, after Tishler had retired

and been replaced by Sarett. After flat period lasting most of the 1960s, the first new antihypertensive agent was discovered late in the decade based on research by a group of steroid chemists who were screening a large library of chemicals trying to identify an effective compound (Palmer & Kleyman 1994). Further research revealed the antihypertensive effects of amiloride, and Merck had quickly launched the new compound under the brand Midamore in 1970. The first beta-blocker, Blocadre (timolol maleate), had been developed in the lab at Frosst not long after Mercks acquisition of it.

Figure 17: Major product launches by decade, first 50 years of R&D at Merck, 1933-1982



Source: Own illustration based on data from company annual reports

As illustrated in Figure 17, Merck launched 9 medications for blood-pressure management (diuretics) based on five chemical compounds discovered in the research labs at either Rahway or West Point. Until the launch of a new product line within the cardiovascular products market in the late 1970s, the company's engagement with learning in antihypertensive drugs had not only afforded the company its major profit center, but also opened a new learning path in protein research that would allow it to enter into the "statins war" against Pfizer, an old rival that had beaten Merck in the penicillin race.

Early engagements in organizational learning in the fledging fields of biochemistry: enzymology and immunology

A group of Merck researchers, in particular at its West Point lab, had grown interested in biochemistry and microbiology in the early 1960s, well before Vagelos' arrival at the company in the mid-1970s. In 1962, Dr. Bruce Merrifield at the Rockefeller University announced "solid-phase" peptide synthesis, opening a new learning path that was to lead to biochemists' making the synthesis of peptides with longer amino chains (proteins) possible. Having secured the support of Tishler and Gadsden, a group of Merck researchers under the leadership of Dr. Robert G. Denkewalter and Dr. Ralph F. Hirschmann embarked upon an ambitious scientific undertaking. Although Merrifield's achievement stimulated interest in peptide chemistry of large industrial research labs in the mid-1960s, experimenting with the synthesis of peptides was of such complexity that it had been pursued by only a few academic institutions in the US: Rockefeller University, the University of Pittsburgh, and the National Institutes of Standards and Technology (Hirschmann, 2007). At the time, however, Max Tishler, Merck's chief scientist and a big protein enthusiast, managed to secure and sustain unanimous managerial support for this basic-research effort even though it offered no immediate aid to the company's ongoing drug-discovery and -development efforts.

Although they had achieved it through independent efforts, research teams at Rockefeller University, led by Merrifield and Dr. Bernd Gutte, and at Merck announced the synthesis of a simple enzyme called ribonuclease, or RNase, at a joint press conference in 1969. This accomplishment was monumental: As a way of illustrating its scale, Cordes (2014) called it "the chemistry analog of putting a man on the moon." Considered a milestone in the evolution of modern pharmaceuticals, the event is thought to have "bridged the interface between chemistry and biology," the opportunity to explore the wonders of the newly discovered world of enzymes having brought together chemists and biologists, who had theretofore rarely been seen in interaction with one another (Cordes, 2014).

This achievement also marked the opening to the organization of a new learning path in protein chemistry³⁷. Having successfully led the research efforts, Hirschmann was promoted in 1972 to head the MSDRL's Medicinal Chemistry Department in West Point, and the peptide research group was transferred there with him from the Basic Chemistry Department in Rahway. Through recruiting prominent academic figures in the fields of organic chemistry and biochemistry as consultants, Hirschmann managed to attract some of the top young scientists to the Medicinal Chemistry Department.

³⁷ Proteins are essentially the bigger versions of peptides comprised of long chains of amino acids (the building blocks of molecules that makes up peptides or proteins). Molecular size of proteins are much larger than organic chemicals used in medicinal products hence protein biosynthesis is a more complex scientific undertaking than the synthesis of organic chemicals. Given their vital functions within organisms such as catalysis of biochemical synthesis.

Merck continued in the early 1970s to increase its investments in the program for the synthesis of peptides or proteins (longer-chained peptides) in order to sustain organizational learning efforts in protein chemistry. Along with the learning efforts the protein chemistry group carried more research in the synthesis of more complex proteins as well as the development of manufacturing processes for high-volume enzyme production. Through this learning process Merck eventually engaged in more learning in the fledging field of immunology, particularly in the synthesis of interferons, which are signaling proteins that activate an organism's anti-viral defense forces in the event that a pathogen tries to infiltrate it.

This learning period in protein chemistry coincided with changes in the research leadership. At the time the synthesis of RNase was announced in 1969, the longtime leader of MSDRL, Tishler, was promoted to senior vice president for Research and Development. Having recognized his distaste for any work outside the research area, and especially on the corporate side, Tishler decided to retire after serving only one year in this post. During his 33 years at Merck, he had served in capacities ranging from organic chemist when first hired in 1937 to senior vice president of R&D, and he was a member of the board when retired in 1970. During a little over three decades, Tishler had involved, in various forms and capacities, in the development of 75 percent of the all products introduced by Merck.

It was shortly after Tishler had been replaced by Sarett as president of MSDRL that a reorganization of the company's R&D operations began with the relocation of the peptide research group from Rahway to West Point, where important company research operations such as pharmacology and vaccines were also locatedSenior researcher leaders such as Pfister, the co-developer of Aldomet, first antihypertensive successfully marketed by Merck, and Denkewalter, the father of the protein chemistry, had left the company after the departure of Tishler, who had recruited them in the late 1930s and early 1940s.

The Gadsden-era diversification campaign coincided with Sarett's tenure, first as the head of basic research between 1962 and 1969, then as head of Merck's entire research operations between 1969 and 1976. Only in vaccines was a boost in the introduction of new products experienced. At the time the vaccines division at West Point was under the absolute control of Hilleman. Under his leadership Merck introduced nine major vaccines in the 1960s and 1970s.

The most notable launches of innovative new products were those of vaccines against viruses such as measles (1963/1969/1971), mumps (1968/1971), rubella (1969/1971), and meningitis (1974). Besides the vaccines, antihypertensives, and orphan drugs, the only notable products launched were Sinemet (1973) for Parkinson's disease; Clinoril (1976) for arthritis; Flexeril (1977) for muscle relaxation; Mefoxin (1978), a broad-spectrum antibiotic; and Dolobid (1978), an anti-arthritis. Sinemet, a byproduct of research on diuretics; Clinoril, an analog of the company's flagship non-steroidal anti-inflammatory drug (NSAID) Indocin; and Dolobid, an analogue of the most popular analgesic, aspirin,

which had been developed as an arthritis-medication alternative to steroid-based drugs, had all been the byproducts of research programs initiated when Tishler headed the research division. Mexfoxin had been developed under his leadership although it wasn't launched until 1978, two years after his tenure as president of MSDRL had ended. Aside from Mexfoxin, it appears, Merck had introduced not one radically innovative new therapy during his tenure as president of MSDRL.

During its nearly 50-year history, Merck Research Laboratories had evolved from an operation staffed by a few men into an industrial powerhouse employing thousands. Despite a couple of flat periods in newproduct launches, Merck's ability to improve its productivity through cyclical and structural changes in markets and technology had been an impressive story followed by many academics, journalists, and practitioners of pharmaceutical innovation. Despite all the changes, some of them disruptive, taking place in the industry Merck, had managed to maintain a stable environment where the company values had, in essence, remained unchanged. Fundamental research had been put on a pedestal, and those in charge of it had been entrusted with extraordinary authority to make decisions that could make or break the entire organization.

Over a period accounting for 40 years of its half-century life, Major and Tishler had transformed a small laboratory with modest research agenda run by a dozen of scientists into a massive organization discovering and developing innovative drugs through the collaborative efforts of more than 2,000 researchers. Sarett's short tenure as the head of MSDRL had coincided with not only a flat period on new-product launches but also a period of major developments in the field of biology.

Over that four-decade period the company's core-competency had been built around organic chemistry, but organic chemistry alone could neither constitute the basis for competitiveness nor yield the productivity the company anticipated. Even the company's top research managers, all trained the field, had recognized that the paradigm in drug research was long overdue for a major shift, as were the company's chemistry-based capabilities.

At the time of the research division's 40th anniversary, the top Merck executives were searching for a candidate to lead it. The MSDRL presidential search committee narrowed the field down to a single candidate, Vagelos, recognized as a prominent scientist and research leader in the field of biochemistry, to captain its organizational-learning efforts in the fledging field of biochemistry.

4.1.3 Vagelos is the chief scientist: A new era for drug research at Merck

In 1976 Sarett had stepped down from an active research-leadership position to a more passive role: As the "Mr. Outside Guy," he was to be the company's spokesperson on science-related matters, dealing with its external scientific affairs at the highest level. As

his predecessors had done, Vagelos received a promotion to head of entire research organization after serving a year as director of fundamental research.

Vagelos initiated a major research restructuring campaign by asking Hirschmann to step in as the new vice president for Basic Research, a critical post that Vagelos himself had most recently held. Hirschmann was at this time among the company's celebrity scientists, having been co-director of the project on the synthesis of RNase with Denkewalter, who had left the company following its completion in the late 1960s.

Since the departure of such high-profile research leaders as Tishler, Denkewalter, and Pfister in the early 1970s, Sarett had brought no one in from outside to fill the vacancies, many of which had been filled by former Sharp & Dohme scientists working at West Point. Hirschmann, a Rahway scientist recruited by Tishler and Folker in 1942, had been promoted upon a recommendation Tishler had made prior to his retirement; as the new head of Medicinal Chemistry he replaced Sprague, who had left the post to go into retirement in 1972. Upon his appointment as vice president of Basic Research by Vagelos four years later, Hirschmann's first marching order was "to restore the calm among the chemists and to recruit heads of biochemistry and immunology" (Hirschmann, 2007). Unrest among members of the company's scientific community had apparently been as troubling as its lack of progress in catching up in the growing field of biology.

In the 1960s, well before Vagelos' arrival at the company, Merck already had a program under way on the development of lipid biosynthesis inhibitors; the drug candidates pursued in the program had, however, failed to produce positive clinical results as an efficient inhibitor of HMG-CoA reductase, an enzyme that induces the production of cholesterol in the liver. As the general knowledge base in protein chemistry expanded in the early 1980s, researchers at Merck began to consider employing a more "rational" approach to designing a molecule that would inhibit the excessive production of low-density lipoprotein -- LDL, or "bad cholesterol" as it is commonly referred to.

Research efforts at the Squibb Institute of Medical Research in Princeton, New Jersey, had led to the development of the first ACE inhibitor, Captopril, in 1977. As Merck had spent years on ACE-inhibitor research earlier, researchers there at first perceived the development of Captopril as a defeat. Vagelos quickly restored the morale and revamped the efforts of the organization. Because Captopril caused an unpleasant side-effect, loss of taste, Merck decided to work on a more effective compound with significantly less prominent side-effects.

Merck quickly deployed extensive resources to a research program aimed at a new ACE inhibitor, putting it under the direction of Art Patchett. This effort led to the development of enalapril, which was launched in 1984 under the brand name Vasotec and quickly outperformed Captopril in the market to become the leading branded ACE inhibitor product worldwide. The only antihypertensive drug to outperform enalapril in the market would be

another Merck ACE inhibitor, lisinopril, branded as Prinivil. Also developed by Patchett, it was launched in 1987.

MSD's research efforts to discover new statins (HMG CoA reductase inhibitors) were also induced by the competition in the drug market. In the mid-1970s two Japanese microbiologists from Sankyo Fermentation Research Laboratories, Akina Endo and Masao Kuroda, had revealed the results of their study on Citrinin as a molecule with a potential for inhibiting cholesterol expression in liver. Citrinin had been first isolated as a chemical compound through penicillin-research programs in the early 1900s and had been known to scientists since then. In 1976 Endo and Kuroda announced the discovery of a new compound, compactin (also known as "mevastatin"), which it subjected to clinical testing" in the late 1970s through the 1980s.

Owing to its long history in penicillin research, Merck was very swift to recognize the opportunity this new breakthrough presented and to make headway in the race to develop the first commercial HGM-CoA reductase inhibitor. This was no surprise, as Vagelos, who led its research division and who was to oversee the development of the world's first successfully commercialized HGM-CoA reductase inhibitor, lovastatin (Mevacor), from discovery to market.

Vagelos, in the 1980s, was at the time the world's leading expert in lipid metabolism. In 1978 a low-density lipoprotein (LDL) lowering agent, lovastatin, was first discovered through a fermentation product for screening project (FERPS), a biological-drug screening process developed by Patchett while he headed Merck's New Lead Discovery department in the mid-1970s. Under the direction of Albert W. Alberts, a longtime colleague of Vagelos from NIH and Washington University in St. Louis, Merck pursued lovastatin as a clinical candidate effectively inhibiting the enzyme inducing the production of LDL within an organism.

The research program on HGM-CoA reductase inhibitor, in which Vagelos had vested enormous faith and confidence, became a top priority for Edward M. Scolnick when the latter succeeded the former as head of research at Merck. When news arrived at Rahway that Endo's statin candidate, compactin, had toxic effects, Vagelos quickly halted the research on the structurally similar compound lovastatin. Once the clinical safety of Merck's compound had been established by medical experts, Vagelos reinstated the program, and lovastatin was first sold, under the brand name Mevacor, in 1987. As the result of further research, a more effective statin, simvastatin, was brought to market under the brand name Zocor in 1991.

New-generation vaccines for the hepatitis B virus (HBV)

In the wake of the molecular biology revolution, many scientists, Scolnick included, envisioned no future for peptides as potential drugs given that the bioavailability of peptide as biochemical agents was perceived as less rich than that of organic chemicals (Hirschmann, 2007). However, large-scale production even of proteins, which are peptides with longer amino-acid chains, had become possible through the recombinant DNA method, a new technology pioneered by young biotechnology start-ups such as Genentech. Through employing the gene-splicing process (expression of a DNA segment intended for cloning in a host organism such *Escherichia coli* –*e. coli* for short- bacteria), the production of a protein through the industrial fermentation process had become possible.

Although the company had already initiated a learning process to acquire the necessary knowledge in microbiology and enzymology, the company's interest in the protecting chemistry and molecular biology was limited in the 1980s. In the late 1970s some of Merck's major rivals -- as among them, Lilly, Roche, Schering, Pharmacia, and Wyeth -- had already undertaken early exploratory research in molecular biology and genetic engineering through collaborations with early biotechnology start-ups such as Cetus (Chiron), Genentech, Biogen, and Amgen. Merck's involvement with this fledging field of biology had been limited to the development of a hepatitis B vaccine through a research collaboration with Chiron Corporation.

By the end of the 1970s, Merck had very focused product strategy, particularly in the anti-hypertensive and anti-inflammatory drug markets. William J. Rutter, chairman of the biochemistry department at the University of California San Francisco (UCSF), decided to consult with Vagelos in 1977 to identify parties in the biopharmaceutical industry who would potentially be interested in a new method that would produce insulin more efficiently through utilizing a genetic-engineering method he and his team at UCSF had developed. Rutter had decided to reach out to Vagelos only because, at the time, Merck had no presence in the insulin market and Vagelos wouldn't be in any form of conflict directing Rutter to one of its competitors³⁸. Vagelos, however, showed an interest in Rutter's technology, observing that it could be useful in the development of the hepatitis B vaccine (HBV) that the company was already pursuing.

Rutter subsequently became concerned about losing two of the key scientists on his research team, as they had been approached by Amgen. In an attempt to keep the team intact, Rutter co-founded Chiron Corporation in 1981 with the team's core members, Edward Penhoet and Pablo DT Valenzuela, as his new business partners. The decision to start a new business followed Rutter's securing a contract under which Merck gained the

³⁸ According to Vagelos (2004) at that meeting Rutter had asked whether Merck would be interested in using the recombinant technology to make insulin. Such offer had been declined given the company's focused growth strategy in the selective markets in which the company had possessed competitive advantage.

right to develop the HBV using Chiron's recombinant technology. Chiron agreed, in exchange for certain royalty rights and financial support that would allow it to acquire lab space in San Francisco Bay Area to work on the project, to out-license the vaccine using the peptides cloned by employing Chiron's recombinant method, as well as to consult with Merck's Vaccine Division during the production phase on the manufacturing of the HBV (Rutter, 2005).

Simultaneously with Merck's pursuit of a contract with Chiron, its scientists were working on a non-recombinant HBV under the command of the world's top vaccine expert, Hilleman. Neither he nor his team had shown confidence or interest in the recombinant method Chiron had to offer. Rutter (2005) argued in spite of overwhelming evidence that the recombinant method yielding higher efficiency during production at industrial scale Hilleman camp had insisted on not fully implementing the new method and therefore experienced significant production issues that resulted in occasional shortages since the introduction of *Heptavax B* in 1982. Once the Merck version of the vaccine had been introduced under the tradename Recombivax HB in 1986, Merck withdrew the Chiron version from the market. The new product was marketed as an original Merck product developed internally. Because this was having significant impact on the validity of both Chiron's technology and its credibility as a company, Rutter launched a public relations campaign disputing Merck's statements and claiming partial credit for the development an iconic product (Rutter, 2005).

It was because of the success Merck had achieved in developing recombinant vaccines that Vagelos decided to recruit Scolnick, one of the nation's leading scientists, from National Institutes of Health to become executive director of virus and cell biology program at Merck in 1982. Through employing some of the top scientists in the field, the Merck's infectious-disease programs had built up momentum for the years to come. It was in 1986, a few years after researchers had first isolated the human immunodeficiency virus (HIV), that Merck joined the race to develop a cure. A series of events, however, interrupted the learning process in the protease- inhibitors program in the late 1980s, undermining the innovation process and placing Merck at competitive disadvantage. Aside from therapies it acquired through the merger with Schering-Plough, Merck still doesn't have a competitive market share in immunology and oncology, one of the most lucrative segments of the drug market. The aforementioned events will be further discussed below.

Merck takes its first steps in exploring new drugs through external partners

The lackluster performance of most of the products Merck had launched in the-1970s were of concern to Vagelos as the expectations of management, investors, and employees grew for the launch of another product with blockbuster potential. That the patents of the company's latest heavyweight products -- Aldomet and Indocin, a blood pressure management medication and an NSAID, respectively – were fast approaching expiry was increasing the pressure to come up with a new product to satisfy Merck's stakeholders. It

was the shareholders, however, for whom Vagelos was particularly anxious to deliver results.

In his autobiography, Vagelos acknowledges the pressure he experienced at the time to deliver blockbuster results:

We were struggling to solve these internal problems [referring to dissonance among research teams and units] and get our momentum back, and I was not at all satisfied with our progress or with my own efforts as president of MRL. All I had to do was read the company's Annual Report that year [1980] to be deeply concerned. These documents are almost always upbeat...

...

When I looked at the report, I wanted to tell everyone, "WE JUST NEEED MORE TIME!" But obviously I couldn't do that, and in the meantime, the report in effect told our employees, the public and the investors that Merck either hadn't broken out a flat period or was encountering a major internal problem, or both."

(Vagelos & Galambos, 2004, p. 148)

A joint-venture agreement with Swedish Astra AB was signed into effect in 1983 for the co-development and co-marketing of various Astra and Merck products in the US and overseas. Astra, which had an expanding pipeline of innovative new drugs, was eager to explore the fast growing drug market in the US, decided to approach Merck on account of the cost associated with getting US regulatory approval. That same year Merck completed a series of acquisitions that included the outright purchase of Laboratorios Abello in Spain and, of greater significance, the acquisition of majority ownership of Japan's Banyu and Torii & Co. The latter move was a major step in Merck's global expansion plan, as it strengthened the company's standing in the world's second-largest pharmaceutical market. As major corporate restructuring efforts began to settle down under new leadership, the share of foreign sales had increased to 44 percent of the total sales (excluding Merck-MEDCO sales in the US) by the end of 1996.

From Merck's period of searching for external sources of new leads, one particular event stands out: A potentially path-altering opportunity, it might, if not overlooked, have opened a completely new avenue of growth to the company. Among Sarett's duties, once his promotion had made him the face of the company for scientific affairs, was to play an active role in scouting for new talent and ideas that Merck could acquire. Among his major tasks involved "The Patent Term Restoration Act of 1981," which, if it had passed, would have amended the patent law then in effect to restore that part of a drug's patent life that had been lost during the FDA approval process. Facing patent cliffs at the time were Indocin and Aldomet, the largest revenue generators among Merck's products at the time.

Among the industry representatives to testify at a hearing of the US Senate Judiciary Committee on the bill in the April 1981, along with Sarett, was Thomas D. Kiley, a vice

president and general counsel at Genentech. According to Sarett (1990), a proposal that Merck acquire Genentech, one of the first biotechnology start-ups to pioneer the recombinant DNA technology in the 1980s, had been rejected by Merck's top management. Having recognized that there was fertile ground in the field of molecular biology, Sarett urged the leadership to pursue the technological changes revolutionizing the biopharmaceutical industry around Merck, and to act upon it by acquiring a firm. Sarett (1990) provides his account as follows:

... During that period, for instance, the recombinant DNA came into being. Genentech was formed and I went out and tried to buy Genentech for Merck, before they even had a laboratory bench. I was unfortunately not able to persuade the management that recombinant DNA technology had any future! [Laughter]

(Lewis Sarett 1990, p. 48)

Although the research community at Merck did not welcome the idea of adopting products “not-invented-there”, the idea of acquiring companies had been embraced by both Tishler and Sarett. As the Merck Research Division was getting ready to celebrate 50 years of developing outstanding products without significant support from outside the company, in the early 1980s Vagelos was formulating a plan to fill the pipeline of potential new blockbusters. These efforts gathered further momentum through the decade as the prevailing research culture at Merck was ruptured and the company began to adopt ideas originating outside its own labs.

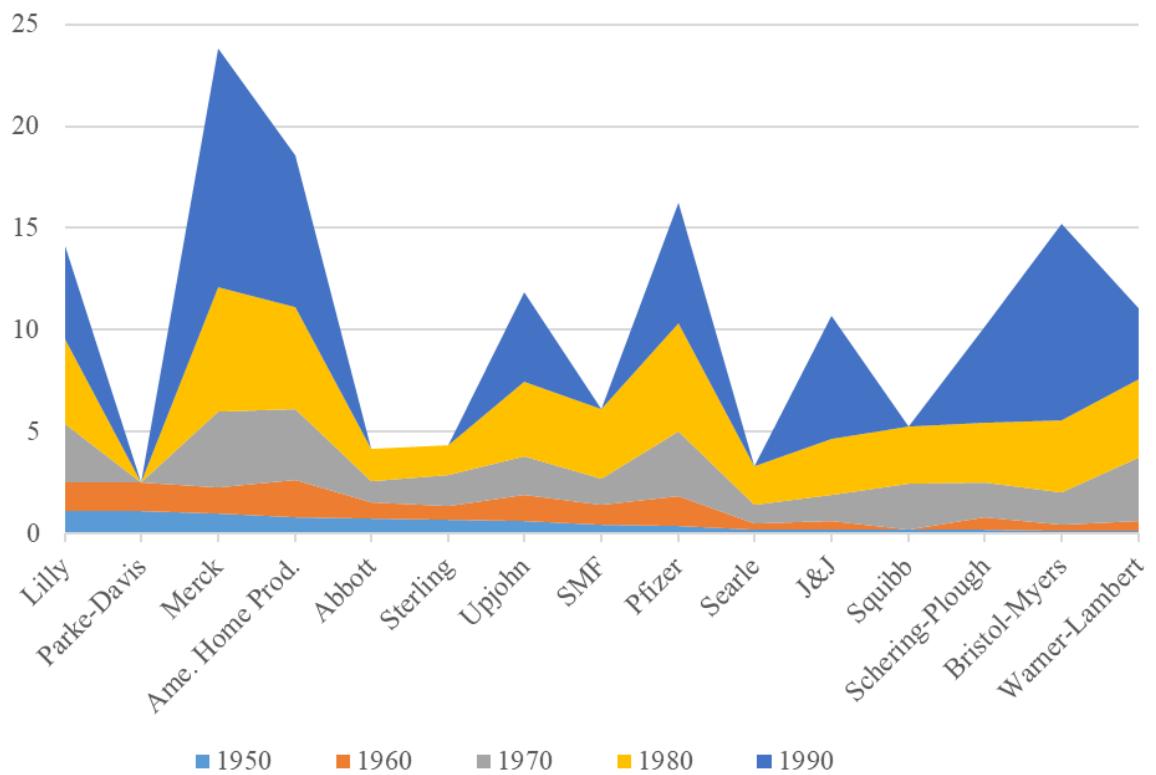
Organizational learning efforts under Vagelos led to one of the most productive periods Merck had experienced, which coincided with Merck's Centennial Celebration in the early 1990s (Figure 18). The company's ACE inhibitors, Enalapril and Lisinopril, became the most successfully products in the market for antihypertensives. By 1996 the combined sales of the company's cholesterol therapies, Zocor and Mevacor, accounted for approximately 40 percent of the global cholesterol-drug market. (MAR, p. 34). With the launch of a new-generation antihypertensive co-developed with DuPont, Cozaar -- and its companion drug Hyzaar, a combination of Cozaar and Hydrodiuril, which was Merck's first-generation diuretic -- the company clinched its position as market leader for drugs treating major cardiovascular diseases.

Proscar (finasteride) represented a major pharmaceutical breakthrough as the only drug on the market in the 1990s able to shrink an enlarged prostate safely and effectively, although its sales had yet to reach blockbuster status. The company's first antacid compound, Pepcid (famotidine), licensed from the Japanese Yamanouchi Pharmaceutical, had by the mid-1990s become the second most prescribed in the United States despite facing severe competition from both generic and over-the-counter (OTC) alternatives. Together with Primaxin, another effective antibacterial agent, in 1985; Prilosec (omeprazole), another antacid compound licensed from Astra AB, in 1987; and Recombinvax, Merck's own

recombinant HBV vaccine, in 1987; the Vagelos-led innovation campaign greatly improved the company's financial position, turning it into America's Most Admired Company in the late-1980s and early-1990s.

Figure 18: Pharmaceutical sales by major American companies, 1950-90 (US\$2016)

(Sales in 2016 \$bn)



Source: Own illustration based on data from Achilladelis (1999) & companies' annual reports

When Vagelos joined the company as director of basic research in 1975, Merck's annual sales were \$1.5 billion. Ten years later, when he was elected CEO and chairman of the board, the company's total sales had slightly more than doubled, to \$3.1 billion. When Gilmartin took over both posts from him in 1995, Vagelos left behind an organization that had been generating \$16.7 billion sales (including \$5.7 billion sales from the newly acquired MEDCO division). At the end of 1996, by which time the last of the Vagelos-era products in cardiovascular (Cozaar/Hyzaar) and osteoporosis (Fosamax) had spent a full year in the market, Merck was preparing to report sales of \$19.8 billion for the year just completed.

During the 20-year period under Vagelos's leadership, as both director of research and CEO, Merck had experienced nearly elevenfold growth. Its success is illustrated by Figure 19, which compares decade-by-decade changes in the sales performance of the leading

pharmaceutical companies in the US between 1950 and 1990. Data on the sales of ethical drugs as shown in the Figure 18 are adjusted for inflation and calculated in 2016 US dollars. In Figure 18 each color-coded area represents one decade, starting with 1950, coded in green at the bottom of the stack, to 1990, coded in blue at the top of the stack.

As indicated in Figure 18, through waves of industrial consolidation activities in the 1970s and the 1980s, the 1950s' top 15 US pharmaceutical manufacturers had merged into eight major organizations forming “big pharma” companies by the 1990s. Since the products launched by the top 15 companies had shown great similarities in the 1950s, the sales performance of Merck and the other 14, as well as their in the list (led by Parke-Davis and American Home Products) had remained the same as in 1960. Thanks to the introduction of some major, first-in-class therapeutics, Merck had managed to outperform its competitors over half a century and to become the industry leader in ethical-drug sales.

4.1.4 Transformation out of Old-Economy enterprise, early-1990s

Without background in running a large pharmaceutical business establishment, most of his managerial skills were developed through on-the-job training. He was apprenticed by Horan in running a large pharmaceutical business and educated by Spiegel and Lewent on matters of corporate finance. Having completed graduate training in finance at MIT's Sloan School of Business and worked as controller at Pfizer, at Merck Lewent introduced new scientific methods -- namely, the Monte Carlo simulator -- to assess project value and aid in making make a keep-or-drop decisions. During this period Merck employed new managerial decision-making tools to assess potential value of a research program before determining the fate of such a program. More marketing and financial consideration began to go into Merck's decisions on the future of a research project. The changes marking this period constituted a major departure from the status quo in that, historically, the research leadership at Merck had overseen the decision-making process almost exclusively.

Judy Lewent had joined Merck in 1980 to fill a newly created post as Director of Acquisitions and Capital Analysis and was promoted to executive vice president (EVP) and chief financial officer (CFO) in 1990. During her tenure at Merck, Lewent developed a management project-assessment tool, “Research Planning Model.” Based on option theory, the tool was designed to assess the value of investment opportunities (i.e., intramural or extramural drug-research projects) by allowing managers to compare and contrast projects during the decision-making process. Her team began to apply financial models such as Black-Sholes and Monte Carlo simulation in an attempt to value research projects and hedging revenues against potential business risks, among them currency fluctuation and policy changes.

During her tenure at Merck, Lewent experienced the ups and downs of the pharmaceutical business. As the “lean, mean and determined” CFO, Lewent managed the financial resources of a highly distressed company on the brink of bankruptcy for a brief period

(Zweigenhaft & Domhoff, 2007, p. 186). Lewent also oversaw the company's massive stock-buyback programs in the mid-1990s, which were primarily financed by the proceeds of divesting assets, most of which had been acquired under the corporate diversification program of the 1960s and 1970s. She played an important role in building JV with Du Pont and Johnson & Johnson, as well as in the acquisition of MEDCO.

Merck had begun to lose researchers in strategic fields, particularly after Scolnick became the head of Rahway in 1984. Among those defecting from Merck in the early period of the biotechnology revolution was Joshua Boger, who left the company to start Vertex Pharmaceuticals in 1989. Concerned over the direction of research at Merck, Boger aspired to build a better version of Merck, one that resembled the Merck at which he had begun working, not the Merck he had left. Other Merck defectors later joined Boger to pursue research on protease inhibitors and competed against Merck in the race to develop the first pharmaceutical products for combating the hepatitis C virus (HPC). Still other R&D personnel left Merck to pursue genomics-based research at the biotechnology start-ups of the time. Upon his appointment as CEO, Vagelos had recognized an important organizational issue: Rebellious leadership within the divisions was making it difficult to restore organizational integration within this fast-growing pharmaceutical company. In the 1980s many divisions were operating almost autonomously, pursuing their own long-term strategies without giving consideration to corporate planning efforts and organizational objectives (Vagelos & Galambos, 2004, p. 181).

Rutter (2005) described Merck as a company that became a united divisions of pharmaceutical whereby operating through divisions with strong organizational attributes to independence in the sense as if they are running like a typical subsidiary with self-appropriated budget and strategy. Rutter (2005) explained that the company's first recombinant hepatitis B vaccine (Heptavax) could have achieved greater success in the market in its early years had the Vaccine Division not had excessive pride in its R&D and insisted on pursuing its own version of the vaccine at the expense of Heptavax, a new-generation vaccine whose co-development program with Chiron was championed by Vagelos but often undermined by the Vaccine group under Hilleman (Rutter, 2005, p. 53).

The rapid growth of Merck's global operations in the 1970s and 1980s led to the addition of so many middle managers and so exacerbated the level of bureaucracy that it became difficult, particularly for the research managers, to function effectively. Merck was already bleeding talent, and the growth of corporate bureaucracy increased the rate of defection to small biotechnology start-ups. Toward the end of his tenure as CEO, Vagelos broke the barrier existing within the organization to seeking opportunities through collaborations with external partners. Merck had devised a commercial partnership deal with Johnson & Johnson in 1989 for co-marketing of the company's off-patent products as over-the-counter (OTC) drugs, an example being offering the antacid famotidine as a new heartburn medication under the name Pepcid. It had similarly formed a joint venture with DuPont for

co-developing and commercializing the company's promising new antihypertensive compound Losartan.

After saving it from closure in 1979, Vagelos established the Vaccine Division in 1991 due to the company's success in the launch of new childhood vaccines such as MMRII and PedvaxHIB, as well as adult vaccines developed using recombinant DNA technique, such as Recombivax HB. Merck then formed a partnership with Connaught Laboratories, an affiliate of Pasteur Mérieux Serums and Vaccines and Europe's leading vaccine maker, to strengthen these vaccines' market share in Europe.

A two-decade long career is coming to an end

Merck was entering its second century with many accomplishments to show for its first. Forbes had declared Merck as the winner of pharmaceutical innovation challenge as the company had topped Forbes's Most Admired Companies List for seven consecutive years. But the company's celebratory mood was short-lived, as another episode the political battle over soaring drug prices was fast approaching in the early 1990s. After having served in the Reagan administration transition team, Sarett had become the company's face in political affairs. In 1981, as Sarett was preparing to retire, Connor, the former CEO who had left Merck in 1965 to serve as Lyndon Johnson's secretary of Commerce, had joined the company's board of directors.

As explained extensively in the section discussing policies governing the US biopharmaceutical industry, the 1980s was one of the key periods defining the industry's growth path. Although most of the legislative changes stimulating industrial growth had occurred during that decade, one of the most significant political battles had been waged in the period as well. During each presidential election cycle the issue of drug prices, had focused policy discussions on reforming the structure of the US healthcare and prescription-drug markets. During his communications with William J. Clinton, whose rising popularity during the had made him a front runner for the White House in 1992, Vagelos had recognized the risk of prescription-drug prices' being regulated as part of a comprehensive healthcare reform was not going away.

The gravity of political situation had escalated when Clinton revealed a plan to reform the US healthcare policy that was destined to have a detrimental effect on profits. During the election campaign, the Clinton family invited Vagelos to attend more than one meeting to discuss the implications of the proposed reform. Having recognized how firmly the Clinton healthcare plans were fixed on its implementation, Vagelos began to devise a plan for securing a competitive position in a market in which drug prices would be suppressed through new price-control mechanisms. In the early 1990s the company's long-term strategies were revised based on a new market scenario envisioning significant price wars instigated by the US government, which would become the single largest buyer in the market. Clinton created a taskforce for his healthcare reform plan immediately after he was

sworn into office in early 1993. By the end of 1993, Merck had completed talks to acquire MEDCO Containment Services for \$6.6 billion, \$2.4 billion in cash and the remainder through a stock transaction.

Founded as National Pharmacies in 1983, MEDCO had evolved from a mail-order drug distributor into one of the nation's largest Pharmacy Benefits Management (PBM) organizations, providing pharmacy services through its extensive drug distribution network. MEDCO had been serving millions of subscribers to prescription-drug benefits programs through their employer- or government-sponsored health insurance programs, such as Blue Cross and Blue Shield or federal and state employee plans. When the Clinton healthcare-reform bill was killed once and for all in the late 1994, Merck found itself stuck with a prescription-drug benefit company that accounted for nearly a quarter of its workforce and annual revenues.

Aside from MEDCO's not being a major source of profit, its acquisition led to a series of problems that Vagelos was to hand over to his successor. Some of these problems were legal, among them a growing number of antitrust cases; some were financial, in particular stock dilution issues in the post-acquisition period, and problems both with proper accounting of various revenue items and with the reporting of net income; and some were organizational, like the confusion among employees caused by the new direction in which the company was heading. In the years leading up to the policy reform actions, which were driven by a growing public outcry over soaring healthcare costs, Vagelos had considered some major corporate policy changes. Most notable among those changes had been a self-imposed cap on price increases, an attempt to change the negative public perception of drug companies in the US and to take regulatory pressure off the back of the company. As part of this plan, Vagelos had pledged to increase the prices of the company's pharmaceutical products no more than the increase in the consumer price index, which would tie the changes in drug prices to the inflation rate for any given year. A way of admitting that previous price adjustments had not been pursued as intended, voluntarily keeping price rises to the increase in the general inflation rate would, Merck hoped, prevent regulatory market intervention to control drug prices.

The decision to adopt a voluntary policy of restricting price increases encountered blowback from both within and outside the organization. Vagelos had anticipated that acting voluntarily would help restore the company's ailing public image and soften the position of regulators, while the company's marketing strategists had adamantly argued that the strategy defied common marketing principles. The marketing leadership reminded their CEO of the most fundamental pricing rule applying in pharmaceutical markets with no price restrictions by tenaciously offering the following line: "Vagelos, you are leaving money on table" (Vagelos & Galambos, 2005, p. 230). Adopting the policy caused backlash in the drug industry because it had obliged other firms to take the same pledge, which resulted in major discontent. After having started a new market trend in a consumer-friendly fashion to repair the industry's ailing public image, Vagelos was declared a

"traitor" by executives of big pharma companies that possessed meager innovative capabilities and lived on shallow profit margins.

Vagelos had also assessed the option merging Merck with another large pharmaceutical company, following a pharmaceutical-industry whereby the winners of a given innovation race gobble up those they have defeated. In the year when he became CEO, a giant of the chemical industry, Monsanto, entered the pharmaceutical field by acquiring G.D. Searle. The future US Secretary of Defense Donald Rumsfeld had been the mastermind of the acquisition, which brought Monsanto into the race to develop new-generation painkillers to compete against the infamous Vioxx, the new-generation NSAID that was to destroy Merck's reputation in the early 2000s.

In 1989 SmithKline Beckman had merged with British Beecham Plc., and Bristol-Myers had merged with Squibb the same year. Since the wartime program in penicillin Squibb had sustained an organizational learning effort that allowed it to pursue emerging opportunities in the fledging field of biology, and had competed with Merck on various fronts, particularly in the race to bring new ACE inhibitors to market in the early 1980s. The merger with Bristol-Myers provided a major boost its modest marketing operations. One of the few companies that had kept its quick during this merger-mania was Pfizer, which would ultimately catch up with its peers owing to an acquisition spree in the early to mid-2000s. At the time when Vagelos was scanning the horizon for a worthwhile merger, Pfizer, a company with a competitive sales force and mediocre products, had appeared to him an ideal match for Merck, a company with an average sales force and a highly innovative portfolio. After various contacts with his counterpart at Pfizer, William C. Steere, Jr., Vagelos' had been inclusive.

Glaxo, with the second-largest share of the global drug market, had been another target to consider. Vagelos, however, had reservations about whether that merger would be worth experiencing the pain that a merger often induces in the organizations that are combining operations. Mindful of Merck's pride in its innovative capabilities, Vagelos had been concerned as to whether the Merck community would welcome any outsider merging into the organization. In 1988, when Merck enjoyed a significant boost in the number of new products in its portfolio, it led all other companies in the global drug market, claiming 3.95 percent of market share worldwide -- slightly below the combined market shares of Roche (1.85 percent) and Pfizer (2.1 percent). Second after Merck, at three percent, was Glaxo, which had acquired the US-based Meyer Laboratories and begun to expand in the US. By 1992 Glaxo had replaced Merck as the company with the largest market share, its 4.81 percent edging out Merck's 4.54 percent. Roche and Pfizer were still far behind, at 2.71 and 2.52 percent, respectively. By the time Vagelos retired, Merck had begun to lose market share to others: While its market share had decreased slightly, from 4.54 to 4.4 percent, in 1994, Glaxo, Roche, Pfizer had each slightly increased market share for the same period, to 5.5, 3, and 2.7 percent, respectively. In the mid-1990s the top ten

companies - most of them based in the US -controlled slightly 34.3 percent of the global drug market (Bogner et al., 1996).

An outsider takes over: Raymond Gilmartin becomes CEO

A corporate policy entrenched in the company's bylaws as if it were carved in stone had forced Vagelos to retire at age 65, but, before doing so, he had cannily prepared to transfer power to a successor of his own choosing, a procedure that had been followed by his predecessors as a corporate leadership tradition. The transition in 1994 led to a chain of strange events that shifted the power dynamics within the organization and altered the company's growth trajectory. Setting it off was the abrupt departure of the company's chief operating officer, Richard J. Markham, a protégé of Vagelos whom the latter had groomed to become the next chairman and CEO. This had forced Vagelos to make urgent changes to the design of the executive team that would lead the organization after his departure (Weber, 1993).

Finding the right replacement for Markham had not been easy. Markham had been a critical member of the executive "dream team" in place under Vagelos that had been responsible for implementing the company's global market strategies. While serving in Merck's human health division in Europe, Markham had developed expertise in marketing and selling pharmaceuticals in major European markets that had adopted nationalized healthcare schemes. Having anticipated that the Clinton administration would pursue the adoption of a federal health insurance program, Vagelos and Markham had devised a new marketing strategy that would place greater emphasis on marketing drugs through institutions providing health services -- large hospitals and health maintenance organizations, or HMOs -- as opposed to marketing through prescribing physicians.

Vagelos had been outspoken about his concern regarding the size of the sales forces big pharma companies possessed, which he felt had become increasingly oversized and inefficient as they competed for the commitment of physicians to push through their drugs. Vagelos had been interested in devising and implementing a more efficient marketing strategy that would employ a leaner sales force and SM&D operations to bring products to consumers. Markham, on the other hand, had been reluctant to settle with the cost-conscious managed-care networks on a preferential pricing scheme (Levy, 1993). Given the sequence of events that unfolded prior to Vagelos' retirement, one can safely conclude that the decision to acquire of MEDCO and pursue an HMO-centered drug-marketing strategy had made it impossible for Markham to accept the job CEO position. Outgoing management had settled on a major strategy in which Markham simply was not a firm believer.

Having predicted that a surge in competition lay ahead, Merck's directors appear to have placed greater emphasis on finding a candidate with a strong track record in sales and marketing, and Gilmartin's sales track record at Becton Dickinson had identified him as the

right person for the job (Weber, 1996). Gilmartin turned out to be one of the last members of the “organization man”-era management species, which was quickly nearing extinction in the 1990s, particularly in the biopharmaceutical industry. Gilmartin immediately stood out as an odd CEO by refusing to follow a fashionable trendline in the industry: He had accepted a pay package that was relatively modest in comparison to those of his peers, whose compensation was in most cases tied to net positive sales performance over competitors (Weber et al., 1994; The Economist, 2002). As an avid scholar of management, he had been tinkering with sustainable business models that would be more inclusive when it came to creating value for all stakeholders.

Vagelos’ retirement and abrupt departure from the company had led to a managerial vacuum. Except for Scolnick, all the members of Vagelos’ “dream team” left the company to take leadership positions at rival companies (Weber, 1996). John L. Zabriskie had been considered among the top candidates to replace Vagelos as chairman before he left Merck to become chairman and CEO of Upjohn. Jerry T. Jackson, executive vice president of Human Health Marketing, took retirement to assume the chairmanship at a biotechnology start-up. Until his retirement in 1996, former Vice President of Finance Francis H. Spiegel, Jr., who had helped Vagelos gain the knowledge he needed concerning corporate finance, after handing over the duties of CFO to Lewent in 1991, took a post overseeing the operations of Merck’s joint ventures with J&J and DuPont. Only a few months after turning down the offer to lead Merck, Markham became president and COO of Marion Merrel Dow. After spending a year in retirement, Vagelos accepted an offer to become chairman of New York-based Regeneron Pharmaceuticals.

As Merck’s board of directors was searching for a new corporate leader to succeed Vagelos, the growing uncertainty over the future of the company’s leadership had exacerbated a turf war among its already territorial divisions. Gilmartin had inherited an organization with a crumbling R&D workforce burdened by a lack of research vision. The Clinton healthcare proposal had gone down to defeated in Congress, and Merck was stuck with MEDCO and the lawsuits brought upon its acquisition.³⁹ While transition of power within organizations is often followed by changes in the upper echelon of management, the change within Merck following the departure of Vagelos was overwhelming in both pace and scale. To restore calm and order within the organization, Gilmartin convinced Lewent to remain as CFO and Scolnick as the senior research leader even as many in managerial positions had left to take leadership positions, primarily at fledgling biotechnology companies.

When Gilmartin became CEO, the biopharmaceutical industry was going through a consolidation phase. Growth in the industry was slow due to the prevailing cost-

³⁹ *Half a dozen Pharmacy Benefit Management (PBM-MEDCO) clients sued Merck for self-dealing transactions violating ERISA and the company settled with the plaintiffs in the same year in 2004 (Freudenheim, 2004)*

containment measures introduced by the HMOs in an attempt to rein in the rising cost of healthcare in the US. The structure of the US biopharmaceutical industry was fast changing, with competition concentrated among fewer players. Although the major competitors consolidated their power within the pharmaceutical market, Gilmartin rejected any strategy calling for inorganic growth through a large-scale M&A transaction. So long as Gilmartin failed to address the company's growing productivity problem, however, the market perception of Merck was rapidly shifting in the late 1990s from that of a potential "predator" seeking profitable targets to acquire to that of attractive "prey" to be swallowed.

Glaxo had merged with Burroughs Wellcome and Swedish Pharmacia had merged with Upjohn in 1995. In the following year Ciba-Geigy had merged with Sandoz to form Novartis and become one of the largest global pharmaceutical companies. In 1999 the French Sanofi and Synthélabo had merged to form Sanofi-Synthélabo and the French Rhône-Poulenc had merged with the German Hoechst Marion Roussel to form Aventis. A year later, recently merged SmithKline Beecham merged again, with Glaxo Wellcome, to form GlaxoSmithKline. As the number of biotech start-ups and big-pharma mergers grew, competition in the drug market became concentrated in a small number of large, established companies, hereinafter to be referred to as "pharmaceutical companies," that were pursuing drugs in both biologicals and pharmaceuticals.

Vagelos had relied on the skills and expertise of his lieutenants in corporate matters concerning finance and shareholder relations, but he had kept a close relationship with the research leadership. Unlike Vagelos, Gilmartin had failed to connect with the R&D workforce and relied too much on his scientific advisers in devising strategic roadmaps for the research operations. An outsider to the company and the industry whose background was in engineering and management, Gilmartin gave unfettered authority to run the research operations until Scolnick retired from Merck in 2003 (Hawthorne, 2006, citing Alberts interview).

4.1.5 Transformation into a New Economy enterprise, late 1990 and 2000s

As the consolidation efforts gained traction within the biopharmaceutical industry, Gilmartin managed not to get enticed by the appeal of a short path to growth. He argued that "[a] large-scale merger does not meet our definition of creating shareholder value, which would be in contributing to our pipeline or through our long-term growth," and decided to focus rather on striking R&D deals with the fledgling biotechnology companies of the time (Herper, 2009). While exploring such opportunities, Gilmartin decided to build the company from within and focused on removing any friction among divisions in order to achieve greater synergy across the organization. As part of this campaign, Gilmartin had formed a global product teams to enable greater interaction among stakeholders within the company (Weber, 1996). Through the establishment of global product-coordination teams, Gilmartin pursued a strategy of integrating divisions that had been crippled by the long-lasting turf wars of the past.

Another Vagelos-era strategy was undone when Gilmartin decided to shut down Merck's generic-drug operations, as producing generics was incompatible with his strategy of returning Merck to its roots, thereby making it a research-driven pharmaceutical company once again. As part of this strategy, Calgon Vestal, Kelco specialty chemicals division, and MEDCO's mental health unit were sold in 1994 to Bristol-Myers-Squibb, Monsanto, and Kravis Roberts⁴⁰, respectively. As the marketing group began to influence development of the organization's research strategy, pursuing the discovery and development of compounds to treat chronic diseases such as rheumatoid arthritis became a research priority. Since the launch of Zocor (simvastatin) in 1991 and Proscar (finasteride) in 1992, Merck had pursued no other major clinical candidate except the compound inhibiting cyclooxygenase-2 (COX-2) enzyme. Merck had proudly announced the result of its COX-2 research, Vioxx, as the "biggest, fastest and best launch ever," organizing a glamorous event to mark the product's release in 1999.

In the period following Vagelos's retirement, some of Merck's major products were facing patent expiration. While troubled by the acquisition MEDCO, Merck under Gilmartin had also faced a major challenge for improving its ailing product pipeline. Following the discovery of the cyclooxygenase-2 (COX-2) enzyme in 1988, many companies joined the race to develop a new inhibitor targeting this newly discovered enzyme to stop inflammation and pain. COX-2 inhibitors were discovered to cause less risk of peptic ulcer than first-generation non-steroidal anti-inflammatory drugs (NSAIDs), in which Merck had historically possessed a strong presence.

Having recognized the threat that the winner of the race to develop an effective COX-2 inhibitor could potentially pose, Merck joined the race to develop its own version to compete against the most serious candidate, Monsanto's Celebrex. Besides unmasking the issues experience within the organization, the case of the discovery of the COX-2 inhibitor is interesting because the winner of COX-2 fight would ultimately be Pfizer, which managed to generate significant profits in the large market for anti-inflammatories without engaging in the learning effort needed to develop the product internally while the other had failed miserably doing so.

During the Vioxx controversy, Scolnick, Antice, and Gilmartin created "reality distortion field" as they used "alternative facts" to dispute medical and support the position that Vioxx was a safe drug. This "reality-distortion field" reached epic proportions, dwarfing even that created by Steve Jobs, who had famously mastered the practice at Apple Computer to sell "insanely great" products that had been the offspring of his own vision. Merck's public-relations group managed to put a positive spin on clinical results indicating a significant increase in the risk of cardiovascular problems among patients taking Vioxx over that among patients taking NSAIDs that had been causing stomach issues. Instead of

⁴⁰A private-equity firm founded by the notorious Henry R. Kravis who had become known in the 1970s as "corporate raider.

admitting that Vioxx had serious side effects and caused heart problems, Merck stated in a press release issued on May 7, 2000, that “findings from Merck’s large outcomes study showed significantly fewer heart attacks were observed with naproxen.” The press release not only claimed that Vioxx was safe but also implied that Roche had been sitting on a gold mine given that the company’s popular NSAID, naproxen, had supposedly had additional benefits such as preventing heart attacks!

The statement reveals the scale on which scientific research was being mismanaged within the organization in this period. Not only had greed reached a new height, but organizational behavior had changed so quickly that the research team was in a state of shock. Nesi (2008) demonstrates the intensity of the pressure upon the employees at Merck to keep an unsafe, and very expensive,⁴¹ drug on the market by sharing a joke employees were telling: They would “be putting Prozac (an antidepressant) in the cafeteria water” (p. 183).

Both Scolnick and Antice had been highly competitive leaders within their respective fields of research and marketing. They had thrived in a very competitive race against Pfizer to bring a product such as Vioxx to market first at all costs. They were also, to some extent, racing against one another as they vied not to be the first one to fail. Teaming the research chief Scolnick with the marketing chief Antice in the absence of supervision was a mistake that turned out to be deadly in the literal sense and that wreaked havoc with the well-being not only of patients but also of the company.

The company’s board of directors as much of the blame for this “deadly” mistake as the CEO, since Vagelos had been ousted quickly and replaced with Gilmartin, an outsider to drug industry, who then gave Scolnick full authority over research operations. Although for Scolnick the 1980s had been a decade of success in launching new products, the products had emerged from the strong product pipeline that Vagelos had left behind when he became Merck’s CEO midway through the decade. Determined to build a legacy of his own, Sconick had chosen Vioxx and Zocor.

Merck under Raymond Gilmartin and Peter Kim

Upon Scolnick’s retirement in 2003, Gilmartin appointed Peter Kim to lead the research division. Hired away from MIT as VP of R&D in 2001, Kim was a reputable scientist who aspired to transform the research at Merck to bring it into the field of genomics. Kim, like many other of the industry’s research leaders at the time, often acknowledged the strategic importance of productivity improvement, particularly in the first two phases of clinical trials. As the popularity of computation genetics grew in the early-2000s, pharmaceutical companies began to place greater emphasis on devising new methods in selecting therapeutic candidates.

⁴¹ Nesi (2008) compared \$3 cost of each Vioxx or Celebrex pill to \$0.35 for each Motrin (a safer NSAID than naproxen) pill.

Merck was in a position to improve its R&D productivity significantly by reducing its rate of early clinical failure through carefully selecting therapeutic candidates with greater chance of clinical success. It had been difficult to steer the organization into a new learning path at a time when the turmoil experienced within the research group was already challenging Merck to retain the company's top researchers (Simons, 2004). Merck under Gilmartin had begun to look outside of the organization for new opportunities for innovation. To do this Gilmartin created a new unit within the R&D division and appointed Dr. Bennett Shapiro to lead it (Koberstein, 2000). To restore peace and order, Kim replaced any dissident managers in top posts undermining the company's new strategy, mainly with outsiders. To improve Merck's relationship with the biomedical community outside the company, he required staffers undergo a training program designed to improve their interpersonal skills. While some researchers complied with the Kim-era reforms, many were infuriated by these new initiatives and began defecting to other companies.

The acquisitions of this period targeted companies with productive drug-development platforms, particularly those with an RNA-based drug-discovery approach, as well as companies with scientific knowledge and technological expertise in fields such as high-throughput-screening, advanced drug-delivery systems, and informational genomics for computational drug development. Merck later dumped some of those high-profile acquisitions –such as the Seattle-based genomics company, Rosetta Inpharmatics, which was acquired for \$630 million in 2001 and later shut down in 2008), which had generated no tangible or intangible returns for the company.

Departure of Gilmartin after the mismanagement of the MEDCO and Vioxx affairs

For most of the ten-year period under Gilmartin, Merck had been highly distressed by crises it was facing. Although some of them had been inherited, Gilmartin had mismanaged -- or, to some extent, ignore -- crises that might otherwise have been resolved in such a way that damage to the company's reputation would have been contained (Simons, 2004). As Hawthorne (2004) argued, a strategic mistake as catastrophic as the decision to acquire MEDCO had been taking too long to divest from this ill-suited acquisition. Failing to make the necessary transition into the fast-developing fields of molecular biology and genomics had placed Merck at a competitive disadvantage, especially as the company's products began to face more intense competition in the market.

For the greater part of Gilmartin's tenure as CEO, Merck had still enjoyed revenues generated by those products launched under Vagelos that were still under patent protection. The company's annual revenues were still increasing, although the profit margin had been suffering a steady decline since Vagelos's pledge to cap price hikes on pharmaceutical products in the early 1990s (see Figure 14). His decision had come after the medical community intensified campaigns in both the public and clinical-research spheres to challenge Merck's safety claims for its super-aspirin, Vioxx, by providing ample clinical evidence that patients taking Vioxx had an increased risk of cardiovascular problems with

lethal complications. On September 30, 2004, after its own clinical studies had shown Vioxx to increase the risk of heart attack after 18 months, Merck voluntarily withdrew the drug from the market. By that time 20 million Americans were estimated to have taken Vioxx, which had generated \$2.55 billion in sales in 2003. After the announcement, Merck's stock began to plummet, immediately losing slightly over a quarter of its value as it fell from \$45.07 to \$33 per share in one trading day. Based on this drop in price, the company lost nearly \$25 billion in market value (Neilan, 2004).

Major legal battles were lying ahead of Merck, not only with patients who had been affected by Vioxx but also with disgruntled shareholders who had taken a financial loss due to the sharp decline in the price of the company's stock. For example, a couple of Merck shareholders petitioned the company's board on October 29, 2004, to take legal action against Gilmartin and other managers for "allegedly causing damage to the Company with respect to the allegedly improper marketing of Vioxx." Although such requests had been rejected by the board, Gilmartin decided to retire from the CEO post on May 5, 2005, one before it was originally set to expire and immediately after the House Committee on Government Reform had released a report (Kaufman 2005).

Merck under Richard Clark and Peter Kim

Merck's stock steadily declined between the withdrawal of Vioxx and Gilmartin's resignation. To repair a damaged reputation among investors the company's directors decided to appoint a longtime Merck executive who was serving as the head of Medco Division at the time, Richard Clark, as CEO in 2005. Clark retained Kim as head of research and sustained the company's new strategy for building a competitive clinical pipeline through corporate acquisitions and R&D deals.

Merck had signed 141 deals for research collaboration and product licensing since Kim had become the head of Merck Research Laboratories in 2003. In 2005 alone, the company had reviewed more than 5,000 partnership offers submitted by companies seeking financial support from big pharma (Salvatore & Davies, 2006). Because the cost of any potential product-licensing or research-collaboration deal is accounted as an R&D expense, the company's R&D grew significantly, but that mainly reflected its exploring opportunities with partners who were primarily outside of the organization.

Kenneth Frazier, who first became a senior vice president and general council with the launch of Vioxx in 1999 was executive vice president and general council in 2006, when the first six Vioxx product-liability cases went to court (FDA, 2005). After the company decided to pay \$4.85 billion to settle the thousands of pending lawsuits, Frazier became executive vice president and president of Global Human Health in 2007, replacing Anstice, who had been the mastermind of the company's Vioxx marketing campaign from 1999 to 2004. It is rather ironic that it was in the year the company finally decided to settle all the cases that Anstice, who sat in the defendant's chair during the trials, decided to take his

retirement. When Frazier joined the board of executive officers, Lewent stepped down from the executive board and handed the CFO post over to the former CFO of Biogen IDEC, Peter N. Kellogg. At the time of their retirement in 2007, Lewent and Anstice held 86,796 and 141,061 Merck shares, respectively, and their compensation, comprising salary plus various stock- or cash-based bonuses and awards, totaled \$3.95 million and \$4.76 million, respectively.

During the period leading up to the settlement of the Vioxx product-liability case, Merck was getting ready to launch several products: a vaccine for human papillomavirus, Gardasil, in 2006; an AIDS drug, Isentress, in 2007; and a diabetes product line with Januvia/Janumet in 2006/2007. Gardasil underperformed expectations due to excessive cost given the drug effectiveness. Zentia and Vytorin, launched in 2002 and 2004 through co-marketing arrangements with Schering-Plough, also underperformed compared with generic alternative, and its sales dropped. The AIDS drug Isentress and diabetes drugs Januvia and Janumet performed well, but that wasn't enough to turn the company's declining revenue performance around.

Clark had overseen the company's most critical acquisition since the merger with Sharp & Dohme in 1953. Although it was Merck that had in reality acquired Schering-Plough (SP), technically the transaction was completed in the form of a reverse-merger (Willens, 2009). Because the most valuable clinical assets of SP, Remicade and Simponi for the treatment rheumatoid arthritis, were developed through a joint venture with Johnson & Johnson, acquisition of SP by another company had the potential to nullify the co-marketing provision of the joint venture. To protect those assets old Merck & Co. had merged into SP before the combined new entity emerged as Merck & Co. once again.

Kenneth Frazier becomes CEO and Roger Perlmutter returns to Merck

On December 1, 2011, Clark reached the age of 64 year, and it was time for him to hand the torch to his successor as required by the company bylaws. Having saved the company from the brink of bankruptcy, to which it had been led by the Vioxx scandal, Frazier had been already selected to succeed Clark as CEO. Clark continued to serve as chairman for another year before leaving that post to Frazier as well. Prior to joining the company in 1992, Frazier provided legal counsel to Merck, one of the major clients of the law firm in Philadelphia for which he worked. When Merck formed a joint venture (JV) with the Swedish firm AB Astra, Vagelos asked Frazier to join the new JV as general counsel. Between then Vagelos's retirement in 1993, Frazier worked closely with Vagelos, who had inspired him with the vision that "creating economic and shareholder value is complementary to and consistent with social and medical value."

In the years leading up to his becoming the company's 10th CEO, Frazier regarded the vision that Vagelos described as having been "at the core of Merck's mission" for more than a century (Seitel & Doorley, 2012). When Frazier was elected CEO he initially stood

out as a maverick who defied the business trends and managerial norms prevailing at the time. Frazier frequently repeated his pledge to remain loyal to Merck's vision and values when speaking before large groups of Wall Street analysts. His decision to do so had followed the company's averting, thanks mainly to Frazier's legal maneuvering, a major business disaster at the height of the Vioxx scandal that might have destroyed the company.

Frazier's first encounter with Wall Street analysts as the company's CEO was a memorable one. In February 2011, discussing the company's fourth-quarter 2010 earnings, Frazier revealed his plan to avoid making any "deeper cost cuts" within the organization to safeguard future growth. In addition, he confirmed his decision to maintain, if not slightly increase, the level of the company's spending on R&D. Such an ardent shareholder pressure appeared shortly after Pfizer's CEO Ian Read had declared his plans to chop the company's R&D expenditures by one-third. Only a few months into his tenure as CEO, Read had announced a major reduction in R&D expenses to boost the company earnings and distribution to shareholders in the name of MSV (Loftus, 2011a). Contrary to Read, who, as predicted, pledged to re-allocate "cash in shareholder-friendly ways", Frazier made a rather striking and unusual move: He dismissed all earlier earnings targets for 2013 and refused to offer the analysts any further earnings guidance, aside from the statement that "investing in our [Merck's] growth is in the best long-term interest of the company."

Frazier purposely withdrew the earning guidance in order to prepare investors for the possibility of lower returns for 2013 than they may previously have expected. Some distressed shareholders, such as Catherine Arnold of Credit Suisse, recognized that his action implied reducing shareholder returns as opposed to pursuing more cost-cutting measures to meet the previously issued earning targets. At the time many analysts and shareholders shared Arnold's sentiment on the issue of decreasing shareholder value and demanded further restructuring programs simply because, as Arnold put it, "there needs to be sharing of pain" (Edwards, 2011). Frazier however dismissed the shareholder demands to cut costs frantically by arguing that "investing in our [Merck's] growth is in the best long-term interest of the company." Within days of the two companies' announcements, Wall Street had rewarded Pfizer's new CEO, Ian Read, for his decision to cut costs by driving Pfizer's stock price up by 4 percent and punished Merck's new CEO, Ken Frazier, for his refusal to issue an earning guidance by driving Merck's stock price down by 3 percent.

The standoff between Frazier and the analysts lasted only a few months before Frazier began to back down from his original proposal to sustain the company's financial commitment to R&D. Frazier was being punished by shareholders, as Jim Edwards (2011) of CBS Moneywatch wrote in a column headlined, "Spanked by Wall Street, Merck CEO Orders U-Turn," referring to Frazier's decision to lay off 13,000 employees in addition to the 17,000 employees that the company had laid off as part of its post-acquisition restructuring program. Edwards's concluding remark was as striking as the headline itself:

.. It is not a coincidence that Merck must now get rid of a similar proportion of its employees. The only mystery is why it took Frazier six months to figure this out.

As evident in this sequence of the events, the tension between innovation and financialization escalated at the outset of Frazier's tenure after his decision to disregard Wall Street's demands to downsize R&D and other operational expenses. Having recognized that such a decision would have repercussions, he was prepared for a potential backlash from Wall Street to such an extent that as Loftus (2011b) reported Frazier was "willing to take a 'few brickbats thrown' in his direction" while staying on course to maintain the company's commitment to innovation although Frazier also acknowledged that he didn't "have a blank check to pour unlimited money into research".

In Frazier's public statements following the face-off with the Wall Street analysts early in 2011, his growing frustration with mitigating the tension between innovation and financialization became more evident as the following statement reported by Loftus (2011b):

... I'm trying to run the company in a way that I can satisfy the short- and intermediate-term needs of investors without sacrificing really what we're about...

Frazier was very attentive to "science and innovation" and aware that they were "in the DNA of the company," and they would lead the company "to another big breakthrough" (Loftus, 2011b). Frazier avoided any major cuts on R&D expenses in the next two years. However he became more conscious of generating high short-term yields for shareholders. As Figure 21 shows, Merck under Frazier began to distribute more earnings to shareholders more than the amount that the company spent on R&D.

In 2013 Frazier rehired a former research manager, Roger Perlmutter, making him president of Merck Research Laboratories. In the same year, Merck announced another restructuring program, this one cutting down the workforce by additional 8,500 employees, mostly in R&D and commercial operations. Ironically, it was Eli Lilly CEO John Lechleiter who was now in a standoff against Wall Street as he refused to budge from his decision to maintain Lilly's financial commitment to ongoing R&D programs, just as Frazier had done two years before (Carroll, 2013). The roles had shifted, however, with Frazier following the path of Pfizer's Read in announcing a new restructuring program to comply with the analysts' earnings expectations.

Merck under Frazier and Perlmutter remained on the path to financialization as management continued to explore M&A as a quick and shareholder-friendly option to acquire new products and boost the revenues while sustaining their commitment to doing stock buybacks to boost stock prices. In 2015, Frazier and Perlmutter spent \$9.1 billion to acquire Cubist and its successful antibiotic Cubicin, a novel and highly potent antibacterial agent for treating gram-positive infections. In February 2015, Merck issued \$8 billion in senior unsecured notes, deploying a large portion of this new debt to finance the Cubist

acquisition but using some of the funds generated to retire outstanding debt and repurchase stock (Merck Annual Report, 2016).

In the US economy, gains realized through exercising stock options and the vesting of stock awards have accounted for the largest portion of total executive pay and been primarily responsible for the explosion in executive pay that has taken place since the early 1980s (Lazonick, 2017; Hopkins & Lazonick, 2016). Despite Merck's prolonged productivity crisis, arduous legal battles, and ailing financial health, its top executives have managed to pay themselves handsomely: In fact, their annual gains have exceeded the industry average.

In the year Vagelos retired from the chairmanship, no top executive reported gains from exercising stock options. At the time of his retirement, however, Vagelos's exercisable stock options were estimated at \$21.6 million. His annual compensation, including a bonus payment, was \$1.94 million in 1994. Vagelos also received nearly \$2.5 million in 1993 and 1994 under the company's long-term incentive program (LTIP). Additionally, Vagelos received a lump-sum payment of nearly \$15.3 million from the Retirement Plan for Salaried Employees (RPSE) and the Supplemental Retirement Plan (SRP) in 1994. Vagelos's total retirement package totaled \$19.7 million for compensation, with an estimated \$21.6 million in additional gains from exercisable stock options.

As Merck began to financialize in the mid-1990s average realized gains from stock options of Merck's top five executives surged in 1995, 1997, 1999 and 2000. Scolnick was among the top executives who had realized nearly \$44.8 million in gains from exercising stock options. Of those \$44.8 million in gains, \$24.8 million were realized on October 25, 2000, when Scolnick and a member of his family to whom he transferred some of the shares he received from exercising options, sold for \$85 per share 381,200 shares obtained by Scolnick at exercise prices ranging from \$16.25 to \$21.19. According to court records from the class-action lawsuit, Scolnick had "personally profited from the sale of Merck stock at artificially-inflated prices" through those stock sales.

According the company's 2010 Proxy Statement, Clark's total compensation, including salary, bonuses, stock awards, and options was \$16.8 in 2009, \$25 million in 2008, and \$19 million in 2007. The total compensation of the top five Merck executives, including Kenneth Frazier, was \$52.7 million. The most conservative estimate places the total compensation of the top five Merck and top four Schering-Plough executives at \$192.4 million for a single year, 2009. Following such a major merger was a number of corporate restructuring programs that had affected the organizational integration at Merck in the next years, which is discussed extensively in the following section.

4.2. Organizational Integration

“Take away everything else but leave me my organization and in ten years I’ll be back on top.”

Andrew Carnegie (Livesay 1979, p. 217)

In Merck & Co.’s early decades as a major research enterprise, its employees aspired to engage in organizational learning “in fighting the battle against disease and suffering,” inspired by the somewhat altruistic mission envisaged by the company’s founders. George W. Merck persuaded the early leaders of the organization to “fight the battle for human life” and “win a greater freedom from suffering and disease” by emphasizing the compassionate and ethical foundation of the organization’s objectives, as articulated in his famous 1950 speech at the Medical College of Virginia:

We try to remember that medicine is for the patient. We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we have remembered it, the larger they have been.

Under the direction of George W. Merck, the company truly altered the trajectory of the biopharmaceutical industry, especially at moments when the industry found itself at a crossroads. Merck wasn’t the only company that made investments in organizational learning; Abbott, Squibb, Eli Lilly, and DuPont also undertook plans to build research operations. Most of their investments followed the 1938 amendment to the Federal Food, Drug and Cosmetic Act in 1933. Proposed in the wake of The Elixir [Sulfanilamide] Tragedy⁴² that had claimed the lives of 34 children in 1937, this amendment required a comprehensive safety review of drugs by the Food and Drug Administration (FDA) prior to their launch in the US drug market.

During the period leading up to signing of this legislation on June 24, 1938, many drug makers were considering new measures designed to improve their organizational research and development capabilities to meet the new regulatory requirements. Merck & Co., however, had already made headway in establishing a highly competitive research and development organization that was not only to be “the finest research laboratory in the pharmaceutical industry” by the end of 1930s, according to Sheehan (1982), but also “rivaled, and in some ways probably surpassed, the research programs in the best academic laboratories in the country.”

At the time when the major US-based drug producers decided to invest in establishing R&D capabilities, recruiting top-quality scientists from the nation’s leading academic

⁴² At the time a novel broad spectrum antimicrobial agent called Elixir Sulfanilamie that had quickly killed 105 including 34 children after the drug was launched in the US market in 1937 before getting tested for toxicity (Akst, 2013)

institutions was extremely difficult. Industrial research in medicinal chemistry was held in contempt by the academic elites to the point that a transition to industrial research was considered career suicide. Many leaders of the scientific community avoided any association with profit-seeking industrial entities in order to avoid isolation by their colleagues in the workplace or by their peers in professional societies.

Having recognized the central role human capital plays in an industrial organization, George W. Merck had been the most vocal figure of his time, repeatedly urging medicinal chemists from both academic and industrial laboratories to collaborate in advancing science and medicine so as to address the medicinal needs of humanity. He had urged his fellow industrialists to invest in human capital and genuinely to pursue both pure and applied research (New York Community Trust, n.d.). To do this, George W. Merck had argued, industry would have to challenge conventional business norms and broaden its vision, tackling larger scientific challenges in order to attract talented researchers with lofty scientific aspirations from the academic world.

During a speech to the members of the American Chemical Society (ACS) in 1935, George W. Merck proposed an early outline for partnerships between industrial organizations and academic institutions, which he described this way:

Industry must be prepared to offer its facilities freely to research workers in medicine. Sometimes this may lead far from what a commercial management might judge to be remunerative territory. It may at times make demands which seem onerous. But a true partnership requires that the load be shared, and, if the medical investigator needs assistance from the industrial research laboratory or development department, industry must be prepared to come forward with the necessary contribution of activity and products.

As postulated by George W. Merck, this partnership was the embodiment of the Merck pledge to advance science and medicine. With this partnership proposal, George W. Merck was extending the scope of the social contract between industry and society to include members of the medical community: To serve the medicinal needs of the larger society, in his view, industry had to serve the intellectual needs of the medical society. Taking advantage of the credibility he had established in the business and academic worlds, George W. Merck began to bring down the barriers down between them and to unify them around the common goal of solving the medical mysteries that threatened the well-being of people at the time.

After he had secured major endorsements from high-profile scientists such as Alfred Newton Richards, the top scientific advisor to Merck, the tenacious public campaign George W. Merck had orchestrated began, to pay off as the company started to recruit young scientists in such fields as organic chemistry and pharmacology from Harvard, Princeton, Yale, and other pillars of the nation's academic establishment. Having recruited

the top talents in their various fields, Merck began to reinvent the market for sulfa drugs and vitamins during the golden age of organic chemistry in the 1930s. As the success of Merck's ambitious plan to grow into the pharmaceutical business by capturing the field of vitamins had attested, the organization's budding innovation capabilities emerged through recently launched learning efforts in organic chemistry. Tishler (1983) described in the following words how he had been introduced to the strategy upon being hired to develop an alternative synthesis of riboflavin (vitamin B2):

Randolph Major came to me and said, "We made up our minds that we're going to specialize in research in the field of vitamins. We're going to isolate every vitamin. We're going to determine their structures if it hasn't already been done and synthesize them and make them available." This was a wise choice because in those days no one was really doing that in the States. They weren't even doing it commercially abroad. (p. 28)

Under Major, the research division passed this test and began to engage in new learning in microbiology and fermentation chemistry with the aim of developing antimicrobial and steroid drugs. Merck and other US-based companies successfully captured the fast-growing antibiotics and steroids market globally and increased their competitive advantage over their longtime rivals, the German- and Swiss-based chemical manufacturers. Excluding these foreign market leaders, who had refused to license their products for manufacture and marketing in the US, from participation in the wartime crash programs had been a highly risky strategy in view of the uncertainties encountered during the learning process. Through successfully coordination of the efforts of scientists from various disciplines in chemistry and biology, the strategy achieved the intended outcome of developing multitudes of vitamin products, which were ultimately to make up a significant portion of US pharma's corporate revenues in the 1940s and 1950s, particularly Merck's revenues as the company played a key in those coordinate efforts

In addition to generating substantial financial returns in the short term, engaging in learning to specialize in the vitamin business had far greater implications for Merck's entry into the pharmaceutical industry in the decades that followed. The company's collective learning efforts in the isolation and synthesis of vitamins cumulated over time, and the expertise it built was reutilized in the synthesis of cortisone, antibiotics, and other major products. Thus, its learning experience in vitamins established the foundation of the company's research tradition in the pharmaceutical industry (Tishler, 1983, p. 29).

4.2.1 Surging productivity and expansion of the workforce at Merck

While the organization's ability to innovate new classes of therapies generally enabled Merck to stay ahead of its competitors (Southwick, 1988), the rising competition often diminished profit margins within these new therapeutic classes over time. Merck had been one of the first to successfully commercialize products in new therapeutic classes such as

penicillin, streptomycin, cortisone, diuretics, and statins (Mevacor, Zocor), but rivals like Pfizer, Squibb, and Upjohn had been quite successful in quickly commercializing me-too drugs to capture the new markets. For instance, Merck had introduced the first generation of cortisone in the late 1940s, but Upjohn was faster in capturing the cortisone market in the early 1950s because the new production process Upjohn developed lowered the cost of production, and therefore the market price, of cortisone. At the time the US-based pharmaceutical companies' interest in the cortisone business had dwindled for the most part owing to the difficulties associated with producing corticosteroids cost-effectively enough to generate profits on a sustainable basis. Sarett, who had first developed cortisone for Merck, continued his research efforts in search of a better method of synthesizing cortisone in order to compete against Upjohn.

However, it wasn't until Philip Hench of the Mayo Clinic reported on cortisone's effects on rheumatoid arthritis in 1948 that many pharmaceutical manufacturers turned their attention back to the cortisone business (Sarett, 1990). After this discovery of a lucrative new market for cortisone, Merck commissioned a new research team under Sarett to explore new methods of synthesis that might improve the economics of cortisone production. This continuing effort, which extended from the wartime steroid crash program through the 1950s, finally paid off when Merck produced the orally administered corticosteroid Decadron in 1958. After the introduction of Streptomycin in 1946, cortisone in 1948, and Hydrocortisone in 1952, Merck's sales and workforce doubled, the latter from 6 thousand in 1950 to 11,300 in 1960 (Table 4). As shown in Table 4, the merger of Merck with Sharp & Dohme, completed in 1953, was responsible for the most part of such a rapid growth from 1950 to 1960.

Having sustained learning efforts in steroids after its success in corticosteroids, Merck was quick to move into non-steroidal anti-inflammatory drugs (NSAIDs), which were emerging for the treatment of arthritis in the 1960s. It launched its first NSAID of the decade, Indocin, in 1965, when the company was about to undertake a substantial internationalization and diversification campaign. Decadron and Indocin drove the company's sales in the pharmaceutical products business and partially contributed to the growth of employment, which nearly doubled to 22.3 in 1970 from 11.3 in 1960 (Table 4). A series of acquisitions the company completed during this period did the most to contribute to this growth.

Since its involvement in the first successful launch of an antibiotic nearly three decades before, Merck had kept alive its learning efforts in microbiology and antibacterial drugs, and it was able to develop and launch a highly potent new-generation antibiotic product, Mefoxin, in the late 1970s. Still, the productivity of Merck's R&D operations had declined, and the company's product portfolio experienced a dry spell that began in the 1970s and lasted through most of the 1980s. As its management decided to transform the R&D operations and to exit some of the non-pharmaceutical business fields, the company's employment growth slowed in the 1980s and remained stagnant throughout the 1990s.

Table 4: Employment at Major American Pharmaceutical companies, 1950-2016

Company	employees (thousands)							
	1950	1960	1970	1980	1990	1999	2006	2016
Abbott	6	9	18.3	31	43.8	57.1	66.7	75
Bristol-Myers	2	6	24	35	52.9	54.5	43	25
<i>Squibb (1989)</i>	<i>6.5</i>	<i>NA</i>	<i>35</i>	<i>27</i>				
Johnson & Johnson	11.2	17	38.2	74	82.2	97.8	115.6	126.4
Lilly	7.7	10.1	26.4	28.1	29.5	31.3	41.5	42
Merck [Sharp & Dohme (1953)]	6	11.3	22.3	31.6	36.9	62.3	60	68
<i>Schering-Plough (2009)</i>	<i>1.1</i>	<i>3.6</i>	<i>11.6</i>	<i>27.4</i>	<i>19.7</i>	<i>26.5</i>	<i>19.2</i>	
Smith Kline & French	1.6	4.6	10.2	31.6				
<i>Sterling (1988)</i>	<i>11</i>	<i>14</i>	<i>23.5</i>	<i>26</i>				
Pfizer	3.4	18	35	41.2	42.5	51	98	96.5
<i>AHP/Wyeth (2009)</i>	<i>11</i>	<i>18.7</i>	<i>41.8</i>	<i>49.8</i>	<i>48.7</i>	<i>51.7</i>	<i>50</i>	
<i>Warner-Lambert (2000)</i>	<i>3</i>	<i>10</i>	<i>55.5</i>	<i>31.0</i>	<i>34</i>	<i>44</i>		
<i>Upjohn (1994)</i>	<i>3</i>	<i>6</i>	<i>28.2</i>	<i>22</i>	<i>18.5</i>			
<i>Searle (1985)</i>	<i>1</i>	<i>1.5</i>	<i>8.2</i>	<i>18.2</i>				
Parke-Davis	8.6	11.8						

Source: Own calculations based on data from Landau, et al. (1999) & companies' annual reports

When he was first hired in the 1930s, “life at Merck,” Folkers explained, wasn’t “at all profit oriented.” The company’s research managers had established a productive environment, and they fostered it by empowering a talented group of creative scientists to pursue original research aimed at fulfilling social needs. This period of “pure science” continued until the merger with S&D in 1953. Concerned over the growing responsibilities of managing industrial research, Kerrigan, who in 1950 had been the first professional manager to assume the role of CEO at Merck, decided to bring in an administrator with experience in the industrial chemicals business to pull Major away from active research management in the newly combined entity. Shortly before the merger, Major was promoted to scientific vice president of Merck & Co., and a former Merck & Co. executive who had originally been recruited from the petroleum industry, Per K. Frolich, was appointed as vice president of MSD’s Chemical Division to take over the duties of research management from Major.

Promoting Major into the position of scientific vice president had not been a symbolic gesture taken to rationalize a significant bump in the salary, it had been part of a deliberate strategy to pull Major away from active research management. According to Folkers (1990), the goal of the decision was to replace an influential research leader who had not shown much inclination to comply with profit-making objectives. It was growing discontent among the new managers in the upper echelons of the Research Division that had prompted the replacement of its longtime head with someone more in tune with the profits motive of the newly merged entity. The strategy ultimately failed, however, as Frolich left the company after proving himself insufficiently “qualified” as a research

director (Folkers 1990). Tishler, who had in fact been groomed for the position, filled the vacancy left by Frolich in the mid-1950s. In 1956, the year when Tishler was named vice president and executive director of the newly created Merck, Sharp & Dohme Research Laboratories Division, Major retired from the company.

Two years after the merger, Kerrigan was replaced as CEO by Connor for a reason similar to the one that had led him to displace Major: He had struggled to maintain control of the company's fast-growing operations. Meanwhile, the former S&D executive and brother-in-law of George W. Merck, Gadsden, had been swiftly climbing the corporate ladder, becoming administrative vice president in 1954, the year after the merger, joining Merck's board in 1957, then reaching the office of executive vice president. Upon Connor's unexpected departure in 1964, Gadsden became CEO. Maintaining short- and medium-term operational profitability became Merck's prevalent business strategy during Gadsden's tenure, as the company slowly abandoned its innovation-driven growth strategy in the pharmaceuticals markets, particularly after the enactment of the 1963 Drug Efficacy Amendment (aka Kefauver-Harris Amendment). During this time, however, profit-oriented business executives had limited influence over the management of research operations, since the Research Division's personnel had become better integrated socially with colleagues working elsewhere in the corporation under Tishler, a strong leader who remained in power for most of Gadsden's tenure as CEO.

4.2.3 Market diversification and setbacks in R&D productivity

The decision in the 1960s to diversify Merck's operations into fields outside the pharmaceuticals market undermined its productivity in R&D, which was no longer protected as the organization's crown jewel. In contrast to its status in earlier decade, the pharmaceutical R&D division had come to be perceived among the company's top business executives more or less as a liability. Introducing new products had become a more complex process, consuming more time and resources, during the period of stringent federal regulation of the approval and marketing of pharmaceuticals. Having already expended a significant amount of the company's liquid assets on recent acquisitions, the top management at Merck introduced various efficiency measures within the organization that were particularly aimed at reining in the Research Division's growing requests for resources to sustain organizational R&D efforts.

Concern over the direction of research reached a tipping point among a group of Merck's most prestigious scientists when Tishler was preparing for retirement in the late 1960s. Among those most concerned, Denkewalter and Pfister had grown frustrated to the extent that they even orchestrated a "leadership coup" within the Research Division in hopes of seizing strategic control upon Tishler's departure (Folkers, 1990; Tishler, 1983; Hirshmann, 2007). After successfully completing the synthesis of RNase with Hirschmann, Denkewalter advocated "design-based" drug discovery that would entail engaging the organization in more learning on peptide chemistry. He was most interested in cancer

research, however, and muddled the coup attempt with a plea to take the cancer research program away from Hilleman, an influential research figure who had overseen research on cancer as part of the immunology program. Their attempt to seize control having failed, Denkewalter and Pfister ended their careers at Merck in the early 1970s. Tishler's, Denkewalter's, and Pfister's retirements were closely followed by others' departures.

According to Firestone (2011), introduction of a conservative approach to research management among pharmaceutical companies in the 1980s that called for research to be carried out in the most orderly and predictable fashion undermined the key characteristics of the drug innovation process: spontaneity (in identifying research opportunities); autonomy (to pursue these opportunities); creativity (utilized in the process of the research); and serendipity (unpredictability of outcome). The company's business operations, both in the pharmaceutical industry and elsewhere, had expanded rapidly through a series of acquisitions in the 1960s, which led to an increase in the complexity of the managerial structure both within and outside of the Pharmaceutical Division. This growing complexity impelled Merck's conservative management to add new layers to middle management and to introduce new managerial tools for monitoring operational efficiency.

Having invested in the development of capabilities in biologics under Hilleman's direction at West Point, Merck managed to introduce lifesaving new vaccines in the 1960s and 1970s, which in turn enabled the organization to develop vaccines, as among them the first Hepatitis B vaccines, in the early-1980s. As part of a move toward building the capabilities to compete in the fledging fields of molecular biology and genetic engineering, Merck co-developed a first-generation recombinant Hep B vaccine (Heotavax-B) with Chiron, while developing another vaccine, Recombivax-HB, entirely through internal efforts.

Having sustained its learning efforts and developed a knowledge base in field of hormones, Merck was quick to recognize the value of an opportunity that presented when Vagelos was head of Basic Research in 1974. The discovery of an enzyme at the time ultimately proved key to enabling Merck's development of an inhibitor for prostate enlargement, Proscar, launched in 1992.

4.2.4 From Major to Vagelos, building a century of research tradition at Merck

Unlike Major and Tishler, Vagelos had been trained as a physician and received an M.D. in 1954, four years after completing undergraduate training in chemistry. During his internship and residency at Massachusetts General Hospital in Boston, a teaching hospital affiliated with Harvard Medical School, Vagelos had briefly practiced medicine, between 1954 and 1956. In addition, he had spent ten years pursuing research in biochemistry at the National Institutes of Health before moving to academia in 1966. Until his next move, which took him to the business sector in 1975, Vagelos oversaw the development of what

was at the time one of the nation's very few prestigious biochemistry departments, at the Washington University in St. Louis, Missouri.

Like Major and Tishler, Vagelos was a very involved leader who kept the distance between himself and the scientists at the bottom of the hierarchy as short as possible no matter how high in it he had climbed. He boosted the morale of the research community by engaging with researchers, often on a personal level. And whether doing research in the lab or writing prescriptions at the hospital, Vagelos had long been involved in the process of drug development. During his brief practice of medicine, Vagelos had recognized the vital role industrial research laboratories play in developing new medicinal products capable of improving the quality of human by curing disease or alleviating the suffering it causes. Having recognized the value of the insight biology had to offer into the functions of organisms at a molecular level, Vagelos had relentlessly pursued a transition to biochemistry through his training and research in chemistry and medicine. Unlike Major and Tishler, Vagelos had managed move up to the tipping point in the upper echelon of corporate hierarchy marking an important period when the company had been run by a scientist for the first time. At the time such an accomplishment was also unique in the pharmaceutical industry.

Vagelos' tenure, first as a top research leader and later as chairman and CEO, coincided with a time when the corporate management ideology that had prevailed for decades within the productive institutions of the U.S economy was undergoing major changes. Activism was on the rise among shareholders who were demanding more managerial oversight, particularly for gaining the strategic control of allocative decisions to ensure that they were made in the name of "maximizing shareholder value" [MSV] (Lazonick & O'Sullivan, 2000). During this period activist shareholders demanded that a greater number of independent directors serve on the companies' boards, which would subject the decisions and performance of public companies' executive teams to monitoring by representatives of the shareholders' interests.

This change in the composition of companies' boards is illustrated in Figure 9 as the George W. Merck-era board appointees began to disappear in the 1970s. Vagelos, as head of research in the late 1970s and the early 1980s, had struggled to revive the company's institutional memory in the midst of the radical change occurring in its leadership. He constantly reminded people to "read up on [Merck's] history" in order that they remember the period when "medicine" was "for people" and, consequently the company remained committed to supporting the innovation process until it led to a productive outcome.

Under Vagelos the productivity of the company's R&D operations had increased in the late 1980s, the boost mainly being credited to improvements in the workplace. Since his arrival in the mid-1970s, Vagelos had transformed the research environment to resemble that of a typical academic institution with such extra benefits a researcher's being allowed to see his or her bright idea all the way through the clinical process until it entered the market as a

new drug to help people with their medical difficulties. Merck, under Vagelos, offered a unique workplace in which scientists were offered the best of both worlds: They were given the opportunity to pursue ideas of their own choosing, as the academic researchers often can, while rendering the routine work assigned as part of their research duty. They were also provided with the opportunity to publicize the results of their scientific work, with the personal aid provided by legal affairs department to obtain the necessary legal protection for the intellectual propriety of such inventions so that the company can recuperate its expenses accrued during the innovation process.

Because the economic success Merck had achieved in the past was driven by the launch of innovative new therapies that often disrupted a segment or segments of the market to secure leadership for the company, fostering and developing the productivity of the innovation process had become the bedrock of the company's growth strategy and its managerial focus. Both the business and research leaders, therefore, had been empowered under this research-driven business model to make strategic investments in long-term learning initiatives in basic science. Because giving researchers time to pursue their personal intellectual interests and enrich their research skills was consistent with both the company's values and their own, Major, Tishler, and Vagelos all extended this opportunity to them, an organizational strategy that then became institutionalized at the company. This feature of Merck's workplace, successfully applied under its three most renowned heads of research, made Merck one of the most desired employers among entrepreneurial and utilitarian academic scientists who were interested in transforming their scientific ideas into marketable therapies that could save lives.

Since no other industrial laboratory could match the quality that Merck's had attained, and no academic research institution could match the wages the company offered, recruiting and retaining talent was not a difficult managerial task. In contrast to the average industrial laboratory, Merck faced only one difficulty: selecting the best candidates from a large pool of applicants. But Merck's turnover rate among the junior researchers, whose development trajectories lagged significantly in comparison to those of the talents surrounding them, was one of the industry's highest (Sarett, 1990; Tishler, 1983).

4.2.5 Changing labor relations and diminishing productivity at Merck

By the mid-1990s the “organization man” phenomenon had come to an end at Merck and most other large pharmaceutical organizations, something that can largely be attributed to the burgeoning of biotechnology startups. Among other examples, Kerrigan had started working for Merck as an “order-bench boy” at age 13 and ultimately rose to become the company's first CEO from outside the Merck family. And when Dr. Harry J. Robinson, VP of Scientific Affairs at Merck, was commissioned by Horan to identify a candidate to replace Sarett, he settled on his old friend and former intern Vagelos. Robinson, a well-respected scientist who built and maintained a bridge between Merck and the medical

community, had remained as a Merck employee from the time Vagelos interned with him in the 1950s until Vagelos had become his boss.

To illustrate the type of career Merck could offer a smart high school graduate in the 1950s and 1960s, Vagelos invokes Robinson's experience:

He had gone to Merck directly out of high school, and the company, which was very paternalistic, had helped him complete an undergraduate degree, a Ph.D., and an M.D. After completing this arduous route to professional standing he had gone on to become one of the firm's important scientists and a vice president of research."

(Vagelos 2004, p. 101)

A Merck employee's commitment could last beyond his or her career. As an example of a researcher's lifelong loyalty to the organization's mission and dedication for science. Folker (1990) offers that of Boyd Woodruff, who collected organisms, screened them in a small home, laboratory, and sent interesting findings to Merck long after he had retired from the company (p. 40). As the productivity boom of the late 1980s began to recede in the early-1990s, Vagelos took some drastic measures to address the company's growing productivity concerns. When he joined the firm in the mid-1970s, he tried centralizing the control of R&D operations; up to then, division leaders had been acting with almost complete autonomy. During the period of diversification between the mid-1960s and the mid-1970s sales and marketing had overshadowed R&D, and innovation -- already divided into two camps, "the Emerald City" at Rahway and "the Country Club" at West Point -- had lost steam (Sarett, 1990).

The arrival of such a well-respected scientist as Vagelos had placed R&D in the spotlight and raised the morale of the research groups at both Rahway and West Point (Hawthorne, 2004; Hirshmann, 2007; Cordes, 2014). Vagelos was an ambitious, disciplined, and demanding manager who pushed the research division hard to excel in drug innovation. Vagelos was also a caring and engaging manager who had a great passion for top-quality research and supported researchers who strived for it. By maintaining a strong presence on the in the laboratory and remaining engaged with the research community, Vagelos managed to rebuild the research operations from the bottom up and eventually regained managerial control over global operations.

Having established control over the operations and put the company onto a productive path, Vagelos handed control over to his successor, Scolnick, when he was promoted to replace Horan as CEO in 1986. But research management took a sharp turn during Scolnick's tenure, as he quickly began micromanaging operations and further consolidating power over decisions concerning research. Although Scolnick implemented flawlessly the efficiency-driven model of management then growing in influence, as his management style became increasingly strict, it began to undermine the productivity of what had been a

highly creative research community. According to Hawthorne (2004), the company's directors decided to hire an industry outsider with no science background to replace Vagelos as CEO in 1994 so that Scholnick could be left alone to run the company's scientific affairs. Scolnick assumed even greater control over the research operations after the arrival of Gilmartin.

Former Merck product manager Michael G. Wokasch, who worked for the company for most of Vagelos's tenure and spent nearly 30 years in the biopharmaceutical industry in various managerial capacities, describes the transition of power from Vagelos to Gilmartin in 1994 as "the most telling example of diminished management depth in the industry" (Wokasch, 2010, p. 119). Wokasch reserves skepticism over the idea of recruiting an outsider to the biopharmaceutical industry for the top executive's post, explaining that such a recruitment strategy can have an undesired effect on the economic performance of a pharmaceutical organization because it makes for:

- (i) *Fewer experienced role models and less effective mentoring;*
- (ii) *Less insightful, less rigorous, and potentially flawed strategic planning that affects the entire business;*
- (iii) *Less attentive organizational oversight, resulting in diminished operational accountability, wasteful spending, and lack of awareness about what is going on in the company;*
- (iv) *Increased vulnerability to regulatory and legal risks;*
- (v) *Unrealistic or meaningless performance expectations, resulting in progressively diminishing operational efficiency and a concomitant reduction in employee morale;*
- (vi) *An inability to recognize and correct mistakes and poor decisions made at lower levels in the organization;*
- (vii) *Publicly disclosed organizational missteps that perpetuate a market perception of executive incompetence; and*
- (viii) *A disconnect from market dynamics and the degree to which the company is meeting customer needs and expectations...*

(Wokasch 2010, p. 119-120)

The laundry list of issues Wokasch underlines above appears to capture everything that went wrong with Merck under Gilmartin, particularly during the period leading up to and including the Vioxx scandal. Gilmartin had not played a part in the acquisition of MEDCO, although he was accused of acting too slowly in divesting the company of it. Acquiring MEDCO was a strategic failure the blame for which, however, falls on Vagelos. How Wokasch explains "what really goes on in the executive suit" may provide a context for Vagelos's decision such that the immediate failure overshadowed the productivity boost the company had experienced under his management:

Even today, the best pharmaceutical executives struggle with the challenges of managing large organizations in a complex and rapidly changing health care market. As mentioned previously, diligent management oversight is one the first casualties to occur in large organizations as executives get caught up in administrative duties, answering queries from Wall Street analysts and journalists, spending time on the Boards of other companies, lobbying with policy makers, and schmoozing with their own Board of Directors (think incentive compensation here). Unfortunately, these distractions interfere with their ability to provide guidance on everything from strategy formulation and goal setting to operation performance expectations. As a result, these executives rely heavily on their management teams (often with limited experience) for business planning, operational reviews, and due diligence oversight.

(Wokasch, 2010, p. 120)

Pfizer and Novartis were later to follow the path Merck had blazed in recruiting an industry outsider to lead a pharmaceutical company. Pfizer recruited Jeffery Kindler in 2002 from the international fast-food restaurant chain McDonald's Corporation, and he served only four years at Pfizer, as a senior executive and vice chairman, before succeeding Henry A. McKinnell, Jr., as the company's CEO. Swiss-based Novartis, another of the world's largest pharmaceutical companies, first recruited Joseph Jimenez from the global food giant H. J. Heinz Company in 2007, only three years before naming him CEO. Interestingly, at the time when the directors of Pfizer and Novartis decided to hire an outsider to lead their organizations, Roche was being run by a manager who had started working for the company as a management trainee after finishing college in the early 1990s. In the meantime, Merck had decided to promote from within and appointed Frazier, the company's long-term general counsel and executive vice president to run the organization.

Growing inertia and organizational disintegration

Drawing from his personal experiences and observations, Merck researcher Raymond A. Firestone discusses how a strict research environment can stifle creativity and undermine productivity in drug research. Firestone (2011)

These middle managers receive little or no credit for new discoveries, but get blamed if they support something that eventually fails. Therefore, the safest thing to do is to disparage anything new. If they kill an Einstein in the cradle, nobody will ever know. (Firestone, 2011, p. 963)

Firestone, a veteran of more than six decades with pharmaceutical companies and an outspoken industry critique, joined the company in midst of this transition period. Since starting work for Merck in 1956, he had been involved in the development various

important products, such as vitamin B6, thibenzole, and Aldomet, and had served as a research chemist alongside scientists such as Tishler, Pfister, and Vagelos before leaving the company to join Bristol-Myers in 1986. During his tenure Firestone had an up-close view of profit-oriented business managers in action while witnessing the efforts of “good research management” as it tried to maintain the integrity of a productive research environment. Firestone (2011) argues that the pharma industry’s current productivity problem was born when “the primary goal of research changed from discovery and social usefulness to making money...”

It was the attempt to impose the maximum order possible on research operations that ultimately led to micromanagement. Making the development and pursuit of new projects contingent upon complying with managerial goals tied to performance targets, milestone events, budget estimates, and other progress metrics discouraged productive researchers from engaging in risky but original research. Placing steady pressure on research operations with the goal of increasing capital efficiency and value extraction became a routine management practice, especially when the productivity of R&D investments began to decline in the late 1960s.

What lay at core of Merck’s scientific success, and therefore its economic growth, was the quality of its scientists and the organizational routines that enabled harmonious interaction among them. In 1977, a year after Vagelos became president of MRL, Horan consolidated all employee relations activities in a new department that had recently been given the name “Human Resources” (HR). Walter R. Trosin, the first manager to lead the department under its new title, argued the reason the company had developed a competitive edge over its rivals had been the quality of Merck employees source (Sturchio, 1991, p. 41). Merck had historically hired employees at a young age, before they had been exposed to other kinds of organizational routines and values. Steven M. Darien, senior VP for Employee Relations and Human Resources who had himself been with for Merck for 30 years before retiring at the same time as Vagelos in the mid-1990s, explains the company’s strategy to “attract, develop and keep talented people” is to “hire the best people off an academic environment and give them a challenge” so they can remain with the company for a long period of time (Hawthorne, 2004, p. 54).

During WWII, when a large portion of the able workforce was drafted into the military, the resulting labor shortage obliged Merck to find new ways of optimizing the productivity of its current employees. Established as early as 1930s, Merck Training School had been responsible for the occupational training of blue-collar workers in various topics (Sturchio, 1991). More emphasis was placed on employee training and skill-development programs in the late 1950s as part of the organization’s human relations policy of filling managerial positions by promoting from within the company. John J. Radigan was appointed director of the newly established corporate Personnel Relations Department and initiated various different training programs to ensure the success of the internal recruitment strategy, which went into effect in 1963. Those training programs included a “revised and extended

program of educational assistance” such that the new human relations strategy would “facilitate the continuing development of Merck employees” and, more important, “help them prepare for possible technological obsolesce of their skills” (Merck Annual Report [MAR], 1963, p. 8).

To follow advancements in science the company scientists kept close connections with the scientific community. Given that the company’s growth strategy was often based on feedback received from its scientists, Merck generally encouraged scientists to pursue graduate education in biology and chemistry (Folkers, 1990; Tishler, 1983; Sarett, 1990; Vagelos & Galambos, 2004). Merck Sharp Dohme Research Laboratories (MSDRL) ultimately became a research institution comparable to the nation’s top research universities, offering research seminars, collaborations between industrial and academic scientists, and the right to publish in scientific journals. To help them in initiating and developing research projects, Merck provided its researchers with easier access to the company’s resources than it provided to academic scientists.

Merck’s publication policy was more relaxed than those of its rivals, as the company had always been interested in showcasing the quality of its research in the hope that it would attract top scientists. Publications showed the company’s investors the progress achieved in preclinical research and provided evidence that the company’s R&D investments were efficient and productive. Roche, in contrast, was secretive about its research progress and often held up publication until the company had gone ahead of its competition by a large margin. Merck, for example, was completely unaware of the progress Roche had achieved in its protease-inhibitor research program and was late in ramping up the organizational learning efforts it needed to catch up with Roche in the race to introduce the first drugs to treat HIV/AIDS and hepatitis C virus (HCV) (Fried, 1998, p. 352)

In the midst of the productivity boom under Scolnick, the research division at Merck began bleeding managerial and entrepreneurial talent. Alan S. Rosenthal, another talented manager, later said he had left Merck to run the US operations of the German company Boehringer Ingelheim simply because it had become too difficult to remain “entrepreneurial within Merck.” Joshua Boger, who was heading the company’s protease-inhibitor research efforts, left to start his own company, Vertex Pharmaceuticals, to “make better drugs faster” and, ultimately, “become Merck, but better” (Werth 2014, p. 50). In a crusade against what had become a bloated and sluggish big pharma, many scientists later defected from “Mother Merck” to join Boger. Merck would recognize the cost associated with losing such a group of talented researchers when a more potent compound Vertex developed for HCV outperformed Merck’s in the market.

Over time, Merck leadership had evolved a vision for drug innovation that rather incentivized incremental progression over radical transformation for the purpose of avoiding any of the risk inherent in drug innovation. In his 2014 book profiling Vertex pharmaceutical, Barry Werth interviewed another Merck veteran, Patricia Hurter, who left

for Vertex around the time Merck withdrew Vioxx from the market in 2004. The following excerpt from the interview (2014) reveals Merck management's changing attitude toward productive employees who engaged in the inherently risky and cumbersome drug-innovation process:

When people take a risk and it doesn't pay off, you've got to be supportive. That's the biggest difference between Merck and here [Vertex]. At Merck, if you took a risk and it paid off, you were a hero. If you took a risk and it dumped on you, you were a disaster, and for the next fifteen years, your performance review reflected that. They were very unforgiving about anybody who did something that didn't pan out. Basically people became very cautious.

(Werth, 2014, p. 161)

4.2.7 Ending “career-with-one-company” (CWOC) as pervasive employment norms at Merck

In the wake of the industry's transformation into the age of biochemistry and molecular biology, pharmaceutical companies such as Merck were struggling to attract scientists from academia, who questioned the integrity of industrial research, especially after many pharmaceutical companies had downsized their investment in research for pharmaceuticals and their R&D workforce. In fact, when Vagelos decided to leave academia for industry, his close friends and colleagues challenged his decision and repeatedly reminded him that he would potentially be looking forward to “selling toothbrushes and combs” (Vagelos & Galambos, 2004, p. 106). Such a statement reflected academic scientists’ perception of industrial research had become during the era of diversification, Merck had extended its product range to include products in the non-pharmaceutical healthcare and personal care segments as all its competitors had done so.

Recruiting top-quality scientists in the fast-growing fields of biology such as biochemistry, molecular biology and genetics has been particularly difficult since the early 1980s. Around this time, entrepreneurial activity was growing in electronics and computer technology, particularly in that part of California’s San Francisco Bay Area later dubbed “Silicon Valley” for being home to a large number of companies developing and manufacturing silicon chips. The Silicon Valley region had also become the birthplace of a new class of private equity investors, popularly known as venture capital (VC) investors, that specialized in providing risk capital to early-stage, high-risk/high-return technology ventures,. As early as the late 1970s VC investors were exploring opportunities in the fledgling biotechnology field, and they funded early biotechnology start-ups such as Cetus, Genentech, Biogen, Amgen, Chiron, and Genzyme. Securing capital from VCs and licensing technologies from the nation’s leading research institutes —among them, UC Berkeley, UC San Francisco, Stanford, and Harvard -- the nation’s prominent biochemists

and molecular biologists were beginning to incorporate biotechnology start-ups and move into new-product development using their cutting-edge drug-development tools.

Early in the biotechnology revolution, many big pharma companies were reluctant to make substantial investments in new learning in molecular biology, but some had shown an interest in inter-organizational collaboration on the development of new drugs using the tools of biotechnology. After having entered into R&D contracts with big pharma, Genentech and Cetus completed successful initial public offerings (IPOs) in the early 1980 despite having no marketable products. Some of these productless-IPOs, termed “PLIPOS” by Lazonick and Tulum (2011), ultimately became major competitors in the job market and began luring talent from big pharma and academia. PLIPOS quickly became attractive employers for scientists in molecular biology and genetics on the strength of the potentially lucrative stock options they offered. More important, research at big pharma came to be perceived as more or less old, bureaucratic, bloated, and sluggish, which drove entrepreneurial young scientists away from big pharma and toward small start-ups.

Merck had begun using stock option plans in 1951, but they were offered only to company officers and other key personnel; the remaining employees were allowed to purchase company stock and invest them in their retirement accounts, which was seen as a way of encouraging them to save on a regular basis. At the time of the company’s centennial in 1991, each of Merck’s 34,500 employees was offered right to purchase 100 shares of the company at a \$127.25 per share option price, set on September 6, 1991. Those options were set to be exercised between September 6, 1996, and their expiration date of September 5, 2001.⁴³ Because Merck’s employees already owned approximately 2 percent of its common shares outstanding when these options were offered, employee ownership in the company would, under the proposed plan, go up to 3 percent before the scheduled expiration in 2001 (Freudenheim, 1991). Critics of Merck’s decision to enact a broad-based employee stock-ownership program argued that it was merely an attempt to divert attention from an already exorbitant executive pay (Weber, 1991)

Having had the reins over MRL handed to him, Scolnick began to abolish the Vagelos-era process of decentralizing decision making power and allowing the leaders of different research groups to practice some autonomy and make strategic decision along with the members of their research team. After Vagelos had retired, Scolnick’s efforts to regain full control of research operations intensified during this period he was left alone by the new CEO Raymond Gilmartin “to run research as his private fief” (Berenson, 2005). Under Scolnick’s control, MRL slowly disintegrated as the company’s productive scientists began to defect from Merck to join the biotechnology start-ups that were galloping to beat big pharma to market with new-generation therapies.

⁴³ Through Centennial Stock Option Grant 100 Merck stocks granted on September 6, 1991 was increased to 300 Merck stocks at \$42.42 after 3-to-1 stock split in 1992; and to 600 stocks at \$21.21 after 2-to-1 stock split in 1999.

Failure under Scolnick to retain top scientists ultimately undermined the company's R&D productivity and clinical pipeline. The only growth in employment in the 1990s occurred through the acquisition of MEDCO in 1993. The company's delayed entrance into the antivirals market is an example of how the deteriorating integrity of research operations had led to the declining innovation productivity of the following decade. Merck had sustained learning efforts in the development of protease inhibitors for a decade prior to its interruption in late 1980s by the loss of two of the nation's top experts in the field of peptidases. Irving Sigal, senior director of Merck's molecular biology program, had been killed tragically at age 35 in the bombing of PanAm flight 103 over Lockerbie, Scotland, in 1988 (Werth, 2014, p. 5). It was the year after the loss of his colleague Sigal, who had championed the protease-inhibitor program under the tyranny of Scolnick, which Boger decided to start Vertex Pharmaceuticals and compete against Merck in the market for antiviral drugs (Fried, 1998).

The loss of Sigal and Boger in the critical phase of the research program on protease inhibitors was a setback that profoundly affected the integrity of Merck's research program and ultimately delayed the company's entry into the market for antiviral drugs, particularly for HIV/AIDS and HCV, market segments captured by Vertex and Roche in the following years. Having failed to develop productive capabilities in recombinant DNA technology (1980s), gene therapy and RNA interference (1990s), and genomics (2000s), the company had no competitive position in such fast-growing fields as immunology and oncology in the early 2000s.

The company's stock price, declining since the early 2000s, were generally thought to reflect loss of investor confidence in the company's management. Gilmartin was ousted mainly for undermining shareholder value by mismanaging the company during the events leading up to the withdrawal of Vioxx – even though the company under his direction had distributed nearly \$54 billion in cash to its shareholders through dividends and stock buybacks. Organizational integrity continued to deteriorate after Scolnick and Gilmartin were replaced by Kim and Clark in 2003 and 2005, respectively. In the mid-2000s the company's revenues experienced sharp declines as the patent lives of its legacy anti-inflammatory, anti-hypertensive, cholesterol, and osteoporosis drugs were coming to an end. During this period the sales performance of the company's newly launched products were disappointing as well.

Determined to revive shareholder confidence, Clark accelerated the company's stock repurchases in 2005, aiming to boost its stock price, which had lost as much as 60 percent of its value from its all-time high level of \$88 in 2000. In November 2007, Merck decided to end the approximately 26,500 ongoing Vioxx product-liability lawsuits by agreeing to pay approximately 47,275 plaintiffs \$4.85 billion, considered at the time to be one of the largest-ever drug settlements (Berenson, 2007). In January 2008 Merck's stock took another dive, when recent clinical studies revealed that Vytorin, a potential blockbuster cholesterol therapy combining Merck's off-patent Zocor and Schering-Plough's Zetia,

failed to show clinical superiority to Merck's generic Zocor in lowering cholesterol when taken as a single-drug regimen. After experiencing repeated setbacks, Clark concentrated his efforts on acquiring another drug company with a strong clinical pipeline in an attempt to end the company's prolonged productivity crisis.

Busting research jobs and capabilities, boosting shareholder value and executive compensation

During Clark's tenure Merck spent over \$50 billion for a series of corporate acquisitions and R&D deals. The company also disbursed over \$36 billion of its cash to shareholders. The former CEO of Merck-Medco Managed Care and president of the Manufacturing Division, Clark was one of the few executives at Merck capable of overseeing a major corporate restructuring program and identifying the assets most eligible for liquidation. These restructuring programs can be placed in two groups: "post-Vioxx," referring to those that followed the voluntary withdrawal of that drug in 2004; and "post-acquisition," referring to those that followed the merger with Schering-Plough in 2009.

The purpose of the post-Vioxx restructuring plans was to restore "the trust and confidence of employees and shareholder," Clark told a room full of investment professionals at the Goldman Sachs Healthcare CEO's Conference on January 6, 2011. During his five-year tenure as CEO, Clark had kept his promise to shareholders and become the second-most successful among the CEOs of the top 11 global pharmaceutical companies in creating value for shareholders (Goldman Sachs, 2011). Clark, however, had also laid off approximately 13.4 percent of Merck's employees through different corporate restructuring programs.

When the Schering-Plough merger was completed in 2010, global employment at the combined new entity reached as high as 100,000. Clark and, later, Frazier have brought global employment down by 32 percent since the beginning of the decade by persistently pursuing corporate restructuring programs during the post-acquisition period. Despite numerous additional acquisitions since the mid-2000s, the company's workforce has been following a trend of steady decline (Figure 15). Aside from a slight increase in 2011, company revenues have also been in decline since 2010 (Figure 14). Despite the reduction in its workforce and its diminishing sales performance, Merck has managed to sustain dividend payments to stockholders and to increase its stock repurchases (Table 8 and Figure 21). Merck's stock price has also increased steadily since the acquisition of Schering-Plough was first announced in March 2009.

As the analysis has shown so far, it was mostly the sense of utility to serve the society's medicinal needs and advance the frontiers of biomedical science that motivated the R&D workforce, or any other employee in this matter, to participate in the organizational learning efforts and remain productive at Merck. Applying financial rewards to harness the productive skills and innovation efforts of the R&D employees had never been a standard

human resources (HR) practice at Merck until the 1990s. At a time when New Economy companies began to emerge in the biopharmaceutical industry in the 1980s, stock options began to gain prevalence among the US pharmaceutical companies not necessarily for stimulating labor efficiency to enhance their productivity, they were rather adopted for remaining competitive in the labor market against the fast growing biotechnology companies to retain productive employees.

The availability of speculative markets in the US gave rise to the New Economy biotech companies in the 1980s and 1990s. It is the speculative nature of the US stock market that often encourages biotech start-ups, even the most risky companies without any product in the market to generate steady stream of product revenues, to raise large sums of capital from the risk-taking stock investors through initial public offerings (IPOs) of corporate stocks. Having dubbed such New Economy biotech companies as “product-less initial public offerings” (or PLIPOs), Lazonick & Tulum (2011) explains how the existence of speculative markets gave rise to the PLIPO phenomenon starting with iconic biotech IPO such as Genentech and Cetus in the early 1980s that gave precedence to many other biotech start-ups to follow a similar path to access capital in the speculative markets.

As stock options gained broader application in the labor force, first to include the manager in the lower-ranks of the administrative hierarchy, then to include some rank-and-file employees, expectations on the future prices of company stocks, rather than the prospect of CWOC, that began to determine the rate of labor turnover, particularly among the most skilled and productive R&D employees. Given how high the scale of financial gains an employee could potentially generate from the increasing stock price of a biotech start-up, it has been difficult for the large and established pharmaceutical companies to lure the new generation of R&D employees into working for large industrial laboratories using stock options as an attractive pay incentive.

In the US economy and elsewhere in the developed economies, gains realized through exercising stock options have accounted for the largest portion of total executive pay and so have been primarily responsible for the explosion in executive pay that has taken place since the early 1980s (Lazonick, 2009). Despite Merck’s prolonged productivity crisis, arduous legal battles, and financial health, its top executives have managed to pay themselves handsomely: In fact, their annual gains have exceeded the industry average. Table 5 compares the average gains of Merck’s top five executives against the average gains of all other employees of the firm. Gains from exercised options are estimated from the information on the gains of employees and the top five executives from exercising stock options that the government has required companies to report annually since 1994.

When a company’s stock price increases substantially, employee stock options can provide significant additional remuneration to those who hold them. As observed in Table 5, on average, across over 47,300 employees, these gains from exercising stock options have been large since 1994. As observed in Table 5, on average, across over 47,300 employees,

these gains from exercising stock options have been large since 1994, however the growth in gains from exercising options was particularly significant between 1996 and 2000.

Table 5: Merck & Co. Inc. gains from exercising stock options, 1994-2016, top five executives and average gains of all other employees

	Average gains top5* \$(per executive)	Average gains, all other employees \$	Ratio top5/average employee	Average number of employees during year
1994	-	4,013		47,300
1995	1,752,877	9,025	180	46,350
1996	186,820	13,368	13	47,150
1997	2,903,784	17,217	153	51,450
1998	456,072	25,323	16	55,550
1999	3,394,198	16,693	185	59,800
2000	12,564,375	23,784	474	65,800
2001	401,002	7,134	51	73,700
2002	948,217	3,513	234	77,700
2003	2,262,089	455	4,302	70,250
2004	8,324,293	3,282	2,252	62,900
2005	847,857	865	819	62,050
2006	236,178	1,620	119	60,750
2007	2,308,707	6,514	329	57,500
2008	-	292	-	53,000
2009	9,754,819	238	20,440	75,500
2010	-	1,667	-	97,000
2011	220,490	1,155	161	90,000
2012	1,947,383	6,000	287	84,500
2013	608,978	4,104	126	80,000
2014	3,953,182	9,044	386	73,500
2015	917,457	4,146	196	69,000
2016	4,070,481	5,901	610	68,000

*The data presented in this table do not represent all of the stock-based pay of top executives.

For example, former top 4 Schering-Plough executives' total exit package valued at \$159.7 million in 2009. This total also includes \$93.2 million termination-related payments. Such a high compensation figure doesn't include \$48.7 million in gains realized through exercising stock options.

Source: Own calculations based on company annual proxy statements and 10-K filings, 1994-2016

Table 5 reveals a trend to confirm this critique; since the surges on Merck's stock prices ended in 2000, employee gains from exercising stock options have yet to match the boom-period performance, although executives' gains have periodically surged. In the year Vagelos retired from the chairmanship no top executive reported gains from exercising stock options. At the time of his retirement, however, Vagelos's exercisable stock options were estimated at \$21.6 million. His annual compensation, including a bonus payment, was \$1.94 million in 1994. Vagelos also received nearly \$2.5 million in 1993 and 1994 under the company's long-term incentive program (LTIP). Additionally, Vagelos received a lump-sum payment of nearly \$15.3 million from the Retirement Plan for Salaried Employees (RPSE) and the Supplemental Retirement Plan (SRP) in 1994. Vagelos's total

retirement package totaled \$19.7 million for compensation, with an estimated \$21.6 million in additional gains from exercisable stock options.⁴⁴

Average gains from stock options of Merck's top five executives surged in 1995, 1997, 1999 and 2000. Scolnick was among several top executives who had realized nearly \$45 million in gains. Of those \$45 million in gains, \$24.8 million were realized on October 25, 2000, when Scolnick and a member of his family to whom he transferred some of the shares he received from exercising options, sold for \$85 per share 381,200 shares obtained by Scolnick at exercise prices ranging from \$16.25 to \$21.2. According to court records from the Vioxx Securities Lawsuit, Scolnick had "personally profited from the sale of Merck stock at artificially-inflated prices" through those stock sales. The plaintiffs in the Vioxx Securities Lawsuits challenged the legitimacy of Scolnick's gains, claiming that Scolnick had acted upon "material adverse non-public information regarding Merck" that he had in his possession. Since Merck ultimately agreed to settle those lawsuits, no verdict was ever reached on the allegations of making "false and misleading statements." Public court documents, however, revealed the intriguing details of how seeking to profit from pharmaceutical innovation can undermine the organizational productivity and put public health at risk.

At Merck, the use of stock options as a form of compensation has served to increase the divide between top executive and other employees—a characteristic of a financialized company. Under Gilmartin, average gains from stock options of the top five executives were 4,302 times greater than the average gains of the 70,250 Merck employed in 2003. Under Clark the average gains of top five executives were 20,440 times greater than the average gains of the company's remaining 75,500 employees. Such a disparity on the average gains of the company's top five executive and the remaining employees occurred after Clark implemented an immediate restructuring plan following the withdrawal of Vioxx from the market to restore "the trust and confidence of employees and shareholders," Clark told a room full of financial professionals at the Goldman Sachs Healthcare CEO's Conference on January 6, 2011. During his five-year tenure as CEO, Clark had kept his promise to shareholders and become the second-most successful among the CEOs of the top 11 global pharmaceutical companies in "creating"—that is, extracting—value for shareholders (Goldman Sachs, 2011). Clark, however, had also laid off approximately 13.4 percent of Merck's employees through different corporate restructuring programs.

Under the "2005 Global Restructuring Program," by 2008 the company eliminated 7,000 jobs worldwide and or closed five manufacturing plants as well as two preclinical sites. One year after Merck settled the Vioxx product-liability lawsuits in 2007, Merck under the

⁴⁴ *The value of gains from exercisable stock options is estimated based on the stock price on December 31, 1994, less option exercise price. Depending on the stock price at the time gains are realized such gains could be lower or higher than the value estimate reported in the company's 1995 proxy statement.*

“2008 Restructuring Program,” reduced its global workforce by another 6,800, with approximately 40 percent of the jobs eliminated being in its US-based operations. Savings were yielded by the operational austerity program mostly through consolidating basic research operations into four global locations and reducing the number of senior and mid-level executives globally.

Through such a program management anticipated generating anywhere from \$4.5 to \$5 billion in savings between 2006 and 2010. The 2008 program was expected to yield anywhere from \$3.8 to \$4.2 billion in savings between 2008 and 2012. The post-merger cost-cutting program, “2010 Merger Restructuring Program,” reduced the global workforce by an additional 15 percent and were expected to yield an additional \$2.6 billion in savings by 2012. Merck under Clark had eliminated approximately 30,000 jobs, five manufacturing plants, and two preclinical sites, yielding savings of anywhere from \$10.9 billion to \$11.8 billion achieved from 2005 through 2012. During the same period Merck spent \$12.3 billion on stock buybacks (Figure 21 and Table 8).

As the pace of transformation into becoming a financialized company accelerated in the period following the retirement of Vagelos, Merck’s innovative productivity diminished. It is difficult to sustain collective and cumulative learning when the company’s labor force is being slashed. As the market pressure became insurmountable in the aftermath of the Vioxx scandal, the top Merck executives came to terms with Wall Street and began to pursue downsize-and-distribute resource allocation strategy in the name of maximizing shareholder value. This new strategy undermined not only organizational integration but also financial commitment. In analyzing financial commitment as a social condition of innovation at Merck, the next section provides a full account of the company’s numerous restructuring programs under Clark and Frazier and discusses the implications of the decisions it took to allocate the savings those programs yielded.

4.3 Financial Commitment

...Retained earnings [are] one of the cheapest sources of long-term capital for investment in commercializing new products.

(Alfred D. [Chandler], 2005, p. 4)

In the first century of its history, Merck’s had been an exemplary case of innovative enterprise. The company had been rewarded financially for relentlessly pursuing its mission of developing safe and effective new therapies “for people” through innovation. The company’s growth, which for decades overshadowed even that of its closest competitors, had depended for the most part on its building a research-driven organization that aspired to advance the frontiers of biomedical science for the sake of scientific progress and public health.

Since the company had lost its access to innovative products when it was forced cut its ties to its German parent in the early 1900s, the founders devised a strategy not only of building research capabilities to develop products internally but also of exploring new opportunities in the then-fledgling field of ethical drugs so that Merck could become a fully integrated pharmaceutical company and an important competitor in the ethical-drug market. To pursue this strategy the company had made significant investments in the development of productive capabilities. Through the utilization of these productive assets, the company had successfully acquired, absorbed, disseminated, and transformed new knowledge into innovative processes and products. Throughout the innovation process, strategic control over the allocation of company resources had remained in the hands of managers who were committed to the company's founding mission and supported organizational efforts in the pursuit of this somewhat altruistic innovation mission, which had inspired people within the organization. Because this mission was so effective, Merck's participation in various medicinal innovation campaigns to challenge diseases had been very high.

At the turn of the twentieth century, the company had had neither the internal capabilities to develop new products nor the impetus to do so. Given its lack of skills and know-how, the young American Merck had lacked the means to match the extremely high-quality German fine-chemical production and so had focused on the sale and distribution of German products in the US market. As tension between the US and Germany in the years leading up to World War I, the American Merck had had to improve its capacity to develop and manufacture high-quality chemical products. Through a very disciplined fiscal management, George F. Merck had managed to retain earnings to reinvest in the development of productive assets until 1917, when the war brought complications that threatened his continued ownership of the company.

Determined to retain control, George F. Merck had offered his personal shares in the company to the Alien Property Custodian (APC) in exchange for being allowed to keep his job as its top executive. By the time APC decided to sell off the company's 8,000 shares in a public auction, George F. Merck had been declared a loyal American eligible to own and run a business and was ready to make a bid. Through Alfred Jaretzki, a senior partner at Sullivan & Cromwell who was one of his advisors on legal matters at the time, George F. Merck had approached Goldman Sachs for help with his effort to reacquire the company. Having secured funding from Goldman Sachs and Lehman Brothers, George F. Merck won the company shares for \$3.75 million (approximately \$45.7 million in 2016 dollars) at auction on May 9, 1919, outbidding serious competitors such as Monsanto and American Aniline (Steen, 2014).

The acquisition of those shares had been costly in that George F. Merck had had to give up 35,000 shares of preferred stock that carried a guaranteed 8 percent annual dividend (Sturchio & Galambos, 2011). George F. Merck and the bankers underwriting the acquisition deal had managed to sell all 35,000 preferred shares in a public offering in

August 1919 designed to raise capital, broaden the shareholder base, and return strategic control of the company to Merck. The preferred shares, whose worth totaled \$3.5 million at their assigned price of \$10, had been oversubscribed prior to their offering in the public market (NYT, 1919). The transaction made Merck & Co. a public company and George F. Merck its largest stockholder.

As part of the reacquisition deal, George F. Merck, had agreed to cut the company's ties with its former parent in Darmstadt. To ensure the separation, APC had appointed a new trust to oversee the company's interactions with Darmstadt. Although still possible informally, the exchange of information had slowly dwindled as the German cousins had become skeptical of Merck's utility as an agent for the sale and distribution of German products in the US. In response to the slowing of the information exchange with E. Merck in Germany, Merck had begun to make investments in organizational learning in a modest attempt to improve productivity. Merck's assets had been leveraged significantly to pay for the reacquisition in 1919, and the company had been struggling to service the debt that had been accruing since the preferred shares were first issued. Although highly profitable, the company's operations hadn't generated sufficient capital in the early-1920s for it to afford substantial investments in the development of a knowledge base.

Having previously served as treasurer, George W. Merck was promoted to manage the company's operations as its new president, while George F. Merck had become chairman in 1925. Trained in chemistry and business at Harvard, the young and ambitious George W. Merck had been fully aware of the challenge that lay ahead for the cash-strapped company. In this context, the infusion of capital that came with the merger with Powers-Weightman-Rosengarten in 1927 had been one of the crucial moments in the company's history. Besides alleviating the company's liquidity and working-capital problems, combining operations and market share had provided economies of scale necessary to generating cash flow and earnings that were adequate for the investments in the knowledge base that George W. Merck envisioned at the time.

Other aspects of the merger were as important as the rapid financial relief it afforded. First, Merck had lacked the know-how needed to improve production quality and efficiency, the merger provided information that could be quickly translated into more efficient manufacturing methods. Second, the scale of operations of, and the market share captured by, the combined entity would justify investment in the development of productive capabilities. And finally, the growth achieved through organizational learning in the fine-chemicals market had quickly opened paths to new markets for high-value, high-profit products such as sulfa drugs and vitamins.

4.3.1 Transforming Merck into a science-driven innovative enterprise

As explained in the earlier sections, Merck had engaged in an intensive learning process that it pursued collectively and cumulatively particularly in the first 50-year period of

Merck Research Laboratories. Having identified a science-based growth *strategy*, George W. Merck had pursued an ambitious recruitment campaign to build an *organization* that had striven for learning in emerging new fields in chemistry and biology. During the process of learning, no matter how onerous and unpredictable it had been, the company resources had been carefully deployed to ensure that the innovation process was well financed until a payout was possible. As had been the case in the previous period, the company's retained earnings had remained the major source of investment in the development productive resources.

The size and duration of financial commitment to the innovation process had varied in different developmental stages of MRL. When the innovative capabilities of a newly created research unit were first tested during WWII, the research group at Merck had risen to the occasion and met the urgent medicinal needs, for which the US government sought industrial support, of the US soldiers fighting the Nazi occupation of Europe. During this period the organizational learning efforts had further intensified, their aim being to develop new means of mass producing penicillin and steroids products to meet surging military demand through one-of-a-kind, inter-organizational research collaboration.

Without anticipating a major payout at the end, Merck had deployed nearly all of its resources, in addition to financial support it received from the US government along the way, to ensure that the company successfully completed this major innovation task through sustaining organizational learning at any cost. Its devotion to learning and innovation in the Second World War ultimately allowed the company to reap returns that whose value was beyond the measure any financial figure could capture. The company's annual sales nearly trebled between the end of WWII and the merger with Sharp & Dohme in 1953.

During this period Merck had remained profitable, which allowed it to finance its major capital expenditures and its merger with Sharp & Dohme. New stock was issued, mainly for the acquisition of smaller chemical manufacturers, and the company's first stock options plan (SOP) launched in 1951, after the Board had authorized nearly 130,000 company shares to be distributed through the SOP. Interest in this incentive program had been limited due to fluctuating stock prices in the three years following the merger. And demand had remained limited despite a successful period of product launches in the late 1950s that had resulted in significant stock-price appreciation and earnings per share that grew more than six times, from an annual average of \$0.47 to \$2.93 between 1953 and 1960.

The trend of rising sales and net income observed in the late 1950s persisted in the years following the enactment of the Kefauver-Harris Amendment of 1962. Having anticipated that further increases in the cost of drug R&D would result from its requirement that safety and effectiveness data be gathered, the biopharmaceutical industry, with Merck marching at its head, lobbied against the amendment. As illustrated in Figure 12 and 13, the company's profitably continued to grow despite the industry's depiction of the amendment's

enactment as an apocalyptic event that would bring drug innovation to an end. The positive trend ended, however, when Gadsden initiated his strategy of diversifying into new pharma or non-pharma markets in the mid-1960s.

The sharp increases in Merck revenues had been driven mainly by acquisitions made in the mid-1960s however the company's profit levels remained stagnant. During this period pharmaceutical products continued to be a major source of profit for all divisions. As illustrated by Figure 21, the company's R&D spending followed the growth trajectory of net income, which increased in the ten-year period following the merger but then was stagnant until the early 1980s. The proportion of revenues (REVs) that Merck spent on R&D was 4.39 percent and 9.44 percent in 1953 and 1963, respectively. Until it went up to 10.45 percent in 1982, the company's R&D spending rate ranged anywhere between the high of 9.9 percent recorded in 1964 and the low of 7.74 percent recorded in 1974. The stagnant growth figure reflects managerial reluctance to engage the organization in further learning, particularly in the fledging field of biology throughout the 1960s, when the company's financial resources were deployed in pursuit of its diversification strategy instead.

The acquisitions of the rapid expansion period were financed largely through the exchange of company stock. Shares used in the acquisitions of Metalsalts, Calgon, Baltimore Aircoil, Pacific Pumping, Kelco, and Hubbard Farm were equivalent to approximately 16 percent of Merck's total stock outstanding. The stock traded for Calgon alone amounted to nearly 10 percent of total stock outstanding. Although these acquisitions quickly boosted the size of company revenues, their contribution to the company's overall profit was less than that of the pharmaceutical products division.

4.3.2 Financing innovation at Merck under Horan and Vagelos

Having recognized the company's need for a fresh, new approach to drug R&D and a more focused, better-formulated growth strategy driven by innovation, Merck initiated an organizational restructuring program and recruited Vagelos to oversee what promised to be an onerous campaign. The company began to launch the restructuring program's first batch of products in the late 1970s: among them, a broad-spectrum antibiotic; analogs of existing analgesics; and new, combination high blood pressure therapies based on existing drugs, an example being Tiolide, a medication that combined the beta-blocker Blocadren with the diuretic Hydrodiuri. In the 1980s, as revenues continued to rise following the new-product launches and Merck began to sell non-core assets -- such as Calgon Carbon and Baltimore Aircoil, which it jettisoned in 1985 -- the company's profit level, as well as its spending on R&D, began to increase.

As Table 6 shows, Merck increased its R&D spending from 8.3 percent in the 1970s to 10.9 percent in the 1980s. During this period Merck was among the biggest spenders on R&D measured as a percentage of total sales, sharing second place with Eli Lilly behind

the leader, Upjohn. Lilly was working with Genentech at the time on the development of the world's first genetically modified insulin while getting ready to market what was to become a blockbuster drug for the treatment of depression, fluoxetine, sold under the trade name Prozac. Also in the early 1980s, Upjohn was intensifying R&D efforts to transition the NSAID ibuprofen, sold under the trade name Motrin, from the prescription to the over-the-counter (OTC) market, as well as to commercialize its new tranquilizer, alprazolam, sold under trade name Xanax, and its new central nervous system (CNS) depressant, triazolam, sold under trade name Halcion.

Table 6: Research and Development Investments of Major American Pharmaceutical Companies as a percentage of total sales by decade

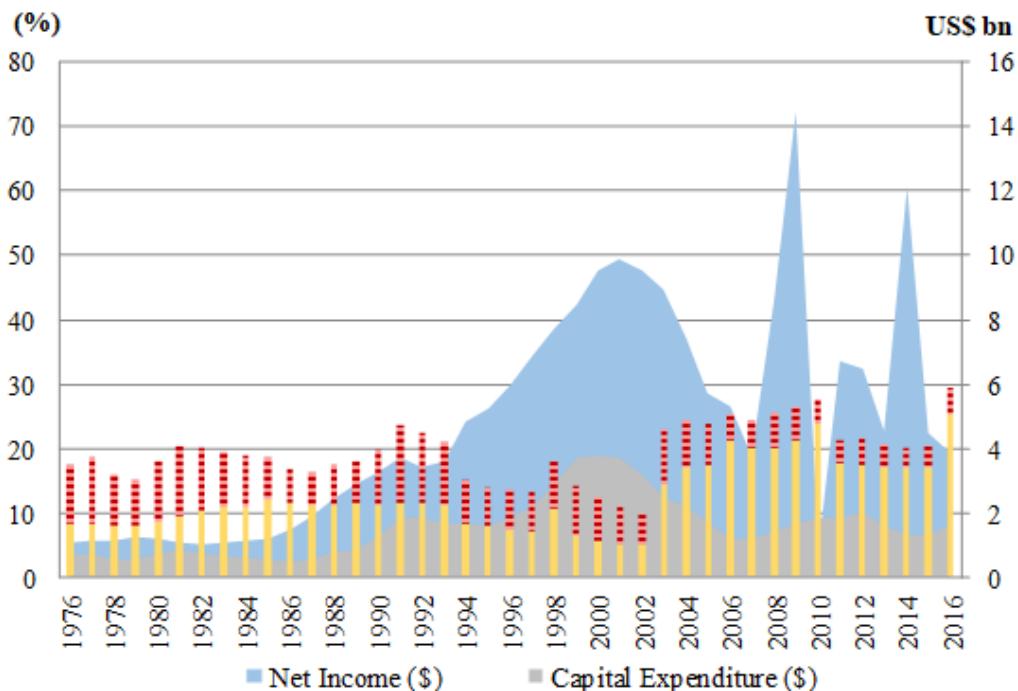
Company	% of total sales				
	1950s	1960s	1970s	1980s	1990s
Abbott	4.00	6.4	5.3	7.3	10.2
American Home Products (Wyeth)	NA	2.0	2.3	4.0	9.9
Bristol-Myers	4.50	3.8	3.6	7.1	8.9
Johnson & Johnson	NA	4.4	4.4	6.6	8.8
Lilly	6.30	10.1	8.6	10.9	16.3
Merck	6.00	9.3	8.3	10.9	8.7
Parke-Davis	4.00	6.7			
Pfizer	4.50	3.7	4.5	7.1	14.5
Schering-Plough	7.80	8.6	5.8	8.3	12.7
Searle (1985)	10.00	9.9	8.2	8.1	
Smith Kline & French (2000)	6.50	9.5	8.2	9.5	
Squibb (merged in 1989) **	NA	NA	4.4	8.1	
Sterling (1988)	2.00	3.0	3.0	4.3	
Upjohn (1994)	8.40	10.3	9.0	12.2	16.0
Warner-Lambert (2000)	2.20	3.4	3.5	5.5	8.6

Source: Own calculations based on data from Achilladelis (1999) & companies' annual reports

As illustrated in Figure 19 tenure as the head of R&D. Having spent five years in that job without introducing any major products, Vagelos began to feel pressure from shareholders and pleaded with upper management to be patient until the company's engagement in new learning finally paid off (Vagelos & Galambos, 2004, p. 148). The period during which Merck's R&D expenses remained flat must, however, be examined in comparative perspective.

As shown in Figure 19, at the time when Vagelos joined Merck in the mid-1970s, the company spent nearly the same for capital expenditures (CAPEX) and R&D that together amounted the equivalent of almost 18 percent of revenues. This high ratio was the result of a massive capital expenditure investment program initiated in 1975. The size of this investment program was nearly \$1 billion (in 2016 dollars) and was financed largely through the issue of long-term bonds. Major construction efforts to increase pharmaceutical manufacturing capacity accounted for a large portion of this investment program.

Figure 19: Merck & Co. Inc., net income (NI), R&D, and capital expenditures (CAPEX), 1976-2016 [adjusted in 2016 dollars]



Source: Own illustration based on data from company annual reports

Horan, who was being groomed for the CEO post at the time, introduced this major strategy overhaul in an effort to refocus the company on its core business, as human and animal health products had been a major contributor to company profits in the previous decades. This investment in capital expenditure to increase production capacity was part of a global expansion strategy aimed at further leveraging the company's pharmaceutical assets. R&D operations underwent a major restructuring in line with this new research strategy, formulated and executed by Vagelos in the late 1980s.

Under Vagelos's direction MRL launched a series of innovative new products, most notably a new ACE inhibitor for blood pressure management, Vasotec (1984); a therapy for stomach ulcer, Pepcid (1985); the first statin ever to succeed in the drug market, Mevacor (1987); the first recombinant hepatitis B vaccine, Recombivax HB (1987); another ACE inhibitor, Prinivil (1987); and another ulcer medicine, Prilosec (1989). Merck's profits rapidly rose to record levels in the late 1980s but the increase in CAPEX and R&D spending was more modest during the period. The accomplishments of MRL under Vagelos were highly unusual: Whether for technological or strategic reasons, no drug company had ever managed, or even attempted, to launch multiple products within a relatively short time period (Hawthorn, 2004).

Table 7 illustrates the scale of this accomplishment and shows that Merck had become the United States' most profitable drug company in the 1980s. During the troubled 1990s, Schering-Plough, a competitor in the cardiovascular drug market, was the only company to perform better than Merck in terms of profitability, which was ultimately to lead to the

merger of the two organizations in 2009. The proportion of net income that Merck spent on R&D steadily declined as the company launched a series of products in the second half of the 1980s, and the decline lasted until the end of Gilmartin's tenure as CEO.

Table 7: Profitability of major American pharmaceutical companies, by decade*

Company	% share of total revenues				
	1950s	1960s	1970s	1980s	1990s
Abbott	11.3	9.6	8.2	13.4	17.1
American Home Products (Wyeth)	8.6	10.2	10.5	15.1	12.9
Bristol-Myers	6.4	8.0	7.8	14.8	17.7
Johnson & Johnson	4.5	7.0	8.5	9.0	12.8
Eli Lilly	13.3	12.6	15.2	15.6	18.9
Merck	10.8	15.5	15.7	19.4	19.9
Parke-Davis	13.8	11.4			
Pfizer	10.7	10.0	8.9	12.2	16.5
Schering-Plough	15.3	11.9	14.4	11.6	20.1
Searle (1985)	21.0	21.5	9.6	11.4	
Smith Kline & French (2000)	15.5	16.1	12.9	17.5	
Squibb (merged in 1989) **	n.a	16.1	8.5	12.2	
Sterling (1988)	7.9	9.0	8.0	7.5	
Upjohn (1994)	12.9	13.1	9.0	10.3	13.1
Warner-Lambert (2000)	7.4	9.0	7.2	5.1	10.2

*Profitability: after-tax profit as a percentage of total sales

Source: Own calculations based on data from Achilladelis (1999) & companies' annual reports

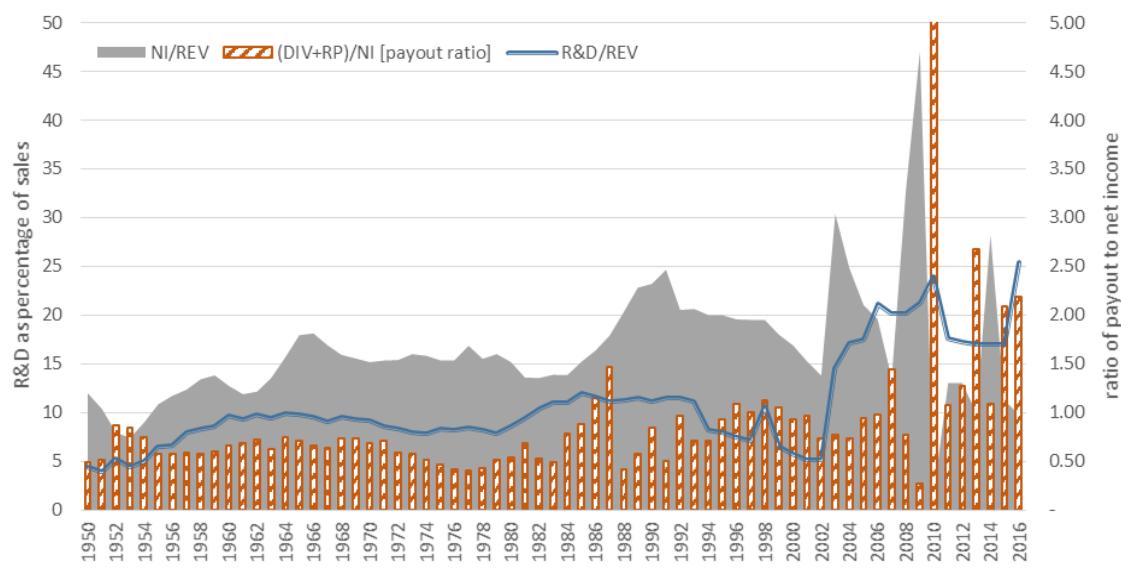
As shown in Figure 20, the proportion of revenues that Merck spent on R&D steadily declined as the company launched a series of products in the second half of the 1980s, and the decline lasted until the end of Gilmartin's tenure as CEO⁴⁵. CAPEX declined from 11 percent to 5 percent in the late 1980s. Except for a couple years in the early 1990s when modest increases in CAPEX were observed, under the manufacturing capacity expansion programs required to launch multiple major products the company's CAPEX program remained below 6 percent of revenues in the late 1990s.

As had been the pervasive industrial norm in the post-WWII decades, the company's retained earnings remained the major source of finance when Merck considered investments in the acquisition and development of productive resources. Between 1946 and 1967 nearly 40 percent of the company's net income was retained and reinvested -along with the selling additional capital stock- in the expansion of capital expenditure and working capital before drug innovation at Merck hit a period of dry spell in the following decade.

⁴⁵ The only exception to steady decline had been 1992, 1993 and 1998. In 1992 the company had initiated the research on Cox-2 inhibitor (Vioxx); in 1993 Merck had acquire and consolidated the R&D operations of Medco with Merck. In 1998 Merck had launched a series of clinical studies on the safety of Vioxx when the company had been challenged by the FDA.

As profit growth stagnated in the early 1980s, CAPEX and R&D ratios reached new maximums. Even as the company's shareholders grew impatient for the launch of new blockbuster drugs, its management sustained its financial commitment to research, devoting to it the equivalent of 80 percent of net income. This is the period when Vagelos was pleading for patience from shareholders and directors while the organization continued to engage in new learning in the emerging fields of biology.

Figure 20: Merck & Co. Inc. R&D as percent of sales and dividends (DV) plus share repurchases (RP) to net income (NI), 1976-2016 [FC]



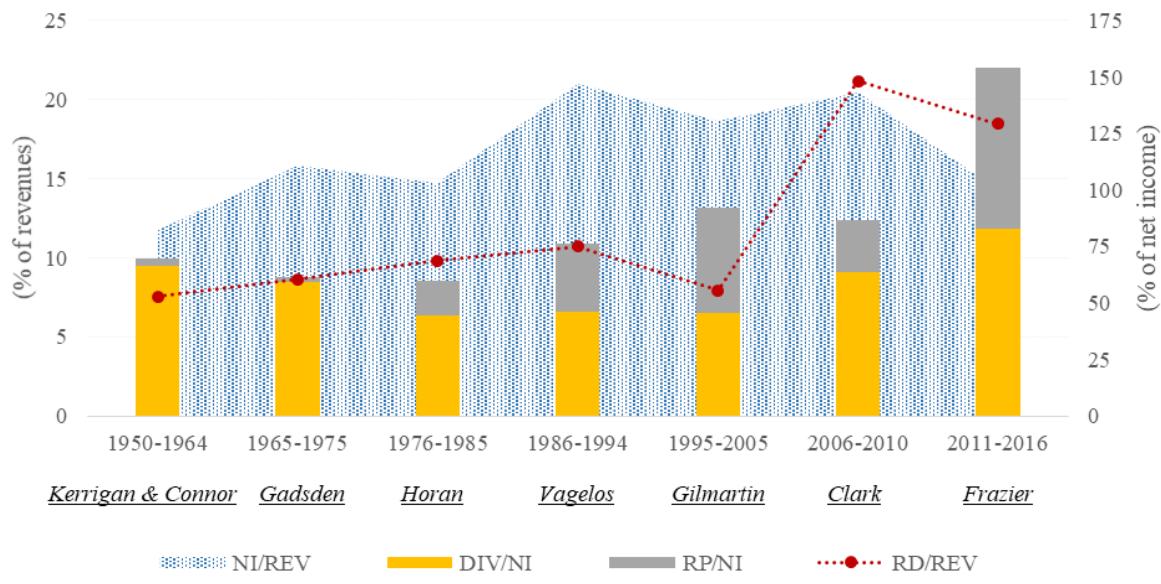
Source: Own illustration based on data from company annual reports

As Figure 20 shows, despite the post-settlement and post-acquisition era restructuring programs, the company's net income was still considerably below its level from 1987 to 1996, the period of productivity boost. But even as Merck's profits diminished, owing largely to the flagging productivity of its research operations, payouts to shareholders continued to increase, and to such an extent that between 2007 and 2016, the combined total of stock repurchases and dividend payments surpassed the company's net income.

Figure 20 also shows that the proportion of distributions that came in the form of stock repurchases grew significantly. From 1987 to 1996, dividends totaled \$10 billion and repurchases totaled at \$8.1 billion, making the total shareholder payout ratio [(DV+RP)/NI] for the period 0.83. In other words, for each dollar of profit the company generated between 1987 and 1996, Merck disbursed 83 cents in cash to shareholders. This ratio rose to 0.91 as \$53.9 billion of the company's total net income of \$58.7 billion was disbursed to shareholders from 1997 to 2006. Between 2007 and 2016 the shareholder payout ratio increased to 1.26, while the company's profit margin decreased to 16 percent from 21 percent between 1987 and 2006.

Figure 21 compares the shareholder payouts ratio $[(DV+RP)/NI]$, profit ratio $[NI/REV]$, and R&D ratio $[RD/REV]$ under different Merck CEOs from 1950 to 2016. The area highlighted in green in each stacked column indicates the percentage rate of stock repurchases (RP) within total revenues (REV); the blue area is the rate of dividend (DV) payments within total revenues (REV); the area shaded in gray indicates the rate R&D spending (RD) within total revenues; and the red dots indicate the profit rate, or proportion of net income within total revenues.

Figure 21: Comparing shareholder payouts by CEO, 1950-2016 [in 2016 \$]



Source: own calculations based on data from company annual reports

As shown in Figure 21 under Horan and Clark the company's disbursement of cash to shareholders was less than the amount spent on R&D. During Horan's tenure the Merck Research Laboratories under Vagelos increased the company's R&D investments and initiated new learning programs in the fledgling fields of biochemistry and enzymology, transforming the organization's research capabilities. Under Clark, however, the company briefly stopped the stock repurchases and deployed its retained earnings to acquire Schering-Plough.

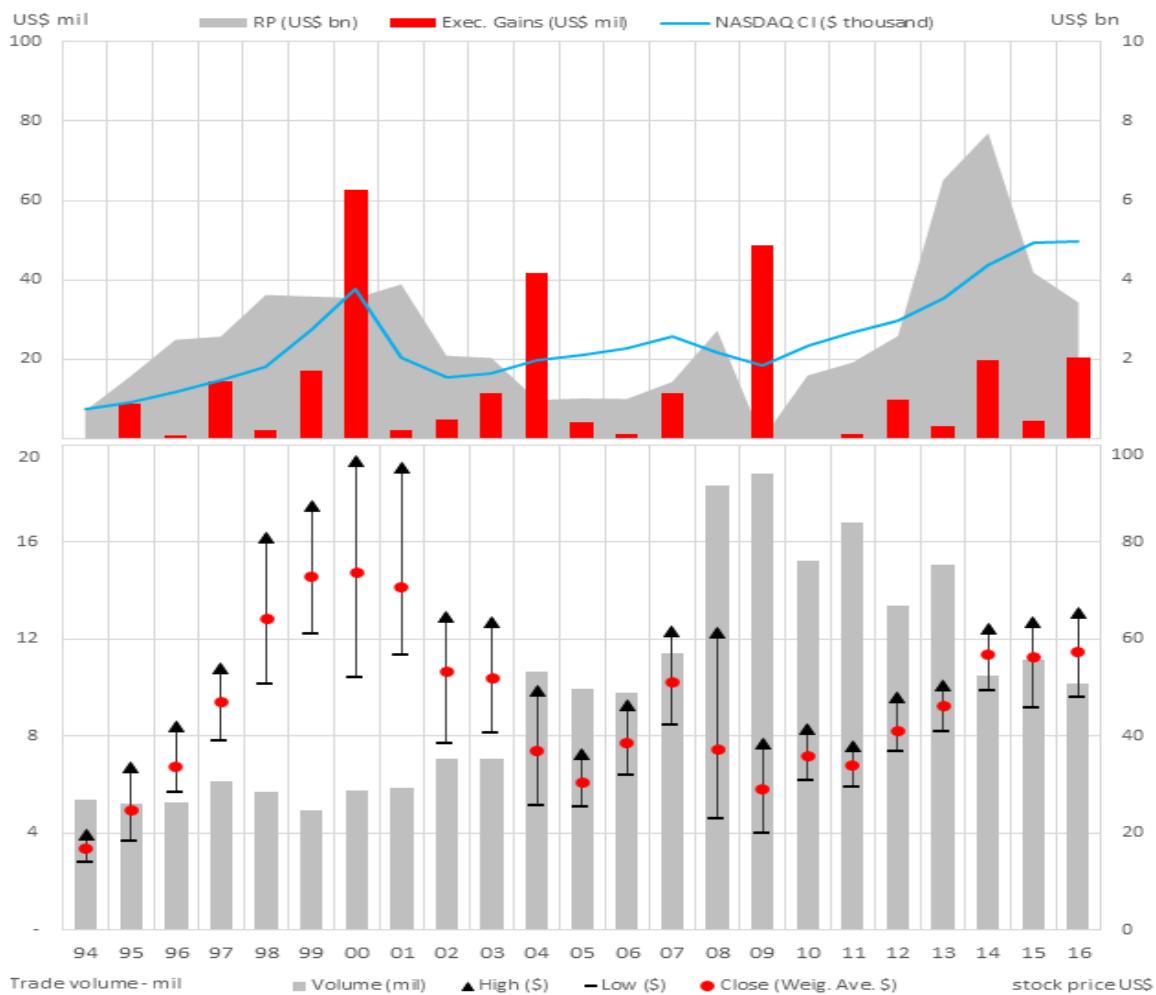
During Vagelos's tenure as chairman and CEO, which lasted from 1986 to 1994, Merck repurchased nearly \$8.5 billion worth of company stock and paid \$12.6 billion in dividends. Nearly two-thirds of the profits generated in this period were distributed to shareholders, an amount 1.5 times greater than that spent on R&D during this period. Figure 21 shows that the company's profit margin (shown by the red dot) under Vagelos surpassed that under any other Merck top executive. As for the remaining one-third of the profits generated under Vagelos, it appears to have been used for partially financing Merck's acquisition of MEDCO in 1993. This was one of the only major acquisition under Vagelos, completed as his tenure was coming to an end in 1994. Once the opposition thwarted the Clinton administration's healthcare legislation efforts, MEDCO quickly

turned from a valuable asset acquired by Vagelos into a significant liability for Gilmartin to handle.

As illustrated in Figure 21 the company's dividend payments have fluctuated under different CEO but its repurchases have been on a significant upward trend since the 1980s. Under Gilmartin and Frazier the company spent as much on stock repurchases as on dividends: 46 percent of net income on repurchases vs. 45 percent on dividends under Gilmartin, 71 percent of net income on repurchases vs. 83 percent on dividends under Frazier. Under Gilmartin the resources allocated for R&D amounted to less than half of the cash disbursed to shareholders. As illustrated in Figure 21, the company's dividend payments have fluctuated under different CEO but its repurchases have been on a significant upward trend since the 1980s. Under Gilmartin and Frazier the company spent as much on stock repurchases as on dividends: 46 percent of net income on repurchases vs. 45 percent on dividends under Gilmartin, 71 percent of net income on repurchases vs. 83 percent on dividends under Frazier. Under Gilmartin the resources allocated for R&D amounted to less than half of the cash disbursed to shareholders.

While dividends reward shareholders for holding the company's stock, repurchases reward shareholders for selling it. The purpose of stock repurchases is to boost the company's stock price, and the prime beneficiaries of these price boosts are the company's top executives, whose pay is overwhelmingly stock based (Lazonick, 2009 & 2013). Figure 22 shows that during the Gilmartin era, particularly in 2000, Merck's top executives generated substantial gains from exercising their stock options. As indicated by the blue line in Figure 22, which represents the NASDAQ composite index's annual average, the period coincided with the peaking of technology stock prices popularly known as the "Dotcom Bubble." The top 5 Merck executives realized \$62.8 million from exercising their stock options in 2000. Strangely, Merck had increased its stock repurchases only after the price of Merck stock had seen its historic high point.

Figure 22: Stock performance, buybacks and executive compensation, 1994-2016



Note: Executive gains (annual realized gains for top 5 executives); stock volume (annual average); price high/low (annual); close (annual weighted average); NASDAQ CI (annual average)

Source: Own illustration based on data from company annual reports and proxy statements, St. Louis Federal Reserve Bank

It is evident in Figure 22 that the surge in executive pay occurred in a year when the company's stock price was highly volatile. The top and bottom ends of the black vertical lines indicate the highest and lowest price of the stock in each year studied. Each red dot indicates the weighted average of the stock's closing price for the year while the gray-shaded columns indicate the annual average of the stock's trading volume.

When the scale of shareholder payouts is placed in comparative perspective, Merck appears to have outperformed its competitors, not only in improving research productivity but also in creating one of the largest shareholder value in the industry. Table 8 provides a decade-by-decade comparison of total shareholder payouts (stock repurchases plus dividends) between 1988 and 2016 among the top five US-based pharmaceutical companies: Johnson & Johnson (JNJ), Bristol-Myers Squibb (BMS), Merck (MRK), Eli Lilly (LLY), and Pfizer (PFE).

Table 8 compares Merck's shareholder payout performance for each decade in the past 40 year period. The first decade (from 1977 to 1986) to the most extent coincides with Vagelos' tenure as the company's head of R&D, which is also the period when the company heavily invested in the acquisition and development of productive resources as a typical retain-and-reinvest company. The second decade (from 1987 to 1996) overlaps with Vagelos' tenure as the company's CEO and Chairman for the most part during which Merck rapidly rose to the top as the leader of the global pharmaceutical market.

Table 8: Stock repurchases (RP), cash dividends (DIV), R&D (RD), and profits (NI), top 5 US firms, 1977-2016

COMPANY	PERIOD	\$ billion		%				
		BB	DV	BB/NI	DIV/NI	(BB+DIV)/NI	NI/REV	RD/REV
Bristol Myers Squibb (BMS)	1977-86	0.0	1.5	0.0	43.0	43.0	10.1	4.8
	1987-96	3.6	11.4	21.6	68.9	90.5	15.7	8.7
	1997-06	8.2	19.7	25.6	61.3	86.9	17.2	13.2
	2007-16	4.9	23.6	13.0	63.3	76.3	20.1	22.2
Johnson & Johnson (J&J)	1977-86	1.3	1.7	30.4	40.2	70.7	8.0	6.1
	1987-96	3.7	5.7	23.8	36.5	60.3	11.6	8.1
	1997-06	23.5	24.1	36.3	37.3	73.5	17.7	11.8
	2007-16	57.6	65.4	43.7	49.7	93.4	19.7	12.0
Eli Lilly	1977-86	0.7	1.9	18.7	46.6	65.3	14.7	9.6
	1987-96	0.0	5.6	0.0	50.3	50.3	20.0	14.6
	1997-06	0.5	12.7	2.3	57.9	60.2	18.6	19.6
	2007-16	4.6	21.1	14.8	68.2	83.0	14.4	24.9
Merck	1977-86	1.1	1.9	25.1	44.2	69.3	14.9	10.2
	1987-96	8.1	10.1	37.2	46.1	83.3	20.7	9.6
	1997-06	24.3	29.3	41.4	49.8	91.3	18.7	9.6
	2007-16	32.1	45.7	51.8	73.8	125.6	16.2	19.5
Pfizer	1977-86	0.1	1.6	3.5	42.9	46.4	11.0	6.0
	1987-96	3.2	4.9	32.3	48.9	81.2	13.5	12.1
	1997-06	45.1	33.0	62.6	45.8	108.4	21.6	18.0
	2007-16	61.2	68.4	59.4	66.4	125.7	19.0	15.1

Source: Own calculations based on data from companies' annual reports

At a time when maximizing shareholder value ideology (MSV) became a pervasive corporate governance norm in the US biopharmaceutical industry the company's top management switched focus from innovation to financialization as Merck began to scuffle with the financial markets due to a series of crises the company experienced in the third decade (from 1997 to 2006). The last decade (from 2007 to 2016) witnessed the demise of Merck during which the company lost internal capabilities to develop innovative new therapies, it began to exhibit the characteristics of a typical new economy downsize-and-distribute company to the most extent.

In the first analysis period from 1977 to 1986 Merck appears to have disbursed only 70 percent of its net income to shareholders while spending 10.2 percent of total revenues on

R&D in this period. Investments on R&D in the previous decade appears to have paid off given that Merck under Vagelos experienced a sizable growth in profit margin (from 14.9 percent to 20.7 percent) in the next decade (from 1987 to 1996). During this period the shareholder payout ratio increases by 14 percent but the company still retained 16.7 percent of net income for future investments.

Table 8 shows that in the second and third analysis periods Merck under Vagelos and Gilmartin maintained the same R&D ratio (9.6 percent of revenues), which was slightly under the first period, however the third period shows a 2 percent decline on the company's profit margin from the previous decade. Despite the diminishing profit margin Merck's shareholder payout ratio shows an 8 percent increase from the second to the third analysis period. Such an increase reflects the distribution of new MEDCO shares to shareholders as dividend payments, after the management decided to spin-out this pharmacy benefits management company in 2002, as well as the stock repurchases Merck under Gilmartin carried out until the end of his tenure as the top executive of Merck.

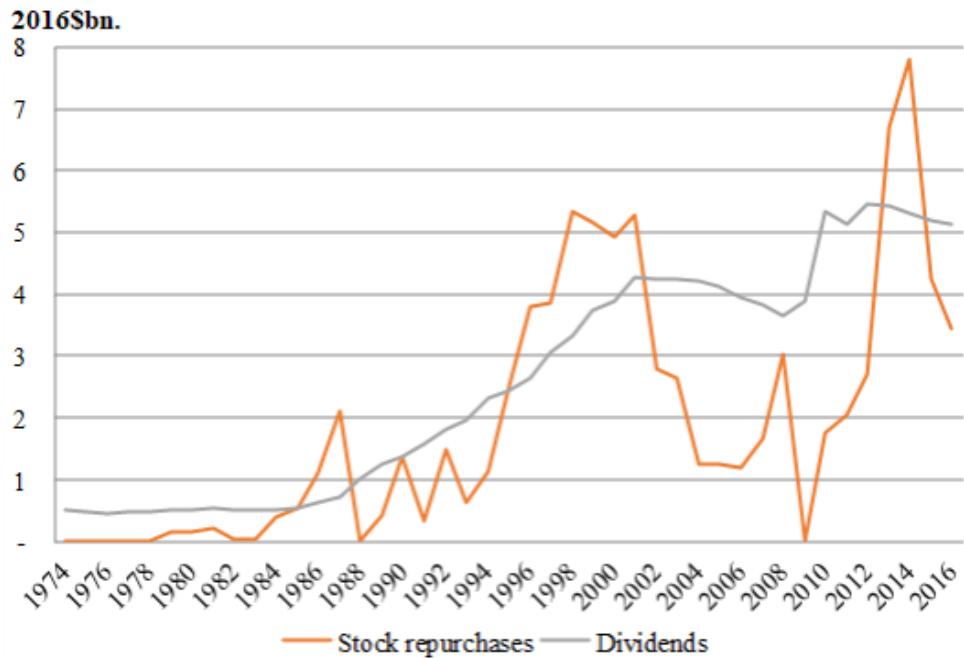
Having suffered from a major setback in developing innovative new therapies, Merck's profit margin experienced further decline the past decade. In the last decade the company's R&D ratio grew nearly twofold, from 9.6 percent in the third period to 19.5 percent in the following period. At a time when organizational learning became the most critical, if not the most vital, condition for the company to rise above the productivity crisis and achieve growth, the top executives appear to have chosen to distribute cash to shareholders instead of further investing in new learning programs and continue to support the innovation process.

As Figure 23 shows, during the late 1980s the company achieved high productivity in innovation and payouts to shareholders grew steadily. Figure 24 shows a sharp growth trend in dividend payments following successful launches in the second half of the 1980s of such innovative new therapies as Vasotec, one of the first effective ACE inhibitors developed for controlling high blood pressure; Primaxin, a new antibiotic; Pepcid, a new antihistamine to inhibit excess acid production in the stomach; Recombivax HB, the first recombinant hepatitis B vaccine; Mevacor, the first statin to be successfully marketed for cholesterol management; Prinivil, a new class of ACE inhibitor to control high blood pressure; and Prilosec, a newly formulated stomach-acid inhibitor. These products drove up Merck's profit margins.

During Vagelos's years at Merck, first as head of research and then as CEO, the company launched more than 20 major products, some of which disrupted the drug market and ultimately became blockbusters. This surge in productivity led to a similar surge in product launches in the short period between 1986 and 1992, something highly uncommon among drug companies, which often prefer to launch products at a more leisurely pace (Hawthorne, 2004). As Merck gained marketing approval in 1986 and 1987 for new drugs

treating cardiovascular diseases, its stock repurchases grew dramatically, from \$524 million in 1985 to \$1.1 billion in 1986 and \$2.1 billion in 1987.

Figure 23: Merck & Co. Inc. dividends and stock repurchases, 1974-2016 [in 2016 \$]



Source: Own illustration based on data from company annual reports

Stock repurchases followed a similar trend in the early 1990s, surging after 1989 and 1991, each a year of successful product launches. During Vagelos's tenure as chairman and CEO, which lasted from 1986 to 1994, Merck repurchased nearly \$8.5 billion worth of company stock and paid \$12.6 billion in dividends. Nearly two-thirds of the profits generated in the period were distributed to shareholders, an amount 1.5 times greater than that spent on R&D during this period. Figure 24 shows that the company's profitability under Vagelos surpassed that under any other Merck top executive. As for the remaining one-third of the profits generated under Vagelos, it appears to have been used for partially financing Merck's acquisition of MEDCO in 1993. This was the only major acquisition under Vagelos, completed as his tenure was coming to an end in 1994. Once the opposition thwarted the Clinton administration's healthcare legislation efforts, MEDCO quickly turned from a valuable asset acquired by Vagelos into a significant liability for Gilmartin to handle.

4.3.3 Financial windfall for Merck shareholders and executives

The retirement of Vagelos also marked a brief period of business growth without a productivity growth in R&D. Figure 14 shows that there was sales growth in the later years of the 1990s, was generated mainly by the MEDCO operations, but, because Merck had no successful product launches in this period, the company's earnings had begun to recede by the late 1990s. Despite Merck's poor innovation performance under Gilmartin, the

company still managed to disburse approximately 91 percent of its net income to shareholders through dividends and stock repurchases. Having already made \$14 billion stock repurchases in the past six-year period since Gilmartin had become CEO, Merck announced another \$10 billion stock-buyback program in February 2000. Between 1994 and 2005, Merck was second only to Pfizer in the size of its payouts to shareholders (see Table 8). Although buybacks were prevalent and substantial, shareholders were distressed by Gilmartin's performance as CEO. Under Gilmartin Merck had yet to bring through its internal R&D operation viable clinical candidates to replace its blockbuster cholesterol drugs, which were facing patent expiry, and a sharp revenue drop, in the early 2000s. Also, research on the company's most anticipated drug candidate for depression was facing significant delays caused by major setbacks in the clinical phases.

In 2002, Gilmartin decided to sell MEDCO stock through an initial public offering (IPO) sometime in mid-2003. Having decided to proceed with an IPO, Merck's management converted MEDCO from a limited liability company (LLC) to a corporation with 270 million common shares issued. But during the US military intervention in Iraq in the early months of 2003, investors were showing no interest in the IPO market, for which reason stock markets were experiencing their slowest year since the Oil Crisis of 1979. Given the condition of the IPO market, Merck decided to distribute the MEDCO shares to Merck shareholders instead of liquidating them through an IPO. Merck completed the spin-off on August 20, 2003, its shareholders receiving in the form of a dividend 0.1206 MEDCO shares for each Merck share they had owned as of August 12, 1993. In other words, shareholders received one MEDCO share for every eight Merck shares they held in a once-off, tax-free transaction.

At the time of this spin-off MEDCO shares were priced at \$23.85, so that the total price was approximately the same Merck had paid to acquire Medco in 1993, \$6.4 billion. By the end of 2003 shares of the newly spun-off MEDCO were trading at anywhere from \$20.50 to \$38, and throughout 2004 they traded in a range running from \$29.40 to \$40.35. This price appreciation allowed Merck shareholders to realize gains of between 23 and 69 percent. Merck's total shareholder payouts remained flat between its distribution of MEDCO's stock to its shareholders and 2007, when stock repurchases began to increase. Buybacks nearly doubled during the period when Merck was preparing its bid to acquire Schering-Plough, which it did in 2009. Unlike Pfizer, Merck continued to make steady dividend payments to stockholders, which it did until acquiring SP, at which point Merck's dividend payment increased according to the adjusted net income of the new, combined entity.

When Clark replaced Gilmartin in 2005 and put the company's research efforts under Kim, Merck was concentrating primarily on looking outside the company for viable clinical candidates to bolster its rapidly aging product portfolio. Desperate to find help quickly and to overcome its prolonged productivity crisis, Merck began under Clark and Kim to pursue the acquisition of larger companies with advanced clinical pipelines. Merck acquired

California-based Abmaxis and Sirna Therapeutics in 2006, NovaCardia in 2007, Insmed and Schering-Plough in 2009, and SmartCells in 2010. The overall cost of these major acquisitions was approximately \$53.2 billion with the individual purchases ranging from \$80 million for Abmaxis to \$1.13 billion for Sirna and \$51.4 billion for Schering-Plough. Merck spent nearly \$130 million to acquire the New Jersey-based biosimilar developer Insmed, and \$138 million to acquire an MIT spin-off, SmartCells, and its glucose-related SmartInsulin products.

Schering-Plough was Merck's first major acquisition since its merger with Sharp & Dohme in 1953. While collaborating with Schering-Plough in the cardiovascular market segment through co-developing a combination therapy for lowering cholesterol, Merck had been competing with it in the antivirals business (i.e., pegintropin for HCV). Because SP had been engaged in new learning to bring its research into the new era of rational drug design since the early years of the molecular biology revolution in the late 1970s, the acquisition improved the productivity of Merck's R&D operations. Schering-Plough's new-generation products were outperforming those of Merck in such segments of the drug market as rheumatoid arthritis, anti-inflammatory, and HCV, and it possessed a clinical pipeline that could help Merck overcome its productivity crisis, which was deepening in the late 2000s. On November 3, 2009, Merck completed the acquisition of Schering-Plough's shares, turning the target company into a Merck subsidiary. Merck had agreed to give the Schering-Plough shareholders 0.5767 Merck common shares for each SP share they owned. Additionally, Merck had paid \$10.50 in cash for each share of SP stock a shareholder possessed at the time the acquisition was announced.

Having completed a complex merger transaction, Clark and Fred Hassan, Schering-Plough's former CEO, rewarded themselves with sizable bonuses despite the austerity measures under which those companies' workforces had suffered in the years leading up to the merger. As Hassan had negotiated a golden parachute clause in his contract, Schering-Plough was required to make a lump-sum payment to him in the event the company's control changed hands. Including accelerated option and stock vesting, as well as the additional payment for a "tax gross-up," the departure of Hassan cost Merck approximately \$60 million in 2009 (Edwards, 2009). From Clark's becoming CEO in 2005 until the Schering-Plough acquisition in 2009, Merck's stock repurchases more than doubled, from \$1.015 billion in 2005 to \$2.725 billion at the end of 2008. The company's stock price steadily increased to \$60.55 per share in early 2008 before dropping to \$22.74 in the first half of 2009, when the company made no repurchases. As the market started trading on the rumors of a potential merger, the company's stock price began increasing, reaching \$39.47 in the early weeks of 2010 but then leveling off until Clark's retirement in 2011.

According the company's 2010 Proxy Statement, Clark's total compensation, including salary, bonuses, stock awards, and options was \$16.8 in 2009, \$25 million in 2008, and \$19 million in 2007. The total compensation of the top five Merck executives, including Kenneth Frazier, was \$32.7 million in 2009. The most conservative estimate places the

total compensation of the top five Merck and top four Schering-Plough executives at \$192.4 million for a single year, 2009. On the heels of the \$51 billion merger, 0.01 percent of the total workforce -- the nine highest-paid employees -- claimed 1.5 percent of the combined new entity's 2009 net income.

4.3.4 Shopping for innovation! Frazier and Perlmutter seek acquisitions for future products

In 2013 Perlmutter, a researcher who had left Merck for Amgen when Gilmartin hired Kim as a potential replacement for Scolnick, accepted Frazier's offer to become president of Merck Research Laboratories, the position he had been denied before. Perlmutter quickly began implementing a new drug discovery and development strategy to revitalize the company's internal R&D operations while seeking clinical candidates through external partners. Merck acquired Idenix Pharmaceuticals for \$3.9 billion to strengthen its product portfolio in viral diseases such as HCV and HIV/AIDS while obstructing the market expansion of Gilead, which had become a major competitor with its 2011 acquisition of Pharmasset and its product line in HCV drugs. After its acquisition of Idenix in 2014, Merck launched a strike⁴⁶ against Gilead, which was fast expanding in the market for HCV therapy at the time. Merck was very aggressive in pursuing the market for HCV therapies. Vertex, a competitor that had been started by a former Merck research director in the late 1980s, had outrun Merck in the race to get to market with new-generation HCV drugs. A big pharma with extensive resources, Merck established a strategic partnership with Roche to explore opportunities for co-marketing the companies' HCV drugs through a new combination therapy.⁴⁷ Since Vertex's Incivek was proven to be clinically more effective than Roche's Victrelis and Merck's Pegasys, the two companies joined forces, aiming to outperform Incivek clinically through a combination therapy and to outspend Vertex on marketing to slow the growth of the latter's HCV drug.

In 2015, Frazier and Perlmutter spent \$9.1 billion to acquire Cubist and its successful antibiotic Cubicin, a novel and highly potent antibacterial agent for treating gram-positive infections. In February 2015, Merck issued \$8 billion in senior unsecured notes, deploying a large portion of this new debt to finance the Cubist acquisition but using some of the funds generated to retire outstanding debt and repurchase stock (Merck Annual Report, 2016). At a time when the company's major competitors, namely Roche, were vying to get into the antibiotics business, Merck had been trying to revive its legacy antibiotic product line its competitors (Cyran, 2014; Mullard, 2014). It is safe to estimate at \$9.1 billion the long-term cost to Merck of failing to sustain its organizational learning efforts for the discovery and development of potent antibacterial agents such as daptomycin,

⁴⁶ Because it was one of the co-founders of Idenix who later started Pharmasset, it opened the legal basis for the intellectual property protecting the two companies' HCV drugs was allegedly overlapped.

⁴⁷ In 2011, Merck had formed a non-exclusive marketing partnership with Roche's Genentech unit for the marketing of Victrelis as part of a three-drug regimen along with to treat patients with HCV in the US

commercialized under the trade name Cubicin. It is interesting to note that daptomycin had been originally discovered in the late 1980s by researchers at Eli Lilly, which later decided to drop the clinically complex antibiotics business, as Merck did, to pursue financially lucrative antidepressants, namely the legacy Lilly product, Prozac (Jarvis, 2008). Cubist, at the time it was acquired by Merck, had paid slightly over \$600 million to Lilly since acquiring daptomycin from Lilly in 1997.

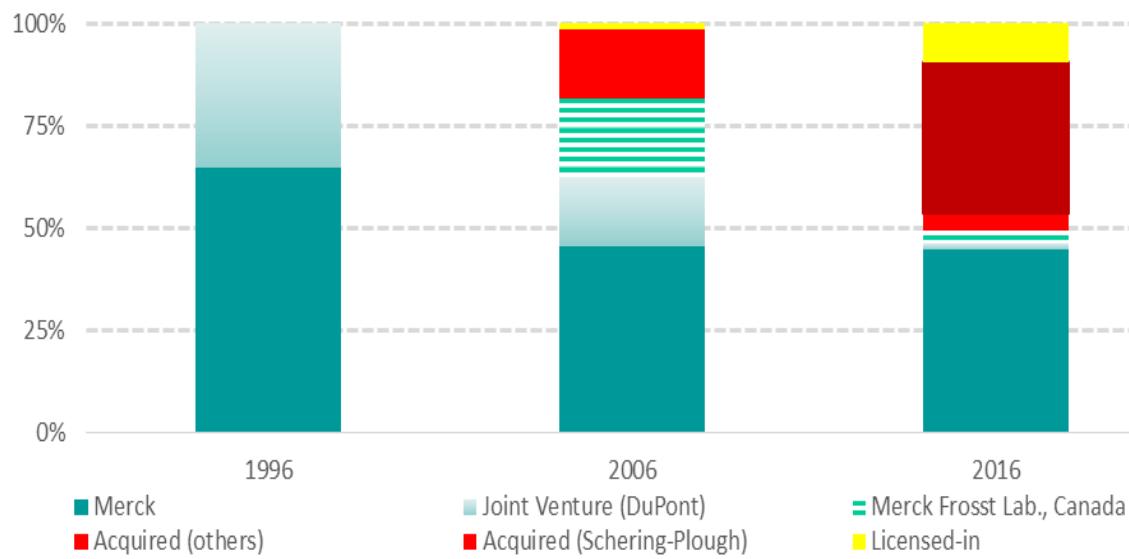
Given the concern over the growth of resistance to many antimicrobial drugs available in the market today, demand for new-generation antibiotics is expected to grow. But the field has been deserted by the same companies that discovered the first-generation antibiotics in the 1940s and 1950s. Merck's acquisition of Afferent Pharmaceuticals and its clinical candidate to treat chronic cough, for which it paid \$1.26 billion in 2006, appears to be the company's attempt to recapture the market lost after Singulair, a blockbuster therapy for preventing asthma attacks, lost its patent protection in 2012. Major acquisitions such as that of Swiss-based Oncoethix SA for \$375 million in 2014, Israel-based cCam biotherapeutics for \$605 million in 2015, and UK-based IOmet Pharma for \$400 million in 2016 appear to align with Perlmutter's strategy of pushing Merck in the direction of cancer immunotherapy, a field the company failed to enter two decades ago. Antibody treatments for cancer feed big pharma's bottom line today, and revenues generated by such products drove Pfizer's and Roche's growth for decades before a slowdown in innovation recently hit the field. Perlmutter aspires to bring Merck to the forefront of the innovation race to "advance the care of patients with cancer by stimulating tumor-directed immune responses," which implies discovering new-generation antibodies through exploring opportunities in the fledgling field of cancer immunotherapy.

Since 1986 Merck has distributed on average 75 percent of its annual net income to shareholders in the form of dividends. Merck expended \$3.4 billion on buybacks in 2016, and has \$5.1 billion remaining under its March 2015 buyback program authorizing the purchase of \$10 billion in shares. The amount expended for repurchases in 2016 was 1.31 greater than the net income the company recorded for the year. Despite the company's legal, technical, and financial troubles, its board of directors has, since February 2000, authorized more than \$50 billion in funds to repurchase company stock. Over that same period its management has reduced the company's workforce by at least 32 percent, liquidated a significant portion of its tangible and intangible assets, and increased product prices to improve its shrinking profit margin, actions that have ultimately freed \$115 billion in cash for making payouts to shareholders through stock repurchases and dividends.

Merck appears to have survived one of the worst crises in its 124-year history, but the company lacks internal drug development capability and has become a downsize-and-distribute company. As of December 31, 2016, Merck had 32 major drugs on the market generating \$30.5 billion in revenues. Among the 32, 10 drugs were enjoying blockbuster status, generating a total of at least \$18.8 billion in revenues for the company. Four of

those 10 blockbuster drugs are facing patent expiry by 2020, which would cause a drop in sales of as much as \$6 billion, or 32 percent of all revenues from blockbuster drugs. Of Merck's 32 major products, 21 are also facing patent expiry by 2020, which could result in a revenue drop of as much as \$15 billion: In other words, Merck faces a potential loss of up to 50 percent of its annual revenues unless Perlmutter finds a way to rush clinical candidates through clinical study and bring new major products to market by 2020.

Figure 24: Internally vs. externally-sourced innovation at Merck & Co., 1996-2016

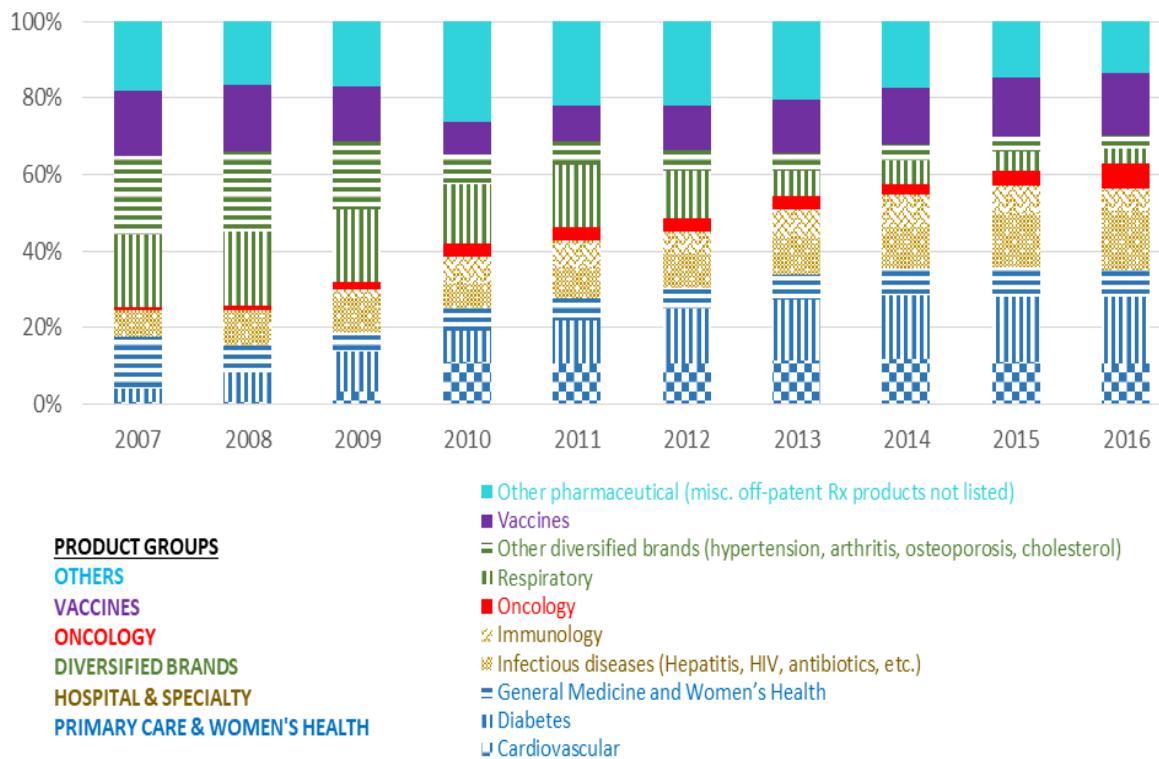


Source: Own illustration based on data from company annual reports & AdisInsight drug development database

As Figure 24 shows, most of the company's major revenue generating drugs were developed internally by the Merck scientists until the mid-1990s. In 1996, nearly 65 percent of the company revenues came from drugs developed internally. Launched in 1995, two major blockbuster drugs (Cozaar and Hyzaar for the treatment of elevated blood pressure) commercialized through a joint venture with DuPont accounted for the remaining 35 percent of the revenues Merck generated in 1996.

Also shown in Figure 24, revenues generated by products obtained from externally sources accounted for 18 percent of the company's total product sales in 2006. Nearly 17 percent of the revenues generated from the two DuPont drugs while 19 percent generated from products (mostly from Singulair, a blockbuster anti-inflammatory drug preventing asthma attacks) developed by Merck Frosst Laboratories in Canada. As Figure 24 also shows, products obtained through acquisitions and licensing deals accounted for nearly a half of the company's product portfolio by 2016. Nearly 46 percent of the revenues generated by products acquired through the merger with Schering-Plough (36.8 percent) or the products licensed from other companies (9.4 percent).

Figure 25: Relative importance of Merck & Co.'s different products as a percentage of total sales, 2007-16



Source: Own illustration based on data from company annual reports

Figure 25 lays out Merck's revenues by product-disease group. During its most productive period Merck Research Laboratories had built significant expertise in vaccines and disease areas such as cardiovascular, infections, respiratory, auto-immune, prostate, and peptic ulcer. Prior to its acquisition of Schering-Plough, Merck's legacy drugs had, or were about to, come out of patent protection and its clinical pipeline possessed no viable candidates to replace its fast-aging products. As Figure 25 illustrates, the company's major legacy products -- included in the "other diversified brands" and "respiratory" categories -- go from nearly 40 percent of product revenues in 2007 to 7.4 percent in 2016.

The withdrawal of Vioxx in 2004 was followed by a couple of major clinical failures that prevented the company from launching products in important markets such as antidepressants, sleep aids, oncology, diabetes, and so on. Merck's nearly \$50 billion acquisition of Schering-Plough can be regarded as the expensive but relatively quick remedy for the company's ailing financial health for the following reason. Figure 26 shows that, until the merger, a large portions of Merck's sales revenues depended on the company's fast aging portfolio of legacy products some of which faced imminent drop in sales as their patents were getting ready to expire.

Figure 25 also shows that Merck began to replace such aging products with new generation drug therapies particularly in immunology, infectious diseases, and cardiology areas most of which were obtained through this acquisition. During the post-acquisition period the

company launched a couple of novel therapies for cardiovascular disease, drugs that had been developed in collaboration with Schering-Plough prior to the acquisition. In 2016 Schering-Plough products accounted for 36.8 percent of Merck's product revenues (see Figure 24).

At a time when the top executives were busy with the completion of merging Merck and Schering-Plough's operations, the company was in a race against a small startup, Vertex Pharmaceuticals, founded by Joshua Boger, who for several years led Merck's protease-inhibitor program in developing new-generation drugs for infectious diseases. Although new drugs for hepatitis C virus (HCV) and diabetes had also been launched during this period, their performance in the market had failed to meet management and investor expectations.

Also to be seen from Figure 25 is that the company has yet to become a major player in the highly profitable oncology and immunology markets -- unlike Pfizer and Roche, which have in the last decade built strong drug portfolios and clinical pipelines through major acquisitions. Until the merger with Schering-Plough in 2009 Merck had achieved no major success in establishing strong foothold in the lucrative oncology and immunology markets. During this period however another major Merck competitor with a strong oncology and immunology product pipeline, Regeneron, had been led by Vagelos, recently retired from the CEO's post at Merck CEO.

In light of the gloomy picture painted by the patent statistics, Frazier appears to have a major dilemma on his hands. Pressure will continue to escalate from analysts and shareholders demanding higher earnings and more cash to "return" to shareholders. To meet these demands, however, the company will have to launch a major innovation campaign such as the penicillin and corticosteroid crash programs in the 1940s. This would require its management to deploy all resources at its disposal -- and perhaps to seek more resources -- in an attempt to engage the organization in a comprehensive learning program that would incorporate growing external innovation efforts with revitalized internal research operation and thereby restore organizational integration. How Merck makes use of its profits may determine its survival: The path that its executives choose to follow at this critical juncture may lead to the company's reinventing itself for growth or to its continuing on its way toward destruction.

Merck can attain the innovative productivity that is foregone along with its financialization in the past two-decade period if and only if the company begins to reinstitute the social condition of innovative enterprise –strategic control, organizational integration and financial commitment- to became an innovative enterprise once again. Restoring the social conditions of innovation within Merck cannot be achieved given that the top executives of Merck are highly immersed in the prevailing corporate governance ideology, MSV, and vested interested in the downsize-and-distribute resource allocation regime.

Recognizing that all business corporations confront a tension between innovation and financialization, the theory of the innovative enterprise provides a framework for analyzing the evolution of the tension between innovation and financialization for US and European biopharma companies operating in the same institutional environment. The next chapter assesses the evidence product-level to evaluate the argument that the less-financialized European biopharmaceutical companies, which are subject to price regulation in their home markets, augment their innovative capabilities by tapping into the immense US knowledge base and selling their products in the United States at high, unregulated, prices.

5 AN ANALYSIS OF THE EUROPEAN BIG PHARMA: THE US NATIONAL INNOVATION SYSTEM AND THE PRODUCTIVITY OF EUROPEAN PHARMA

While this research so far has shown that the major US pharmaceutical companies are highly financialized, these characteristics of the US pharmaceutical drug industry provide an ideal environment for a non-financialized company that is willing to reinvest its profits in drug development to generate innovation. Such should be especially the case for European pharma companies that are subject to price regulation in their home markets if they can tap the immense knowledge base in the United States and sell their products in the United States at high, unregulated, prices. The basic hypothesis is that, based in what are often called “social market economies”, European pharma companies will be less influenced by MSV ideology and hence exposed to its destructive impacts on drug innovation. The purpose of this chapter is to undertake an exploration of the operation and performance of major European pharma companies that are highly active in developing and selling drugs in the United States to gain insight into this “innovation versus financialization” hypothesis.

The findings in this section support the hypothesis that the possession of an innovative business model has given major European firms a competitive advantage over US firms because the US-based competitors have increasingly turned from an innovative to a financialized business model (Lazonick & Tulum, 2011; Lazonick et al., 2017). If such is the case, it provides a strong argument to European policy-makers to recognize the destructive impacts of MSV ideology and erect barriers to its pernicious spread from the United States to Europe. The market analysis in this chapter focuses on Europe’s most competitive companies in the global drug market that have historically had a well-established presence in the drug industry and persisted through various different restructuring periods during the evolution of this industry. Novartis and Hoffmann-La Roche from Switzerland; GlaxoSmithKline and AstraZeneca from the United Kingdom; Bayer and Merck KGaA from Germany; and Sanofi-Aventis from France are the most competitive drug companies globally that are based in Europe, and all have a long history in the industry.

The analysis conducted on the products of those seven companies revealed that in 2015 Roche was the top performer in various different dimensions among the seven companies examined. Based on the financial figures filed with the US Securities and Exchange Commission (SEC) for 2015, Roche was second after Johnson & Johnson in terms of consolidated corporate sales. However, when the comparison is made based on pharmaceutical product sales only, Roche outperformed all the global competitors.⁴⁸ Roche's 2015 position represents an impressive improvement from its number 11 ranking in 1990 with \$2.9bn global sales figure in a list that was headed by US-based Merck & Co. (not to be confused with German Merck KGaA) with \$5.2 global sales. Merck & Co., the most innovative pharma company in the world in the 1980s and early 1990s, was ranked number 6 in 2015, falling behind Roche.

5.1 The growth of European biopharmaceutical companies in the US market

The postwar era of growth in the biopharmaceutical industry has been an important enabler of recovery among many European drug makers whose access to major markets in the world had been disrupted during the Second World War (Quirke, 2004; Chandler, 2005). Such growth was also major stimulant for innovation among the American drug makers who had accumulated considerable skills and capabilities in the development and manufacturing of medicinal products but had lost a major consumer: the governments of the Allied forces in World War II (Chandler, 2005; Godley & Hughes, 2014).

Newly introduced innovative therapies in the 1950s and 1960s, such as antihypertensive, antibiotics, anti-inflammatories, tranquilizers, and antidepressants would quickly face competition in the market since organizational capabilities to develop competitive products were steadily converging among both domestic and foreign drug makers that competed in the United States (Landau et al., 1999). Competitors in the US drug market responded differently to a gradual decline in the profitability of conventional therapies due to increasing market competition and cost of drug development in addition to declining macro conditions of the US economy in the 1970s (Achilladelis, 1999; Chandler, 2005). While some companies decided to diversify into unrelated industries such as food/nutrition, medical equipment, cosmetics, etc., some others decided to merge with the competitor of a similar size to boost their sales and marketing operations and strengthen their competitive position in their existing markets. Recognizing the potential of the fledgling new field in molecular biology, some drug makers however made a strategic decision to steadily transition away from organic chemistry into biochemistry.

⁴⁸ The global ranking of top pharma company for 2015 was published by a pharma market intelligence company, Igeahub, access via <https://igeahub.com/2016/05/06/top-10-pharmaceutical-companies-2016/>. In this list J&J is the world pharma leader in term of total revenues (\$70 billion) including sales from consumer health, pharma and medical device division. As far as the pharma product sales are concerned Roche outperforms J&J given the pharma revenues generated in 2015 respectively \$38.8bn vs \$31.4bn.

Table 9: Biopharmaceutical product revenues and % share in total revenues by the Top 7

Company (# of products)	(€ bn)	as a % of total revenues				
	REV [c]	PREV (%)	US PREV [d]	REV [159]	NI	RD
Roche (23)	44,995	78	54	72	19	18.41
Novartis (20) [a]	44,437	62	34	49	36	18.08
GlaxoSmithKline (26)[b]	32,775	60	34	45	35	14.88
AstraZeneca (30)	22,219	96	40	90	12	24.27
Bayer (15)	46,324	30	31	24	9	9.24
Merck KGaA (7)	12,844	54	39	38	9	13.31
Sanofi-Aventis (38)	34,542	73	49	59	12	14.71

Notes: REV: Total Revenues (€ bn); PREV: Revenues from pharma products; US PREV: United States [or North America] pharma [or healthcare] revenues; REV. [159]: Revenues from 159 products identified for the study; NI: Net Income; RD: Research and development.

[a] Novartis' above average net income performance in 2015 was a result of extraordinary increase in the pre-tax gains (\$12.7 billion) from the net sales to third parties from discontinued operations including the sale of Animal Health (\$4.6 billion) to Eli Lilly Company as well as the completion of series of asset swap transactions with GlaxoSmithKline (GSK) (\$8.7 billion) including the sale of vaccine division in exchange for GSK's oncology drug portfolio and the creation of a joint venture over which over-the-counter drugs within the consumer healthcare division were transferred as part of the JV agreement. Net income/revenues ratio and R&D/net income for the previous year was 19.7 percent and 0.88 respectively. [b] GSK's relatively high net income reflects the sale of assets in oncology product-line to Novartis for \$8.7 billion. [c] AstraZeneca revenues only include the sales of biopharmaceutical products; Roche revenues include the sales of diagnostic which makes up 22 percent of total revenues; Novartis revenues include the revenues from Alcon (eye care) and Sandoz (generic/biosimilar) divisions which constitute 20 percent and 18 percent of total revenues respectively; Sanofi revenues include consumer health (10.1 percent), generic (3.5 percent) and vaccine (13.7 percent) revenues but excludes animal health; Merck revenues includes healthcare (54 percent), life science (26 percent) performance materials (20 percent); GlaxoSmithKline revenues vaccines (15 percent) and consumer health (25 percent); Bayer revenues include healthcare (49 percent); crop science (22 percent) and material science (26 percent). Excluding the consumer health revenues (20 percent), Bayer's pharmaceutical revenues made up only 30 percent of the group revenues. [d] Bayer and Merck revenue figures are for the North America region. AstraZeneca, GSK, Sanofi and Bayer figures other healthcare products including consumer health products. Also, any revenue figures published in foreign currencies are converted into Euros using the annual average of exchange rates in 2015 provided by companies in their annual reports. GSK figures in British pound, AstraZeneca and Novartis figures in USD, and Roche figures in Swiss franc were converted into Euros.

Source: Company SEC filings and annual reports

The revenue figures included in Table 9 reveal a diverse composition of concentration on biopharmaceutical products among big pharma companies in Europe. Roche leads the competition among the other European companies in terms of total pharma revenues and net income. With a long history in high-volume product markets such as agriculture and industrial chemicals, Bayer's total revenues surpassed Roche's, whose core competencies have historically depended on the development of ethical drugs and specialty chemicals.

Pharmaceutical revenues make up 78 percent of the company's total revenues while Bayer only generates 30 percent of revenues from pharmaceuticals.

AstraZeneca appears to be the only company whose focus is almost exclusively on the development of biopharmaceutical products (96 percent of total revenues are generated from biopharmaceutical products). Roche and Sanofi follow AstraZeneca with 78 percent and 73 percent concentration rate on pharma sales respectively. Despite pioneering in the field of ethical drugs in the late-19th and early-20th century, the two German companies, Bayer (30 percent) and Merck (54 percent), appear to be the least concentrated, or the most diversified, drug makers in the list.

The Table 9 also indicates higher net income ratios observed among the non-German companies that appears to be the consequence of larger concentration on higher value biopharmaceutical products. Given the portion of pharma product revenues, the US market appears to be the major consumer of such premium products. Once again, Roche leads the European companies in taking advantage of highly profitable product markets in the US, with 54 percent of total pharma sales in the US in 2015. With nearly half of the revenues generated in the US, Sanofi-Aventis follows Roche in capturing value in the US pharma market. Although the diversity attained by German companies seeks to maintain stability at the cost of lower operational profitability and slower economic growth, a strategy to focus heavily on pursuing pharmaceuticals, especially in the higher value segments, can pose a risk given that it would require a solid commitment to organizational learning and sustainable innovation practices to attain superior innovation competence and performance.

The 159 products identified for analysis constitute a significant portion of group (54 percent) and pharmaceutical market (65 percent) revenues and generated nearly €130 billion revenues globally for the top European companies in 2015. According to *EvaluatePharma* World Preview 2016, a popular periodical forecasting future economic trends in the global pharmaceutical market published by Evaluate, a global healthcare market analytics firms based in London, the worldwide sales of prescription drugs in 2015 was nearly €700 billion in size and roughly 25 percent of that market consisted of prescriptions of orphans and generics. Such an estimate indicates that, through the marketing of those 159 products, anywhere from one-fourth to one-fifth of the worldwide prescription market is being captured by the European companies identified in this study.

Placing the market share of the top seven drug makers in the global context illustrates the importance of sustaining innovative performance for global competitiveness in the biopharmaceutical industry. As an enabler of such performance attained today, one carefully needs to examine the sources of innovative capabilities in the past. The following analysis seeks to accomplish such goal. The following approach is an attempt to identify the sources of growth through tracing the path of learning back to its origin and by reverse engineering the process of innovation through which an innovative product is generated today.

5.2 An analysis of product portfolios and clinical pipelines of the leading European biopharmaceutical companies

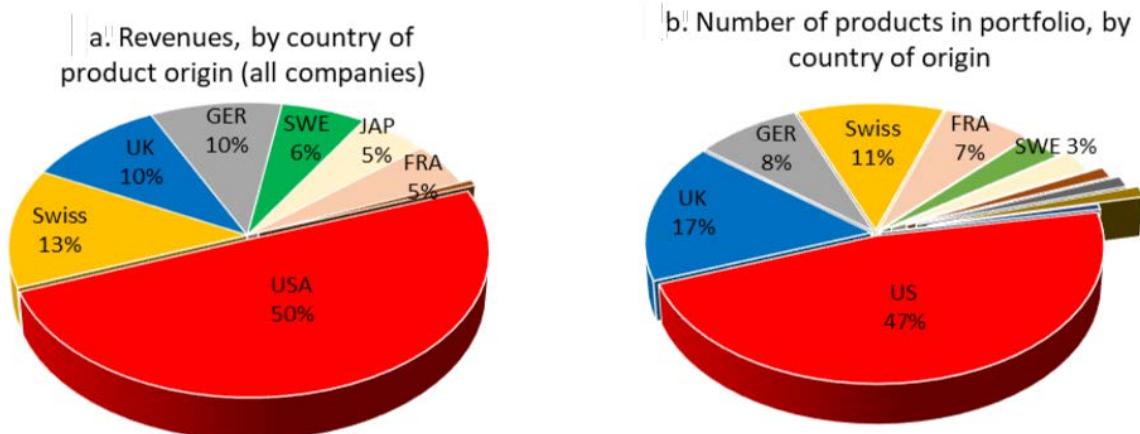
As discussed earlier, in the rise and decline of the European biopharmaceutical industry in the first half of the 20th century, the expansion of the US drug market aided the postwar recovery efforts of the European biopharmaceutical companies. Since the US-based research institutions were leading the global drug discovery efforts in the postwar period, major European drug makers were expanding their research operations in the major US science and technology hubs such as New Jersey/New York corridor in the 1950s through 1970s and California since 1980s (Cohen, 1986; Casper & Kettler, 2001; Quirke & Gaudillière, 2008; Quirke, 2014).

Of the 159 products identified in the top seven European BP companies, 47 percent originated from the US (where the discovery of key drug component took place). Those products made up nearly half of the total product revenues in 2015. While the total number of products originating from Switzerland constituted only 11 percent of total products, revenues from such products made up 16 percent of total revenues. Such a ratio indicates that the products originating from Switzerland tend to be higher value-added therapies.

The pie charts in Figures 26 illustrate the breakdown of product revenues based on their origin in three distinct time periods based on the product launch dates. The time periods considered in this illustration reflect different drug discovery/development methods (i.e. random screening/synthetic chemicals; recombinant upgrades of existing products such as insulin/chemical or biologics; genomics and high throughput screening/advance biologics, etc.) that were employed by the BP companies at the time. This illustration compares the common discovery methods employed at the time of product launch. Such a distinction confirms that given that German and Swiss firms were highly competitive in organic chemistry Europe was the country of origin for chemistry-based products launched in the 1980s. But, in the era of biochemistry and molecular (1990s and 2000s), a new generation of biotechnology product emanated from the innovation networks in the US and UK.

While the drugs first launched in the 1980s were the byproducts of the organic chemistry era, the product launches in the 1990s included a new generation of recombinant therapies but they were often the re-engineered versions of molecules known to scientists at the time (and therefore were considered to be “low-hanging-fruit” such as human insulin, growth hormone, etc.) (Alafi 2013). More innovative and complex therapies such as monoclonal antibodies for oncological indications were mostly being introduced in the early decades the 21st century, particularly following the completion of early drafts of human genome mapping, made available by the Human Genome Project (Scannell et. al. 2012).

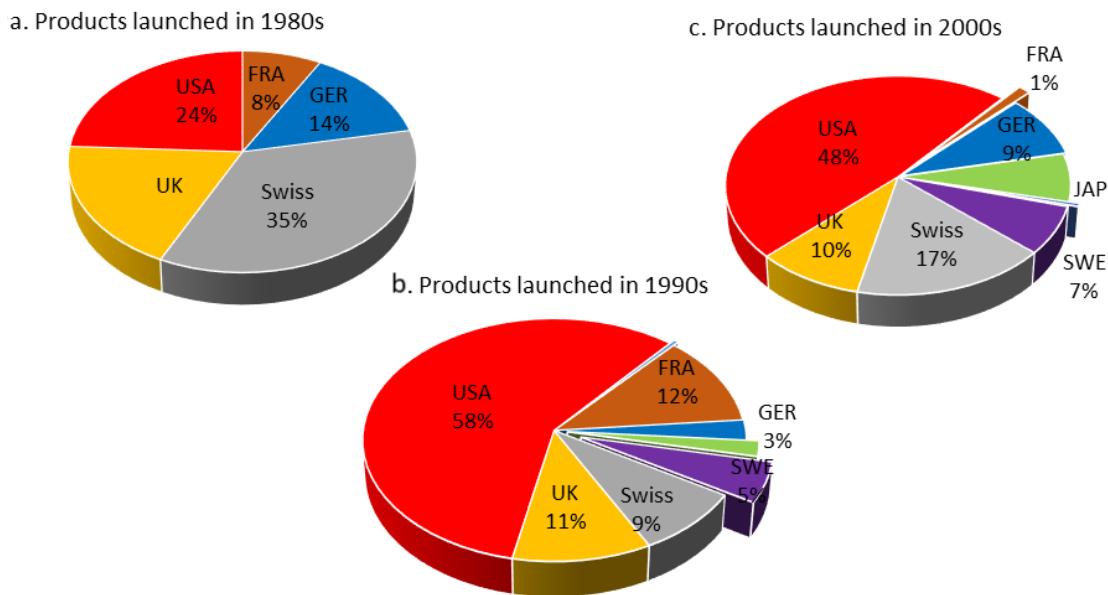
Figure 26: Total revenues, by country of product origin, all years



Source: Own illustration based on data from company annual reports

In addition to completing the acquisition of pharmaceutical and biotechnology companies especially in the 1970s through 1990s, the top European companies were also active in pursuing drug research and commercialization deals to strengthen their share of the US market. Such efforts are reflected in pie charts in Figures 27 illustrating the distribution of the total number of products and revenues generated by country of origin.

Figure 27: Total revenues, by country of product origin and decades in products launched

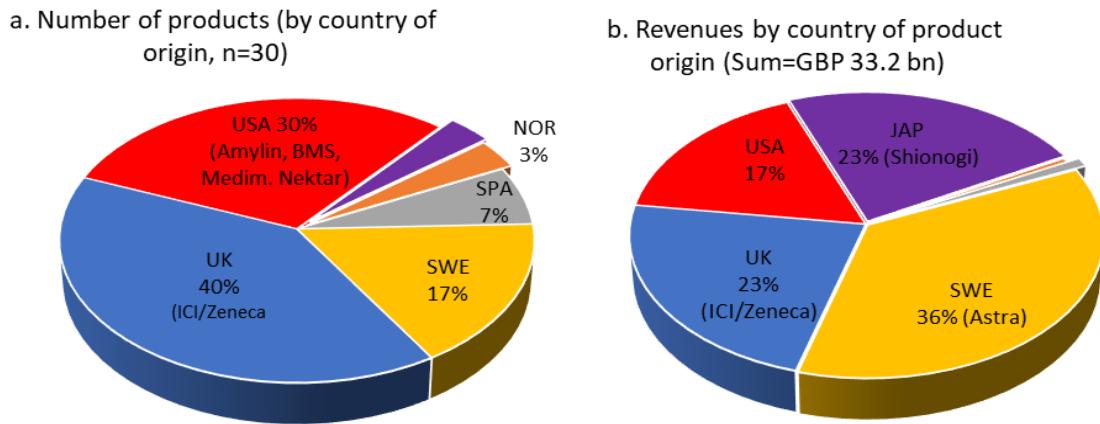


Source: Own illustration based on data from company annual reports

As indicated in Figure 27a, at least a half of the product revenues launched in the 1980s came from products of Swiss or German origin while the revenues from the US-sourced drugs made up only a quarter of the total revenues from products launched in the 1980s. The ratio, of the revenues based on the sales of products originating in the United States quickly jumped from 24 percent to 58 percent with the introduction of new generations of biochemical products in the 1990s. Within a decade, products originating in the United

States began to make up a very significant portion of total pharmaceutical sales. A notable change is observed in the share of revenues from products originating in Switzerland and Germany, respectively, from 9 percent to 17 percent and 3 percent to 9 percent in the 1990s and 2000s.

Figure 28: AstraZeneca (AZ)

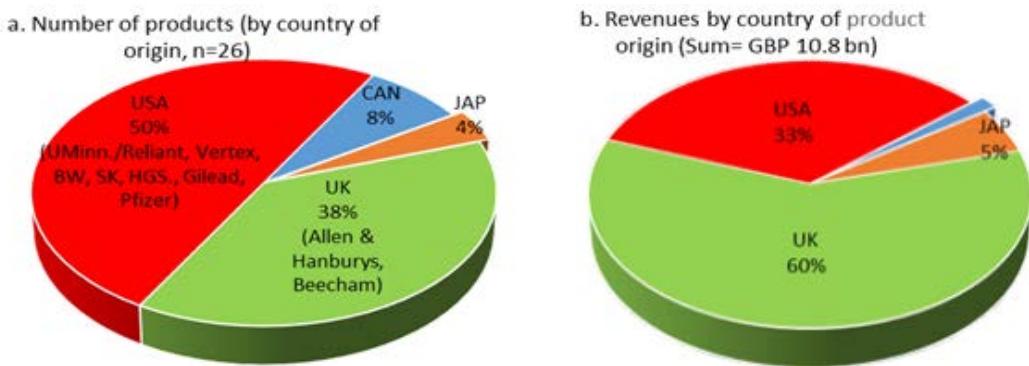


Source: Own illustration based on data from company annual reports

As illustrated in Figures 28a and 28b, the products originating in the United States constitute 30 percent of the total products marketed by AstraZeneca while the same products contributed only 17 percent of total pharma product revenues. Products developed by Swedish Astra appear to be the major revenue generators for AstraZeneca, given that 17 percent of the products with Swedish origin make up 36 percent of total revenues. Products with U.K. origin are 40 percent of total products but only 23 percent of total revenues.

The other major U.K.-based pharma company, GlaxoSmithKline, shows even greater dependence on the sourcing of new products from the US-based product development operation, as shown in Figures 29a and 29b. Half of the total products originating in the United States make up one-third of the revenues, while 38 percent of the products originating in the U.K. still make up 60 percent of total revenues. This result is due to the company's strong sales in established products such as therapies for respiratory conditions, epilepsy and infections obtained mostly through mergers and acquisitions in the U.K.

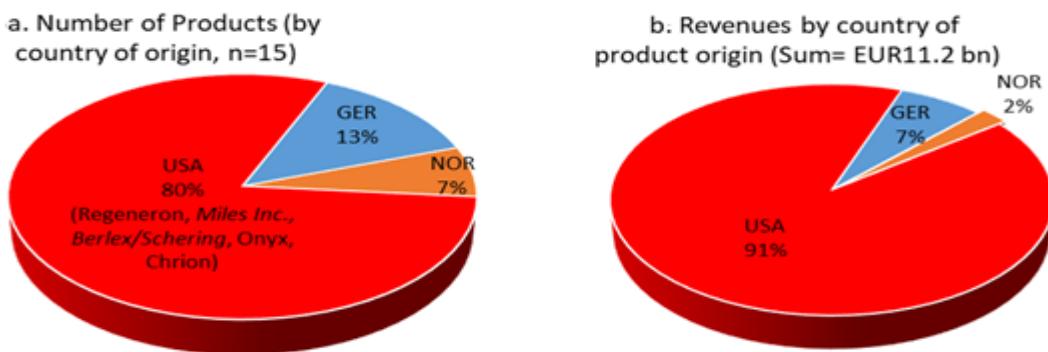
Figure 29: GlaxoSmithKline (GSK)



Source: Own illustration based on data from company annual reports

In the case of German companies, the graphical illustration of Bayer's product data, in Figures 30a and 30b, reveals some interesting results. The maker of the legacy over-the-counter pain killer, Aspirin, has been steadily increasing its presence in the prescription drug market. Such growth in market share appears to have been achieved through major acquisitions that the company has completed in the United States since the 1970s.

Figure 30: Bayer



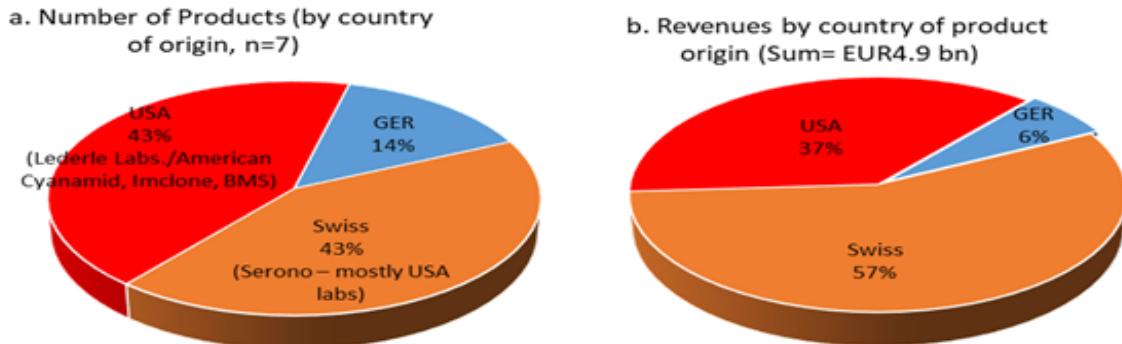
Source: Own illustration based on data from company annual reports

Nearly 80 percent of products marketed in 2015 came from the company's US acquisitions such as Miles Laboratories, Berlex (which came with the acquisition of Schering AG, another German company with a major presence in the United States under the name Berlex Laboratories) or technology collaborations with companies such as Regeneron, Onyx and Chiron. The products originating in the United States made up 91 percent of the company's prescription drug sales in 2015.

The data for German Merck, also known as Merck-Serono, also reveal an interesting case, with 14 percent of total products originating in Germany generating 6 percent of prescription drug revenues. As illustrated in Figures 31a and 31b, the acquisition of Swiss Serono, a leader in reproductive health field, appears to have boosted the product portfolio, with 43 percent of products, constituting 57 percent of product revenues, originating in Switzerland and the other 43 percent from the United States contributing 3 percent of total product sales. As a company with significant R&D operations in the United States, it is

likely that some portion of that 43 percent product ratio was enabled by the R&D capabilities developed through the company's US operations.

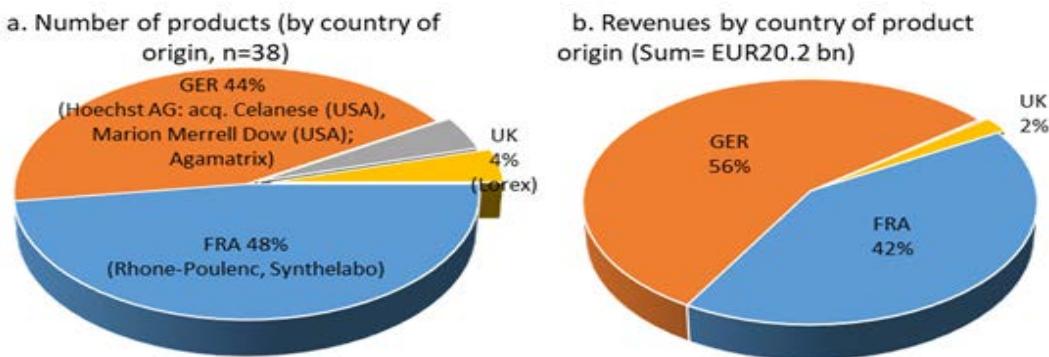
Figure 31: Merck KgAA (Merck-Serono)



Source: *Own illustration based on data from company annual reports*

The graphics in Figures 32a and 32b illustrate the analysis of product data based on the country of origin. Sanofi-Aventis, the only French company included in the study, also appears to have boosted its product sales by acquiring one of the very few large dedicated US biotechnology companies, Genzyme, in 2011.

Figure 32: Sanofi-Aventis

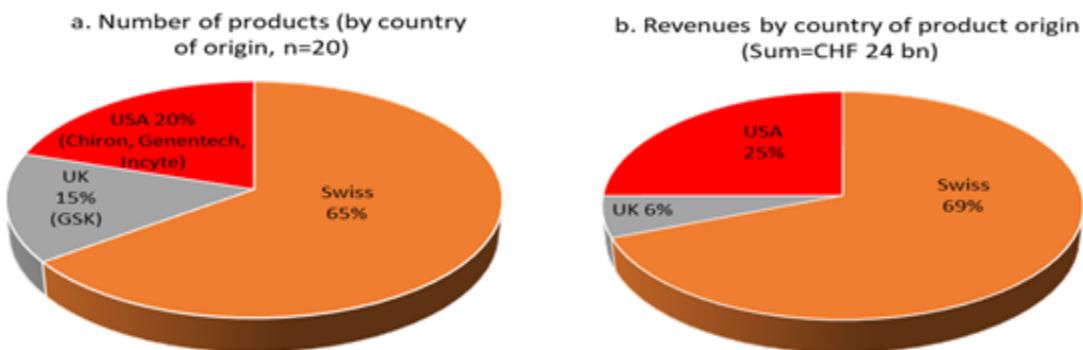


Source: *Own illustration based on data from company annual reports*

As discussed earlier in the historical background of the biopharmaceutical industry in the postwar period, Swiss companies were the first explorers of the fledging biotechnology from the early years of enlightenment in molecular biology. Today, Novartis, formed in 1996 after the merger of Ciba-Geigy and Sandoz, is one the world's most successful pharmaceutical companies in terms of financial and innovative strength. Among all the other top pharma companies in Europe, Novartis has the largest number of products that originated in the company's R&D operations in Basel, Switzerland. As illustrated in Figure 33a and 33b, of the total products marketed, 65 percent originated in Switzerland, contributing 69 percent of the company's total pharmaceutical revenues in 2015.

The reason for such success could be the company's clever strategy to pursue close collaboration with the top scientific establishments in the United States through generous support provided by the Genomics Institute of the Novartis Research Foundation (GNF) since the late 1980s. A notable relation that GNF forged with The Scripps Research Institute (TSRI), one of the nation's leading biomedical research institutes at the time, was instrumental for facilitating interaction between academic and industrial scientists from the earlier years of the genomics revolution (Zeller, 2004). Such learning efforts would later extend to pursuing partnerships with Chiron, the first company to clone molecules for the treatment of cancer and infectious diseases, in the 1990s before the company was acquired by Novartis in 2006.

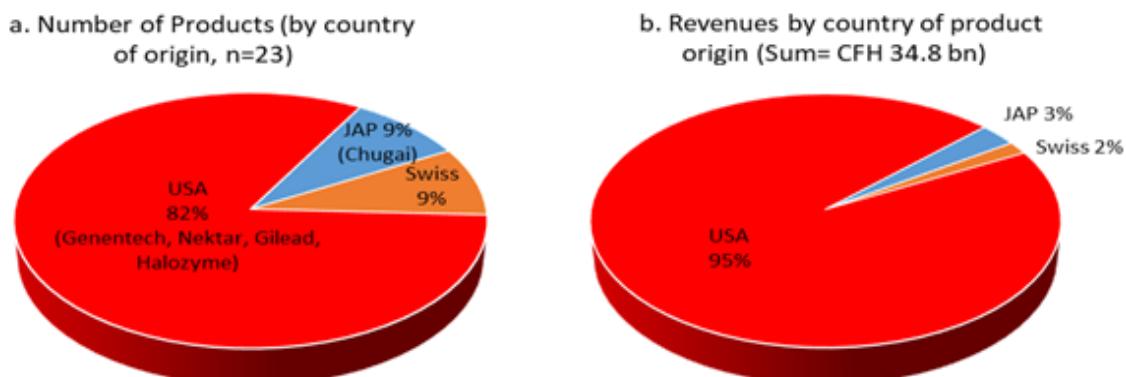
Figure 33: Novartis



Source: Own illustration based on data from company annual reports

Contrary to the product data on Novartis, 82 percent of Roche's products originated in the US and contributed to 95 percent of the company's pharmaceutical revenues in 2015. As illustrated in Figures 34a and 34b, Roche's dependence on US-based R&D operations should come as no surprise given that the survival of the company depended heavily on the expansion of the company's R&D operations in Nutley, NJ during the Second World War. Through the R&D operations at Nutley, Roche discovered and developed Valium, one of the very first blockbuster tranquilizers. Valium made Roche the largest pharmaceutical company in the world by the end of 1960s.

Figure 34: Roche Holding AG (Hoffmann-La Roche)

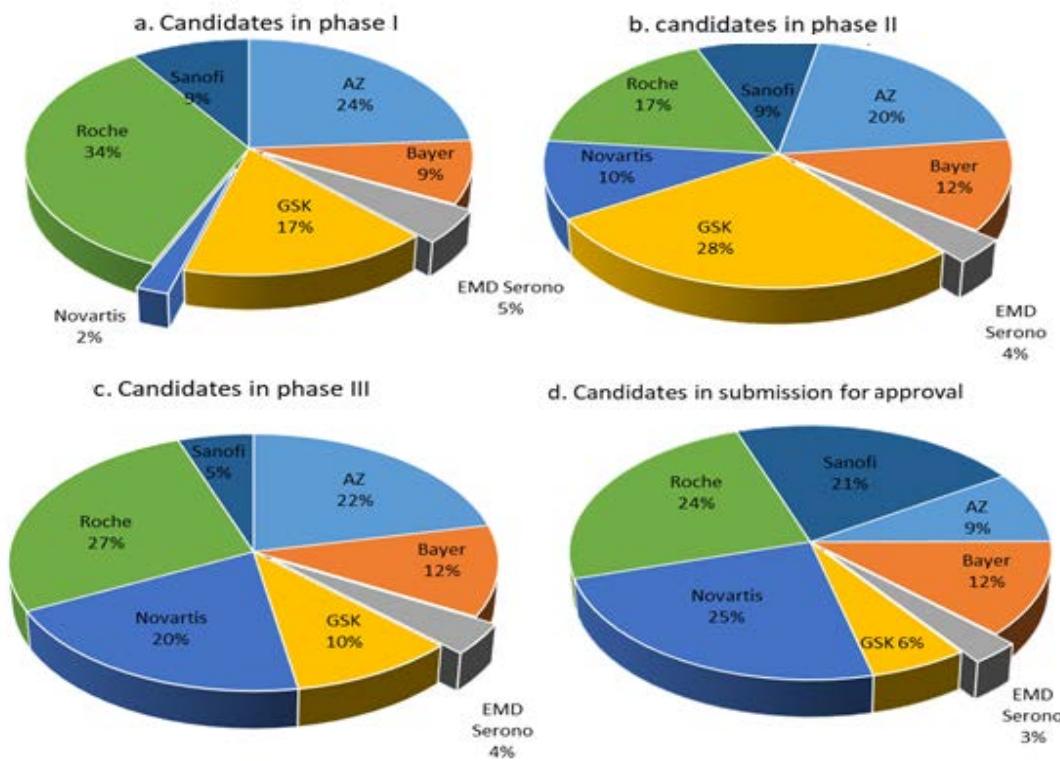


Source: Own illustration based on data from company annual reports

A significant portion of Roche's products are highly innovative new therapies co-developed through partnering in R&D with Genentech since 1979. A biotechnology icon of the 1980s, Genentech, arguably the world's first biotechnology company, is now a wholly-owned subsidiary of Hoffmann-La Roche. Roche became an important competitor in the biotechnology market through the company's close collaboration with Genentech in the past decades. Nevertheless, the company's interest in moving into biotechnology even predates the establishment of Genentech in 1976.

Roche has been making substantial R&D investments in basic and applied research in molecular biology since the establishment of the Roche Institute of Molecular Biology (RIMB) in 1967. Through this new addition to the company R&D powerhouse in Nutley, NJ, in which the company's legacy products such as vitamins, tranquilizers (namely Valium) were discovered, Roche would engage in extensive organizational learning in the fledgling field of molecular biology. Such learning efforts at Roche depended on what Lazonick calls the social conditions of innovative enterprise, as examined extensively below.

Figure 35: Europe top 7 product candidates in pipeline, by clinical phase



Source: Own illustration based on data from companies' annual reports

An overview of the top European pharmaceutical pipelines indicates a similar performance that was observed in company-by-company analysis of the product portfolios. In terms of products nearing commercialization (products in phase III clinical trials or in the

submission stage), the two Swiss companies show great strength in the development of late stage products. As illustrated in Figures 35c and 35d, nearly the half of late-stage product candidates belong to Roche and Novartis, so the two companies are likely to surpass the innovative performance of the other big pharma companies in Europe as far as new product launches are concerned in the near future.

British companies are populating their product pipeline with early stage candidates as illustrated in Figures 35a and 35b below. Nearly the half of phase II candidates are pursued clinically by GlaxoSmithKline and AstraZeneca and a similar performance is observed among the phase I candidates, with nearly 41 percent coming of them being pursued by the two U.K. companies. However, Roche appears to dominate the competition among the seven European companies given that 34 percent of the phase I candidates pursued by the top seven are belong to Roche. The company comes third after the after GlaxoSmithKline and AstraZeneca as Roche's phase II candidates constitute 17 percent of the entire phase II population identified for the seven European companies.

The analysis thus far has traced the products back to their origins and illustrated the importance of the US not only as a major product market that has been the primary driver of profitable growth but also as the focal point for transforming organizational capabilities to remain adept in overcoming the hurdles of changing market and technology conditions. Innovating new therapies becomes more challenging as BP organizations' capabilities to capture and process knowledge are tested during the age of genomics due to oversupply of new information. Enabled by advancements in molecular genetics and computer science, the production of information can sometimes be greater than how much an innovative company can handle for timely processing and analyzing such information (Pollack, 2010).

From the perspective of Chandler (2005), information overflow in the genomics age requires much greater economies of speed to keep up with such learning challenge. Only a small group of big pharma companies have been consistently investing in the building of new learning bases to make the radical move into the biotechnology market since the early years of the molecular biology revolution. And the top performers in the global drug market today are leading the race in pharmaceutical innovation.

Identified as one of the most productive pharmaceutical company in the world who exhibits the characteristics of an innovative enterprise, the social conditions of drug innovation are analyzed in the context of Roche in Chapter 6. Through a systematic case analysis of Roche the Chapter 6 provides insights into the ways in which innovation-led growth can be attained through the abilities and incentives of strategic managers engage in innovation for the sake of the growth of the firm. The case analysis of Roche's two key acquisitions will explain how a non-financialized outsider to a national economy can benefit from productive resources of an organization in ways that financialized insiders, undermined by MSV, cannot. Finally, through the case analysis of the first biotech PLIPO, Genentech, this study adduces evidence that by undermining the social conditions of

innovative enterprise the value extraction efforts of financial interests in the United States enabled an outsider, Roche, to gain access to valuable US-based knowledge flows that it would have otherwise been far more difficult to attain.

6 AN ANALYSIS OF THE TRANSITION FROM INNOVATIVE ENTERPRISE TO GLOBAL LEADER: ROCHE HOLDING AG

Today, I hear completely the opposite of what was said 20 years ago [1990s]. Now, there is an emphasis on the long-term stability that family businesses can bring.

*André Hoffmann
Non-Executive Vice-Chairman
Hoffmann-La Roche*

The analysis mentioned earlier conducted on the products of top seven European biopharmaceutical companies --GlaxoSmithKline, AstraZeneca, Sanofi-Aventis, Bayer, E. Merck of Darmstadt (EMD or German Merck), Novartis, and Roche Holding (Hoffmann-La Roche) – in chapter six revealed that in 2015 Roche was the top performer in various categories. Based on the financial figures filed with the US Securities and Exchange Commission (SEC), Roche was second to Johnson & Johnson in consolidated corporate sales. When the comparison is made based solely on sales of biopharmaceutical products, however, Roche outperformed all global pharmaceutical companies in 2015 (Table 2).

Roche's 2015 position represents an impressive improvement from its No. 11 ranking in 1990, when its \$2.9 billion global sales figure placed it well behind the leader, US-based Merck & Co., which recorded \$5.2 in global sales. Merck & Co., the most innovative pharma company in the world in the 1980s and early 1990s, was ranked No. 6 in 2015, falling behind Roche. As Table 2 shows, Roche came to top the ranking in 2015 from being No. 9 in the list that was topped by Merck & Co. in 1993.

Roche's current global position is the result of its organizational commitment to building a competitive knowledge base, which dates to the late 1960s. At that time, the company was enjoying the financial success that resulted from the introduction of the first pharmaceutical blockbuster, an iconic tranquilizer marketed as Valium. Recognizing the potential value of the new fields of biology, biochemistry, and molecular biology, Roche ploughed back the funds generated by Valium into the acquisition of new knowledge in molecular biology.

Based in Basel, Switzerland, Roche Holding AG is the leader of the global pharmaceutical markets. Since it was first established by Swiss banker Fritz Hoffmann in 1896, Fritz Hoffmann-La Roche aspired to bring industrial standards to manufacturing medicinal products and marketing them in the international markets. Having set the goal to become an international business establishment, Fritz Hoffmann turned his small manufacturing

operations in Basel into a multinational business enterprise in the late 1890s and early 1900s.

By the Second World War Roche had established branches in 35 different countries worldwide that were overseen by the headquarter in Basel (Roche Historical Archive, n.d.) however as potential Nazi occupation of Basel became major concern for Swiss companies in the onset of the war, the top management decided to assign the administrative responsibilities of Roche's global operations to Roche USA, based in Nutley, NJ, and Roche UK, located in Welwyn Garden, England in the late 1920s.

During the Second World War Roche decentralized and fragmented R&D operations as a consequence of the company's deliberate strategy or safeguarding its Basel assets and operations against the potential occupation of Switzerland by the Axis Powers and shifted most R&D functions and personnel from its headquarter in Basel to other global locations, particularly to Roche USA in Nutley, NJ, and Roche UK located in the outskirt of London, Welwyn Garden City, England (Bürgi & Strasser, 2009).

By the time WWII ended in the mid-1940s, Roche restructured the global R&D operations to concentrate in there major locations in Basel, Welwyn, and Nutley (Peyer 1996, p. 158). By this time Nutley had become the company's most important affiliate not only for being responsible for nearly half of the company's global sales, but also making the most significant contribution into the company's drug innovation efforts. Furthermore, by the early 1960s the size of employment in Nutley had grown as much as the number of personnel employed in Basel (Roche Historical Archive, n.d.). In 1956, Roche Research Management Group (RRMG) was established as a global research-strategy group including the top research and operation leaders of the major R&D centers for coordinating the company's already fragmented R&D operations.

Nutley remained integral to the company's global R&D operations until the acquisition of Genentech and Syntex in the 1990s when the company began its transition from the mecca of pharmaceutical industry in the east coast, New Jersey, to the birthplace of biotechnology in the west coast, California. Having spent nearly 22 percent of its total revenues in 2016, Roche innovation activities pursued by nearly 22 thousand R&D employees along with more than 150 external partners in the global drug innovation network. Currently, all these global efforts are coordinated through three pharma R&D units: Pharma Research and Early Development (RED) is located in Roche's headquarter in Basel, Switzerland; Genentech Research and Early Development (gRED) is located in San Francisco, California, USA where Genentech headquarter is located; and the third innovation center in Tokyo, Japan that has become a major innovation hub in the far east region after the acquisition of Chugai in 2016. Among all the major global centers the company's US-based operations have critical importance though. As Figure 10 shows, nearly 82 percent of the drugs, which generated significant revenues for the company in 2015, in fact have been

developed in the US, particular through Genentech. The revenues generated by those drugs developed in the US account for nearly 95 percent of the entire product revenues in 2015.

During the biotechnology revolution of the 1980s and 1990s Roche was one of the very few big pharma companies that was strategically positioned at the forefront of an emerging science, molecular genetics, which would disrupt the pharmaceutical industry. Roche had acquired and developed a competitive knowledge base in molecular genetics through its close relationship with Genentech, arguably the world's first biotechnology company. Established in 1976, at the onset of the biotechnology revolution, Genentech was formed with the purpose of becoming an independent and fully integrated pharma company (FIPCO) by leveraging a powerful drug discovery and development tool, recombinant DNA (rDNA) technology.

Genentech and Roche were among the very few companies that possessed the technological capabilities and scientific skill to utilize this powerful tool in the innovation of new therapies. Started as a drug-development partnership in the late 1970s, the relationship between Roche and Genentech would take a new turn in the late 1980s, when Genentech's financial resources had depleted and it sought help from Roche to push the innovative therapies in its pipeline through clinical development.

6.1 Strategic Control

During perhaps its most formative years, a direct descendant of company founder Fritz Hoffmann-La Roche served on the board of directors from 1960s through mid-1990s. After the death in a traffic accident of Fritz's son, Emanuel Hoffmann, his widow, Maja Hoffmann-Stehlin, married a Swiss music conductor, Paul Sacher. Jakob Oeri-Hoffmann, the son of a former chief editor of a Swiss newspaper and former member of the Swiss Parliament, had joined the family in 1943 through his marriage to Vera Oeri-Hoffmann, Emanuel and Maja Hoffmann's daughter. Jakob, along with his brother-in-law, Lukas Hoffmann, and his stepfather, Paul Sacher, served on the company's board until the mid-1990s. Lukas was survived by four children, one of whom, André Hoffmann, is currently the Hoffmann's representative on the board. His fellow board member Andreas Oeri, one of Vera and Jakob Oeri-Hoffmann's children, currently represents the Oeri clan.

The Hoffmann-Oeri family has sustained its strategic control of the company through a collective voting scheme first established in 1948. By pooling their total 50.7 percent stake in the company, the eight heirs of the Hoffmann-Oeri family have been able to outvote all the other Roche shareholders. Although Maja Oeri is no longer part of the collective voting scheme, having withdrawn her 5.06 percent share from the voting pool in 2011, she has been committed to voting the family line in order to sustain its strategic control (Nicholson, 2011).

Under the strict governing regime that allows the Hoffmann-Oeris to dominate shareholder voting, no outsider could possibly infiltrate the company and seize the strategic control, not even the powerful Novartis, despite the one-third share it has held in Roche for the better part of two decades. Agility and patience are the two of many virtues the family offers to the managers of a global organization. Although the family has absolute power over the company's productive assets, the family allows the holders of the non-voting shares (Genussscheine) to monitor, and engage in, the decision-making process. The company "can't ignore short-term investor sentiment because it affects our [Roche's] cost of capital," said Hoffman in the same FT article. Unlike many other family-run companies, Roche manages to integrate a shareholder perspective into its corporate governance structure while keeping the company's long-term vision intact and immune to speculative attacks.

The long-term vision of excelling in the pharmaceutical business set forward by the company's founder, and fostered by his descendants, inspired the company's business and science leaders to initiate an ambitious organizational transformation campaign in the 1970s and 1980s to pursue new learning in the fledgling fields of biology. Those efforts began to pay off in the early 1990s, and Roche's market value rose. Roche's stock outperformed that of Merck & Co., declared by *Fortune* magazine to be the "Most Admired" company in the US for seven consecutive years as the company enjoyed a productivity boost of a magnitude rarely seen before (Välikangas, 1995; Hawthorne, 2004). Aside from its market value, Roche also nearly doubled Merck's investments in R&D, as well as the R&D spending of the other 18 top US competitors.

This long-term oriented vision, combined with a proven track record in sustainable growth, has made Roche attractive among long-term investors. Thanks to its reliability in generating profits regardless of conditions in the drug market, Roche has never had trouble raising cash in the capital markets to finance its growth initiatives. Even in the midst of the financial turmoil accompanying the collapse of the global financial system in late 2008 and early 2009, Roche managed to raise the cash to fund the \$46.8 billion deal that made Genentech its wholly owned subsidiary. The acquisition was funded by the company's retained earnings, as well as by capital raised in the bond market (Baldwin et al., 2010). Roche's purchase of Genentech was completed shortly after Pfizer had acquired Wyeth for \$68 billion and Merck had acquired Schering-Plough for nearly \$50 billion.

The company's ability to raise nearly \$700 million among US investors in the early 1990s, considered one of the largest borrowings ever by a foreign company in the US, speaks for Roche's credibility. Roche funded other major acquisitions, such as its \$5.3 billion purchase of Syntex Corporation in 1994, with the cash raised mainly through bridge loans. Roche's longtime CFO and director Henri B. Meier has been credited for the effective use of financial markets to access cheap capital and finance innovation projects in careful ways that kept the "Hoffmann family's controlling stake undiluted" and intact (WSJ 1993).

André Hoffmann shares the outlook of George W. Merck as to the mission of Roche as a drug company and the family's interest in the drug business:

I always quote three numbers to bring some perspective to our ownership... One is eight, the number of family shareholders in the pool. Two is 91,000, the number of employees at Roche. And three is 23 million, the number of people that took our current drugs last year. For us, there is absolutely no contest: the interest of eight people is nothing compared with the other numbers.

(Ernst and Young 2016b, p. 177)

With Emanuel's death at a young age in 1932, the Hoffmans had to hand the reins over to professional managers. The voting pool emerged as a way of exercising control over management and gradually reinforced the subtle separation between the principles and the agents. In contrast to past practices -- Sacher had been "adamantly against the members [of the family] coming in to run the business" -- André advocates greater family integration into the business and recognition by the family members that Roche is more than merely a "financial investment."

Once the family builds an "intimate relationship" with the business, its engagement could provide the "long-term stability that family business can bring," André said during an interview for the 2016 Ernst & Young Family Business Yearbook. After surviving the calamities of the Second World War, Roche made a significant debut in the ethical-drug market with the discovery of Valium in the late 1970s. Nor did it join the "one-hit wonders" club when stifling market competition and the inevitable patent expirations brought its torrent of profits to an end in the 1970s.

It is always difficult to initiate change within an organization that is experiencing business growth, and this had been the case at Roche, as the research division under the reign of organic chemists resisted any transition into biology in the 1960s. Focused in the long-term performance of the company, the members of the Hoffmann-Oeri family, namely Paul Sacher, Jacob Oeri-Hoffmann, and Lukas Hoffmann, oversaw a truly remarkable transformation at the company from chemistry into biology and molecular diagnostics during their active participation in the strategic control of the organization from the early 1950s through mid-1990s (Peyer 1996; Roche Historical Achieve, n.d.).

6.1.1 Evolution of dual-share structure at Roche

Having two classes of shares traded on the Swiss stock exchange (SIX), 160 million bearer shares with the voting rights and 702.6 million non-voting equity securities (Genussscheine: dividend-right [participation] certificate), Roche Holding AG has the most peculiar ownership structure among the global pharmaceutical companies. The company's

dual-class share structure has a long and complex history that goes back to as early as 1920s.

Roche was first founded as a private company in 1896 and later emerged as a joint-stock company in 1919. The company's diminishing market performance during the First World War dragged Roche into financial troubles at the end of the war. When the company's operations required additional capital Fritz' Hoffmann's brother-in-law Albert Koechlin Hoffmann came to his rescue to recapitalize the company with a loan secured from Basler Handelsbank whom Albert K. Hoffmann was its chairman of at the time. The new joint-stock company had an equity capital totaling 4 million Swiss francs and 4,000 shares issued whom Fritz Hoffmann had received 3,790 of those shares and deposited at Basler Handelsbank, one of the largest banks in Switzerland, as collateral for the loan he received.

The company's board of directors and top three executives bought the remaining 210 shares including Albert K. Hoffmann, who became Chairman of the new joint-stock company after incorporating, Albert A. Hoffmann, Fritz Hoffmann's cousin, Emil Barell, an old-time Roche chemist who later became an executive officer, and some other trusted colleagues (Peyer 1996, p. 73). After Fritz Hoffmann's death in 1920 the Hoffmanns had to hand the reins over to professional managers. The first professional manager to replace Fritz Hoffmann, Emil Barell, had become the company's most influential shareholder after acquiring Fritz Hoffmann's younger son Alfred Hoffmann's interest in the company in 1924.

Having struggled to restore financial stability in the early 1920s, Roche was once again in need of additional capital to remain solvent. Distressed economically due to the financial liability Fritz Hoffmann's descendants inherited after his death, no heir of F. Hoffmann could subscribe for the newly issued shares after the management decided to double the company's equity capital. Basler Handelsbank not only subscribed to acquire majority to the new shares issued but also later managed to purchase some of the old shares from Emil Barell who he had acquired from Alfred Hoffmann in 1924.

By the mid-1920s Roche's majority control was held by a ten-member syndicate including top executives and some key managers from affiliates who had later become owner-managers as Barell encouraged them to purchase company stocks. In the late 1920s the company's strategic control was divided between the ten-member syndicate led by Emil Barell and Emanuel Hoffmann who, unlike his younger Alfred Hoffmann, was keen to hold Roche stocks he inherited and represent the family's large minority stake in the company (Peyer 1996).

Although Basler Handelsbank played a mediator role between the two groups as an attempt to protect its equity stake in the company, Fritz Hoffmann's brother-in-law Albert K. Hoffmann, who represented the bank's interest in the board as the joint-stock company's first Chairman, often clashed with Barell, as well as the syndicate led by him, and kept the

power struggle between the shareholder groups in balance until his death in 1927 (Peyer 1996, p. 115).

Following the death of Emanuel Hoffmann at a young age in 1932, who was the last Hoffmann to remain active in the company management, the family then had to hand the reins over to the company's managers led by Barell. Emanuel Hoffmann's widow, Maja Hoffmann-Stehlin, married a Swiss music conductor, Paul Sacher in 1934. At a time when Emil Barell continued to extent his reign in the company Sacher increased his involvement with Roche's business affairs upon Maja Hoffmann's urging and joined the Roche's board in 1938. Jakob Oeri-Hoffmann, the son of a former chief editor of a Swiss newspaper and former member of the Swiss Parliament, had joined the family in 1943 through his marriage to Vera Oeri-Hoffmann, Emanuel and Maja Hoffmann's daughter.

As WWII was coming to an end in the mid-1940s some of the most influential figures in the company management began to disappear. Having lost the battle against Emil Barell to gain absolute control of the company's US operations, Elmer H. Bobst, a successful American executive who attempted to take Roche's most profitable foreign subsidiary in Nutley, NJ public in 1928 and 1936, resigned from the company in 1944. Succeeded Albert K. Hoffmann in 1927, Dr. Max Brugger, the representative of Basler Handelsbank on the Roche board died in 1945. Already having suffered significant losses during the war that had come to an end recently Basler Handelsbank decided to sell its equity stake in Roche after Brugger's death. This event gave Paul Sacher the opportunity to regain the voting equity that was lost in the early 1920s on behalf of the Hoffmanns. Sacher and the Hoffmanns liquidated a large portion of their wealth including the non-voting Roche shares to acquire the company's voting stocks held by Basler Handelsbank (Peyer 1996, p. 155).

As Emil Barell implemented an organizational overhaul to rejuvenate the top management in Basel after his return from Nutley at the end of WWII, Paul Sacher eventually convinced Barell to prepare for a gradual but orderly transition of the chairmanship post to the next person. Recommended by Sacher, Roche's directors appointed Dr. Albert Caflish, an expert in finance and a board member of the Swiss Bankers Association, to the board in 1946 who later became Vice-Chairman in 1947, and CEO in 1951.

After forestalling Bobst's ploy to spin-out the US subsidiary and removing any division between Nutley and Basel after the war ended, Alfred J. Fuchs retired from his post as the head of finances and the chairman of the executive committee in 1948. The voting pool also emerged in 1948 as a way of exercising control over management however such a voting scheme gradually reinforced the subtle separation between the Hoffmann-Oeri family and the company managers. In 1953 when Barell died, Jakob Hoffmann, along with his brother-in-law, Lukas Hoffmann, joined his stepfather, Paul Sacher, on the board of directors and they all served as directors of Roche until the mid-1990s.

Lukas Hoffmann was survived by four children, one of whom, André Hoffmann, is currently the Hoffmann's representative on the board. His fellow board member Andreas Oeri, one of Vera and Jakob Oeri-Hoffman's children, currently represents the Oeri clan. During this period, according to André Hoffmann, Sacher had been "adamantly against the members [of the family] coming in to run the business" which stood in sharp contrast to past practices prior to the emergence of the voting pool (Ernest and Young, 2016). Unlike Paul Sacher though André Hoffmann has been advocating greater family integration into the business since he joined the board of directors in the mid-1990s arguing that the family should perceive Roche something other than merely a "financial investment" (Ernst and Young, 2016).

Although the family has absolute power over the company's productive assets, the family allows the holders of the non-voting shares (Genusscheine) to monitor, and engage in, the decision-making process. The company "can't ignore short-term investor sentiment because it affects our [Roche's] cost of capital," said Hoffman in the same FT article. Unlike many other family-run companies, Roche manages to integrate a shareholder perspective into its corporate governance structure while keeping the company's innovative vision intact and immunizing the company from speculative and manipulative attacks.

Both the voting and the non-voting shares are subject to same ownership benefits and liabilities except that those who control the voting shares have the power to make corporate resource-allocations decisions. The Hoffmann-Oeri family has sustained its strategic control of the company through a collective voting scheme first established in 1948 (Ernst and Young, 2016). By pooling their total 50.7 percent stake in the company, the eight heirs of the Hoffmann-Oeri family have been able to outvote all the other Roche shareholders. Although Maja Oeri is no longer part of the collective voting scheme, having withdrawn her 5.06 percent share from the voting pool in 2011, she has been committed to voting the family line in order to sustain its strategic control (Nicholson, 2011; Ward, 2015).

There have been two major challenges for control of Roche occurred in 1936 and in the early 2000s. A direct descendant of company founder Fritz Hoffmann-La Roche has always served on the board of directors or always involved in any corporate decision that would alter the company's ownership structure or future growth strategy (Peyer 1996; Ernst and Young, 2016). One exception to the family reign in the strategic control had been a brief period between 1932 and 1938. The first major challenge emerged during this period in which Roche had nearly lost its most profitable subsidiary in the US at a time when the survival of the company's operations in war-ridden Europe had depended on the profits generated through this affiliate.

At a time when the majority control of Roche's voting stocks changed hand, Elmer Bobst, head of Roche Nutley at the time, conspired a managerial takeover with the intention of taking the company's most profitable affiliate in the US through offering its shares in the US stock market in 1936. It wasn't the first time that Bobst had tried to personally profit

from Roche's most successful subsidiary in the US. Having played a major role in building a successful subsidiary for Roche in the US in the 1920s, Bobst had attempted to generate personal profits after receiving an offer from an American investor to acquire Roche's entire pharmaceutical operations in the US in 1928. After realizing how discontented some of the company's major shareholders in Basel became with the acquisition offer, Bobst had decided to put his pursuit of generating greater personal gains from the profitable Nutley operations on hold, but not to rule out the possibility that it could be possible someday.

On the eve of the Second World War, Roche made radical changes in its ownership structure to ensure that its operations would be sustained in the case of the complete Nazi occupation of continental Europe. While responsibilities pertaining to Roche's European operations were assigned to its wartime headquarters in Lausanne, Switzerland, operations in the rest of the world, including those of its subsidiary in the United Kingdom, were assigned to a newly created twin company, SAPAC Inc., based in Uruguay. This dual structure provided insurance against the potential loss of proprietorship in the company: In the case of a Nazi sequester of Roche assets in Continental Europe, SAPAC Inc. would still be able to operate independently (Kurosawa, 2015)

As German occupation expanded toward Western Europe maintaining ties with subsidiaries became highly challenging for Roche. In fact, Roche was in the brink of losing control over the company's most critical two subsidiaries in Germany and the US. Despite surging demand for drugs, and vitamins in particular, maintaining profitability, or even achieving growth, was a challenge. Access to Roche's production sites in Nazi-occupied territories was highly restricted, and moving goods and personnel was highly uncertain and costly across Europe. The Roche subsidiaries within the Nazi-occupied territories attempted to declare independence from the Group. However, Dr. Waldemar Hellmich, the head of Roche Grenzach in Germany, worked with the subsidiaries' leadership and succeeded in preserving the ties with the subsidiaries (Roche Historical Archive, n.d.; Peyer 1996).

In 1936 when the anti-Swiss sentiment reached to the maximum in the wake of the Second World War such that Roche was also in the brink of losing its American affiliate to the US government (Peyer 1996). Bobst argued that the only way to sustain Roche's profitable operations in the US was through offering Roche Nutley's major stake in the US stock market and turning the US affiliate into a truly "Americanized" business enterprise (Peyer 1996, p. 152). Bobst was being paid well through various profit-sharing arrangements. He was interested, however, in obtaining the controlling stake in the profitable pharmaceutical business, to whose building he had contributed heavily, after opening the company to public. At a time when Roche, faced intense political pressure both in Europe and in the United States, Bobst attempted to persuade Dr. Emil Christopher Barell, CEO of the parent company, to take Roche-Nutley to public.

Temporarily based in Nutley along with Bobst at the time, as a precaution against potential fall of Basel to the control of Nazi Germany, Barell, who suffered health issues was kept isolation from the rest of the company directors in Basel. Alfred J. Fuchs, the director of finance for the entire Roche group companies, averted such a threat of losing the company's most profitable operations in the United States, after travelling to Nutley to handle the situation in person on behalf of the Board in 1936 (Peyer 1996; Kurosawa 2015).

The second major challenge to strategic control was that since the early 2000s Roche has lost a third of the company's voting shares to its longtime rival, Novartis. The Hoffmann-Oeris clan dominates shareholder voting under the strict governing regime in a way that no outsider could possibly infiltrate the company and seize strategic control, not even the powerful rival Swiss pharmaceutical company Novartis, despite the one-third share it has held in Roche for the better part of two decades (Hirschler & Reid, 2010).

Novartis had become an issue after the Hoffmann-Oerie family successfully defeated activist shareholder Martin Ebner to acquire a seat on Roche's strictly controlled board of directors. The collective voting agreement has ensured the integrity of family control over the business and it has repelled attacks in various shapes and forms, such as from activist shareholders like Swiss financier Martin Ebner, designed to exploit weaknesses in corporate governance to gain control over allocative decisions. Martin Ebner interest in Roche as a financial investment goes back to as early as mid-1980s when Ebner first established his investment firm BZ Gruppe Holding (Bilanz, 2004). Focused only on companies with good management and strong growth potential, Ebner gradually increased his stake in Roche's voting stocks through open market transactions in the 1990s particularly after obtaining a large number of Roche's voting shares in the early-1990s through acquiring the majority control of Pharma Vision 2000 AG, a Swiss-based closed-end mutual fund that had held significant amount of equity stocks of major global pharma companies including Roche (Knechtli, 2000).

Ebner had increased his stakes in Roche when the company's managerial control was under Fritz Gerber, who was the first Roche executive to "follow the call of shareholder value" in the 1990s (Bilanz, 2004). At a time when the scientific and technological frontiers of drug development was rapidly expanding, Paul Sacher had handpicked Gerber, who was still serving as the chairman of Zurich Insurance Company, to lead Roche in its quest to discover a new growth path and a new organizational structure in order to remain competitive in the fast changing pharmaceutical business. Like his predecessors Fritz Gerber had to assume the top executive post in the middle of a crisis in 1978. In the aftermath of Severo crisis, one of the major industrial accidents that took place in 1976, contaminated regions surrounding the company's first manufacturing site in Severo, Italy with the potent chemical compound in a herbicide commonly known as Agent Orange. Such a massive industrial accident as Severo began to strain Roche in the late 1970s that was cash rich until recently as from Valium's market success earlier in the same decade.

Having recognized the need for further investing in the company's core business in pharmaceuticals, Gerber's first course of action was to adopt extensive cost containment methods to boost the company's efficiency in production. Gerber also decided to divest any division that wasn't in line with the company's core business activities in pharmaceutical. In the onset of his tenure as CEO, Gerber identified building innovative capabilities in biotechnology as the company's strategic priority. While the size of the company operations were shrinking elsewhere, Roche increased its investments in pharma business as the company accelerated the organizational learning efforts in the fast advancing fields of molecular biology and immunology in the 1980s, as well as investing in the acquisition of new technological capabilities in genetic engineering (Peyer 1996, p. 271).

In order to boost the company revenues in the short-term Roche under Gerber began to pursue drug commercialization deals with external partner and pursuing M&A deals to expand the company's product portfolio. Starting early in Gerber's tenure as CEO Roche invested in organizational capabilities to develop, drug commercialize and market new drugs to remain competitive in the world's most profitable drug market in the US. Desperate for leveraging such a growing salesforce in the US, Roche signed a drug co-promotion agreement with British Glaxo for the launch of Zantac, the second heartburn medicine, after SmithKline Beckman's Tagamet, to become a blockbuster drug with over a billion dollar annual sales by 1987 in the US (Wright, 1996).

This co-promotion deal came a year after Merck also entered into an agreement with Swedish pharmaceutical company Astra AB, to sell the company's products in the US. Although Roche quickly generated a steady stream of revenues from the Zantac deal and invested in the new organizational learning efforts in biotechnology, it had taken Merck more than a decade to profit from a partnership deal with Astra after the first major byproduct of the joint-venture, Prilosec, a new generation ulcer and heartburn medicine, was approved for marketing in the US in 1996. At a time when Vagelos pushed the R&D workforce hard to overcome the "not-invented-here" syndrome and seek for more collaboration with external partners in the early-1980s, Gerber had faced similar challenges with Roche scientists to look for opportunities beyond the organization.

The partnership deal with Glaxo and Astra were the first major experience for Roche and Merck to shatter the tall glass surrounded the R&D workforce that had isolated them from the external networks of innovation for a long time. Having vested focus heavily in biotechnology and already integrated into the national innovation network in the US pursued Roche had already made a headway in exploring new market opportunities in the fast growing genetic engineering field in the 1980s.

During this period both the business and science leaders at Roche, particularly through the Roche Institute of Molecular Biology at Roche Nutley, had developed an extensive relationship with their counterparts at Genentech. Through the acquisition two California companies both in grave financial distress, Genentech in 1990 and Syntex in 1994, Roche

accelerated its efforts to pursue a more competitive position in the US drug market in the 1990s. Interestingly, already in a better position financially, the top science and business leadership at Merck had decline the opportunity to acquire Genentech when the former head of Merck Research Laboratories, Lewis Sarett, presented the opportunity to so when Genentech was merely a brand new start-up in the late 1970s.

The changes in the company business model, the organizational restructuring efforts, and the new investments in biotechnology had begun to payoff so much so that Roche had become a highly profitable company in the mid-1980s all the operational restructuring efforts had company under Gerber. In order to streamline the company's global operations and bringing more transparency to the company's financial affairs, Gerber decided to end Roche's six decade old twin-share structure splitting the company's domestic and international operations into two administrative units.

Originally established as a subsidiary and intended for the marketing arm of the company's finished Worbla celluloid products and other diversified products, Roche decided to repurpose S.A. Pour Papplication du Celluloid (SAPAC) after failing to pursue the company's diversification strategy into unrelated markets in the mid-1920s. In 1927, Roche transformed SAPAC into a holding company to oversee operations of all Roche subsidiaries and their finances (Peyer 1996, p. 112).

The decision to repurpose a subsidiary into holding company based in Liechtenstein came after Roche successfully recovered from the financial troubles the company had experienced in the early 1920. Having successfully undertaken a global expansion strategy in the pharma business line in the early 1920s, Roche's top executives began devising a new corporate structure with tax saving benefits in order to address the company's growing tax liability and other international fiscal problems at the time. SAPAC's ownership structure was designed to mirror Roche's shareholder equity structure. In addition to receiving dividends from Roche stocks, the company shareholders began to receive dividend from the earnings of all the foreign affiliated whose financial ineteres had been pooled in this new international holding company.

As Roche continued to grow profitable in the late 1920s the management decided to repay such equity contributions of early investors as Basler Handelsbank who was interested pursuing other investment opportunities with the repayment of its earlier capital contributions (Peyer 1996, p. 114). While continued to repay its shareholders and reduced the size of the company's share capital (from 4 million CHF in 1928 to 2 million in 1931), Roche also began to issue non-voting shares during this period. Such changes in Roche's share structure also reflected the share structure of the company's twin sister organization, SAPAC Corporation. Historic origin of Roche's current dual-share structure traces back to these events in the late 1920s and evolved over time as the company issued new non-voting shares (Genusscheine) in 1971 and 1983 (Peyer 1996, 115.)

Gerber-led corporate restructuring efforts in the 1980s eventually brought the company's complex twin-share ownership structure to an end in 1989 when the company directors approved the retirement of all the SAPAC shares. The retirement of those shares was immediately followed by the restructuring of SAPAC and F. Hoffmann-La Roche to become the subsidiaries of a global new enterprise, Roche Holding AG. Having ended the twin share structure with the unveiled much of the secrecy around the company's business and financial performance, Roche under Gerber became more shareholder friendly company in the 1990s. Roche began to implement more detailed reporting on financial matters since the secrecy around the company financial figures was a major concern for shareholders until the late 1980s (Peyer 1996, p. 250).

Already vacated the CEO post for his successor, Franz Humer, in 1998, Gerber announced his decision to retire from the chairmanship post in the early 1999 at the time when the US justice department launched an investigation into "Vitamins Inc," seven foreign producers of bulk vitamins who controlled more than 80 percent of the world vitamin market in 1999: the "ringleader" Roche and co-conspirer German BASF AG later joined by French Rhone-Poulenc, German the Hoechst Marion Roussel, Japanese Takeda Chemical Industries, the Eisai Company and Daiichi Pharmaceutical, colluding illegally to fix the prices of bulk vitamins in the 1990s (Barboza 1999).

The US government investigation later followed by various legal charges that brought the seven companies to courts in the US and overseas including a class-action lawsuits brought by the largest US buyers of those bulk vitamins. Roche decided to quickly settle the legal charges made by the US government after agreeing to pay US\$500 million in May 1999. The company agreed to pay additional \$632 million to settle the class-action lawsuit with the major American buyers in later in the same year.

Having accumulated significant amount of Roche shares throughout the 1990s to own 20 percent voting stake in the company through his investment firm BZ Gruppe Holding, Martin Ebner, who anticipated a major breakup in the upper echelons of the company's management in light of these recent legal troubles, embarked an intensive shareholder campaign to question the company's dual-class stock scheme and call for a single-class stock system by joining the company's voting and non-voting stocks (IHT, 2000). Ebner argued that once Roche adopts the new single-share structure the company management then deploy the company's stockpile of cash, along with the company's stocks, to pursue major M&A deals to acquire some of the major competitors as it was the popular trend in the industry in the early 2000s (Bilanz, 2004; Tagliabue, 2000).

Ebner often complained about the Roche's board for failing to enhance the shareholder value under strict control of the family and called for the empowerment of other shareholders through appointing more independent directors on the board. Ebner argued that Roche took an unnecessary financial with the price-fixing scandal because the company's board had failed to supervise the management adequately. Ebner advocated for

greater supervision of the top management by the company's board comprised of additional independent directors he asked for a seat on the board (Swissinfo, 2001).

Having no interest in a single-share structure or a major acquisition, on April 13, 2000, the Hoffmann-Oeri family announced their decision to reject Ebner's request to join the company's board of directors especially after Enber accused the family for not taking sufficient interest in the company to steer it in the right direction. Replacing the outgoing director, Werner Stauffacher, in the next company annual general meeting in May, 2000, the family decided to endorse Peter Brabeck-Letmathe, CEO of Nestlé, another Swiss company that had been engaged in similar dual-class share system to the retain the majority voting stocks of a French cosmetic company, L'Oréal, since the mid-1970s (ICIS, 2000).

Having failed in his plot to gain a seat on the board and influence over strategic control of the company, Ebner offered 16 percent of Roche voting shares in his possession to the company's long-time arch nemesis, Novartis. On May 8, 2001, six years after came into being through the merger of Sandoz and Ciba-Geigy, Novartis acquired 20 percent of Roche's voting shares from Swiss investor Martin Ebner by agreeing to pay \$87 for each share and a total of \$2.78 billion for the 32 million voting shares acquired.

Anticipating a landmark merger between the two companies to form the world's largest drug company, Novartis quickly accepted Ebner's offer, paying \$2.78 billion in the hope that it would eventually gain access to Roche's innovative pipeline. When Daniel Vassella, CEO of Novartis at the time, announced the decision to collect Roche shares on the open market after acquiring the Ebner block of shares, he also revealed the future sources of innovation at Novartis. Vassella told investors that acquiring the 20 percent stake in Roche was "a long-term financial investment, which is also strategic in nature" (Olson, 2001). At the time of acquisition Vassella repeatedly stressed the fact that Novartis didn't anticipate a set timeline for a potential merger given that it was "not a must" thing for the both companies to pursue although he often repeated that "it [a merger between the two companies] would be great" (Olson, 2001).

As part of this "strategic investment" plan the company acquired additional 1.3 percent stake in Roche through the stock market later in the same year. As the biopharmaceutical industry continued to consolidate through major corporate mergers among large global pharma companies in the early 2000s, Novartis gradually acquired an additional 11.4 percent stake in Roche by the end of 2002 for the total of \$1.8 billion. By the end of 2003 Novartis had acquired an additional 0.6 percent and already tied up nearly \$6 billion in capital to 33.3 percent of Roche's stocks, making a significant bet on the future success of a competitor that would reward Novartis regardless of whether the two firms ultimately merged.

Despite the size of the voting stakes owned, Novartis remained as the largest minority shareholder of Roche and has yet to make any attempt to acquire seats on Roche's board

due to regulatory issues (Langley, 2003). Aside from occasionally pressuring Roche's majority shareholders, the Hoffmann-Oeri family, to consider a potential merger Novartis possesses very limited power to exercise over Roche's strategic decisions (Langley, 2003). Having recognized the slim prospect of a merger after ten years of waiting, the next CEO of Novartis, Joseph Jimenes, began to evaluate alternatives open to the company with regard to its Roche shares. Jimenes, however, decided to put any plans for the Roche stock on hold, knowing that that 33.3 percent ownership stake Novartis possessed would be worth more than \$12 billion in the market based on Roche's 2013 share price, which was bolstered by the company's innovative pipeline (Hirschler, 2013).

Novartis' possession of Roche's 33.3 percent voting shares doesn't appear to pose a grave danger for the integrity of corporate control at Roche as long as the voting-pool remains intact to safeguard the company's legacy as an independent drug company (Ward, 2015). During one of his very few interviews with a journalist, André Hoffmann explicitly dismissed even the slightest possibility of collaboration with Novartis. He explained to Andrew Ward of the Financial Times in 2015 that Novartis would not be a threat for Roche for much longer because the amount of capital it had invested in Roche was too great even for a company such as Novartis.

According to André Hoffmann the opportunity cost of tying over \$12 billion capital in Roche's stocks will continue to "burns a hole in their [Novartis] pocket" (Ward, 2015). Time appears to be proving André Hoffmann right given that the market value of Novartis' 33.3 voting stakes in Roche has yet to increase significantly since Novartis began to consider the option to sell those stocks in 2013. As of December 31, 2016, the market value of Novartis' 33.3 percent voting stake in Roche was \$12.4 billion. Those 33.3 percent of Roche's voting stakes owned by Novartis account for 6.3 percent of Roche's total equity (both the voting and non-voting shares) and since their first acquisition in 2001, Novartis has received slightly over \$4 billion cash through dividend payments. Instead of cashing out its investment in Roche stocks, Novartis has been divesting its animal health, vaccine, and over-the-counter (OTC) drug units since 2015.

And understanding of the ways in which Bobst, Ebner, Novartis, and the Hoffmann-Oeri families decide to exercise power demonstrate the centrality of strategic control to the pursuit of enterprise growth by focusing on innovation and mitigating financialization. Roche entered the 1970s after the success of a series of innovative new sedative drugs known as tranquilizers. Librium, introduced in 1960, was a major breakthrough in the market for psychoactive drugs, and Valium, launched in 1963 become one of the most popular psychotropic medications worldwide by 1969 (Tone, 2008).

6.1.2 Evolution of Fritz Hoffman-La Roche & Co. into innovative enterprise

In 1893, with the financial support of his father, who was a wealthy silk merchant, a young banker from the Swiss city of Basel, Fritz Hoffman-La Roche, invested 200,000 francs in

Bohny, Hollinger & Cie., a small chemical manufacturer located there (Roche Historical Achieve, n.d.). An entrepreneur who envisioned a blooming future for the innovative marketing of branded biopharmaceutical products, Hoffmann soon found himself in disagreement with factory management, which led him to join in 1894 with the company's pharmacist, Max Carl Traub, in acquiring the factory and forming Hoffmann, Traub & Co. When Hoffmann and Traub decided to part ways in 1896, shortly after establishing the company's first foreign subsidiary in Grenzach, Germany (Peyer 1996), F. Hoffmann-La Roche and Co. was first incorporated.

Although Fritz Hoffmann envisioned building a company with the characteristics of the “innovative enterprise”, from the very first days of Roche his journey to that goal was never an easy one. Despite not yet having brought a successful product to market, Fritz continually added subsidiaries and invested heavily in building a research facility capable of developing high-quality products. Since product launches were delayed as capital expenditure increased, the company faced bankruptcy only years after its incorporation (Roche Historical Archive, n.d.).

Fritz managed to recapitalize the company with funds from family members and hired a talented young chemist, Dr. Emil Christopher Barell, and an apothecary, Carl F. Schaegers, who helped develop and introduce a series of new products, including Sirolin, a flavored cough syrup (Bürgi & Strasser, 2009; Roche Historical Achieve, n.d.). The growth achieved through the successful launch and marketing of Sirolin encouraged Fritz to maintain his internationalization efforts in the early 1900s. By 1912, Roche had managed to establish its presence in many major markets, among other things by opening its first US office in New York in 1905 (Peyer, 1996).

Although Roche was introducing highly innovative products, such as a heart tonic (Diagalen) and a pain killer (Pantopon) to the market, the growth that followed their successful launch was hampered by the onset of the Great War. Roche's products were boycotted both by French and German consumers, who were expressing their anger at the company for doing business with their enemy. Additionally, the company's access to its production facility in Germany, where the majority of production took place, was restricted. Finally, Roche lost one of its most important markets, and some major assets along with it, during the Russian Revolution of 1917.

The toll of the Great War and the Russian Revolution was heavy, and in 1919 the company was once again facing the threat of bankruptcy in 1919 (Roche). In dire need of capital, Fritz Hoffmann decided to restructure the company as a limited partnership and accepted outside capital to form F. Hoffman-La Roche & Co. Ltd. Barell and some other associates also invested in the new partnership, and with the financial backing of Basler Handelsbank, which was headed by Fritz's brother-in-law, Rudolf Albert Koechlin-Hoffmann, Fritz managed to recapitalized the company and put the insolvency issue to rest before the year was out (Peyer, 1996).

The challenges Fritz faced in the early years of his growing company took a heavy toll on his health, and he died in 1920 at the age of 52. Upon his death Barell was appointed as the new managing director of Roche. Upon acquiring the interest of Fritz Hoffmann and Adèle La Roche's younger son, Alfred Hoffmann-La Roche, in the company, Barell one of its largest shareholders and took over its management. A young, bright chemist and innovator, Barell was known to be a very tough manager who often applied harsh austerity measures to restructure the company, which was trying to recover from the calamities of the recently ended war, for a path to healthy growth.

Despite the hefty restructuring measures imposed by Barell early in his tenure as managing director, the research division at Roche, under the leadership of Markus Guggenheim, managed to launch more innovative products in 1920s, most notably the company's first semi-synthetic product, Allonal, a sedative marketed as a sleep aid. By 1920, Barell had appointed Elmer Holmes Bobst, initially hired by the New York office as a salesman in 1911, manager and treasurer of the Hofmann-La Roche Chemical Works. To capture a greater share of the fast-growing US drug market, Bobst restructured the small sales office in New York into an independent subsidiary, then, in 1928, relocated US operations to their new home in Nutley, New Jersey. (Peyer, 1996)

During the interwar years Barell was successful in recruiting highly talented scientists and chemists, as among whom was Tadeusz Reichstein. Reichstein, a young scientist at the Swiss Federal Institute of Technology in Zurich, accidentally synthesized vitamin C while spending most of his time in the 1920s trying to synthesize the aroma of coffee at his laboratory (Steffen, 2012). Once he had successfully managed to synthesize a form of vitamin C in 1933, Reichstein began to search for the right industrial partner to adopt his revolutionary synthesizing technique for its mass production (Steffen, 2012).

In 1933, Roche and Reichstein joined forces to develop a new production process that allowed the company to scale up production without causing bacterial contamination of the production site -- a method often referred to as the "Reichstein process" -- a manufacturing issue not many drug manufacturers had success but Roche resolving it at the time (AoT - Roche). Another chemist, Otto Isler, was hired in 1936 from ETH in Zurich and assigned to find new synthetic pathways to vitamins. He eventually made the company the largest producer of vitamins in the world market (Bürgi & Strasser, 2009).

The economic success achieved by the introduction of the company's first synthetic chemicals, Allonal and vitamin C, persuaded Roche's management to intensify its research focus on developing new products through synthesizing new chemicals. A shift in focus to synthetic chemistry resulted, which was accompanied by an increase in investment in the company's in-house R&D capabilities. The number of research personnel it employed nearly tripled over the next two decades, growing from 26 in 1924 to 75 in 1944 (Bürgi & Strasser, 2009).

Roche's recovery efforts at the end of the Second World War were accelerated by the discovery in 1945 of a new application for vitamin B in the field of haircare. This application was launched through a new subsidiary, Pantene AG, which turned out to play a major role in the success of Roche's post-war recovery efforts. Barell's return to Basel in 1946 signaled the beginning of a normalization period, and the company managed to develop innovative new therapies such as Gantrisin, a sulfa drug for the treatment of bacterial infections, and Rimifon, another antibiotic, which was mainly developed by the scientist at the Nutley laboratories and was used in the treatment of tuberculosis.

After Barell's death in 1953, Dr. Albert Caflisch, who served as a board member both at Roche and the Swiss Bankers Association at the time, became the new leader of Roche. During his tenure Caflisch replaced the autocratic management practices that had characterized the Barell era with practices founded in a more liberal leadership vision. Caflisch's new regime was to align with the building of the more modern corporate structure he envisioned for Roche as the company continued its efforts at internationalization in highly competitive drug markets. The new practices supported an increase in functional and regional autonomy that was intended to empower local leadership to pursue a long-term growth vision driven by innovative practice.

Caflisch was also concerned about the highly decentralized and fragmented R&D operations concentrated in three major centers: Basel, Nutley and Welwyn in the UK. Established in 1956 as a small, global research-strategy group consisting of eight members, including the top research and operation leaders of the major R&D centers, Roche Research Management Group (RRMG) was responsible for coordinating the company's R&D operations. R&D had been fragmented at Roche as a consequence of the company's deliberate strategy or safeguarding its Basel assets and operations against the potential occupation of Switzerland by the Axis Powers (Bürgi & Strasser, 2009).

A discovery made in 1960 by Leo Sternbach, a Polish research chemist who had been transferred to the US from Europe at the onset of the Second World War, would mark another turning point in the history of Roche. Desperate for a big hit in the early 1950s, Roche management requested that Sternbach synthesize a compound similar to the popular anti-anxiety drug Miltown soon after its market launch in 1953 by Wallace Pharmaceuticals (Tone, 2008). However, instead of pursuing what he considered a boring task, Sternbach decided to return, without informing his superiors, to his earlier work on some compounds that he had studied in his native Poland in quest of new dye applications. After two years of intensive work in 1955, Sternbach's studies on the compounds anticipated for potential dyes led to the discovery of benzodiazepine, a compound with chemical properties that demonstrated sedative effects. (Maugh, 2005).

Since the work was done in secrecy, Sternbach waited for half a year to share his discovery with Lowell Randal, the head of the pharmacology division at Roche-Nutley (Maugh, 2005). Initial experiments with the new chemical compound on animals were to lead to the

discovery of new tranquilizers, although it was only after years of hard work by the two scientists that first one of those new tranquilizers was introduced in 1960. The success a series of innovative new sedative drugs -tranquilizers; Librium, which in 1960 was a major breakthrough in the market for psychoactive drugs; and Valium, in 1963 became the world's first billion-dollar medicine - brought Roche a vast fortune in the 1960s and into the 1970s. Valium's success surpassed that of Librium: By 1969 it had become one of the most popular psychotropic medications worldwide; it was to become known, rather widely, as "Mother's Little Helper" (Tone, 2008).

6.1.3 Shifting the focus of drug discovery from chemistry to biology: Factors requiring drug manufacturers to transform drug R&D in the 1960s and 1970s

Surging demand for penicillin and vaccines during the Second World War stimulated academic/industrial drug R&D efforts in the Allied nations, primarily in the United States and the United Kingdom. As discussed extensively in chapter five, the winners of the wartime penicillin challenge such as Merck managed to scale up their R&D efforts in the years following the war (Bud, 2005; Quinn, 2013). Those who had been excluded from the wartime penicillin programs further advanced their knowledge base in organic chemistry and built extensive libraries of newly synthesized chemical compounds during the postwar era (Bürgi & Strasser, 2009).

However, these libraries' screening of compounds against a wide array of biological targets, along with conducting clinical tests for potency and toxicity in living organisms, was, in the 1950s, increasing the cost of drug discovery. In the absence of a radically different approach, based on further substantiated insight into pathology and pharmacology, to the conventional "random" or "programmed" screening of newly synthesized compounds (Galambos & Sturchio, 1998), the conventional drug screening tools were becoming a bottleneck for the discovery of innovative new therapies. On the strength of the advancements achieved in biochemistry and biology in the first half the 20th century, biochemistry was about to challenge organic chemistry for superiority in drug discovery and development (Galambos & Sturchio, 1998).

A medical tragedy came to light in 1962, when thousands of babies were born in various European and Commonwealth nations with defects caused by a sleeping pill considered safe for pregnant women, Thalidomide, developed by the German firm Chemie Grünenthal. In the wake of this tragedy, the US government adopted comprehensive drug-safety measures through the enactment of the US Kefauver-Harris Amendment in 1962 (Temin, 1980).

By amending the Food, Drug and Cosmetics Act of 1938, this statute shifted the burden of proof in the drug-approval process from the FDA to drug companies, requiring a company to provide sufficient evidence of a drug's being safe and effectiveness before it could be marketed. The new regulatory pressure to produce evidence for the safety and

effectiveness of a new therapy intensified the pressure on drug manufacturers to question the sustainability of their existing innovation strategies and to make necessary investments in knowledge acquisition and capability improvement.

In studying the changes Roche adopted in the 1960s, when the pharmaceutical industry was approaching one of the major turning points in its history, Bürgi and Strasser (2009) benefited from an extensive library of communications among the scientists, leaders of the research community, and top management at Roche. The communications they analyzed reveal the scientists' concern about the newly emerging technological and regulatory issues the company would inevitably face in the very near future should it dismiss the need for a new, radically different approach to drug discovery.

Bürgi and Strasser (2009) observe that the difficulty of sustaining growth without exploring the new approaches to drug discovery that had been enabled by advancements in the fields emerging within biochemistry received more frequent mention in reports submitted to RRMG during the 1960s than it had earlier. In these reports some leading scientists at Roche's research centers, particularly those in the US and UK, urged top managers to consider making investments in basic research in biology.

Aside from biological screening of synthesized chemicals, Roche had accrued very limited knowledge in biology -and thus the company had shown no interest in the discovery, development and manufacturing of biological drugs previously - at a time when the emerging fields of biology, such as biochemistry, immunology, and enzymology began to show more promise attract the interest of some scientist at the nation's major industrial laboratories in the mid-1960s (Bürgi & Strasser, 2009).

In the field of organic chemistry, which was responsible for the innovation of the company's legacy products, those who led the crafting of research strategy had been reluctant to engage the organization in new learning programs in the emerging fields of biology for the most part of the 1950s and 1960s. This apathy toward biological learning resulted in the company's withdrawal from the markets that then emerged. Given Roche's limited knowledge in the field of biology, its researchers were concerned about the risk associated with the fermentation process for producing biosynthetic antibiotics, and hence decided to opt out of biological drug manufacturing, a new market in which major competitors such as Merck and Pfizer were building capabilities at the time (Peyer, 1996).

Similarly, the research team dismissed the idea of manufacturing vaccines and antivirals because they could not be manufactured synthetically. Therefore, instead of investing in organizational learning for vaccine development and manufacturing, a potentially faster route to developing effective treatments for viral diseases, the leadership decided to adhere to the organic chemistry approach for the development of chemotherapeutic compounds. Such efforts in the antiviral program ultimately failed to deliver the anticipated productivity and capture a significant share in the emerging antivirals market.

At the same time that the company's recent attempts in entering new markets were failing miserably, a group of scientists from Welwyn was offering a gloomy perspective on the prospect of business growth based on the chemistry-focused, traditional drug-discovery approach. The Welwyn report argued that top management had to make major investments in basic biological research that would ultimately eliminate the need for increasing investments in the random screening of a growing library of synthesized chemicals, as such screening efforts were failing to deliver the anticipated productivity in drug discovery (Peyer, 1996).

Growing disparity between the number of newly synthesized chemical compounds and that of viable drug candidates based on the screening of an increasing number of chemicals was the most urgent issue to address among the leading pharmaceutical companies in the US. RRMG began to recognize the consequences of its failure to fully engage in basic research in the emerging fields of biology: The company's early antiviral research program, in progress for most of the 1950s and 1960s, had been able to deliver only a single compound due to the chemical approach that failed to give the necessary attention to acquiring biological insight into disease pathology and clinical pharmacology

Engaging in new learning in the fledgling field of biochemistry and exploring new market opportunities in the US

Until 1960, the company's innovative capabilities had been vested in organic chemistry, and the research leadership wasn't eager to join the post-war antibiotics and vaccine rush, given the company's limited capabilities in developing and manufacturing drugs through biological means. The company's leading chemists, including the man behind the discovery of new synthetic pathways for vitamins, Isler, argued that its current success had been achieved solely on the basis of its competitive strength in organic chemistry and that that could be further strengthened for future innovation (Bürgi & Strasser, 2009). Isler also argued that biological research was based merely on theory or speculation and that, given its impractical nature, pursuing fundamental biological research would not result in new drugs.

In the late 1960s, some leading scientists at Roche's research centers, particularly those in the United States and United Kingdom, urged Roche's top executives at Swiss corporate headquarters to consider making investments in basic research in biology (Bürgi & Strasser, 2009). At a time when Roche enjoyed a significant financial windfall from the unpreceded success of Librium and Valium, the company's recent attempts in entering newly emerging fields in biology were failing miserably, with a group of scientists from Welwyn UK offering a gloomy perspective on the prospect of business growth based on the chemistry-focused, traditional drug-discovery approach.

In a series of reports submitted to Roche Research Management Group (RRMG), a small global research-strategy group consisted of eight members, including the top research and

operation leaders of the major R&D centers, in 1966, the scientists from Welwyn expressed their concern, echoing the sentiment growing among scientists in Roche's other research centers, that managerial apathy about biological learning could have detrimental effects on the long-term growth of the company (Bürgi & Strasser, 2009).

The establishment of the members of RRMG began to play an integral role in devising and overseeing innovation initiatives and organizational learning efforts in ways that allowed drug discovery at Roche to be guided by emerging knowledge in biochemistry. In making a transition in drug development from chemical extraction compounds from natural substances to deriving organic compounds employing tools made available by organic chemistry during the interwar period, Roche became the world's largest drug producer in sales by 1967. The enormous success that its vitamins and sedatives brought resulted in a financial boon and recognition throughout the international science community. This financial and reputational capital could be deployed in supporting organizational learning efforts while attracting world-class scientists to join these efforts through the forging of much closer relationships with academic research centers.

Although it was a tall order to get top management to prioritize the investments in fundamental research in biology, and to commit resources to funding a long-term learning strategy carrying a high level of uncertainty, the efforts of those visionary scientists at Roche were aided by the rising popularity of long-term-planning , an administrative-science paradigm new to the field of corporate management (Bürgi & Strasser, 2009). Encouraged by the company's strong financial condition and motivated to maintain its market position, in mid-1950s Roche's top management established an independent committee as part of the research operations at Nutley to devise and oversee "long-range planning" for the organization (Bürgi & Strasser, 2009, p. 427).

Building innovative capabilities internally: creating an army of molecular geneticists through the Roche Institute of Molecular Biology (RIMB)

In 1967, Roche established RIMB as an independent research body within the company solely for the purpose of engaging in deep learning in the field of molecular biology at the most fundamental level. Among many individuals, Sidney Udenfriend, first director of RIMB; Herberth Weissbach; John J. Burns, executive VP; and Alfred Pletscher, VP of R&D at Roche in Basel, who had worked together at the National Institutes of Health in the 1950s, were key to the establishment of this institute (Udenfriend, 1995; Weissbach & Witkop, 2003).

Under the leadership of the nation's highly respected scientists, the Institute gradually evolved until it was nearly indistinguishable from an academic equivalent, as its learning environment inspired those working there to excel according to academic norms (Pollack, 1982). Fostering such an environment had helped Roche to recruit top scientists in their fields, especially during the period when federal support for biomedical research was in

sharp decline. The Institute hosted a number of international symposia on different topics in molecular biology, which created an ideal environment for academic and industrial scientists to exchange ideas that would benefit Roche immensely in the years to come (Peyer, 1996).

In fact, the topic for the second symposium, in 1973, was the latest developments in recombinant genetics. The symposium was held in the same year that Stanley Cohen of Stanford and Herbert Boyer of the University of California San Francisco announced their success in cloning a gene through recombinant techniques. Four years later, at the 1977 RIMB Symposium, the two scientists were presented with the Virginius D. Mattia Award for their scientific achievements (Boyer, 2001). The symposium was held around the same time that Dr. Philip Handler announced Genentech's successful undertaking of cloning the first human growth hormone, Somatostatin. At this event, Boyer had the opportunity to discuss the progress achieved in cloning Somatostatin at Genentech and introduced the scientists in attendance to the capabilities that this new start-up then possessed (Boyer, 2001).

Roche placed heavy emphasis on fostering learning efforts at RIMB, continuing to allocate resources to keep this basic science program running while dismantling some other research programs and downsizing its Basel operations. The institute gradually grew in size from 70 scientists in 1967 to nearly 200 by 1975 and over 500 by 1987 (Bürgi & Strasser, 2009; Weissbach, 1987). Attracting high-quality postdoctoral research fellows was critical to staffing the institute with the right amount of high-quality biomedical scientists, who were still in short supply at that time, for pursuing high-quality research.

As the only non-academic institute at the time operating as an affiliated research unit within an industrial organization, Roche took part in an international visa program for improving the mobility of academic researchers that was coordinated by the State Department (Peyer 1996). RIMB developed a partnership with local universities to design a new Ph.D. program that would allow students to attend classes at the degree-awarding institutions while pursuing their research at the labs within the institute (Weissbach, 1987). Although some basic research of a similar kind had already been established in the interwar years at DuPont, Merck & Co., and Squibb, RIMB became one the largest organizations in research and training, particularly in the field of biomedical science, supported by industry (Bürgi & Strasser, 2009; Weissbach, 1987).

Although management had no expectation that this basic research institute would produce results in the short term, the scientists at RIMB managed to turn out some important work that was successfully translated into commercial products. Abu-screen (a diagnostic tool for screening drugs of abuse) and Roferon (interferon-alfa, developed through recombinant DNA) are among the notable examples (Peyer 1996). However, the most important contribution of this institute was the building of one of the most productive molecular

genetics departments at Roche, as measured by the careers of the people who were trained at the institute.

The role that RIMB played within Roche was instrumental to the company's organizational learning efforts. Intellectual accomplishments within the institute were key to crafting the company's long-term growth strategies and steering it into high-growth markets along the trajectory of the fledgling molecular genetics field (Bürgi & Strasser, 2009). Roche's place among the most innovative companies in the field of molecular genetics and its possessing one of the most successful portfolios of recombinant products today can be credited to the research and training efforts of this institute. As the visibility of the Institute grew, Roche was able to recruit some of the most prominent scientists, one of whom was Severo Ochoa de Albornoz, a Nobel laureate who served from 1974 to 1985 as director of RIMB, where he led a large group of highly accomplished scientists (Peyer, 1996). Sidney Pestka was another important figure who was instrumental in the success of RIMB: A team of RIMB scientists under his leadership was one of the first groups in the US to isolate pure interferon (Heyneker, 2002).

For decades, RIMB would remain devoted to the Institute's original principle that its scientists be independent in choosing broad scientific questions in which they would pursue basic research as passionately as they might in an academic setting regardless of the time involved. It is this devotion to scientific independence that constituted the most critical element of the Institute's successful recruitment performance. Notwithstanding the great service that it rendered to the company, the Institute's physical distance from the center of the molecular genetics network in California was becoming an important hurdle in attracting and retaining talent. In fact, the management at Roche was unable to find a suitable candidate to replace Weissbach, the Institute's last director, whose retirement was fast approaching at the time (Udenfriend, 1995). After its acquisition of Sytex in 1994, Roche decided to move the Institute to Palo Alto, where Sytex's US headquarters was located. Roche management was confident that a more suitable candidate, especially in the field of genomics, could be identified at the epicenter of the information and communications technology (ICT) and genomics revolutions (Udenfriend, 1995).

6.1.4 Penetrating the early biotechnology network: Roche joins the cloning rush on the West Coast

Fostering such an environment had helped Roche to recruit top scientists in their fields, especially during the period when the US federal support for biomedical research in sharp decline as the mounting cost of Vietnam War began to impact the US economy in the late 1960s, which ultimately led to the enactment of the 1969 Mansfield Amendment to limit the US government nondefense R&D spending in the early 1970s (NAS, 1995, p. 45; Teitelbaum, 2014, p. 49). The Institute hosted a number of international symposia on different topics in molecular biology, which created an ideal environment for academic and

industrial scientists to exchange ideas that would benefit Roche immensely in the decades to come (Peyer, 1996).

At a time when molecular biologists and geneticists were in short supply in the 1970 and 1980s, Roche gradually embedded itself in the fledging network of prominent scientists in the US through a team of world class scientists at RIMB, (Peyer, 1996). Through this network, Roche was monitoring the latest developments in gene-cloning technology being pursued by Cohen and Boyer in 1973. Despite the promise of those scientific accomplishments, which had the potential to disrupt the ways in which the discovery of drugs could be pursued, the majority of big pharma establishments, rolling in the riches of the penicillin and antibiotics era, overlooked such advancements in molecular biology.

The wider reluctance to explore the commercial viability of this technology had some basis to it, however. Various regulatory issues revolved around the new technology that stemmed from public fear over risks associated with the science of manipulating living cells on a molecular level. Some medical scientists urged the NIH to put together a guideline for geneticists to adhere to during their experiments. These concerns were echoed in different communities around the world, and the governments of a few nations took extreme measures, discouraging the work from being performed by subjecting it to severe restrictions.

It was because Switzerland was one of those nations that adopted strict guidelines for conducting experiments using recombinant DNA technology that Roche management decided to establish RIMB within the US headquarters at Nutley. Under Pestka's leadership, a research group at RIMB joined the race to isolate pure interferon (alpha), one of the members of a protein group that at the time was considered the silver bullet for the treatment of cancer (Peyer, 1996). Genentech, Cetus (later Chiron), and Biogen (in collaboration with Schering-Plough) were all working on the same protein, which would lead to the discovery of other members of the interferon family (beta and gamma) (Vettel, 2006, c. 8). During these innovation efforts, another Roche research team, based in Basel, discovered a new method of identifying different types of interferons. They revealed significant applications in the field of diagnostics and opened a new growth path for Roche to pursue.

Building core competence in molecular biology diagnostics: Roche, Cetus, and Polymerase Chain Reaction (PCR)

Roche had been active in the diagnostics field since the 1960s but had not been the market leader. An opportunity to assume that position emerged in 1989 after its decision to collaborate with Cetus in development of the PCR method. The PCR method was considered revolutionary and declared by *Science Magazine* to be the most important discovery of 1989 because it was outperforming the other diagnostic tools at the time in efficiency and accuracy. The diagnostic application of this method was powerful: While a

complex virus such as AIDS could be detected through conventional blood tests only months after the first infection, with the use of the PCR method the same virus could now be detected almost instantaneously (Peyer, 1996).

Roche's acquisition of PCR technology would not have been possible if the management at Cetus had recognized its value and pursued it as a viable business opportunity (Rabinow, 1996; Glaser, 2006; Fore, Wiechers & Cook-Deegan, 2006; Cohen, 2009; Alafi, 2013). Because of its financialized business model, Cetus had failed to develop the necessary productive resources -- managerial, monetary, or human -- to deploy the PCR technology commercially. We now examine briefly how financialization affected the innovation of the PCR method at Cetus and led to the acquisition of the technology by Roche.

The birth of Cetus, a venture-backed biotechnology company initially formed in 1971 and incorporated in 1973, was a testament to a new, technology-driven industry in which technology and finance were converging the fashion experienced throughout the evolution of ICT in Silicon Valley. Although Cetus was considered to be the first biotechnology company ever to be established in 1971, it did not truly become a biotech company until after Genentech had emerged to develop recombinant therapies. Moshe Alafi, lead investor and chairman, former academic and physician, Ronald E. Cape and Peter Farley, along with the world-renowned Nobel laureate in physics Donald Glaser, co-founded Cetus with the initial purpose of providing commercial services for the fast screening of microorganisms using a device invented by Glaser to identify new antimicrobials. The first entrepreneurial initiative of its kind, Cetus managed to attract some major scientific figures as consultants, such as two Nobel laureates, Joshua Lederberg (for the discovery of bacterial conjugation) and Stanley Cohen (for the co-discovery of genetic engineering), and the two influential figures at Mexico-based Syntex Laboratories, Carl Djerassi and Alejandro Zaffaroni, whose successful collaboration on the synthesis of first oral contraceptive had been key to the company's rapid growth in the 1950s and 1960 (Alafi, 2013; Glaser, 2006).

Despite possessing an all-star scientific advisory committee, a pool of scientific talent, and an astounding level of capital -- nearly \$120 million, secured through an all-time record initial public offering (IPO) in 1981 -- from very early on Cetus suffered from a lack of the strategic vision needed for transforming technology and markets in order to pursue sustainable growth. The absence of such strategic vision constrained organizational learning and ultimately resulted in the loss of other productive resources. Various insider testaments reveal that Cetus was presented with various opportunities to pioneer the development of novel biological therapeutics by employing the techniques then emerging in the genetic engineering field. Although they had recruited Cohen, co-inventor of the recombinant DNA technique, as the Cetus's top consultant, Cape and Farley, the executives in charge of the organization's daily operations, still insisted on pursuing as its business line providing commercial services to top pharmaceutical companies using Glaser's screening technology.

Despite all the effort by Cetus to attract a big pharma contract, the only drug company that decided to explore what it and Glaser's new technology had to offer was Schering-Plough. Through this collaboration, Cetus agreed to assist Schering-Plough in efforts to improve the production efficiency of Gentamycin, a powerful antibiotic used at hospitals as a drug of last resort in the most complicated cases of infections. Bob Swanson at the time a member of Cetus's board representing junior partner Kleiner Perkins, developed an interest in the recombinant technology that Cohen had presented on various occasions. Approaching Cape and Farley, Swanson asked them to hire him to pursue this new technology more extensively within Cetus. Not only was his request declined by Cape and Farley, Swanson was also let go by Kleiner Perkins, reportedly because the duo did not want a third partner. According to Vettel (2006), this was the second time Cetus declined a proposal to pursue recombinant DNA for pursuing Glaser's screening machine, as Roche had approached the company with a proposal to pursue this technology jointly a year before (p. 212).

Unable to convince Cetus and parting ways with his former partners, Swanson decided to approach Boyer, the other inventor of recombinant DNA technique at the University of California San Francisco. Swanson pursued Boyer about exploring commercial applications of his disruptive technology through a new start-up with the prospect of securing financial backing from Kleiner Perkins. Not only did Cetus lose a talented technologist highly motivated to pursue the recombinant DNA engineering technology internally, it also created a fierce competitor that would later beat Cetus, and its successor Chiron, in the race to clone the top items on any biotechnology start-up's to-do list in the late 1970s: the first human growth hormone, somatostatin, – a relatively small molecule in size) which would be produced in bacterium in 1977, insulin in 1978, and growth hormone in 1979.

Cetus decided to move into the cloning business when Genentech (1976), Biogen (1978), and Amgen (1980) had all joined the race to pick the ripe fruits that were hanging low, including human insulin, human growth hormone (HGH), and interferon (alfa, beta, and gamma). In response to growing pressure from shareholders, Cetus's board decided to make some radical changes in its business model. This decision was accompanied by a shake-up of top management in 1981, after the company had completed the largest IPO ever recorded, when hiring the former president of Biogen, who would later replace Cape as CEO upon the resignation of Farley in 1982 (Vettel, 2006).

Cetus attempted to make the leap into developing new therapeutics through forging strategic partnerships with other biotechnology start-ups. Through an R&D collaboration with a subsidiary of Royal Dutch Shell, Triton Biosciences, Cetus began to pursue its first major therapeutic candidate, beta-interferon b1 (Betaseron) in 1985 (Kinch, 2016). However, after failing to show effectiveness for the treatment of the cancer agent, it would take years to discover that Betaseron could be an effective therapy for Multiple Sclerosis

Prior to the partnership on Betaseron, Cetus had already been pursuing another anti-cancer agent, interleukin-2 (IL-2), in the early 1980s. During a fierce competition against Immunex, Genentech, and a Japanese researcher, Tadatsugu Taniguchi, Cetus aggressively pursued the development of IL-2, and, in collaboration with the nation's leading IL-2 expert, Dr. Steven Rosenberg at the National Cancer Institute, pushed the new therapy through clinical trials (Lax, 1985). In addition to boosting investment in R&D, Cetus was heavily investing in the expansion of its manufacturing and sales & marketing operations to prepare the organization for the launch of this experimental new therapy that was still in the clinical phase (Lehrman, 1992).

The cost of this ambitious innovation strategy mounted fast as the clinical progress on interferon project was delayed. Fildes began to sell the company's major assets in non-drug business lines, including one that was soon to become a major revenue-generating technology, *polymerase chain reaction* (PCR). A technique for amplifying the production of copies of DNA on a large scale, PCR had been discovered and developed by Kary Banks Mullis during his tenure at Cetus in the early 1980s and would win him the Nobel Prize in chemistry along with Michael Smith in 1993 (Cohen, 2009; Alafi, 2013; Glaser, 2006).

From early on, Fildes had been unable to recognize the importance of this powerful tool, with its important diagnostics and research implications, and he decided to pursue the further development of the technology through partnerships as its popularity grew among the scientific community (Cohen, 2009; Alafi, 2013; Glaser, 2006). Cetus first formed a partnership with Kodak, in 1986, for the development of an *in-vitro* diagnostic tool powered by the PCR technique, then formed a joint venture with Perkin-Elmer in 1987 to develop and manufacture the diagnostics instrument GeneAmp PCR Kit for biomedical research. (Fore, Wiechers & Cook-Deegan, 2006)

With the expiration of the Kodak partnership approaching, Cetus was looking for a new partner for the commercialization of PCR kits. And since the company was preparing to launch Proleukin (IL-2), a treatment for kidney cancer in which it had invested heavily, in the European market, Fildes was interested in avoiding any potential IP dispute against Roche, which had acquired the marketing rights for IL-2 both from Immunex, a Seattle-based biotechnology start-up founded in 1981, and Ajinomoto, a Japanese company that held the IP rights for Taniguchi's recombinant IL-2 (Rabinow, 1996). In fact, he was willing to give up on PCR if that would mollify Roche, which for its part was not only eager to avoid a legal battle with Cetus in Europe upon the launch of Proleukin but also seriously interested in the PCR technology.

Roche agreed to discuss terms with Cetus, which, in 1989, licensed its PCR technology to Roche in exchange for being allowed to market *Proleukin* in Europe without facing legal action. Based on this agreement, Roche would supply \$30 million in cash to fund the

PCR-based diagnostics research during the following five-year period, in addition to purchasing one million shares of Cetus (Fore, Wiechers & Cook-Deegan, 2006).

As the expiration of the partnership with Kodak was approaching, Cetus was looking for a new partner for the commercialization of PCR kits. As a serious competitor in the IL-2 market heading for a legal battle with Cetus in Europe upon the latter's launch of Proleukin there, Roche showed significant interest in the PCR technology and agreed to discuss terms with Cetus. Given how much Cetus had invested in *Proleukin*, Fildes was willing to give up on PCR if that would mollify Roche, which had acquired the marketing rights for IL-2 both from Immunex, a Seattle-based biotechnology start-up founded in 1981, and Ajinomoto, a Japanese company that held the IP rights for Taniguchi's recombinant IL-2 (Rabinow, 1996). Fildes was interested in avoiding any potential IP dispute against Roche as the company was getting ready to launch *Proleukin* (IL-2), a treatment for kidney cancer, in the European market. In 1989, Cetus agreed to license its PCR technology to Roche in exchange for being allowed to market *Proleukin* in Europe without facing legal action from Roche. Based on this agreement, Roche would supply \$30 million in cash to fund the PCR-based diagnostics research during the following five-year period in addition to purchasing one million shares of Cetus (Fore, Wiechers & Cook-Deegan 2006).

With the FDA's decision to disapprove interleukin 2 (IL-2) in 1990, the experimental drug expected to provide a miraculous cure for Cetus's failing financial health, the company was forced to proceed onto a new path, as it faced a loss of nearly \$120 million stemming mostly from its risky bet on IL-2. In 1991, Chiron showed interest in acquiring Cetus in a stock-based transaction worth \$660 million. However, that transaction depended on a legal challenge by DuPont to the validity of Cetus's PCR patents, which had to be resolved before the sale of Cetus's PCR business to Roche could be completed. Acquisition of this powerful diagnostics tool, a deal worth \$300 million in cash plus subsequent royalties stemming from the technology (Rabinow, 1996), would make Roche an important competitor not only in the diagnostics market but also in pharmaceutical. PCR's functionality in drug research would enable Roche to create economic value measured in the billions of dollars in the years that followed.

Travelling in the fast lane in the transition into genetic engineering and the new era of biologics: Roche, Genentech, and the First Generation of Recombinant Therapies

Even as Roche was pursuing the PCR technology to strengthen its position in the diagnostics market, the company was already pursuing a number of research partnerships centered on recombinant therapies with biotechnology start-ups in the San Francisco Bay Area. At the time, recombinant interferons were considered as the silver bullets to fight cancer that could potentially become blockbusters quickly.

Although Genentech had the technology to clone such a protein, the company needed to acquire a protein source to initiate the cloning process. It turned out that Pestka and his

team had been working on cloning the protein at RIMB and had a cell line that could source it. As Boyer had had constructive talks with the management at RIMB a year before, Genentech decided at the time Boyer was presented with the Mattia Award in 1977 to approach Roche about forming a research collaboration with the research team at RIMB. Although an initial research collaboration was not productive, one positive outcome was that the management at Roche began to recognize the technological capabilities Genentech possessed, while Genentech discovered one of the best research partners it could collaborate without the fear of losing the technology (Perkins, 2002; Goeddel, 2003; Raab, 2003).

A young venture capital investment enthusiast trained in chemistry and management at MIT in the late 1960s, Robert (Bob) Arthur Swanson initially arrived in San Francisco in 1970 to open Citibank's first West Coast office, which was for its recently established venture capital arm, Citicorp Venture Capital (CVC). In the following years Swanson met Eugene Kleiner, co-founder of Silicon Valley's famed venture capital company Kleiner Perkins, while serving on the board of a nearly failed venture in which Kleiner Perkins had an equity interest.

Impressed with his passion and abilities, Kleiner asked Swanson, who was only 27 years old at the time, to join Kleiner Perkins in 1974 as a junior partner. One of Swanson's first major assignments was to evaluate an investment opportunity at Cetus Corporation, the nation's first biotechnology start-up, which had been established a few years before. During Kleiner Perkins's involvement with Cetus, Swanson had the opportunity to get to know more about genetic engineering and cloning from the company's world-renowned scientific advisors. Although Swanson, along with some other top science advisors and investors, were highly captivated by the commercial potential of this emerging technology, there was no imminent impetus to pursue such technology being acknowledged by management (Alafi, 2013; Hughes, 2011).

At the time Kleiner Perkins was getting ready to let Swanson go (Perkins, 2002; Alafi, 2013), Swanson asked Perkins to connect him with the top management at Cetus so that he could explore the possibility of employment there (Perkins, 2002). After Cetus had turned down his proposal to pursue rDNA technology commercially for the company, Swanson decided to pursue it in partnership with someone who held the right scientific credentials and using seed capital promised by his former boss, Tom Perkins.

While surviving on unemployment benefits and looking for a new job to sustain a decent living, Swanson was assessing the commercial viability of the emerging rDNA technology and searching for a potential scientist-partner in the early months 1976 (Swanson, 2001). After hitting it off quickly with Boyer and convincing him to partner in a venture that would explore commercial opportunities using Boyer's technology, Swanson began his attempts to identify a potential product candidate, and the two agreed to pursue the idea of

synthesizing human insulin chemically, as the molecule was small enough that that was possible, and devising a plan to mass manufacture it using bacteria.

The basic idea behind their value proposition, as mentioned in the first business plan, was that using rDNA technology to produce human insulin would be a much more cost-effective way of producing insulin than deriving it from animals (Swanson, 2001; Hughes, 2011). Because the new venture was on a very limited budget and would not be able to afford to build infrastructure ideal for conducting proof-of-concept experiments, Swanson decided to form Genentech as a virtual company, contracting with university scientists and facilities.

Boyer suggested collaborating on making human insulin with Arthur Riggs and Keiichi Itakura, two City of Hope scientists who had been turned down by NIH for a grant to produce somatostatin, a growth hormone embodying a very simple amino acid structure. Riggs and Itakura were willing to make the human insulin but argued that it would make more sense to deal with a smaller molecule to test the idea. Although Swanson wasn't thrilled with the idea of following a small detour in the path to making insulin, Boyer and Riggs convinced him to pursue engineering somatostatin as a proof of concept to demonstrate to the world that rDNA was a commercially viable technology.

Swanson and Boyer contributed \$500 each to incorporate Genentech on April 7, 1976 (Swanson, 2001). As the CEO, Swanson's first order of business was getting some funding to set up contracts with the University of California, the City of Hope, and Caltech that would allow Riggs and Itakura to initiate the research. Kleiner Perkins would initially invest \$100,000, as agreed, for the completion of the legal work with the universities. With infusions of additional capital from Kleiner Perkins and other private-equity and institutional investors, the total outside capital committed had reached around \$1 million by the time the somatostatin experiment was initiated in February 1977 (Hughes, 2011). By that August the first human growth hormone, Somatostatin, had been cloned.

At the time, this success was certainly considered as a major scientific achievement. However, there was an even more important implication of this achievement: The visibility that the event brought to Genentech, and to biotechnology in general, was invaluable. Even as an article was pending for publication in *Science* that was to share the study results with the scientific community, , the president of the National Academy of Sciences, Dr. Philip Handler, had announced the results during his testimony before a Senate subcommittee studying gene research in November 1977 (Schmeck, 1984). Some additional endorsements from prominent figures in the scientific community followed Handler in praising the accomplishment, and these high-level endorsements would lift up the public image of genetic engineering, which at the time was unknown to most.

In the years following the Somatostatin success, Swanson was busy raising additional money to hire new technical staff and start bringing in some revenues from licensing and

royalties. To clone the first human insulin was the top item to the agenda. A third round of fundraising was completed, new contracts were prepared, and a team was assembled to start cloning human insulin. After its completion in August 1978, Swanson signed a licensing agreement with Eli Lilly for the commercialization of recombinant insulin. Genentech followed a similar model for funding R&D and operations, and a revenue model for the commercialization of the next two products that the company worked on, in 1978 and 1979: human growth hormone (HGH) for Swedish Kabi and interferon-alfa for Roche.

Only a few years after its incorporation, Genentech managed to develop multiple products with which a modest revenue stream was established. Although there was no shareholder pressure to achieve operational profitability in the early years of its existence, top management insisted that the company's income statement produce results around the break-even point, if not a very small amount of profit (Swanson, 2001). Given the heavy emphasis placed on gradually improving corporate financial strength starting from the break-even point, Genentech was developing engineering skills both in corporate finance and molecular genetics so that the company's R&D operations would be adequately funded without risking the integrity of shareholder equity and organizational productivity.

Swanson hired his college roommate, Fred Middleton, as the company's first Chief Financial Officer. Middleton and Swanson had both attended classes in chemistry before pursuing a graduate education in business at MIT's Sloan School of Management, although Middleton had gone on to complete his graduate education at Harvard Business School. They both had spent some time in the consulting field before switching to finance. The infusion of education both in engineering and finance at Sloan must have been the source of inspiration for engineering tools to address the corporate finance needs. Since the day it was incorporated, Genentech was envisioned as becoming a Fully Integrated Pharmaceutical Company (FIPCO) at some point in the near future. This vision was explicitly spelled out in the company's early business plans as first drafted by Middleton in 1979 (Middleton, 2002; Swanson, 2001). Fiscal responsibility was to be at the core of the financial operation, which was designed to achieve steady growth. Any income generated was to be plowed back into funding product innovation.

The first genes that Genentech cloned were relatively easy targets. The first major product, human insulin, was chosen deliberately because the molecular structure of insulin was already known to scientists and a major market for it already existed: A recurring treatment for diabetes, insulin had the potential to provide Genentech with a major revenue stream (Swanson, 2001). Since the safety and efficacy of conventional insulin had already been established, getting the FDA approval for a recombinant version was not expected to be too difficult; at least that was what Boyer and Swanson had originally anticipated. By contracting out the work to be completed externally, Genentech could pursue product innovation without major upfront capital expenditures or investment in full-time staff.

The lean operation model would not have been sufficient for a company that aspired to become a FIPCO. After the insulin and growth hormone project, Genentech had to hire some full-time scientists to complete certain tasks in-house. These tasks gradually became the company's core competence in winning contracts with big pharma and spinning out projects to form joint ventures. After the insulin project was completed in 1978, management decided to pursue multiple products simultaneously, which ultimately required increases in the size of the workforce. As the organization grew exponentially in the first years of its operations, the demand for new sources of finance increased significantly (Middleton, 2002).

One way of generating new revenues would be through signing contracts to out-license products. In return, the company could receive some upfront payments that would be followed by additional milestone-based payments plus royalties down the line. Additionally, Genentech could engage in what Swanson and Middleton coined *Pay-As-You-Go* (PAYG), a product development partnership plan stipulating a reasonable up-front payment with further payment required only if pre-defined milestones were achieved (Middleton, 2002), which they devised to appeal to the leadership at big pharma companies.

There were couple of important risks inherent in the model. First, Genentech would still need to find new sources of working capital sufficient to maintaining operations between milestone payments. Second, meeting such milestones could create pressures on the workforce as well as the management given that making the payroll payments would depend on the receivables based on the upcoming milestone payments. Third, as far as the products being cutting-edge, Genentech would have to rely on marketing partners for the successful translation of innovation into economic growth. After all, the size of future royalty-based revenue streams would depend on the sales performance of the marketing partner. And finally, such relations could be ill-pursued by the other party, which had occurred during a partnership deal with French Mérieux in which the development process for hepatitis vaccine was deliberately slowed so that their colleagues at Pasteur Institute could launch their version and license it to Mérieux (Swanson, 2001; Kiley, 2002).

Swanson was aware of the fact that PAYG wasn't the right path for Genentech to take if it was to become a FIPCO, given that the products being considered for out-licensing were major market products. If they had been commercialized and marketed by Genentech itself, then those products could quickly have placed the company on the path to becoming a FIPCO. However, Genentech had neither the resources to afford the costly clinical trials nor the sales and marketing workforce to launch a major product effectively. Therefore, PAYG was suitable temporarily, while new product opportunities in rare diseases were being pursued for the purposes of forward-vertical integration and developing capabilities in product commercialization.

Given how little value Genentech captured from its deal granting Eli Lilly an exclusive license for the production and marketing of insulin, management decided to pursue the idea of breaking up the market and negotiating separate licensing deals with multiple partners. Because the demand for recombinant products increased significantly after the successful cloning of human insulin, Genentech's management decided to negotiate multiple R&D contracts for the same product so that the product license for each of the major markets -- North America, Europe, and Japan, to name a few -- could be sold separately.

Pursuing the strategy of selling a product "three times" allowed Genentech to capture greater value from its innovative new therapies, since negotiating separate deals entailed no cost increases. (Middleton, 2002; Swanson, 2001). If Genentech could only manage to finance the costly clinical trials, then the company would have the upper hand to negotiate better licensing deals, and better yet, market its own products in North America by building its own sales and marketing workforce (Middleton, 2002).

In the meantime, Tom Perkins and some other shareholders had been seeking ways to liquidate their equity in Genentech. Hoping they could cash in on its success with insulin, some Genentech shareholders approached Eli Lilly first and Johnson & Johnson next in an attempt to interest them in acquiring the company, but both declined their offer to sell at around \$80 million (Perkins, 2002). Unable to attract buyers to take Genentech over, these shareholders decided on an IPO as the best route to an exit. Perkins pressured Swanson for some time to look into the option of doing an expeditious IPO (Perkins, 2002).

Although skeptical at first, Swanson gave the green light for an investment banker to file the necessary paperwork with the SEC. Swanson (1997) later recalled that the reason he changed his mind was that he wanted to beat Cetus in the race to become the first biotech company to go public. The Supreme Court had decided on whether patents were to be granted on genetically modified organisms in the case of *Diamond v. Chakrabarty*, a few months before Genentech offered its stock on the New York Stock Exchange (NYSE) as the first biotech company to be traded in a major market.

Genentech's IPO, held on October 14, 1980, stirred a great frenzy among investors, and Genentech's shares rose to \$88 from the opening price of \$35 within moments of the start of trading in the stock. Aspiring to become a FIPCO in the near future, Genentech had become the first PLIPO in 1980. The irony of the positive market reaction to a product-less biotech IPO is captured in the explanation given by Middleton, Genentech's first CEO, of speculative markets' role in creating substantial financial returns for those who had made a leap of faith to work for a highly risky business venture:

I looked at all this [replacement of preferred stocks with common stocks] and tried to figure out a way of creating this incentive [a big bump-up in the value of stock at the time of an IPO] for new employees and management in a company that is already public. Companies continue to be risky. They only difference at Genentech

was that we used to be a private company without products and now we're a public company without products. [laughter] Is the risk really that much less to an employee coming in?

(Middleton 2002, p. 59)

Not anticipating such high demand for Genentech's stock, Swanson and Middleton had decided to sell only one million shares (up-to one percent oversubscription) to generate \$38 million. Money raised through the IPO would be used for building a production facility for growth hormone and tissue plasminogen activator -tPA- (Activase), a recombinant protein used for dissolving blood clots (Middleton, 2002).

Even with the financing plans for pre-clinical research and a production site in effect, the company was in need of devising a plan for financing clinical trials for its products. Going after two goals, targeting an orphan indication for the fast launch of products in small markets and being able to finance the clinical trials to launch its own products, Middleton devised a new method, the R&D partnership financing (RDPF) program. This highly complex financing method, previously used among high-technology companies in the semiconductor industry (Middleton, 2000), involved establishing R&D investment funds to function similarly to venture capital funds. Under the scheme, Genentech would establish a new subsidiary as fund manager and start raising capital for a new fund to finance the clinical trials for product candidate, let's say drug X, after which the CEO would go out to raise funds as typical venture capitalists do.

Taxpayers in high-income brackets were usually attracted to such funds as tax shelters, and some of Genentech's shareholders, including Perkins, had invested in them at some point (Middleton, 2002). An RDPF fund typically offered a royalty payment of anywhere from five to seven percent over a period 12 to 15 years in addition to the R&D tax benefit based on the initial amount invested (Middleton, 2002). For the riskier clinical programs, a fund would offer the option of receiving 1,500 shares in return for the investment instead of royalty payments. In certain instances, the stock price went up anywhere from four to five times and the investors decided to exercise their options (Middleton, 2002).

The cost of clinical trials for the new-generation Genentech products such as tPA, a new version of growth hormone, and interferon-gamma, were all covered by the funds generated through RDPF until 1986 (Middleton, 2002). What made RDPF appealing to investors was the incentive available under the tax law, which in the early 1980s allowed the companies to pass along a tax benefit to their investors: A portion of the R&D expense that the company accrued, its size dependent on the income-tax bracket of the investor in question, could be claimed as a deduction dollar for dollar against the profit generated.

Such investment tools had been popular among high-income investors seeking tax shelters until the removal of these incentives with the enactment of the Tax Reform Act of 1986. Funding R&D through such funds appealed to Genentech shareholders because it allowed

costly clinical trials to be financed without diluting shareholder equity and diminishing value. In fact, shareholder equity grew along with the economic value of intangible assets as the products progressed through clinical trials.

Management had been considering ways to start building sales and marketing capabilities by amending the R&D partnership on HGH with Kabi to launch this product in the US market. An opportunity emerged as the company discovered a new therapeutic application that had shown greater commercial prospect that the treatment of a pituitary dwarf (Swanson, 2001; Middleton, 2002). HGH (Protropin) could be used in the treatment of a condition called constitutionally delayed short stature (CDSS), a temporary delay in skeletal growth, and initial projections indicated that a US marketing campaign could be successful simply because there were around 500 US pediatric endocrinologists treating CDSS in young children. Because these specialists were concentrated in certain medical centers, the product's marketing could be handled by a small team (Swanson, 2001; Middleton, 2002).

The company considered a similar marketing strategy for the marketing of tPA among the medical experts who treated stroke patients. The market for tPA appeared to be structured similarly to that for Protropin in that a relatively small population of cardiologists clustered around certain medical centers in the US, to which the company could reach out directly through a small sales and marketing operation. Despite the relatively small size of this market, the product was a potential blockbuster, considering that it was priced at over \$2,000 in the late 1980s and was alone in the market, with no real competitor expected to come in given the difficulty of matching Genentech's high quality (Pollack, 1990; Goeddel, 2003).

During the 1980s Genentech pursued various product-development initiatives through in-house research or joint ventures. Innovation efforts were sustained through a period in which raising large amounts of capital was not an easy matter. After the changes in the R&D tax credits, raising capital through RDPF funds was no longer an option. A follow-on stock offering would not be feasible in the market conditions of the late 1980s. As the size of Genentech's operations and workforce grew, so did its operating costs. And sales of tPA, the company's flagship product, had failed to meet market expectations in the late 1980s due to its high price tag (Pollack, 1990).

For a hands-on manager such as Swanson, managing Genentech's affairs ultimately became a difficult matter as disappointment with share price, innovation productivity, and sales performance grew. As a response to declining operational performance, Perkins, the chairman of the Genentech's board, and Swanson, its CEO, decided to recruit a seasoned executive to help with management. A former CEO of Abbott, Kirk Raab, was chosen as the right candidate to support Swanson in operational affairs (Perkins, 2002).

The decline of its stock price was especially troubling to the company, given that it had used stock as a currency when it was short of cash. Aside from the collateral function of raising funds to finance clinical trials, stock served as a speculative currency to attract and retain some of the country's most talented scientists in molecular biology, who were in short supply in the late 1970s and early 1980s. Middleton (2002) credits himself above all for the innovative use of junior common stock to manage workforce and organization-wide motivational alignment effectively.

Highly-qualified candidates, who are most likely to have stable employment at a university or big pharma, can be attracted to work for a start-up only by allowing them to purchase founders' stock, a type of stock issued to the company's founders when it is formed, at a price significantly below the price of its common stock. Once the start-up company goes public, those with founders' shares have an incentive to remain with the company, since the value of the stock is likely to appreciate (Middleton, 2002). If it does not, however, it will be easy to sell it on the stock market.

The real challenge for Genentech was to find a way to manage the price risk for the stock following the IPO event. Because the PLIPO status remains in the post-IPO period, the stock price may be volatile at times, with sharp moves occurring on negative news, whether or not it involves the company. These risk factors associated with a PLIPO such as Genentech could deter top candidates from taking jobs at PLIPOs, given that another early-stage start-up would always come along, and it would offer founder's stock with a great chance to generate a higher return, especially at the time of the IPO. By offering junior common stock (also called "earnings-convertible" or "restricted" stock) to employees at discounted rates, calculated at any given time using a probabilistic method, Genentech addressed a significant business risk associated with the increasing flow of labor along with the number of new start-ups that were entering the competition (Swanson, 2001; Middleton, 2002).

As seen in the case of Genentech, the very first biotech PLIPO, a stock can serve various functions and create different classes of shareholders with different sub-identities -- employee-shareholder, scientist-shareholder, VC-shareholder, founder-shareholder, etc. -- within the organization. As long as achieving a scientific goal (for example, being the first company to clone a gene, or bringing a recombinant product to market that would cure a disease for which no therapies had existed) remained the primary motivation of most employees, stock-price performance did not do much damage to organizational integration at Genentech.

But once the main motivator was replaced by, or came to be represented in, stock-based performance indicators like earnings per share or shareholder value, meeting company goals was not as effective a driver for some competitive scientist-shareholders as it had been when those goals had been scientific. Excessive dilution of stock and plummeting prices also made it difficult for Genentech to raise more capital through equity sales

(Middleton, 2002). Despite its strong pipeline, the company failed to sustain its financial commitment to maintaining its learning efforts. Its share-price decline of the late 1980s was seen as a foregone conclusion, the result of a variety of strategic miscalculations, and the downward trend was considered irreversible by many observers.

The new managerial perspective developed during these crises only increased the division among different classes of shareholders, with many board members positioned in the Raab camp while some core employees rallied around Swanson. This division would ultimately contribute to further decline in the clarity of corporate vision. Exercising strategic control over resource allocation is highly difficult if the leadership cannot motivate enough people to commit to complying with strategic objectives and engaging in the action plans within an organization that has disintegrated into too many shareholder choirs singing different tunes.

6.2 Organizational Integration

...It is good to have a rich uncle in America. Genentech had a rich uncle in Switzerland.

(Steve Krognes, Head of mergers and acquisitions, Roche Holding AG⁴⁹)

At the time Genentech was underperforming financially, the company still had a strong product pipeline. It was disappointing to let the very strong pipeline of innovative products go, but the board members knew that the current state of corporate finances and the stock performance could not be fixed without outside help. The company had to find a “rich uncle” to help to push the pipeline out to explore the opportunities in global markets (Baldwin et al., 2010). During an interview in 2001, Tom Perkins shared a story that illustrates the shareholders’ frustration with Genentech’s market performance and how the company was derailed under the close watch of David Packard, at the time Chairman of Hewlett Packard and a member of Genentech’s board:

I remember the meeting we had with the shareholders where we presented all of this [disappointing market performance, the report on which required the board’s approval for the company’s sale to Roche]. One lady stood up and said, "I have a question only for David Packard [who was perceived to be a mentor for both Perkins and Swanson]. How could you permit this to happen, Mr. Packard? It's like leaving New York on a train to San Francisco, and you're making us get off in Denver. How could you permit this?" His answer was, basically, "I'm doing what I was told." [laughter] He didn't use those words, of course. But she was so disappointed. We all were. It wasn't a happy thing. But we all felt that we had to do it [approve the acquisition deal]. The loss of independence. It's still an independent

⁴⁹ This statement of Krognes summarizes the nature of relationship between Roche and Genentech during the period followed by acquisition, as cited in Baldwin et al. (2010).

company, more or less. It's still a public company, at least. But it's no longer the baby Jesus.

Roche had been aware of the scale of financialization that had taken place within a once-innovative organization that had managed valuable assets but had run out of gas before the next pit stop. It was a general consensus among the people at Genentech that Roche was the most appropriate candidate to acquire its valuable pipeline (Goeddel, 2003; Perkins, 2002).

On March 2, 2010, a year after the acquisition, Levinson joined Roche's board of directors, serving on Remuneration Committee along with André Hoffmann. Levinson left Roche in 2014, one year after being hired as CEO of Calico, Google's new biotechnology research initiative on aging. During his three years on Roche's board, Levinson had overseen the process of consolidating the company's global research operations by turning Genentech into one of three Roche R&D centers. Levinson was not the only former Genentech executive that remained within Roche to help with the transition. More Genentech expatriates had risen to the upper echelons of management in Basel to keep in sync pRED and gRED operations that were running parallel to each other. Richard Scheller, a former senior VP and chief research officer of Genentech, became head of the newly created gRED division; Ian Clark became CEO of Genentech and head of North American Commercial Operations for Roche; and Hal Barron became the head of global product development and chief medical officer of Roche's Pharma Division.

Other US-trained scientists and managers Roche promoted to executive positions in 2010 were Pascal Soriot, who had been COO of [Sanofi]Aventis US until 2004 and served briefly as interim CEO of Genentech during the acquisition in 2009, while at the same time serving as a member of Roche's Corporate Executive Committee (CEC);, Dan Zabrowski, a former Syntex director of drug regulatory affairs, who became head of Roche Partnering, which oversaw the company's relations with more than 150 partners globally; and Daniel O'Day, COO of Roche's Diagnostics Division. These and other key managerial figures enabled Basel to adopt Genentech's uniquely American corporate culture.

In the early period of the merger process these influential figures played a critical role in designing a new organizational strategy for Roche that enabled Genentech to preserve its uniquely "West Coast" culture. Sustaining that culture allowed Genentech to recruit and retain productive researchers and to maintain its organizational productivity in the years thereafter. Today, three key positions in Roche's CEC are occupied by American expatriates: O'Day, now CEO of Roche's Pharmaceutical Division; Christina A. Wilbur, head of human resources at Roche Group; Michael D. Varney, head of gRED; and John C. Reed, head of pRED. All currently hold leadership positions and are involved in designing science, technology, and human-resource strategies at Roche Group in Basel (Roche Historical Archive, n.d.).

Despite gloomy predictions, the partners in the Basel-San Francisco marriage appeared to have a healthy relationship immediately after the merger. The openness of top management in Basel, which comprised young and agile Swiss-American executives, played a significant role in Roche's building a productive relationship with a company whose style clashed with Swiss business culture. A rather humorous incident (Doherty & Waters, 2010) illustrates how keen Roche was to build and sustain a productive relationship with Genentech at the highest level. At an investor event in New York that took place in early 2010, an observant analyst from Morgan Stanley oddly asked Roche CEO Schwan whether "the Genentech team "[hid]" the ties of the Roche executives," given that the analyst had "never seen them without suits and ties before." As it turned out, Scheller, the former Genentech CRO who had become the head of gRED, did not wear a tie in Basel, as ties had been considered a symbol of corporate culture despised by the Genentech scientists in California (Doherty & Waters, 2010). Schwan and other executives then decided to ditch their ties in an attempt to ensure that Genentech and Roche didn't appear out of sync (Doherty & Waters, 2010).

6.2.1 Dealing with New Economy biotech: Integrating Genentech into Roche

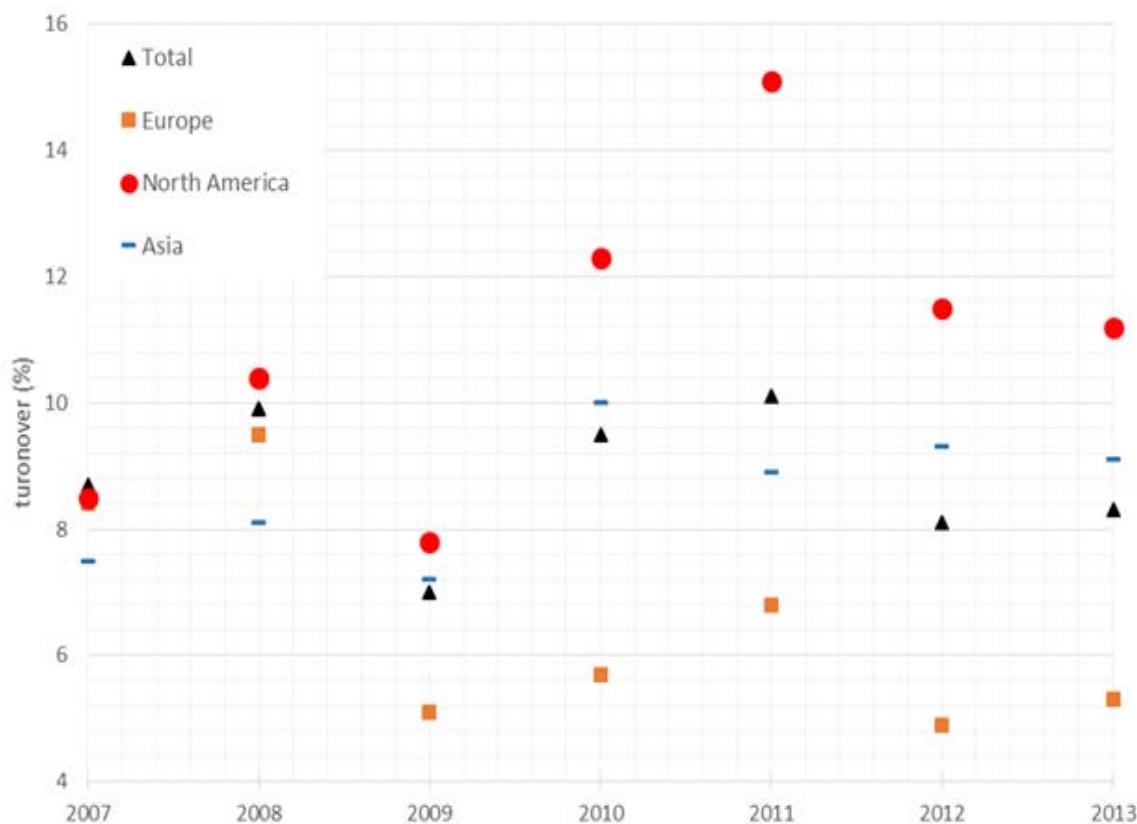
The critics of the merger predicted the disappearance of the entrepreneurial "West Coast" culture that had driven Genentech's organizational productivity – and of the productivity along with it -- as Roche forced Genentech to assimilate to its Swiss-style, big pharma culture. Based on the evidence, however, one can plausibly infer that the opposite took place, or at least that a midpoint was found, as the relationship ended up a symbiotic one. The composition of executive committee at Roche has been changing fast since the merger, as the company has invited more executives familiar with a contemporary, American-style corporate governance perspective and business model to join its executive team. Additionally, the two organizations have become more interdependent to sustain productivity -- although, as time has gone by, Roche has become more reliant on the productivity achieved in San Francisco to sustain its growth. As a consequence of this ongoing power shift, Roche's corporate strategies have come to be geared more toward preserving the West Coast-style corporate culture, to the point that Roche has begun to resemble a typical New Economy business enterprise.

Aside from the scale of the transaction, the timing of the acquisition had serious effects on the company's short-term financials. It had taken major effort for Roche to gather up \$41 billion in cash through internal and external sources and complete the merger in the midst of the 2008 Great Recession. In the years following the merger, Roche implemented major austerity measures to improve the company's cash flow and retained earnings, which allowed it to service the debt accrued during the expansion of its capital expenditure, as shown in Figure 36.

As Roche took extensive precautions to prevent a mass exodus from Genentech immediately after the merger, the company also implemented a major organizational

overhaul in the North American operations. On November 17, 2010, Roche announced a restructuring program called “Operational Excellence” through which the company anticipated saving CHF 1.8 billion savings in 2011 and an additional CHF 2.4 billion in 2012. Along with plant closures and major layoffs employment turnover at Roche had begun to increase in years to follow.

Figure 36: Changes in labor turnover by region at Roche during the post-merger restructuring period, 2007-2013



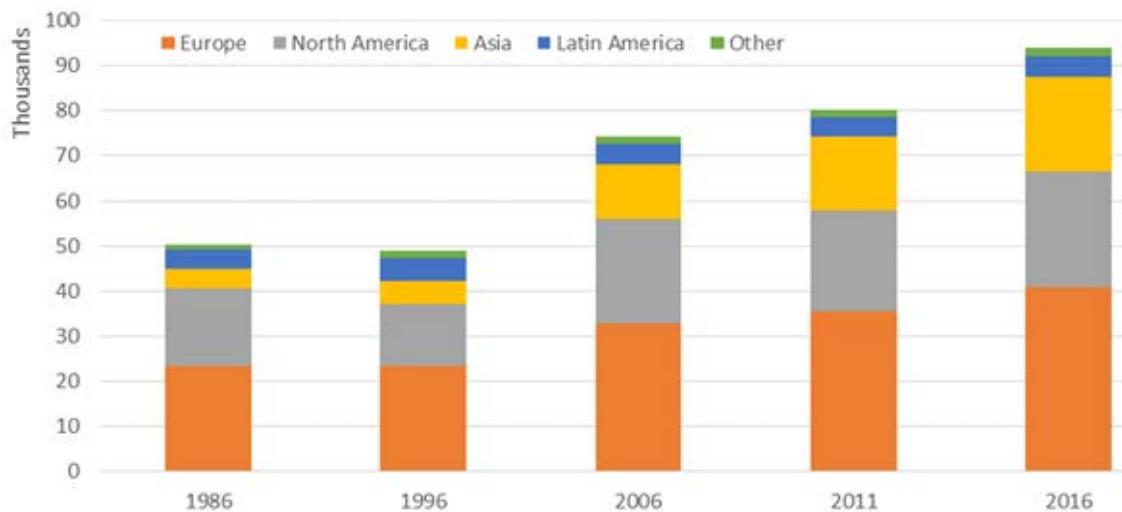
Source: Own illustration based on data from company annual reports

Figure 37 shows that the company’s worldwide labor turnover rate increased from 7.8 percent in 2010 to 12.3 percent in 2011 before peaking in 2012, as its labor turnover rate in North America went as high as 15.1 percent of the total workforce. Nearly 51 percent of the departures had been initiated by employees, compared with a rate of voluntary departure for the overall US economy of 9.2 percent on average between 2010 and 2011. According to Figure 37, the impact of the restructuring efforts on employment had been greater in North America than in other regions. While the turnover rate in North America (marked by red circles in Figure 37) closely trailed the overall turnover rate (marked by black triangles) until 2009, that gap grew as high as five percent after the Operational Excellence program took effect in 2010.

In 2010, Roche decided to move its US headquarters from Nutley, New Jersey, to Genentech’s headquarters in San Francisco, California, marking the initial phase of an

extensive restructuring plan. Roche had already moved some functions of its sales, marketing, and R&D operations from Nutley to Palo Alto, following the acquisition of Syntex in 1994 (Todd & Jones, 2012). As much as it was an operational one, the decision to move its headquarters from the historic “Pharm Belt⁵⁰” region of New Jersey to the “birthplace of biotechnology” in South San Francisco, California, had been a symbolic one.

Figure 37: Changes in employment at Roche by region, 1986-2016



Source: Own illustration based on data from company annual reports

In 2009, prior to moving the headquarters out of the “Pharm Belt,” Genentech had announced its decision to withdraw from the pharma trade group, Pharmaceutical Research and Manufacturers of America (PhRMA), and to join the biotech trade group, Biotechnology Innovation Organization (BIO). This decision had been another symbolic action meant to realign the company’s identity with its new strategic vision of aspiring to remain the largest biotechnology company in the world (Todd, 2009). As the post-merger restructuring programs continued, Roche decided, in 2012, to close the Nutley site permanently. The Nutley site was a historical landmark for the company; as a research-driven pharmaceutical company, Roche had put down roots and emerged in this location. The decision to move meant leaving a legacy in chemistry and pharmaceuticals behind to embark on a new learning experience in the still-fledgling field of biotechnology, which has yet to be fully explored commercially.

Roche’s organizational restructuring involved drastic measures that went beyond site closures. Like the site erected during the golden age of organic chemistry, the jobs created at that time were being retired during Roche’s complete transition into biotechnology. As Figure 37 shows, the largest labor turnover of the post-merger restructuring campaign was seen in North America, where Roche had already reduced its workforce from 23,200 employees in 2006 to 22,400 in 2011. Although the decline in actual numbers may seem

⁵⁰ See Fried 1998, p. 243

immaterial, such a decline can be considered significant when it is measured against the region's contribution to Roche's growing revenue performance.

As the proportion of Roche's revenues generated in North America went from 40 percent in 2006 to 44 percent in 2016, North America's share of Roche's employment went from 31.3 percent in 2006 to 27.1 in 2016. The post-merger restructuring period had coincided with a decline in the European drug market. Due to severe austerity measures taken by governments in Europe to get their rising national-accounts deficits under control, drug prices were under tremendous pressure. During this period Roche's European revenues were 27 percent of its revenues worldwide in 2016, down from 37 percent in 2006, even though Europe's share of Roche's worldwide employment remained relatively unchanged at around the 44 percent level. The only growing economies at the time, those in Asia, were driving growth in employment and revenue, the former going from 16.3 percent in 2006 to 22.6 percent in 2016, the latter from 15 percent in 2006 21 percent in a decade later.

6.2.2 Changing structure of the executive pay at Roche?

The implications of the cultural differences for the organization's compensation strategy have been striking. Genentech's entrepreneurial culture had been mainly driven by the company's stock-based employee incentive scheme, which is a common compensation mode used by New Economy companies to recruit and retain skilled high-tech workers. As explained earlier, Genentech was among the first companies to adopt and implement this compensation model, which was originally employed by the first-generation computer and electronics companies in the region popularly known as Silicon Valley.

Many other biotechnology start-ups had, in the late 1970s and 1980s, begun to imitate this new business model, which, in the field of pharmaceutical, was first employed by Genentech. In the last decades of the 20th century, stock options had been heavily used by biotechnology start-ups to lure productive scientists and researchers away from stable employment at universities or large industrial research laboratories and into highly volatile science-based business ventures. As labor mobility has increased within the biopharmaceutical industry in the 21st century, companies' stock option programs have become more lavish, such that potential gains realized through exercising stock options have become the primary motivator for start-ups wishing to boost their workforce and research productivity. One caveat on this strategy is that it can sustain its utility for a company so long as its stock prices keep rising. Part of why Roche found itself with the unique opportunity of acquiring a productive company such as Genentech at an arguably bargain price is that Genentech's stock price had stopped increasing in the late 1980s.

By selling the majority stake to Roche in 1990, Genentech had secured the financial stability required at the time to support innovation efforts within the organization. This stability paved the way to the productivity boost of the 1990s and 2000s that saw the

company's market capital go from \$2.6 billion in 1990 to approximately \$100 billion in 2009. When Roche acquired Genentech in 2009, Roche's market capitalization was nearly 40 percent greater than Genentech's⁵¹ --but the annual compensation of Genentech's CEO, Levinson, was 2.5 times that of Schwan, the CEO of Roche Group and the highest paid employee at Roche in 2008.

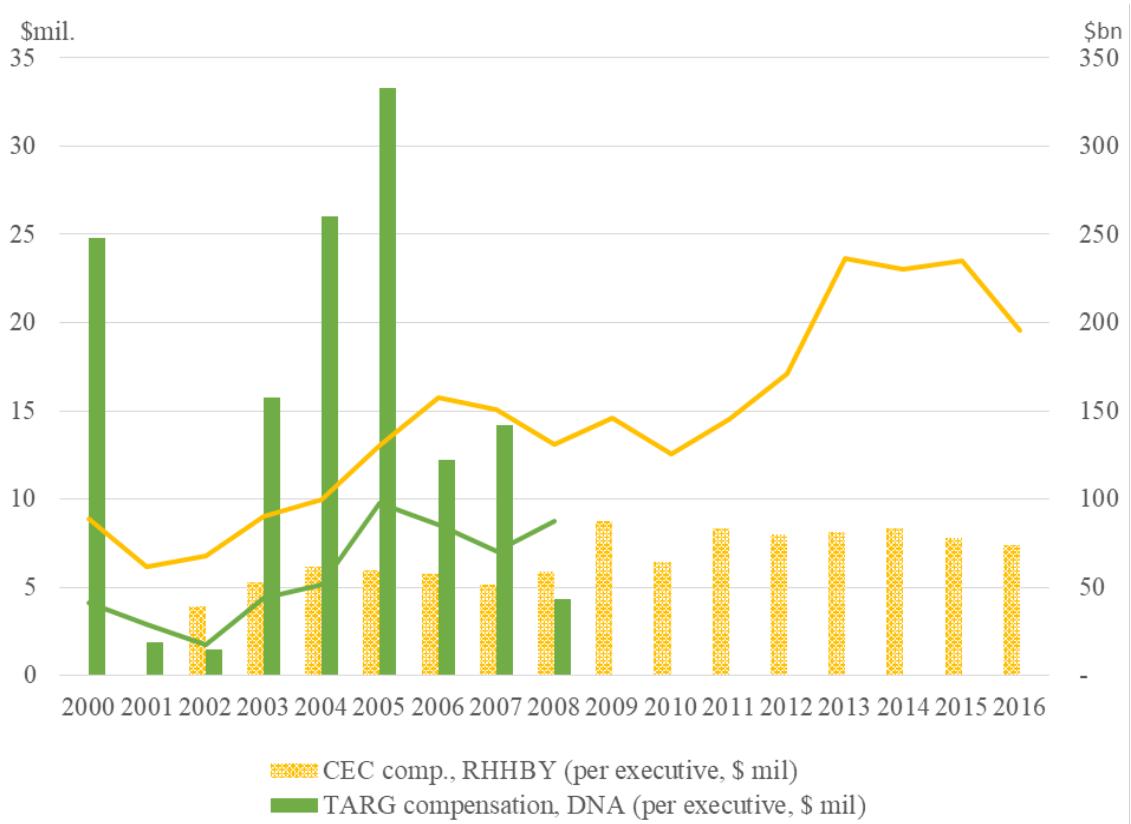
Nearly two decades later, in 2009, when Roche acquired the remaining outstanding shares of Genentech, Roche's market capitalization was nearly 40 percent greater than Genentech's. But, in line with the financialization of US corporation, the annual compensation of Genentech's CEO, Levinson, was 2.5 times that of Schwan, the CEO of Roche Group and the highest paid employee at Roche in 2008. Behind this disparity were the generous stock-option awards that the US executives were receiving. In the decade leading up to the acquisition, Genentech had doubled its market capitalization as a result of the productivity growth experienced under Levinson, whose total compensation, including gains from exercising options, was approximately \$260 million for the period.

Levinson received \$8.74 million as retention bonus after Roche acquired Genentech in 2008. In the last year prior to acquisition, Levinson's total actual realized gains compensation was \$23.8 million in 2007. Cash-based and non-equity incentives accounted for only 17.4 percent of the total actual realized gains (TARG) compensation of Levinson in 2007. Figure 38 shows a similar trend for other top Genentech executives. Between 2000 and 2005 the compensation of the top five Genentech executives skyrocketed along with the company's market capitalization, but it then began to decline along with the stock price. Average actual realized gains of top 5 Genentech executives went up to as high as \$33.3 million in 2005, which was more than five times larger than average compensation of top 5 Roche executives for the same year.

As a newly appointed CEO, Schwan received annual remuneration with social security contributions of CHF 8.3 million in 2008, or approximately \$7.7 million. Salary and cash-based bonus payments accounted for 66 percent of Schwan's annual compensation, with another 27 percent coming as stock-settled stock appreciation rights (S-SAR), an additional benefit determined by the appreciation of the company's non-voting share price. Although Schwan's compensation had, by 2016, increased by 48 percent (60 percent) to CHF 12.3 million (\$12.4 million), it still came nowhere close to the 2016 compensation of Merck & Co. Chairman and CEO Kenneth Frazier, which came in at \$21.8 million, plus \$17.6 million in gains realized through exercising stock awards and options.

⁵¹ Arthur D. Levinson annual compensation Levinson \$18,212; Severin Schwan \$7,425 (CHF8.019 million). Roche As of December 31, 2008 Roche's market capitalization was CHF140.7 around the time when Roche paid \$95 per share to take Genentech private. 1.05 billion Genentech shares at \$95 per share put nearly \$99.8 billion market value.

Figure 38: Changes in market capitalization and average compensation of top executives at Roche vs Genentech, 2000-2016



CEC comp., RHHBY (\$ mil.): Roche corporate executive committee average compensation, in million USD; TARG compensation, DNA (\$ mil.): Total actual realized gains of top 5 Genentech executive, per executive, in million USD; MarCap, RHHBY (\$ bn.): Roche market capitalization [as of December 31, 2016], in billion USD; MarCap, DNA (\$ bn.): Genentech market capitalization [as of December 31, 2016], in billion USD.

Source: Own illustration based on data from companies' annual reports [Form 20-F] and Genentech annual proxy statements [Schedule 14A]

The remuneration committee of the board, headed by André Hoffmann, began 15 years ago implementing major changes to the compensation and incentives programs for the members of the CEC. Starting in 2002 Roche introduced a performance share plan (PSP) determined by the changes in two factors: the company's stock-price performance and the total shareholder return (TSR) produced. Since its introduction in 2005, stock-settled stock appreciation rights (S-SAR) offer additional benefits based on the price appreciation of the company's non-voting shares. Also introduced in 2002 was a voluntary employee stock purchase plan (Roche Connect) that allows employees worldwide to purchase Roche non-voting equity securities (NES) at a discounted price.

Although it is no longer being offered, the restricted stock unit (RSU) is a form of equity-based individual award that would take three years to vest after it had been granted and that would be blocked for up to 10 years before it could be exercised. While PSP is available to only 42 key Roche executives around the globe, S-SAR and RSUs have been made

available to approximately 19,000 Roche employees worldwide. PSP replaced RSUs in 2016 and, together with S-SAR, were the metrics used for the company's long-term incentive (LTI) scheme for corporate executives. Since then, however, the price performance of NES and TSR have become the only determinants of LTI for top executives.

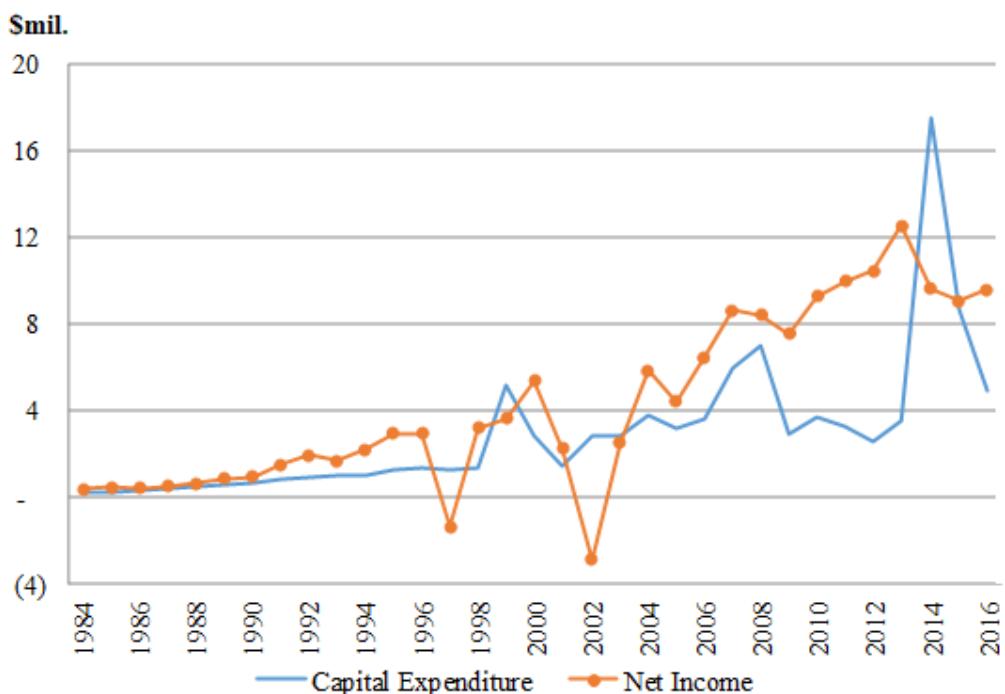
Figure 38 illustrates the results of changes implemented in Roche's compensation strategy for top executives and key managers. The compensations of CEC members have grown slowly but steadily since the new incentive programs were first implemented, between 2004 and 2005. With public pressure growing in Switzerland, companies have been required to take measures to close the pay gap between average employee and top executives. Swiss policy makers were working on new legislation to limit excessive executive pay, a policy initiative triggered by the excessive pay received at the time by the top executives at Novartis and major Swiss banks, Roche's shareholders backed the new compensation plans for executives and other top managers proposed by the board at the company's annual general meeting in 2013.

6.3 Financial Commitment

Considering Roche as more than merely being a "financial investment", the youngest members of the Hoffmann-Oeri clan has been eager to build the "intimate relation" to ensure that the family provides the company with the "long-term stability" the business of pharma needs especially at a time when the relationship between companies and their shareholders is becoming more transactional. Such an "intimate relation" the family has more or less maintained for nearly a century enabled the company to survive through various different catastrophic world events, industrial crisis, or turbulent times in the world markets periods. In fact, Roche is among the very few companies that have managed to maintain its traditions, corporate identity, and independent sprit by avoiding any major merger with another drug company at all cost.

As the case discusses extensively, the strategic clarity provided by the founder and his descendants provided greatly contributed into the company's success in keeping the integrity of the organization well intact. Long before the fledgling biotechnology disrupted the biopharmaceutical industry, Roche had sensed that the growing body of new knowledge would disrupt the ways in which innovative new therapies were discovered and developed in the US pharma. The management had established the Roche Institute for Molecular Biology (RIMB) in 1967 as part of the company's new market strategy, which mostly entailed broadening Roche's market perspective to pursue new avenues for growth in the 1960s by fast adopting highly robust drug discovery and development techniques emanated from the fast growing field of biology.

Figure 39: Roche's capital expenditure and net income, 1984-2016



Source: Own illustration based on data from company annual reports

Agility and patience are the two of many virtues the family offers to the managers of a global organization. Although the family has absolute power over the company's productive assets, the family allows the holders of the non-voting shares (Genussscheine) to monitor, and engage in, the decision-making process. The company "can't ignore short-term investor sentiment because it affects our [Roche's] cost of capital," said Hoffman in the same FT article. Unlike many other family-run companies, Roche manages to integrate a shareholder perspective into its corporate governance structure while keeping the company's long-term vision intact and immune to speculative attacks.

Figure 39 compares Roche's capital expenditure to the company's net income between 1984 and 2016. Roche's net income had been already on the rise in the early 1990s due to the addition of new products to the company's portfolio through both R&D and co-marketing arrangements with external partners. While Roche was engaged in basic research in emerging fields such as molecular biology, it was through acquisitions such as that of Syntex that enabled it to enter a number of interesting therapeutic areas, including analgesia, rheumatology, and transplant medicine.

As Figure 39 shows, Roche's net income began to grow faster in the mid-1990s than it had grown before the acquisition of Syntex in 1994. The loss Roche accrued in 1997 was due to special charges that stemmed from the acquisition of Corange, a German company incorporated in the Bahamas and the parent of medical diagnostics and devices companies Boehringer Mannheim and DePuy. After its acquisition of Genentech in 2009, Roche's

capital expenditures dropped precipitously due to the company's post-acquisition restructuring efforts, namely the Operational Excellence program announced in 2010.

The retained earnings has always been the company's main source capital to invest in productive resources. In the following excerpt taken from his autobiography Elmer Bobst explains why his wealth – that was already significantly higher than his peers in the industry at the time- could have been higher while serving as the head of Roche-Nutley if it wasn't for the company's strong urge to retain earnings:

One of the Basle company's so-called "secrets" is that it has always skimped on dividends, resulting in an enormous accumulation of capital within the company; so much in fact that Hoffman-La Roche is probably the only major company in the world today [in the early-1970s] that finances all of its capital needs out of its own resources, never from banks or public money markets...

(Bobst, 1973, p. 197)

Concerned over the dilution of stock, Roche has considered using retained earnings and debt issuance to finance the previous acquisitions as well as that of the recent acquisition of InterMune completed in 2014 for \$8.8 billion all in cash. Roche funded other major acquisitions, such as its \$5.3 billion purchase of Syntex Corporation in 1994, with the cash raised mainly through bridge loans. The company's ability to raise nearly \$700 million among U.S. investors in the early 1990s, considered one of the largest borrowings ever by a foreign company in the U.S., speaks for Roche's credibility (WSJ, 1993). Roche's longtime CFO and director Henri B. Meier has been credited for the effective use of financial markets to access cheap capital and finance innovation projects in careful ways that kept the "Hoffmann family's controlling stake undiluted" and intact (WSJ, 1993).

A long-term oriented vision, combined with a proven track record in sustainable growth, has made Roche attractive among long-term investors. Thanks to its reliability in generating profits regardless of conditions in the drug market, Roche has never had trouble raising cash in the capital markets to finance its growth initiatives. Even in the midst of the financial turmoil accompanying the collapse of the global financial system in late 2008 and early 2009, Roche managed to raise the cash to fund the \$46.8 billion deal that made Genentech its wholly owned subsidiary. The acquisition was funded by the company's retained earnings, as well as by capital raised in the bond market (Baldwin et al., 2010). As Roche took extensive precautions to prevent a mass exodus from Genentech immediately after the merger, the company also implemented a major organizational overhaul in the North American operations. On November 17, 2010, Roche announced a restructuring program called "Operational Excellence" through which the company anticipated saving CHF 1.8 billion savings in 2011 and an additional CHF 2.4 billion in 2012.

6.3.1 Genentech: Roche's most productive investment

As part of its corporate strategy of expanding into the biotechnology field, Roche announced its decision to acquire majority stakes at Genentech on February 2, 1990. After gaining Genentech shareholders' authorization for the sale to Roche of the company's stock in a vote held on June 8, 1990, and the Federal Trade Commission's (FTC) consent for the acquisition on August 31, 1990, Roche completed its purchase of 60 percent of Genentech shares for \$2.1 billion on September 7, 1990.

The total acquired shares comprised 50 percent of Genentech common stock purchased for \$1.5 billion, as well as an additional 10 percent equity interest granted in exchange for approximately \$490 million cash infused by Roche as a direct investment to fund various Genentech research programs. Roche had also offered \$36 cash and a new Genentech share listed on New York Stock Exchange for every two old Genentech shares. Through open-market purchases Roche subsequently increased its equity share in Genentech 65 percent (Genentech 1990). Under this merger agreement, signed in 1990, Roche also had the option to acquire Genentech's remaining 43 million shares (40 percent) by June 30, 1995, at a price ranging from \$38 to \$60.

Having spent \$5.3 billion to acquire Syntex Corporation of Palo Alto in 1994, Roche was unable to exercise the option and negotiated another deal to extend the option date. On October 25, 1995, Roche and Genentech entered into a new agreement (Amended Governance Agreement) extending the expiration date for the option until June 30, 1999. By doing so Roche had gained a four-year extension however the option price had gone up from \$60 per share to \$82.5 per share, due by June 1999. On June 14, 1999, Roche decided to exercise the option to buy the remaining 40 percent at the \$82.50 exercise price, and an Affiliation Agreement was signed the following month. After signing the Affiliation Agreement, Roche decided to sell the newly acquired shares on the open market.

The first open-market sale of stock took place on July 23, 1999, when Roche completed an IPO to sell 44 million Genentech shares at \$97 per share. The demand for Genentech stock was so high that the stock had gone up to \$132 before closing at \$127 per share at the end of the first trading day. Roche completed a secondary offering on October 26, 1999, selling an additional 40 million Genentech shares, which contributed to bringing Roche's ownership stake down to 66.1 percent by December 31, 1999. As the price of Genentech shares continued to rise in the early 2000s Roche decided to sell an additional 17.3 million shares, for which it realized approximately \$3 billion on March 29, 2000. By the end of 2000 Roche's equity stake had been reduced to 58.4 percent.

At the time of the stock offerings, Roche was facing takeover threats from a popular Swiss corporate raider, Martin Ebner, and later from Novartis, an old hometown rival that had acquired 32.7 percent of Roche's voting shares and was urging Roche shareholders to approve a merger. This maneuver had cleverly allowed Roche to exercise its option on Genentech stock and to generate nearly \$650 million in profit by selling on the open

market the shares thereby acquired. It had also alleviated the growing concerns of Genentech employees, who had anticipated a complete corporate takeover by a big pharma company that would have turned independent Genentech into a corporate subsidiary.

By allowing Genentech to continue floating its shares in the stock market, Roche had iterated its proposition to keep the life and business at Genentech as usual. The move had been strategic in the sense that significant value could have been lost if Roche had failed to preserve the culture at Genentech and retain the talent it had gathered. In fact, some the new shares issued had been used to retire some of the previous stock option programs or to make up to 13.7 million additional Genentech shares available for future purchase through existing programs, such as the 1991 employee stock option plan (ESOP) that extended through December 31, 2007.

Acting carefully to avoid any indication that they might be embarking on a corporate takeover, the executives at Roche in Basel declined to take a majority position on Genentech's board, appointing only two of the company's directors. Roche was first represented by Franz Humer, chairman of the board and CEO of Roche Group, and Jonathan K.C. Knowles, head of group research. Although careful to keep relations with Genentech at arm's length, the group leadership was keen to exercise some degree of strategic control over operations through (the Affiliation Agreement with Genentech, which provided that two members of Genentech's three-member Nominations Committee would be appointed by Roche. By doing so Genentech could determine the nominees for independent directors to protect the integrity of the Board. Having reserved the right through the Affiliation Agreement to seek proportional representation on the board, Roche decided to appoint an additional director to expand its representation on the Board in 2004.

Also based on the Agreement, Roche required Genentech to establish a stock repurchase program in order to avoid excessive dilution of Roche' holdings through Genentech's granting of additional shares through its employee stock option plans (ESOP). Under the program, Genentech would be authorized to repurchase up to 150 million of its own shares, or \$10 billion worth, if Roche's ownership stake in Genentech decreased by two percent of a predetermined minimum ownership ratio (55.7 percent) at any time through June 2009. As employees began to exercise granted options Genentech was authorized to repurchase stock on the open market to meet the obligations.

With the new affiliation arrangement, Roche and Genentech had also revised the licensing agreement on certain Genentech products, extending Roche's right to commercialize Genentech products from 2005 until 2015. One caveat on this arrangement was that the Affiliation Agreement was not applicable to all Genentech products. The financial stability provided through the affiliation with Roche allowed Genentech to develop innovative new therapies to the point that Genentech became a competitor in certain markets for specialty drugs both in the US and overseas. Genentech also began to negotiate deals for collaborative research and co-marketing with Roche's rivals in the drug market. Roche was

obliged to negotiate separate deals for those new therapies not covered by the licensing agreements, and, more important, Roche would have to negotiate a new licensing deal with Genentech once the licensing agreement then in effect came to an end. Negotiating a favorable deal with Genentech, now that it had restored its financial stability would certainly be a challenging affair for the executives in Basel if they waited until the licensing agreement's expiration in 2015.

Along with its sales revenues and net income, Genentech's cash reserves grew significantly as the company accrued cash over time through retaining earnings. Under the existing Affiliation Agreement Roche's access to Genentech's cash reserves was restricted: Genentech paid no dividends to Roche, or to any other shareholder for that matter, in order to avoid paying dividend tax. Buybacks were also limited to those needed to maintain Roche's majority stake, so there were no other cost-effective ways to distribute excess cash to Roche (Baldwin et al., 2010).

Hoping to avert the risks associated with allowing Genentech to maintain its operational independence through the affiliation arrangement, Roche executives, under new CEO Severin Schwan, decided in July 2008 to acquire all of the 43 million shares of Genentech that remained outstanding for \$89 per share. Genentech shareholders, having recognized Basel's intention to acquire the company's competitive portfolio and clinical candidates at a bargain price before the current licensing deal expired, declined Roche's offer immediately upon its presentation in August 2008.

The executives in Basel had to walk on a thin ice during the negotiations, wanting to acquire Genentech without destroying the latter's most valuable asset: its pool of talented scientists and entrepreneurial research leaders. Through a tender offer made directly to shareholders Roche could have acquired the remaining Genentech shares at a better price, but such a move would certainly have alienated the executives and other key employees at Genentech. Unless Roche was tough in negotiations, the cost of the acquisition would be astronomical: Genentech had come up with an offer of \$112 to \$115 per share to counter Roche's \$89-per-share offer price difference that could drive up the acquisition's cost by as much as \$27 billion. In September 2008, as the negotiations turned sour, Genentech's stock price dropped below the original offer price of \$89. By January 2009 Roche had adopted a more hostile tone in the negotiations and revised its bid downward to \$86.5 per share, reflecting the declining price of Genentech stock. By February 2009 Genentech shareholders had declined the offer, arguing that it significantly undervalued the company and its innovative clinical pipeline.

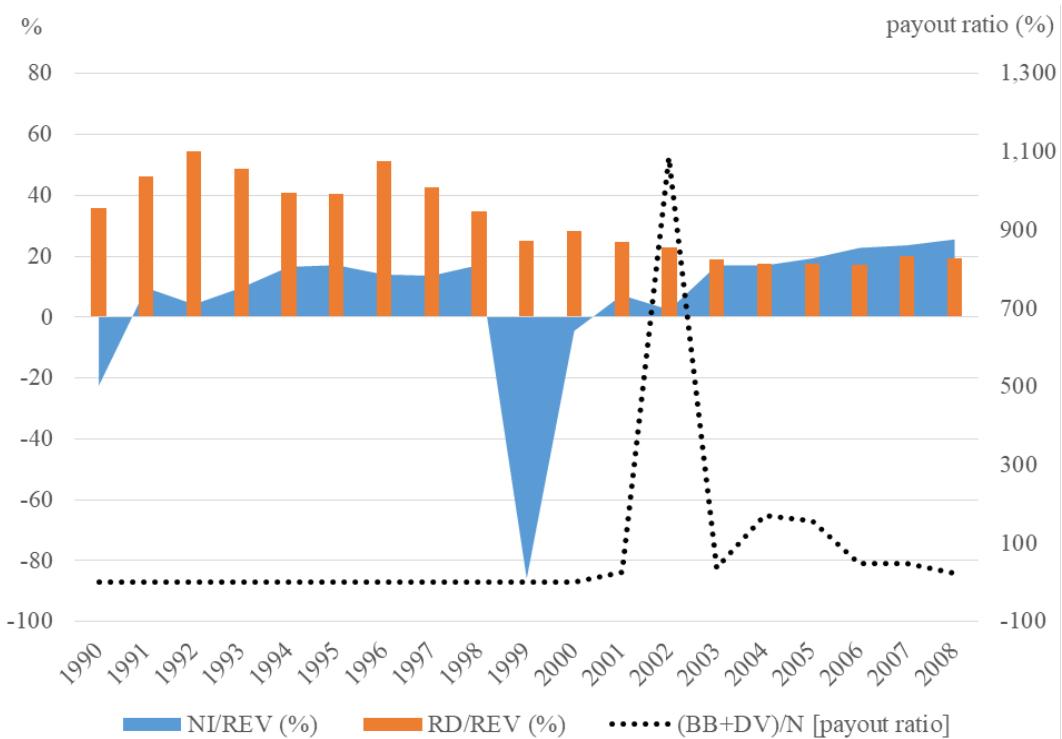
In conjunction with announcing the company's quarterly earnings in March 2009, Genentech issued a strong growth projection based on an increase in the sales of its blockbuster cancer therapy, Avastin, to as high as \$10 billion annually. This projection reflected further increases in the product's retail price, as well as positive results of ongoing clinical trials that would potentially open new therapeutic applications. Because

the positive results Genentech expected were to be released in April 2009, Roche quickly revised its offer price to \$95 on March 6, 2009. A day after the tender offer's expiration date, Roche announced the completion of its acquisition of Genentech for \$46.8 billion in cash, with the remaining 40 percent of Genentech shares to be purchased at \$95 per share on March 26, 2009.

6.3.2 A different kind of stock repurchases: maintaining strategic control of Genentech after the merger

As discussed earlier, Roche's contribution to restoring Genentech's financial stability had been critical, as it brought Genentech back from the brink of insolvency in the late-1990s and made of it a highly profitable business rich in cash. As figure 40 shows, aside from 1999, when it incurred a loss, Genentech remained profitable from the time Roche acquired a majority of its shares 1990 through 2008. During this entire time payouts to shareholders had been minimal; as mentioned above, it paid dividends neither to Roche nor to any other shareholder. In fact, Genentech had rarely made dividend payments or engaged in stock repurchases from the time it went public in 1980.

Figure 40: Genentech Inc. net income, R&D, and payouts to shareholders



Source: Own illustration based on data from company annual reports

As Figure 40 shows, the only exception had been the period when Roche required Genentech to make open-market repurchases in order to enable Roche to retain its majority stake in Genentech, as Roche's holdings had been diluted through Genentech's granting of new options under its employee stock option plans. From the signing of the Affiliation Agreement in 1999 until its acquisition by Roche in 2008, Genentech spent \$7.4 billion to

repurchase its stocks. Nearly 45 percent of those repurchases were made in 2004 and 2005 such that the company's market capitalization had peaked in the same years (Figure 40). Not coincidentally, the compensation of the top Genentech executives also peaked at that time, as the top five took home a total of nearly \$129 million, including gains realized from exercising options, in only those two years.

Emergence of stock buybacks following the merger

As the negotiations for the merger turned hostile, Genentech shareholders, company employees for the most part, headhunters in the industry were already preparing for a business recruitment season to find employers for soon-to-be Genentech expats (Krognes, 2010). The consensus at the time was that Genentech employees would quickly flee the company once the acquisition was completed and Roche abolished the stock option plans. It was one of the most urgent issues to tackle in the post-acquisition period if the Genentech operation was to be successfully integrated into Roche's.

Prior to the acquisition many of Genentech's key research and managerial staff had been not only loyal employees but also shareholders who adamantly monitored the performance of the company stock. Growing tension between Roche and its affiliate over the assigning of a stock value acceptable for Genentech shareholders had ultimately turned a friendly acquisition request into a hostile takeover attempt. Amid employees' growing concerns over the state of research and employment under new leadership, Genentech, quickly after rejecting Roche's bid of August 18, 2008, to take it private, declared a broad-based employee retention program (ERP) instead of proceeding with the renewal of the previous stock option program that the company had originally planned for 2008.

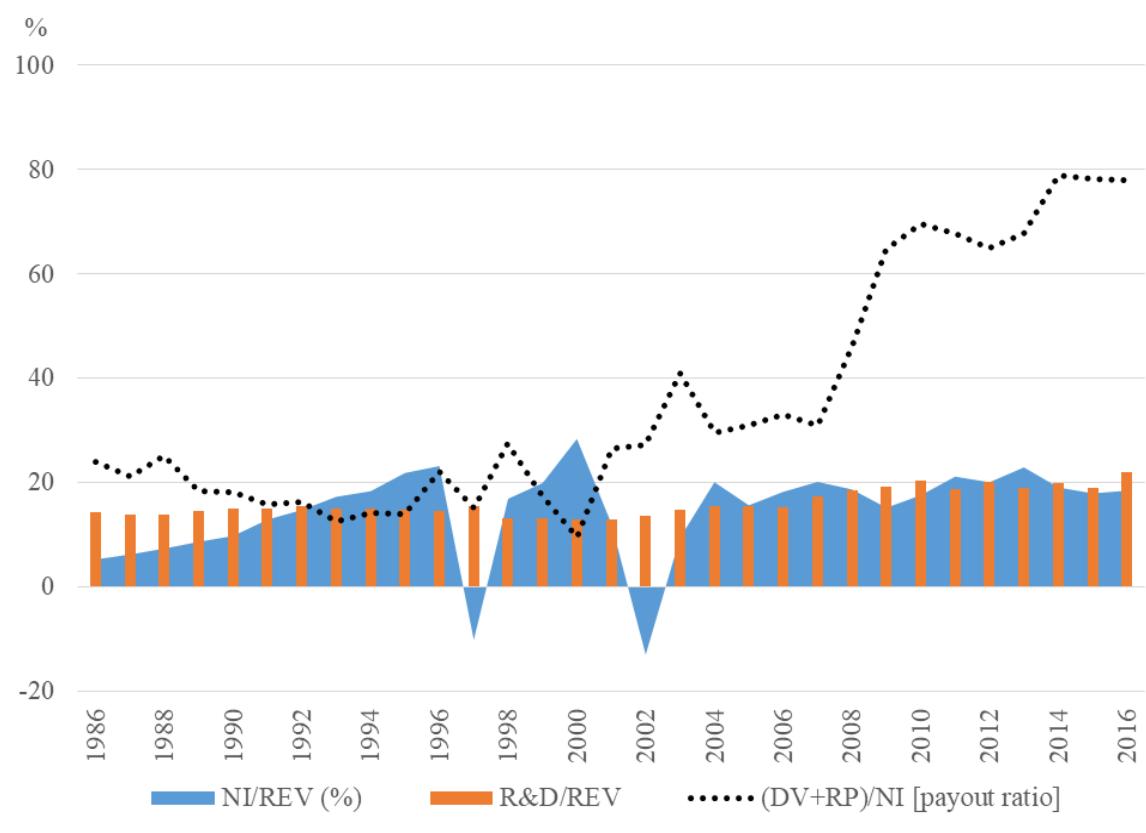
The ERP, whose fair-market value was estimated at approximately \$375 in 2008, offered a severance package as well as a retention bonus, including a \$21.5 million bonus package for the company's top five executives. Because Roche would still have to pay the program bonuses in four-year period until the options offered through bonuses were fully vested following the completion of the acquisition, Genentech had assured for the most part the safety of employment at Genentech through the new program.

In contrast to the prediction that most of the jobs at Genentech would be slashed following the merger, Roche was concerned that a large number of the productive researchers who had made Genentech's success possible would be lost in a mass exodus following the acquisition. Under the Genentech Employee Retention Program (GERP), Roche had taken over ERP along with other employee option plans previously granted, and all were being vested as part of the merger agreement signed into effect on March 12, 2009. The company also began to offer additional incentive plans to keep the company competitive in the market for scientists, technology and managerial talent. Combined with some disappointing results in the clinical or market performance of products with high shareholder expectations, Roche had increased the payouts to shareholder starting in 2008.

6.3.3 Growing shareholder payouts at Roche

With its ownership concentrated in the Hoffmann and Oeri families, Roche had been the symbol of stability in the biopharmaceutical industry when it came to creating shareholder equity. Roche has two classes of shares: bearer (voting) shares traded on the Swiss exchange (SIX); and (non-voting) equity securities (NES) traded on stock exchanges both in Switzerland and in the United States. As of December 31, 2016, 50.07 percent (nearly 80.1 million shares) of the total 160 million bearer (voting) shares were held by the members of the Hoffmann and Oeri families (45.01 percent) or by Maja Oeri (5.06 percent).

Figure 41: Roche Holding net income, R&D, and payouts to shareholders



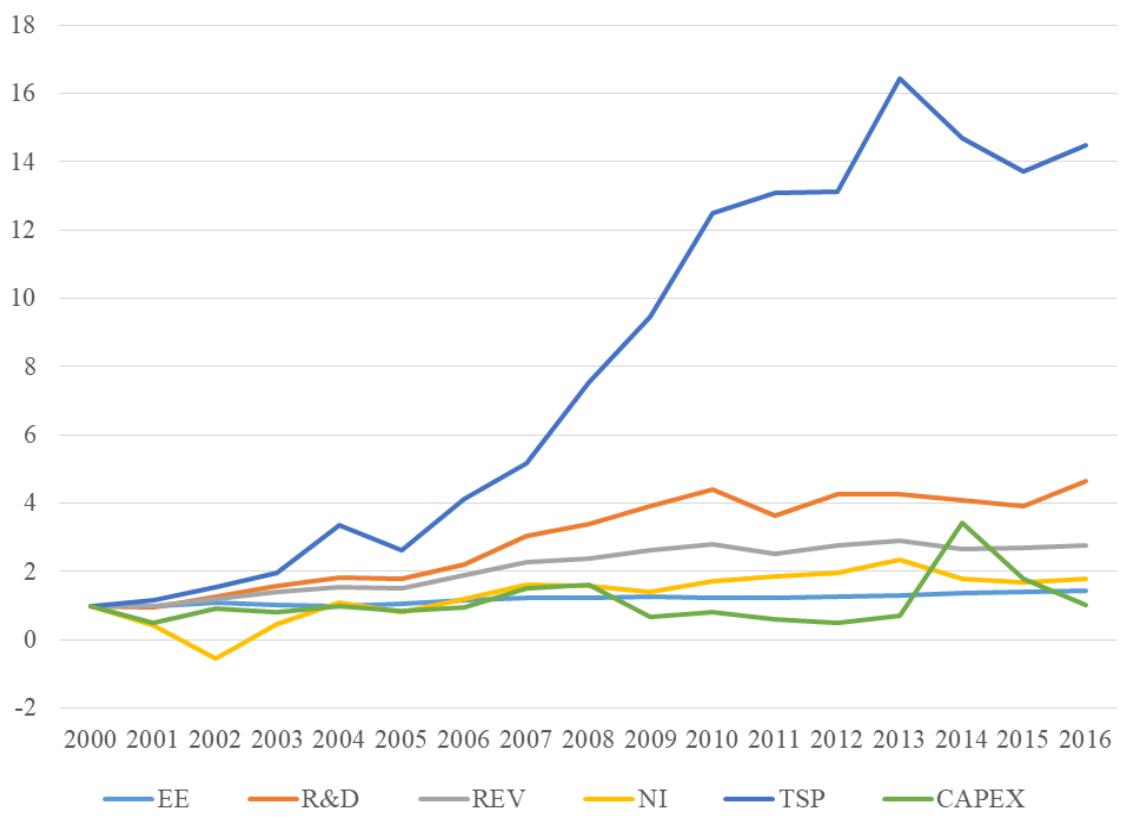
Source: Own illustration based on data from company annual reports

Given that the company has 852.6 million shares outstanding counting both bearer and NES, the Hoffmann and Oeri families-Maja Oeri consortium has managed to retain the majority stake despite possessing only 9.3 percent of the total shares outstanding. At any given period of the company's history, the Hoffmann and Oeri families have been represented by at least two directors on the company's board. The two current representatives, André Hoffmann, vice-chairman of the board of directors, and Andreas Oeri have held important posts on critical committees such as the remuneration committee, corporate governance and sustainability committee, and presidium/nomination committee. The family is, however, not represented on the audit committee, which carries the function

of monitoring the activities of the corporate executive committee on behalf of all other shareholders.

Until the acquisition of Genentech was completed in 1999, Roche's total shareholder payout (TSP) had followed a fairly steady trend line, as shown in Figure 41 and 42. Although the dividend payment jumped by 27 percent from 2002 to 2003, and again by nearly 57 percent from 2005 to 2006, TSP spiraled upward only when the company began repurchasing its stock for the first time in 2008. Figure 41 exhibits the changes between 2000 and 2016 in Roche's growth index across all major indicators: employment (EE), R&D, revenues (REV), net income (NI), total shareholder payout (TSP), and capital expenditure (CAPEX).

Figure 42: Growth index in employment (EE), R&D, revenues (REV), net income (NI), capital expenditure (CAPEX), and total shareholder payout (TSP)



Source: Own illustration based on data from company annual reports and Compustat database

The significant jumps in the TSP growth index observed in the periods of 2002-2003, 2005-2006, and 2008-2009 coincide with important milestones in the company's history. In 2002-2003 and 2005-2006, Roche's directors introduced new employee incentive programs mainly geared toward incentivizing corporate executives to generate higher returns for shareholders. The performance guidelines for the long-term incentives (LTI: i.e., PSP, S-SAR, RSUs) are directly tied to the company's stock price performance, and the proportion of LTI in overall executive compensation has been growing since 2008.

The period of 2008-2009 was the start of a new era for Roche, as the company was integrating with Genentech under Schwan as CEO and a new executive team. To retain the members of the team, made up of US-trained managers as well as Genentech veterans, Roche revised its compensation strategy in a way that would allow it to make competitive offers to those executives who were then in high demand. At the same time, being obliged to fund the sizable employee retention program it had inherited from Genentech, Roche began doing buybacks to meet the demand for its stock, which was growing as the options began to vest and be exercised (Figure 42). Finally, eager to retain the footloose scientific and managerial talent that Roche had counted on acquiring along with Genentech, the company began to promise compensation schemes sufficiently competitive Genentech and Roche would remain attractive places to work after the merger in 2009.

7 DISCUSSIONS ON ANALYSIS AND FINDINGS

In his elaboration of *the theory of innovative enterprise* (TIE), Lazonick (2013b) argues that business enterprises, as productive agents of a market-based economic system, transform productive resources into innovative outputs. The economic output that results from such a productive transformation process constitutes the basis for the growth of business enterprises as well the growth of the industries or regions in which they are embedded. Innovative output refers to goods and services that offer greater consumer value in terms of quality that is higher, and cost that is lower than existing alternative. TIE posits such a transformation process that yields higher value outputs at lower unit costs as the definition of innovative enterprise.

According to the TIE perspective, there are certain social conditions embedded within the innovative firm that influence the decisional dynamics in the ways in which the firm distinctly engages in three generic business activities—*strategy*, *organization*, and *finance*—so that the innovation process yields a greater economic outcome given the productive resources at the firm’s disposal. The firm (i) devises and implements *strategy* that determines the ways in which resources are allocated in the most productive manner to invest in tangible (i.e., laboratory, machinery) and intangible (i.e., new skills, knowledge) resources; (ii) builds an *organization* that can enable such tangible and intangible resources to augment productive capabilities so that a productive transformation can occur; (iii) ensures that it has access to *finance* so that the firm can successfully execute the strategy and develops the organizational capabilities to carry out the productive transformation until the anticipated returns are captured from it.

The productive transformation process is inherently “uncertain” simply because, at the onset of the innovation process, whether or not such a productive transformation would yield the anticipated economic return cannot be foreseen with a great deal of confidence. Additionally, what productive resources the productive transformation process would require cannot be known at the outset of the process. It is through immersing in an organizational learning process that the firm identifies issues challenging the productive

transformation process, and through developing learned-capabilities that the firm overcomes such challenges.

The learning process is collective given that such a process exceeds the ability or capacity of an individual, namely the entrepreneur, to carry it out alone. The process is cumulative in the sense that the organizational capabilities that the firm would need to overcome inherent uncertainties of the innovation process are attained through collective learning that the firm previously engaged. This also implies that any capabilities the firm will need to overcome challenges can only be developed over time through continually engaging in collective learning.

The innovation process results in superior economic performance that varies among firms depending on the business model, including whether it aspires to achieve productivity growth, or to enhance the financial performance, of a firm. At any given time, firms face a tension between innovation and financialization. However, the social conditions—*strategic control*, *organizational integration*, and *financial commitment*—that are encoded distinctively in the organizational routine, culture, or the collective organizational memory of the innovative enterprises can come into play to mitigate this tension.

Based on the *social conditions of innovative enterprise* (SCIE) framework, this research closely examines how the changes induced by the financialization of such social conditions whose strategic, organizational and financial decisions can determine the productivity of the innovation process and the economic performance of the firm. *Governance*, *finance*, and *employment* are the three major economic institutions constituting an environment that can “enable” or “proscribe” the *social conditions of innovative enterprise* embedded in such an environment. As discussed extensively in chapters 1 and 3, the US institutional environment has undergone a significant transformation process since the fast growing high-technology companies, adopting the principles of the *New Economy Business Model* (NEBM), began to dominate the US economy since the 1980s.

Based on the *maximizing shareholder value* ideology, NEBM has generally given rise to a financialized resource allocation regime within major US corporations. Merck is among those US corporations that have transitioned from innovation to financialization since the company abandoned the core governance principles that were rooted in the *Old Economy Business Model*, to adopt the principles of NEBM in the 1990s.

This research argues that such a transition from innovation to financialization is the real culprit behind the *productivity paradox* that puzzles the scholars of pharmaceutical innovation: despite having access to the most well-funded science and technology infrastructure, the most productive knowledge-base and innovation networks, and spending the greatest amounts on drug R&D, the productivity of the US biopharmaceutical industry is diminishing in terms of bringing innovative (high-quality, low-cost) new drugs therapies to meet growing patient needs in the market.

Table 10: Comparison of Merck and Roche's business models

	MERCK & CO.	ROCHE HOLDING
Strategy (product)	<p>Acquiring advanced technology platforms or clinical candidates to commercialize</p> <p>Accumulating new capabilities through the acquisition of start-ups or clinically-advanced biopharma companies</p> <p>Bolstering revenues through major merger and acquisition (M&A) deals and active management of product lifecycle</p> <p>Accessing new markets through strategic acquisitions</p> <p>Scaling-up national and global drug sales, marketing and distribution operations to defend competitive position in therapeutic segments the company has legacy</p> <p>Marketing and finance functions heavily influence new product decisions; it is no longer exclusive to R&D leadership</p>	<p>Pursuing growth through leveraging internal innovative capabilities</p> <p>Accumulating new capabilities through organizational learning – more conservative on the decision to pursue M&A deals – especially to boost product revenues</p> <p>Strategic business expansions into new product markets; based on related technologies (i.e. extension into companion-diagnostics field through PCR-technology)</p> <p>Investing on national and international sales, marketing and distribution operations to capture markets upon new product launches (rationalizing the economies of scale)</p> <p>R&D leadership still controls the process of new product decision; marketing and finance functions still involve in the process</p>
Strategy (process)	<p>Decentralizing corporate R&D and descaling investments on early-research for boosting late-stage clinical candidates</p> <p>Early-stage research and drug discovery efforts carried through innovation networks</p> <p>Cross-licensing of technology based on open systems principle – smaller biopharma companies as well as universities and other non-profit medical centers</p> <p>Vertical specialization of the value chain that is more oriented toward clinical development and commercialization of new drugs</p> <p>Outsourcing and offshoring of certain routine activities in addition to certain basic research, clinical, regulatory and administrative functions</p>	<p>For decades, maintained a relatively centralized corporate R&D structure through three innovation centers: <i>Basel, Swiss; Nutley (until mid-1990s), and Syntex/Genentech, USA; Chugai, Japan</i></p> <p>Development and patenting of proprietary products that were often considered as the industry standards</p> <p>Vertical integration of the value chain, at home and abroad; investing in improving operational quality and process efficiency to maintain high quality standards associated with the brand</p> <p>Established a competitive environment for the evaluation and selection of product candidates the process mainly controlled by R&D leaders, accepted only limited input from marketing and finance leadership</p>

<p>Finance</p> <ul style="list-style-type: none"> Growth finance from retentions plus stock as acquisition currency; Repurchasing own stocks to support stock price. Adopting value-based pricing strategy, which enables the company to maintain high profit margins that also allows the company to recover the R&D cost through price increases in the US, Pursuing various form of pricing strategies – i.e. value-based in the US, and differential pricing system worldwide- to maximize product revenues 	<p>Growth finance through leveraging retentions and bond-markets</p> <p>Stringent but regular distribution of cash dividends</p> <p>Known to be shareholder-value “unfriendly” company until the early 2000s:</p> <p>Strong operational performance allowed steady relations with investors</p> <p>Pursuing various form of pricing strategies – i.e. value-based in the US, and differential pricing system worldwide- to maximize product revenues</p>
<p>Organization</p> <ul style="list-style-type: none"> Diminishing employment security: layoffs became prevalent following the acquisition of a new company Difficulty in recruiting and retaining R&D personnel as internal capabilities diminish Decline in the proportion of unionized-labor Broad-based stock options for employees and stock-based awards for key R&D employee became more prevalent Employee began to bear greater burden of medical insurance and responsibility of saving for retirement 	<p>Secure employment opportunities, and salaries often around the industrial average (stock-based pay never prevailed);</p> <p>Attracted and retained productive scientists from academia or start-ups through Genentech</p> <p>Seeking internal candidates to promote for managerial role</p> <p>Adopting policies to pursue more diverse workplace that can participate in the management process</p> <p>Implementing a rigid protocol for drug development to ensure product safety and quality; but still seeks employee input -from R&D and production employees to middle- and upper-level management through feedback channels</p>

Source: Adapted from Lazonick (2009, p. 17). *Sustainable prosperity in the new economy? Business organization and high-tech employment in the United States*. WE Upjohn Institute.

Adopting a financialized business model can undermine the productivity of even the most innovative firm such as Merck, a company that Forbes Magazine named Merck as the Most Admired Company in the United States for seven consecutive years in the late 1980s and early 1990s. The case analysis in chapter 4 extensively examines the process through which Merck’s social conditions of innovation began to weaken to support the innovation process as the managerial orientation switched from innovation to financialization.

While the major US drug makers suffer from diminishing productivity, Roche, in the meantime, a foreign competitor based in a different institutional environment, has transformed itself, through better leveraging the productive resources in the United States, to become the global leader of the biopharmaceutical industry. Table 10 summarizes the

results of comparative case analysis this research employed on two global pharmaceutical companies, Merck and Roche. As Table 10 shows, the resource allocation regime adopted by the firm—i.e., innovative *retain-and-reinvest* vs. financialized *downsize-and-distribute*—determines how the firm engages in three generic activities—*strategy*, *finance*, and *organization*—that ultimately determines the productivity of the innovation process and economic growth.

7.1 Strategy, ownership, and control

According to TIE, the firm's growth strategy is determined by the abilities and incentives of those who are in strategic positions to make allocative decisions whether the firm should *retain-and-reinvest* in productive resources that would further enhance its innovative capabilities and the prospect for future growth, or the firm should *downsize-and-distribute* its productive assets to enhance the value of those who holds the company shares. The analysis in this research shows that it was under family control that Merck and Roche had completed a major transformation from manufacturers of fine chemicals to research-driven fully-integrated pharmaceutical companies in the early 20th century.

One should not infer from the ownership pattern the research identified that family-owned companies are more likely to develop productive capabilities that are superior to those whose shares are publically-owned. In fact, Roche is one of the very few global pharmaceutical companies, if not the only one, under family-control, but still faces competitive pressure from other publically-owned pharmaceutical companies. Also, such an ownership pattern revealed by the analysis does not imply that public companies cannot be innovative. In fact, the analysis shows that Merck sustained the founder's vision even well after George W. Merck handed corporate control over to professional managers in 1950, to continue building a corporate research laboratory in the “equal footing with the academic labors” and to excel as a profitable pharmaceutical business enterprise even based on the moral premise that “medicine is for people, not for profit.” This research rather argues, while under family-control, the social characteristics of these companies resembled the characteristics of the innovative enterprise.

Although the Hoffmann and Oeri families control slightly over 50 percent of the Roche's voting shares through pooled-interest, the company is not a typical family business. It is a business organization run by a Corporate Executive Committee (CEC), including the company's chief executive officer (CEO), selected by the company's Board of Directors. Although two family members, André Hoffmann and Andreas Oeri, represent the family on the company's directorial board, no family member serves on the executive committee who are responsible for managing the company's day-to-day operations. Unlike a typical family businesses, the family has shown no interest in intervening with the managerial authority of the executive committee since the death of the company founder Fritz Hoffman. On the contrary, through directors representing the family on the board of

directors, the family has been carefully engaging with the corporate executives so that the company's founding principles continue to influence Roche's vision and values.

Until adopting a financialized business model in the 1990s, Merck's leadership had carried the torch for the Merck family and remained committed to being a science-driven pharmaceutical company that engaged in innovating new drug therapies primarily for the improvement of human health, not necessarily for maximizing profits. Such a corporate mission was set forward by George W. Merck as the company went through a major transformation from being a manufacturer of fine chemicals to becoming major player in the global pharmaceutical market, in the 1950s, which is discussed extensively in chapter 4. Such a period also marked the beginning of a new era where the Merck family decided to withdraw from the active management of the company and transferred the control of the company's day-to-day operations to professional managers. Although no longer a family-run company, the traces of family influence in maintaining a corporate culture aligned with the value of George W. Merck were visible to some extent in the 1960s through the 1980s. However, in the 1990s Merck leadership abruptly abandoned such corporate principles to adopt the prevailing corporate governance ideology: maximizing shareholder value (MSV).

Although MSV was already prevailing the US economy from the mid-1980s, the reason for such an ideology to gain slow acceptance among the Merck executives may have had something to do with some influential figures in the company's top leadership who had been with the company since the late 1950s, which was the period when George W. Merck still exercised control over crafting a long-term corporate strategy for growth as the company went through a major transformation to become a managerial corporation. Individuals such as John T. Connor, who served as CEO of Merck from 1955 to 1965, was the second professional manager, after James J. Kerrigan, to serve as a top executive who was not a member of the Merck family. After returning from public service to join the company's board of directors in 1981, Connor had remained with Merck until retiring from the company's board of directors in 1987. Having stepped down from the directorship post in 1974, Adolph G. Rosengarten had remained involved with Merck as a director emeritus until his retirement in 1990. His father, Adolph G. Rosengarten, Sr., had been a major Merck shareholder since the late 1920s. However both Rosengarten Sr. and Jr. had allowed the Merck family to exercise strategic control while the two families controlled the majority stake in the company.

And finally, Albert W. Merck, the second son of George W. Merck who was the last Merck to serve on the company's board of directors, decided to retire from the directorship post in 1994 at a time when the top leadership at Merck was transitioning from Roy Vagelos, a long-time Merck leader, to Raymond Gilman, an outsider to the company and the drug industry. Currently, there exists no single holder of a major equity stake at Merck who can advocate for long-term economic growth, but a large number of shareholders who are anxious to generate greater yields for their investment on company stocks. This thesis

argues that such an absence of equity control concentrated in a group of shareholders that influences strategic decision making by advocating for a productivity-driven corporate growth that can be sustained in the long-term and that maximized value for all the stakeholders is what distinguishes Roche from Merck.

Strategy for innovation (process and product)

Merck used strategy (product and process), organization, and finance, distinctively prior to 1990s, in the ways in which they resembled the characteristics of the Old Economy Business Model (shown in Table 1). Table 10 shows the changes in the ways in which the company engaged in strategy, organization, and finance after abandoning the retain-and-reinvest mode of resource allocation strategy, which lies at the core of the Old Economy Business Model (OEBM) that drove productivity in the company previously, to adopt the downsize-and-distribute mode of resource allocation strategy, which constitutes the basis for the corporate governance regime in the New Economy Business Model that essentially prioritizes shareholder value maximization as the top managerial priority.

As the case analysis shows, Merck and Roche both faced tensions between innovation and financialization that intensified particularly in the 1990s. Within a matter of one decade, Merck went from being the poster child of the biopharmaceutical industry in the early 1990s that had envied the rivals with its corporate research lab known for high scientific integrity and superior innovative productivity to join the ranks of “corporate crooks” in the early 2000s when the company was accused of “wittingly” and “aggressively” marketing a deadly painkiller, Vioxx, that was supposed to provide the boost that the company’s ailing product revenues needed at the time. As elaborated in the case analysis, Merck had desperately pursued Vioxx into the market simply because Merck’s ailing research operations were still bleeding productive researchers, after Roy Vagelos, Merck CEO and the former director research operations, and a number of prominent research leaders had left the company in the mid-1990s. As a result Merck failed to replicate the legacy in drug innovation Merck had been known for decades.

As the analysis shows, a vast majority of the drugs that generated a significant portion of the company’s product revenues until the mid-1990s had been developed by the company’s own scientists. For instance, the drugs that were developed internally accounted for nearly 65 percent of the company’s total revenues in 1996. The remaining 35 percent of revenues came from drugs for which Merck scientists played a major role in their development process although such top-selling drugs were commercialized as part of a joint-venture agreement with DuPont where the events leading up the key discovery took place. Excluding the products acquired through the merger with Schering-Plough, the products developed internally by the company scientists accounted for nearly half of the company’s total revenues in 2016.

As shown in the analysis, Roche, unlike Merck, had maintained its strategic investments in the acquisition of productive resources to bolster organizational learning in the field of

biotechnology in the 1990s through the 2000s. Roche has been pursuing growth mainly through leveraging internal capabilities that led to the development of many innovative drug therapies in highly lucrative markets for specialty drugs such as oncology, antiviral therapies, etc. Roche had rarely considered major acquisitions or corporate mergers but those such Syntex, Genentech, Chugai acquisitions had been strategic in the sense that Roche had managed to enrich its innovative capabilities through successfully integrating the R&D operations of those companies into its own.

Aside from a brief period of diversification, Roche mainly pursued strategic business expansions into new product markets in related technologies such the extension into the companion-diagnostics field through the acquisition of polymerase chain reactor (PCR) technology from Cetus Corporation (later acquired by Chiron Corporation) in 1991. The company has been investing in national and international sales, marketing and distribution operations to capture markets more effectively after launching innovative new therapies (rationalizing the economies of scale).

In various events through its history, Merck had shown how a firm that is innovative; it could transform market, technological and competitive uncertainties that challenged every drug maker in the industry into a competitive advantage through developing distinct organizational capabilities that were difficult to imitate by the competitors. As the analysis shows, the 1930s had marked an important time period for Merck. During this period, the top management had empowered a group of entrepreneurial research leaders to oversee an ambitious investment strategy for building a research laboratory in the corporate setting that would be comparable to the leading academic institutions in the United States. In the decades following the initiation of such an ambitious organizational transformation project, the top leadership had shown great commitment to sustain the organizational learning efforts as Merck continued making investments in new products and processes, as well as building and fostering a unique environment encouraging collective and cumulative learning within the organization. By the end of World War II, Merck had developed highly productive skills and innovative capabilities to develop new drugs so that the company transformed from one manufacturing bulk and fine chemicals to supply national drug marketers and distributors with the chemical intermediaries necessary for producing biopharmaceutical products, into a major competitor of its former clients developing its own branded medicinal products.

The research leadership at Merck had begun to undergo a major transformation toward the end of Roy Vagelos' tenure as CEO under whom Merck had enjoyed significant productivity growth from the time he was hired as the research leader in 1975 until he stepped down from the top executive post in 1994. Also, some of the key managers began to leave the company soon after the top executive post transitioned from Roy Vagelos to Raymond Gilmartin, an outsider to the pharmaceutical industry who joined Merck from Becton Dickinson. The analysis shows that such a transition of corporate and research leadership Merck experienced in this period marks a crucial turning point in the company's history. Such a transition came at a time when the US pharmaceutical market was facing a

great deal of uncertainties due to a major healthcare policy overhaul that the newly-elected United States President William [Bill] J. Clinton proposed in the early 1990s. Prior to its defeat by the industry lobbyist, Pharmaceutical Research and Manufacturers of America (PhRMA), such a landmark policy reform included a major regulatory overhaul that was intended for getting soaring prescription drug prices under control through adopting a new regulatory control mechanism in the US drug market.

At a time when a major regulatory overhaul for controlling drug prices appeared imminent, the company's product strategy went through some changes to address the uncertainty in the US prescription drug market that was induced by the proposed new regulations in the early 1990s. The company's new product strategy involved diversifying into the drug distribution business for more effective management of profits projected to be much smaller if and when the US regulators increased pressure on the drug companies to lower their prices. Medco Health, a major pharmacy benefit management (PBM) company in the United States acquired by Merck in 1993, quickly became a major liability as the Clinton healthcare reform was defeated in the US Congress soon after Merck completed the acquisition.

Prior to the Medco acquisition, the management had already increased investments to increase the company's global operations in sales, marketing, and distributions (SM&D) following the launch of a number of new drugs in the late 1980s and early 1990s. The pressure on the research leadership grew significantly as the top management raised expectations on R&D and projected greater innovative productivity to rationalize the company's fast growing SM&D operations. As part of a new product strategy the management considered various options such as extending into generic drug business, seeking more in-licensing, and co-marketing deals with external partners. As the management became friendlier with the idea boosting product revenues through product-lifecycle management strategy (finding new therapeutic applications for existing drugs), the company began to place more emphasis on incremental innovation.

Merck under Raymond Gilmartin, in the early period of his tenure as CEO, did not consider inorganic growth through a major merger or acquisition deal (M&A). The company's shareholders raised concerns over the company's shrinking future product pipeline as some of the company's major drug candidates failed to make the necessary leap forward in the clinical trials in the early 2000s. Prior to his retirement in the mid-2000s, Merck under Gilmartin then began to consider smaller M&A deals as a strategic option to pursue. Having lost confidence in the R&D operations, Richard Clark, who succeeded Gilmartin in 2004, had been more aggressive in accumulating new capabilities through seeking a series of M&A deals. Merck under Clark implemented a series of organizational restructuring plans that involved the downsizing of global manufacturing and R&D operations. Such restructuring plans not only intended to address the declining investor confidence on the company's ability to deliver greater investment yields that reflected on the company's plunging stock prices in the mid-2000s, but also allowed Clark to pursue a

major M&A deals such as the company's merger with Schering-Plough in 2009. During Clark's tenure, Merck spent over \$50 billion to complete a series of M&A deals.

Roche's R&D operations have become highly globalized in recent decades. However the management of information flow within this complex R&D network has been coordinated through three major innovation centers: Pharma Research and Early Development (pRED) in Basel, Switzerland; Genentech Research and Early Development (gRED) in California, USA that had replaced the company's legacy US headquarters in Nutley, NJ in the early 1990s; and Chugai R&D center in Tokyo, Japan. As my analysis shows, Roche's US-based R&D operations have become of critical importance to the company's innovation efforts since the early 20th century. Organizational learning that took place in the company's Nutley site had been highly productive such that many of the company's innovative products came out of this site that was also home for Roche's US headquarters. New learning in molecular biology had been also initiated in the 1960s through the Roche Institute for Molecular Biology (RIMB) in Nutley. Since then the company has been investing heavily in improving organizational capabilities.

As the analysis shows, Roche under the family's control has been more strategic than it previously had been in retaining the control of the company's strategic resources to sustain organizational learning and support the innovation process. As the analysis shows such efforts have become especially challenging after the acquisition of Genentech, one of the first New Economy biotechnology companies to emerge in the late 1970s. Embodying the characteristics of the Old Economy Business Model, Roche's social conditions of innovation have been put on a pedestal for testing the limits since the company initiated the efforts to integrate its R&D operations with Genentech, a company who grew up within a financialized economy. As the analysis shows, Roche has increasingly struggled to mitigate the tension between innovation and financialization as the use of company stocks to acquire highly-skilled labor and improve employee motivation to participate in the collective and cumulative learning process that was adopted from Genentech, finds greater acceptance in the company's global operations.

While the patent life of Valium was running its course throughout the 1970s, Roche's researchers were struggling to develop a new drug to replace its first blockbuster. Rocephin, an antibiotic effective for common bacterial infections, had been its only major product launch in the early 1980s, and Roche was getting ready to license Zantac, the second-in-class but popular antacid drug, from Glaxo to launch it in the US market. The unprecedented financial success achieved by the company prior to 1990s had mostly depended on very few products, for which reason the lack of diversity in generating product revenues began pushing leadership in the direction of a major overhaul in the company's drug R&D operations.

Although every major pharmaceutical company acknowledged interest in the microbial biochemistry and enzyme inhibition in the mid-1970s, very few were willing to undergo the ordeal of transitioning their entire research operations and deploying the resources

involved in committing to the long-term learning process demanded in molecular genetics and recombinant DNA technology (Galambos & Sturchio, 1998, p. 260). Merck under Vagelos had intended to extend the company's presence in the market for biologics in the late 1980s and early 1990s, but growing industry concern over President Clinton's proposed healthcare policy agenda led the management to pursue a different growth path in the 1990s. The preceding chapter discussed the underlying causes of Merck's decision to abandon an innovation-driven growth path and the consequences that managerial action had on the company, which had bolstered its productivity and enjoyed substantial economic growth in the previous decade.

Table 11: Productivity and economic performance of R&D at Roche, 1993

Company	1993							(% of 1992 Sales)	
	Market Value (\$bn)	R&D (% of sales)	Number of products			US Patents			
			Total	Own	Under License	# of patents	per mil sales		
Roche (CH)	42.1	23.2	115	72	43	358	6.8	0	
Merck (US)	38.0	11.2	113	94	19	728	8.3	0	
J&J (US)	30.3	15.2	79	48	31	177	3.9	4	
Glaxo (UK)	27.9	15.2	80	51	29	151	1.8	72	
Pfizer (US)	20.4	13.0	57	43	14	245	4.8	8	
Sandoz (CH)	18.7	18.1	85	57	28	117	2.4	32	
Ciba-Geigy (CH)	17.8	12.7	102	71	31	356	6.9	35	
SmithKline									
Beckman (US/UK)	16.6	14.2	101	61	40	264	5.1	27	
Eli Lilly (US)	14.6	14.7	93	67	26	248	5.3	30	
Schering-Plough (US)	12.8	15.1	52	27	25	145	3.9	48	

*Source: Adapted from "Upon the shoulders of giants," by L. Välikangas, 1995, *Iryo To Shakai*, 5(1), p. 8, [Figure 11].*

Having already engaged in comprehensive learning in molecular biology and foreseen the growth potential of the emerging biotechnology market, the science and business leadership at Roche decided to diversify the company's research approach, traditionally centered on organic chemistry, and agreed upon pursuing a growth strategy in the emerging biotechnology field. Aspiring to become one of the largest biotechnology⁵² companies,

⁵² In 2010, Roche announced it was quitting the US industry lobbying group Pharmaceutical Research and Manufacturers of America (PhRMA) to join the biotechnology association BIO (Todd, 2009)

Roche had invested in a new research institute and built its innovative capabilities from the bottom up, a decision that began to realize its promise in the early 1990s.

Table 11 shows the state of R&D productivity at Roche at the time when the company's market value exceeded those of its rivals in the competitive pharmaceutical market. Not only in market value and overall spending on R&D, but also in the size of its product portfolio had Roche outperformed the competitors, including Merck, which was still harvesting the financial benefits of its productivity boost under Vagelos. In contrast to Merck, whose organizational culture often led it to overlook the benefits of collaborative research with external partners, Roche had put in place a science leadership that recognized the importance of penetrating emerging innovation networks through collaborative research efforts in the biotechnology field. As Table 11 shows, the sharp contrast in the number of products the two companies marketed under license reflects the difference in the two companies' attitudes toward exploiting the potential of the fast-growing US biotechnology research network in the 1980s.

The last column in Table 11 shows the percentage of total 1992 sales accounted for by products whose patents were set to expire between 1993 and 1995. The contrasting figures exhibited by the top 10 pharmaceutical producers can explain the variance in market valuation of those companies. Having enjoyed a recent productivity boost, Roche and Merck had no products whose revenues were facing a patent cliff between 1993 and 1995. An interesting note on the companies which had underperformed in research productivity at the dawn of biotechnology age is that, aside from Eli Lilly, which has been pursuing an intensive innovation program for the past decade, all the low performers were obliged to merge in the years to come in an attempt to stay ahead of the competition. One of the better innovation performers, Merck, had acquired the lowest performer, Schering-Plough, in 2009, while Glaxo merged with SmithKline Beckman to form GlaxoSmithKline in 2000. Novartis emerged in 1996 from the merger of Ciba-Geigy and Sandoz.

7.3 Finance, innovation, and stock repurchases

Merck and Roche, like the other global pharmaceutical companies, have been implementing various different pricing strategies to maximize product revenues from global sales and marketing operations. While pursuing a differential pricing strategy to comply with the government drug pricing and reimbursement policies that vary across national markets in the world, the two companies pursue a value-based pricing strategy in the US, the world's only major drug market without a price control mechanism, that allows the companies to maintain their high profit margins through regular price increases in this market. As the analysis in this research shows, the ways in which pharmaceutical companies allocate such earnings generated in the highly profitable drug market in the US vary significantly.

As the analysis in chapter 4 shows, Merck has generally remained as a profitable company, which allowed the company to finance its major capital expenditures since the 1950s. Merck issued new stocks mainly for the acquisition of smaller chemical manufacturers in the 1950s and the 1960s. Merck launched the company's first stock-option plan (SOP) in 1951 but such a plan was very modest and limited to key employees in managerial positions. As my analysis shows, at the time when Vagelos joined Merck in the mid-1970s, the company spent nearly the same for capital expenditures (CAPEX) and R&D that together amounted to the equivalent of almost 18 percent of revenues. This high ratio was the result of a massive capital expenditure investment program initiated in 1975. The size of this investment program was nearly \$1 billion (in 2016 dollars) and was financed largely through the issue of long-term bonds. Major construction efforts to increase pharmaceutical manufacturing capacity accounted for a large portion of this investment program.

The company's highly fluctuating stock-price performance in the late 1990s reflected stock-market uncertainty concerning Merck's fast-diminishing innovative productivity, which gave rise to downsize-and-distribute mode of corporate resource allocation regime since the late 1990s. Determined to revive shareholder confidence, Clark accelerated the company's stock repurchases in 2005, aiming to boost its stock price, which had lost as much as 60 percent of its value from its all-time high level of \$88 in 2000. Merck under Clark disbursed over \$36 billion of its cash to shareholders. As the analysis shows, Merck distributed on average 75 percent of its annual net income to shareholders in the form of dividends from 1986 to 2015. Merck expended \$3.4 billion on buybacks in 2016, and has \$5.1 billion remaining under its March 2015 buyback program authorizing the purchase of \$10 billion in shares.

Historically, Roche has leveraged the company's retained earnings along with the funds raised through the bond-markets in the United States and Europe to finance its growth. As the analysis shows Roche has distributed cash to shareholders through dividend payments at the rate that were considered to be below the industrial average. A historical review of the company's allocative strategies shows that Roche retained a large portion of its earnings to invest in the acquisition of new skills and resources. Because the company's voting stocks are key to retaining strategic control, Roche avoided using its shares as a currency to finance corporate acquisitions. Furthermore, historically, the company stocks have never been used as compensation currency to attract and retain executives or any other key employees, so that Roche has not felt compelled to repurchase of company shares for this purpose.

Some investors holding minority stakes at the time increased their criticism over the company's *retain-and-reinvest* resource allocation strategy. Some of the most vocal critiques such as Martin Ebner argued that the company's large cash reserves could be deployed more efficiently through pursuing M&A deals as opposed to investing in intramural R&D activities. The Hoffmann-Oeri clan, who at the time still had held the majority control of the company's voting stocks, turned down various different shareholder

requests in the late 1990s demanding the management of the company's large cash-resources in a more "shareholder-friendly" way, which essentially implied switching to a *downsize-and-distribute* mode of resource allocation that prevailed among the US pharmaceutical companies at the time. Having retained the strategic power, the Hoffmann-Oeri family repelled such shareholder attacks as Martin Ebner launched in the early 2000s. However, Novartis came to acquire Ebner's shares with the expectation, which was unsuccessful, of gaining Roche's strategic control along with all the company's productive resources.

The savings generated through the restructuring program were retained to offset the cost of expansion in capital expenditure the company undertook in the previous decade unlike the financialized US big pharma such as Merck who distributed cash savings from organizational restructuring to shareholders as discussed in the previous section. Figure 43 depicts the extent to which Roche's shareholder payout ratio has changed over the past two decades in comparison to those of other companies in its industry. In this figure, the top five US-based pharmaceutical companies are compared against Roche and Novartis, another Swiss-based pharmaceutical company.

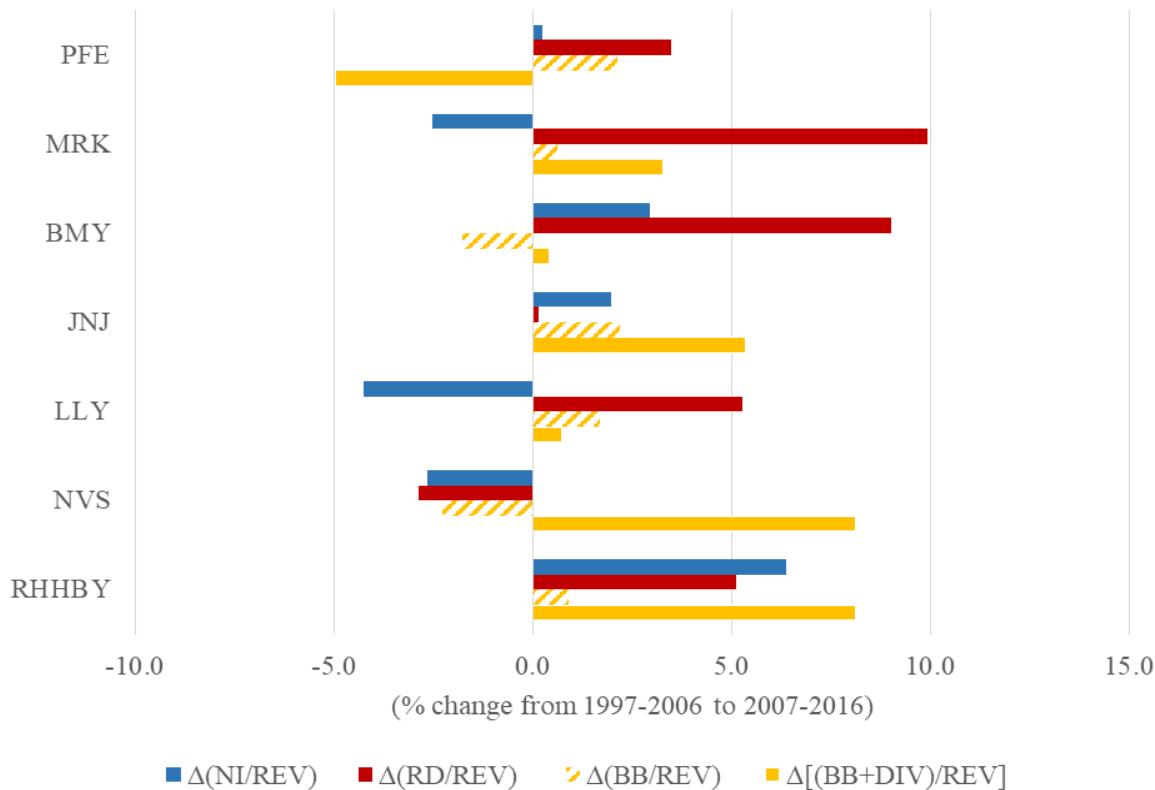
Figure 43 shows the the extent to which Merck and Roche's shareholder payout ratio has changed over the past two decades in comparison to those of other companies in its industry. In this figure the top five US-based biopharmaceutical companies are compared against Roche and Novartis, another Swiss-based pharmaceutical company. The seven companies are ranked based on their payout performance $[(\text{DIV}+\text{RP})/\text{NI}]$ in the period from 1997 to 2006; Pfizer (PFE), on the top, paid out the most and Roche, on the bottom, the least.

As Figure 43 shows, Bristol-Myers Squibb (BMY) is the only company that reduced its shareholder payout while increasing R&D expenses by additional 9 percent (from 13.2 percent to 22.2 percent) in the past ten-year period. Although Merck shows the largest increase in the R&D ratio (9.6 percent from 1996-2007 vs. 19.5 percent from 2007-2016), the company's profit margin suffered a decline (from 18.7 percent to 16.2 percent) in the past decade. While Eli Lilly (LLY) outdid Merck in experiencing the largest decline on profit in the past decade, the company also shows the highest percentage increase on the stock repurchase ration [RP/NI].

Merck (MRK) appears to follows Pfizer (PFE) in the list of companies ranked based on their shareholder payout performance in the period from 1997 to 2006. Also, Merck appears to come second after Novartis (NVS) when the same companies are ranked based on how their shareholder payout performance changed from the period between 1997 and 2006 to the period between 2007 and 2016 (35 percent for Novartis vs. Merck: 34.3 percent). Since the company's shareholder payout ratio increased by an additional 30.8 percent (from 34.5 to 64.3 percent) Roche follows NVS and MRK in third place. However

the proportion of stock repurchases within this change in total shareholder payout is only 4.4 percent (Figure 43).

Figure 43: Comparing the shareholder payouts of top 7 pharmaceutical companies, % change from 1997-2006 to 2007-2016



Pfizer (PFE); Merck (MRK); Bristol-Myers Squibb (BMY); Johnson&Johnsons (JNJ); Eli Lilly (LLY); Novartis (NVS) and Hoffmann-La Roche (RHHBY); $\Delta(NI/REV)$: Change in net income as a percentage share of total revenues from 1997-2006 to 2007-2016; $\Delta[(BB+DIV)/NI]$: Change in shareholder payout; $[(BB+DIV)/NI]$ as a percentage share of profits from the period of 1997 and 2006 to the period of 2007 and 2016; and $\Delta(RD/REV)$: Change in research and development as a percentage share of total revenues from 1997-2006 to 2007-2016; $\Delta(BB/REV)$: change in buybacks as a percentage of profits

Source: Own illustration based on data from company annual reports and Compustat database

Among all the company's previous investments, the Genentech acquisition has been the most strategic in the sense that by extending the traditional knowledge-base in medicinal chemistry into biotechnology, hastened by such a major acquisition, Roche became the global leader in pharmaceuticals in the 21st century. Roche developed a significant competitive advantage in the pharmaceutical industry as an innovative organization engaging in learning that is collective (through a global R&D operation networked around three major innovation centers in California, Basel and Tokyo) and cumulative (since the late-1960s with the establishment of the Roche Institute for Molecular Biology) in biotechnology.

Having retained the majority vote, the Hoffman-Oeri family ensured the sustenance of the necessary strategic control to oversee the successful execution of a long-term strategy spanned through the tenure of at least four CEOs. The economic result of executing its long-term strategy is evident in Figure 43, which shows that Roche outperformed the major US pharma companies as well as the hometown rival Novartis in boosting profitability. Comparing the percentage rate of net income within total revenues [NI/REV] in the past decade (from 2007 to 2016) against the decade before (1997-2006) Figure 43 shows that Roche's net income as a percentage of total revenues grew by 6.4 percent during this period; a change in profit rate that is nearly 2.2 times greater than the competitor with the second highest profit rate [NI/REV], Bristol-Myers Squibb (BMY).

At the time it was acquired by Roche, Genentech was underperforming financially, but the company still had a strong product pipeline. It was disappointing to let the very strong pipeline of innovative products go, but the board members knew that the current state of corporate finances and the stock performance could not be fixed without outside help. The company had to find a "rich uncle" to help to push the pipeline out to explore the opportunities in global markets (Baldwin et al., 2010).

By selling the majority stake to Roche in 1990, Genentech had secured the financial stability required at the time to support innovation efforts within the organization. This stability paved the way for the productivity boost of the 1990s and 2000s that saw Roche's market capitalization go from \$2.6 billion in 1990 to approximately \$100 billion in 2009. As shown in the case of the relationship between Roche and Genentech, in the absence of such financial stability, those biotechnology start-ups emerge as product-less initial public offering (PLIPOs) almost never transform into fully-integrated pharmaceutical companies (FIPCOs).

7.4 Organization

Well into Vagelos' tenure as CEO in the early 1990s there were already some major changes to the labor practices at Merck underway. Until the 1990s, "career with one company" (CWOC), which had been a pervasive employment norm in the biopharmaceutical industry in the post-World War II decades, had prevailed as a common employment practice at Merck. Many Old Economy companies such as Merck had long cherished such an employment practice for incentivizing organizational learning, but more importantly, it was pursued for protecting their valuable investments in productive resources, often in the form of intangibles and encoded in the productive skills and capabilities of research employees. These accumulated organizational capabilities constituted the basis for the company's competitive advantage.

By the mid-1990s, however, the "organization man" phenomenon had come to an end at Merck and most other large pharmaceutical organizations, a change that can largely be attributed to the burgeoning of biotechnology startups. The prospect of working at the

cutting edge of biotechnology, which held out the possibility both of making a major impact on the world and of garnering a significant financial reward, proved alluring to many young scientists. Pharma had historically paid scientists above the average pay that their academic counterparts used to receive. Historically Merck had been the place where an employee could have a fulfilling and lucrative career without feeling the itch to look for employment someplace else. As New Jersey had been the Mecca of the entire pharmaceutical industry since the middle of the 19th century, the barrier to switching employers was relatively low, but doing so had not been normal practice within the pharmaceutical industry until the 1990s.

Like their microelectronics counterparts (Lazonick, 2009), biotech startups used stock options to lure scientific and managerial personnel from the “career-with-one-company” (CWOC) employment model that characterized Old Economy companies to new ventures at which careers would be inherently uncertain. As stock options gained broader application in the labor force to include a broad base of professional, technical, and administrative personnel, the prospects of future prices of company stocks rather than a career with one company began to determine the rate of labor turnover as high-tech personnel flowed from Big Pharma to PLIPOs, particularly among the most skilled and productive R&D employees. Given the high financial gains an employee could potentially reap from the increasing stock price of a biotech start-up, it has been difficult for the large and established pharmaceutical companies to attract and/or retain the new generation of R&D employees to work for large industrial laboratories.

From “career-with-one-company” (CWOC) to high-velocity market for biopharma talent

If during the period of innovation until the 1990s Merck suffered from the not-invented-here syndrome, in the subsequent period of financialization the organization seem to be suffering from a cannot-invent-here syndrome. At a time when biotech startups quickly became attractive employers for scientists in molecular biology and genetics on the strength of the potentially lucrative stock options they offered, Merck under Vagelos revised its employee compensation scheme and extended the offering of stock options and performance-based cash bonuses to those on lower rungs of the managerial hierarchy (Vagelos & Galambos, 2004). According to some critics, Merck’s decision to enact a broad-based employee stock-ownership program in 1991 was merely an attempt to divert attention from an already exorbitant executive pay (Weber, 1991).

Because the company’s stock price was less volatile they offered greater price stability as well as steady dividend payments. However, new-generation scientists were more attracted to the young and dynamic startups challenging “old and slow big pharma.” At least part of the attraction was that the startups granted stock options at low prices, often comparable to the grant prices of their founders’ options—meaning their employees had the potential to

realize much higher returns, if and when the company reached the IPO phase, than salaries at big pharma would have offered them (Lazonick & Tulum, 2011).

Under Scolnick's control, Merck slowly disintegrated as the company's productive scientists began to defect from the company to join the biotechnology start-ups that were galloping to beat big pharma to market with new-generation therapies. The company's delayed entrance into the antivirals market is an example of how the deteriorating integrity of research operations had led to the declining innovation productivity of the following decade. Merck had sustained learning efforts in the development of protease inhibitors for a decade prior to its interruption in late 1980s by the loss of two of the nation's top experts in the field of peptidases.

At Merck, the use of stock options as a form of compensation has served to increase the divide between top executive and other employees—a characteristic of a financialized company. Such a disparity in the average gains of the company's top five executives and the remaining employees occurred after Clark implemented an immediate restructuring plan following the withdrawal of Vioxx from the market to restore "the trust and confidence of employees and shareholders," Clark told a room full of financial professionals at the Goldman Sachs Healthcare CEO's Conference on January 6, 2011. Through various organizational restructuring programs leading up to, and in the aftermath of, the merger with Schering-Plough, Merck under Clark had laid off approximately 13.4 percent of its employees. Merck under his successor Kenneth Frazier have brought global employment down by 32 percent since the beginning of the decade by persistently pursuing corporate restructuring programs during the post-acquisition period.

Currently, Roche appears to be the least financialized and most productive of the large drug makers. By adopting a highly-focused growth strategy, Roche has made a highly risky bet on the innovation of scientifically challenging specialty drugs to capture the most lucrative segments of the drug market, such as oncology, anti-inflammatory, and infectious disease. If successful, Roche will gain a significant competitive advantage over its rivals as all face intense competition in a market for small-molecule drugs characterized by diminishing profit margins. The prices of specialty drugs, mostly highly complex large-molecule therapies, are much more immune to competitive pressure. Unlike small biotechnology start-ups, which are its main competitors in the market for specialty drugs, Roche has the necessary skills, capabilities, and resources to push viable drug through the clinical process. Building a sales force highly trained in marketing specialty drugs can ultimately become the company's competitive advantage over its rivals.

Innovating specialty biotechnology drugs can be highly rewarding. It is, however a risky proposition and requires the upmost organizational commitment to sustaining innovation. In the absence of an alternative revenue stream, the company would fail to generate the cash flow needed to keep the company afloat when the productivity of R&D hits a dry spell. It was the net income generated from Valium that had afforded the organizational

engagement in new learning in biology, so the success of this new strategy will be determined by the company's ability to keep producing new blockbusters. As in the case of many small biotech start-ups today, any hiccups in a company's cash-flow can quickly undermine the innovation process.

Genentech was great in developing innovative new therapies but lacked the strategic control to acquire, develop, and deploy in a timely manner the productive resources needed to support the innovation process. Having lacked the strategic control, Genentech ultimately failed to navigate financial crises. In contrast, the descendants of Fritz Hoffmann, being in possession of sufficient strategic control, have managed to preserve the company's legacy, and along the way Roche has accumulated highly valuable skills and capabilities, allowing it to come out of any type of crisis stronger through innovation. Combining Genentech's entrepreneurial skills and innovative capabilities with Roche's managerial and financial stability, as well as the latter's survival skills, a Roche-Genentech partnership can continue to reign over the biopharmaceutical industry.

The strong appreciation for, and commitment to, science that Roche and Genentech possessed was what made the partnership work in the years following the acquisition. Genentech had been brought to its knees by its financialized business model. When the opportunity emerged, the top executives of Roche were smart enough to evaluate the situation correctly and to come up with the right approach to acquiring a highly innovative company without losing the element most important to making the company highly innovative: human and intellectual assets.

The executives in Basel also knew what was not needed in the equation for a successful drug business -- too many shares and shareholders -- and therefore eliminated them! Solutions? Since employee motivation had been extensively tied to the company's stock, let the shares continue to float in the market; since Genentech had been an organization extremely proud of its independent spirit, let the company own the other half of itself. After all, 50.07 percent is all it takes to run a company efficiently, as the descendants of the Hoffmann and Oeri families have been doing it for over a century!

The partnership can sustain its market leadership so long as the partners preserve the unique skills and capabilities that have made it a success up to now. As financial interests continue to tout managerial commitment to creating greater shareholder value, those who have a long-term stake in Roche need to remove the history books from the dusty shelves of the corporate library and read up on the company's history once again, to try to figure out when, if ever, share-sellers contributed to the value creation process that built the Roche we know today. This is at least what Roy Vagelos, former chairman and CEO of Merck & Co., suggested his employees do in the 1980s, but it appears that not much of attention was paid to his advice at the time. In light of the evidence laid out in the latter part of this chapter, the critical question lying ahead of the members of the Hoffmann and

Oeri families is whether they can stay in the way of financial interests and prevent an all-out invasion by the profit-sucking vampires of Wall Street.

CONCLUSION

Given the industrial subsidies and the market incentives available for the drug companies, whether they are based in the US or globally, the environment in the US is highly conducive for drug innovation. Yet there are widespread claims that a crisis of productivity afflicts the US biopharmaceutical industry. Within such a consensus on the existence of this crisis, there are numerous, often competing, theories seeking to explain the origins of this problem. Such theories are categorized within three overarching themes: (1) those which focus on issues stemming from the limitations of available science and technologies (S&T); (2) those which focus on the role of regulations and government interventions; and (3) those which look to the issues stemming from governance of innovation.

A growing number of studies in the third group reveal “financialization” as the real culprit behind the industry’s productivity crisis. According to Lazonick (2009) an innovative enterprise becomes financialized if and when managerial decisions to allocate productive resources are driven to create gains for a group of people, including the senior executives themselves, that is well in excess of their contribution to the value-creation process. Revealing the perils of the US biopharma’s financialized business model, Lazonick and Tulum (2011) explain such a business model driven by *maximizing shareholder value* (NSV) ideology poses a serious threat against the productivity and performance of the US biopharma business enterprise. Through a comparative business history research, this thesis developed an in-depth understanding of the mechanism linking the industry’s productivity crises with the financialization of the US biopharmaceutical industry. Through comparative cases analysis, using the *theory of innovative enterprise* (TIE) framework, this research explains the process through which the productivity of a previously innovative company diminishes as it transitions to financialization.

The analysis of this thesis revealed the highly-financialized character of the major pharmaceutical companies focusing on distributions to shareholders and the stock-based pay of pharmaceutical executives. While chasing greater financial gains through exploiting the market opportunities for blockbuster drugs to the full extent, financialized pharmaceutical companies often run into problems with innovating new drugs to replace the existing products that are falling off the “patent cliff.” During the period leading up to a major patent cliff, the top pharmaceutical executives in the United States often follow a very predictable decision-making pattern, including merging and acquiring new drug companies to access their pipelines of innovative new drugs; laying off employees and downsizing corporate R&D spending to boost profitability. These decisions are made in the name of maximizing shareholder value, which ultimately enables insider shareholders to

extract value from the company while it loses its capabilities to create value, and hence innovate.

This imbalance between value creation and value extraction has not always been the case in US pharmaceutical research. In their letter to the company's shareholders in the 1957 company annual report, Merck's Chairman of the Board, Dr. Vannevar Bush, and President, John T. Connor, listed the company's product accomplishments in 1957. In this letter, Bush and Connor indicated that in 1956 pharmaceutical companies spent nearly \$127 million on medical research including \$13.1 million that Merck had spent in that year. At a time when the US regulators began to investigate the causes of increasing drug prices Bush and Connor felt the need to highlight the fact that the combined Federal income tax paid by pharmaceutical companies had come close to matching the entire Federal government spending of \$211 million on medical research through the National Institutes of Health (NIH) in 1957.

Nearly six decades later in 2015, the amount that Merck spent on R&D spending was slightly over 10 percent of the amount spent by the members of the industry's top lobbyist, Pharmaceutical Research and Manufacturers Association (PhRMA). An analysis conducted by Lazonick et al. (2017) shows that the 18 healthcare and pharmaceutical companies in the S&P 500 are highly profitable when compared with the other companies in the same index. A further analysis conducted on the domestic (federal and local) taxes paid by the 18 healthcare and pharmaceutical companies reveals that these companies paid total taxes that were only 30 percent of the federal R&D spending on biomedical research through the NIH. The same 18 companies were responsible for nearly half the prescription drug sales in the United States.

The analysis in the second part of thesis assessed the hypothesis under a system of corporate governance that supports innovation rather than financialization, the US innovation not imply that there exists no innovation in the US biopharmaceutical industry at all. Innovation appears to be coming from companies that are taking better advantage of this supportive environment than others but one needs to look at the companies individually within the US biopharmaceutical industry to identify what companies are superior innovators, and more importantly to determine what constitutes the basis for such a cross-company performance variance in drug innovation.

Chapter 1 offered an extensive summary of the literature on the “productivity paradox” of US biopharmaceutical industry including the discussions on the highly-financialized character of the major pharmaceutical companies, focusing on distributions to shareholders and the stock-based pay of pharmaceutical executives. Discussing the theoretical and methodological challenges inherent in *the theory of the market economy*, Chapter 1 then explains why *the theory of the innovative enterprise* as the most appropriate framework for analyzing the evolution of the tension between innovation and financialization for pharmaceutical companies operating in the US institutional environment.

As explained in Chapter 2, the analysis in this thesis has initiated a long-term research project for developing a more comprehensive understanding of how, why, and to what extent transitions from innovation to financialization occur in the pharmaceutical companies and the implications of these transitions for the productivity of the biopharmaceutical industry. For this purpose, the stage of the research project on innovative pharmaceutical enterprise in comparative perspective by studying the US company Merck and the Swiss company Roche. In the case of the United States, I chose Merck & Co. (previously Merck Sharp & Dohme) because coming into the 1990s it had had a highly innovative business model, under the leadership of CEO Roy Vagelos. With the retirement of Vagelos, however, the company made an abrupt transition from innovation to financialization in the mid-1990s. In the case of Europe, I chose Roche Holding (previously Hoffman-La Roche) because it is a highly innovative company that has outperformed its US-based competitors to capture the most profitable segments in the US drug market such as oncology and immunology.

The most appropriate methodology for analyzing possible transitions from innovation to financialization is the company case study that integrates the theory of innovative enterprise with the historical evolution of the company in question. Through comparative historical analysis of two companies, this thesis offers an analysis to understanding of how, why, and to what extent transitions from innovation to financialization occur in the pharmaceutical companies. The thesis then examines the implications of such a transition for the productivity of the biopharmaceutical industry as part of the research agenda aspiring to reveal the mechanism linking financialization and the declining productivity of the US biopharmaceutical industry.

Chapter 3 analyzes the evolution of the US innovation system for pharmaceutical drug development since the 1980s, emphasizing the ways in which it has sought to support innovation, even as major US pharmaceutical companies have in fact undermined innovation through the financialized corporate resource-allocation behavior that this research documented through the first case-based analysis in the following chapter. As the analysis shows in Chapter 4, a US-based company like Merck, under the influence of MSV, has abused the US institutional environment as the company's innovative capabilities lapsed over time since it adopted a financialized business model to pursue a *downsize-and-distribute* resource allocation strategy in the 1990s.

As strategic control inside the major US pharmaceutical companies changed from innovation to financialization, managerial priorities made the *downsize-and-distribute* resource allocation strategy a managerial goal, legitimized by MSV. The most explicit indicator to measure whether, or to what extent, a public company is financialized is the level of resources the company allocates in purchases its own stock (stock repurchases), which can vary across companies in the spectrum from none to multiples of its net income. Arguing that the financialization of the US pharmaceutical business model is the real

culprit behind the diminishing productivity of the US pharma companies, the thesis explained in detail why and how Merck transitioned from innovation to financialization.

The analysis in chapter 4 offers an extensive inquiry into the sources of the financing that enabled Merck to grow during different phases of its history. Against a background of the heavy emphasis the company has placed on its stock-price performance in recent years, chapter 4 also explored the role that the stock market has played historically in financing the company's growth. It also examined the implications for Merck's future of its decision to complete over \$60 billion in payouts to shareholders since 2010, during which time the company also spent over \$40 billion to acquire a longtime rival as a remedy for its ailing sales performance and product pipeline.

Lazonick (2014a) argues that stock buybacks done as open-market repurchases have no constructive role to play in productivity improvement, but can have destructive consequences. The evidence compiled in Chapter 4 supports this argument; adopting *downsize-and-distribute* resource allocation mode in fact stands out as the foremost factor driving the growing imbalance between innovation and financialization within a pharmaceutical company, and contributing to growing inequity in the distribution of financial gains in the companies and in the economy as a whole.

Within the innovative enterprise, these gains, when they accrued, were shared with the company's career employees in the forms of employment security, higher pay, and better retirement and health benefits. This "career-with-one-company" (CWOC) employment in turn enabled and incentivized employees to invest their skills and efforts in the collective and cumulative learning that generated the innovative drugs that in turn generated the profits out of which these returns to employees could be paid. As shown in the case of Merck, incentivizing research personnel with the lure of gains from stock options rather than career employment security, the use of broad-based stock options as a mode of compensation research employees contributes to a breakdown in CWOC.

As shown in Chapter 3, the US institutional environment has been critical to the growth of major European biopharmaceutical companies. In addition to providing the knowledge base required for drug innovation, the US drug market, with its unregulated prices, has become a major source of European profits, especially for those innovative products developed in the United States. The US institutional environment makes the United States the most lucrative place for global drug companies to launch their innovative new therapies. The question is then to what extent these companies use these high profits for innovation or, alternatively, financialization. To answer this question, one has to look at the social conditions of innovative enterprise that prevail at these European companies and the relation of these social conditions to innovative performance in developing and marketing pharmaceutical drugs.

In Chapter 5, the discussion is based on the analysis of the US product strategies of following seven major European biopharmaceutical companies in the United States: Novartis and Roche (Switzerland), GlaxoSmithKline and AstraZeneca (UK), Sanofi-Aventis (France), Bayer and Merck KGaA (Germany). Through this analysis of product strategies, the thesis assessed the validity of the hypothesis that under a system of corporate governance that supports innovation rather than financialization, the US innovation system could result in a much more innovative biopharmaceutical industry that would focus on treating medical problems at affordable costs rather than on boosting stock yields to increase the financial gains of senior executives and the Wall Street bankers and hedge-fund managers with whom they have become allied.

The results of the second analysis in Chapter 6 suggests that a European-based pharmaceutical company like Roche that has been protected from the influence of MSV in its home country are in fact better positioned to make use of the US environment to enhance its innovative capabilities. The analysis of Roche shows that the company built core competencies in developing highly profitable specialty drugs through engaging in collective and cumulative learning, supported in part by the US institutional environment, in the emerging fields of biology since the 1960s. Roche's most important US competencies were obtained through the acquisition of Genentech in 1990, but these competences became productive only after Roche managed to restore order within Genentech's rapidly disintegrating organization due to the company's deep financial troubles.

As detailed in Chapter 7, the ways in which Roche managed to bring stability to Genentech illustrates how a change in strategic control can improve an acquisition's productivity by the implementation of organizational integration and financial commitment required to support the innovation process. Combining Genentech's entrepreneurial skills and innovative capabilities with Roche's managerial and financial stability, as well as the latter's survival skills, the Roche-Genentech partnership has had a profoundly productive influence on the US and global biopharmaceutical industry.

There are two factors that stand out in explaining how Roche ensures that the company's strategic control is vested in top corporate executives who have the abilities and incentives to pursue a growth strategy through innovating new drugs. First and foremost is the company's unique ownership structure. It is rare today for a family who are the direct descendants of the founder to retain full control of a major pharmaceutical company in Europe or elsewhere. The second factor is that, given this ownership structure, Roche has maintained drug innovation as its corporate goal. As the analysis shows, Roche has achieved this goal through leveraging its retained earnings along with the funds raised through the bond markets in the United States and Europe to finance its growth. A historical review of the company's allocative strategies shows that Roche retained a large portion of its earnings to invest in the acquisition of new skills and resources, which in part

was possible because the company distributed cash to shareholders through dividend payments at the rate that were considered to be below the industrial average.

Research Contributions

Among the most significant methodological contributions of this research is demonstrating the analytical power of the *social conditions of innovative enterprise* (SCIE) framework, when combined with the *historical-transformation* methodology, in the context of two pharmaceutical companies. Large pharmaceutical companies such as Merck are among the most complex social organizations. It is often difficult to analyze their operation and performance, given that the value-creation process within those organization occurs through social interactions among individual who participate in collective and cumulative learning process. The analysis of this research demonstrates that theoretical and methodological issues concerning the economic analysis of industrial organization, which deters scholars from pursuing in-depth case-base studies, can be overcome by employing a coherent combination of theoretical perspective, analytical tools, and methodological approach. This thesis supports the proposition that, with the relevant set of research tools, academic scholars and analysts interested in studying organizations can effectively make use of a significant amount of qualitative and quantitative data that can be gathered from electronic resources.

In line with Pisano's (2017) call for scholarly efforts to employ more rigorous analysis examining the links between capabilities and competitive advantage of firms, this research provides an empirical insight into the evolution of capabilities within two pharmaceutical firms, Merck and Roche, following two distinct business models prescribing two contrasting allocative decision-patterns (*retain-and-reinvest* vs *downsize-and-distribute*) for managers to follow. As this research shows, following such allocative decision patterns can enhance or undermine the competitive advantage of the innovative firm. Guided by the *theory of innovative enterprise*, using the *social conditions of innovative enterprise* as the analytical apparatus, comparative economic analysis based on two company cases conducted in this research explains the mechanisms linking decision-making patterns that are rooted in two distinct corporate resource allocation regimes and key to determining in which particular capabilities firms decide to invest, and the economic performances of those firms that follow the distinct decision-making patterns.

The analysis in this research shows that two distinct institutional environments, the United States and Switzerland, have different implications for the tension between innovation and financialization at two major pharmaceutical companies, US-based Merck and Swiss-based Roche. The research also shows that the change in the US institutional environment to one guided by MSV ideology has affected the US company but not the European company, even as they have both competed in the US market. Such findings have significant implications for the Chandlerian and Penrosian theories of the growth of the firm, both of

which tend to neglect the linkages between the organizational capabilities that the firm accumulates over time and the institutional environment in which the firm is embedded. Without including the major economic institutions related to *governance*, *employment*, and *investment* in the theoretical construct, one can only develop a limited understanding of the process through which the firm accumulate organizational capabilities, and hence why certain firms develop the unique set of capabilities in different institutional settings.

For instance, over the past two decades, US government investments in the nation's science and technology infrastructure, through the National Institutes of Health (NIH), have more than doubled. The NIH is the world's single largest supporter of basic and applied research in life sciences, providing over \$30 billion funding annually to support biomedical research in the United States. Universities and biotech start-ups are among the largest recipients of such funds. Since the 1980s, the National Association of Securities Dealers Automated Quotation (NASDAQ) system, itself founded only in 1971, has become the single most important stock exchange for biotech startups, based in the United States or overseas. When they are listed on NASDAQ, these young firms have no marketed drugs to generate product revenues, but they can access substantial amounts of capital through stock offerings. The speculative stocks of such high-risk, high-reward biotech startups became an attractive compensation currency for biotech companies to recruit and retain highly-skilled employees, using stock-based pay. Both the doubling of NIH funding and the availability of NASDAQ funding for young companies illustrates major changes in the institutional environment and industrial conditions in the United States that have impact the operation and performance of pharmaceutical companies in the United States.

As discussed previously, the market-based economic theories such as the *resource-based view* (RBV) of the firm or the *transaction-cost framework* are inadequate to explain how within the firm the tension between innovation and financialization gets resolved. In these lines of research, there are studies using in-depth case study methods to explain that the long-established US pharmaceutical companies (Big Pharma), after adopting a financialized resource-allocation strategy, have begun to downsize productive assets and cut costs in the name to maximize shareholder value. Although this thesis establishes a link between financialization and vertical disintegration that prevails at Big Pharma in the United States, the study however offers no insight into the ways in which such vertical disintegration impacts the innovative performance of the economy but concludes that such an in-depth analysis is needed to gain a better understanding of the dynamics of financialization.

This research contributes to the literature by updating the story on the evolution of the biopharmaceutical industry from where Chandler left off in the 1990s by focusing on the transition of the US biopharmaceutical industry from innovation to financialization over the past two decades. While, with the constraints of this thesis, I have studied two major companies, in future research the methodology can be extended to an analysis of all the major companies in the global biopharmaceutical industry. Since Chandler's analysis ended

in 1993, five of the top ten U.S. core companies in the pharmaceutical industry have been acquired by the other five; four of the top six non-U.S. chemical companies have merged their pharmaceutical operations to extend into the drug market; and five of the top eight non-U.S. (i.e., European) pharmaceutical companies either merged amongst or were acquired by the U.S. core pharmaceutical companies. More importantly, almost every single biotech start-up that Chandler analyzed in the later chapters of the book have been acquired by the large US or European biopharmaceutical companies over the past 25 years.

Chandler's comparative-historical analysis has established the foundations of the analysis of the evolution of the multidivisional corporation under strict managerial control. Penrose (1959) stressed the critical importance of the unique innovation capabilities, which the modern industrial firm accumulates over time through engaging in collective learning, to overcome managerial constraints on the growth of the firm. As Froud et al. (2006), Lazonick (2001), and Lazonick (2012) argue, however, the theoretical frameworks that Chandler and Penrose developed are unable to explain whether, or to what extent a corporate governance system, driven by *maximizing shareholder value* (MSV) ideology that supports financialization, encourages strategic managers to undertake innovative investments and create or maintain the productive capabilities of the firm.

The research in this thesis also has theoretical implications for the dynamic capabilities (DC) framework. Through an application of the DC framework to the US biotechnology industry, Pisano (2006) explains that the growth of the industry was not necessarily driven by innovative productivity; however, such an analysis fails to provide the firm-level empirical evidence to explain why and how such a science-driven industry as biotechnology managed to expand rapidly in the 1990s through 2000s while productivity of the pharmaceutical firms to the most extent suffered in terms of bringing innovative new therapies to market during the same period.

The DC perspective fails to tackle those issues fundamentally by avoiding to address this key questions concerning whether and to what extent the abilities and incentives of those who exercise strategic control within firms deploy resources in ways that firms (a) search for new capabilities, from a wide array of options with varying risk attributes (supply- and demand-side uncertainties); (b) choose the most economically feasible option to pursue; and (c) sustain their commitment until such capabilities are fully-developed and settled in the organization. By employing the *social conditions of innovative enterprise* analytical framework and the *historical-transformation* methodology, this research overcomes the conceptual and methodological challenges inherent in the dynamic capabilities approach.

As Pisano (2017) admits, the DC approach has failed to evolve theoretically as the scholarly interest has diminished over time to engage in the empirical work needed to fill the conceptual gaps in this theoretical construct. In his recent attempt to develop a more robust capabilities perspective, Pisano lays out a number of theoretical and methodological issues that challenge the scholars of the DC framework to do the required empirical research. Pisano calls for more industry-specific empirical insight into the extent to which

firms are inclined to commit resources on the “capability enhancing efforts”. The research in this thesis adduces the evidence that the inclination to commit resources would vary depending on the system of corporate governance under which firms operate; that is, whether the prevailing system of corporate governance supports innovation or financialization.

It is evident in the heterodox view of the firm, whether it be Chandlerian, Penrosian, resource-based, or in the dynamic capabilities, what is key to the growth of the firm, if not to industrial growth and economic development of nations, is organizational learning. The broad implication of organizational learning is clear: without organizational learning, the firm cannot develop organizational capabilities; without a set of integrated organizational capabilities, productive investments will not yield innovation; without generating innovation, there will be no productivity growth and economic development. This thesis adds to our understanding of the implications of organizational learning in the context of the discovery and development of innovative new medicinal drugs.

The social conditions of innovative enterprise can keep the tension between innovation and financialization from becoming vastly problematic in the medicinal-drug innovation process. These social conditions restrain financialization from decimating the organizational learning processes that generate new drugs. From the perspective of *the theory of innovative enterprise*, we gain insights that are illusive from the perceptive of the neoclassical theory of the market economy. The studies that analyze the US biopharmaceutical industry’s productivity crisis within the neoclassical-economic paradigm tend to construe the state as the source of the problem either because it regulates the market excessively, which consequently undermines the productivity of industrial R&D, or because it underinvests in science and technology infrastructure, which ultimately undermines the productivity of the national innovation system. This thesis confronts those theoretical arguments by adducing compelling evidence to the contrary, while demonstrating the effectiveness of *the theory of innovative enterprise (TIE)* for analyzing the economic performance of organizations. These contributions may help to attract more scholar in fields such management, strategy, organizations, economics, policy, and other to employ TIE in their work.

The findings of this research have major policy implications that can contribute to the debate on the role of the “national innovation system” in the development and commercialization of pharmaceutical drugs. It is important for legislators and regulators to understand the governance, structure, and performance of innovative enterprise to ensure that the institutions that they put in place to support innovation do not in fact encourage financialization on the part of the companies upon which they rely to bring innovative drugs to market.

For instance, US legislators often face vigorous opposition from pharmaceutical companies lobbying against market regulations to control drug prices in the United States. The opponents of regulation to control pharmaceutical prices often argue that the main reason

why the United States has some of the world's most innovative drugs companies is because companies can profit from drug innovation and therefore they are highly incentivized to continue innovating. Although this was true to some extent until the 1990s, this research shows that it is hard to argue that since then the market environment has been incentivizing companies to innovate. They are rather motivated to boost drug prices and extract monopoly profits. In this thesis research, an historical assessment of the US biopharmaceutical industry has revealed that the leading US business model that resulted in high levels of industrial productivity was primarily concerned about the generation of innovative new therapies. This innovative business model ultimately led the companies to create value for stakeholders, and especially for patients who are in dire need of those innovative new therapies.

As the historical analysis of Merck shows, the company was at the forefront of the biopharmaceutical industry's lobbying efforts against the regulation for price control as early as the late 1950s. Indeed, at a time when Merck and other pharmaceutical companies asked consumers to pay high prices on those drugs successfully developed in the past for the sake of innovative drugs in the future, the business model that prevailed at those companies was innovation-oriented. Such a business model entailed making substantial investments to acquire and develop the necessary organizational capabilities to generate innovative new drugs, which consequently led to a productivity boom that the biopharmaceutical industry enjoyed in the post-World War II decades. As Lazonick et al. (2017) reveal, and this research confirms in the case of Merck, the largest US pharmaceutical companies, during the period from 2006 through 2015, were allocating the profits derived from high drug prices to distributions to shareholders. Hence in charging these high prices the US companies have been engaged in price-gouging rather than funding innovation. This evidence in this thesis supports that argument that a company that engages in the financial behavior of Merck should be regulated for the sake of medical-drug innovation and public health.

The companies that grew up in the United States and became financialized have been abusing the productive US environment as they continue to make use of massive NIH funding and other government support to develop new drugs, and to take advantage of the US drug market by increasing drug prices arbitrarily for bolstering corporate earnings, which can be used to boost the repurchase of the company stocks, and subsequently the market prices of such stocks. Of particular importance, not just for the biopharmaceutical industry but for the US economy more generally is legislation and regulation concerning the widespread practice of stock buybacks. As Lazonick and his colleagues have shown in a number of empirical studies, "stock buybacks manipulate the market and leave most Americans worse off"—to quote the subtitle of his *Harvard Business Review* article "Profits Without Prosperity" (Lazonick, 2014a). Consideration of how and why US companies have turned from innovation to financialization then raises a host of issues concerning corporate governance, employment relations, and investment finance that, in

line with the arguments in this research, are treated in a forthcoming book by Lazonick and Shin (2018) on what they call “predatory value extraction”.

Confirming the findings of Lazonick et al. (2017), what this research revealed in the case of the US company Merck is that major pharmaceutical companies that seek greater financial gains by controlling the revenues from patented blockbuster drugs run into problems related strategic control, organizational integration, and financial commitment that undermine in-house processes innovating new drugs to replace the blockbuster revenues when the patents expire—what is known as the “patent cliff”. During the period leading up to a major patent cliff, senior pharmaceutical executives in the United States tend to focus on the acquisition of other drug companies to access their pipeline of innovative new drugs to replace the aging drugs. In the process, the in-house innovative capability of Big Pharma degrades further, manifested by layoffs of once-valued employees and the disruption of organizational learning. The strategic goal of the company is profits, not products, and the purpose of the profits is to boost the company’s stock price. If the goal of public policy is to generate effective medicines at affordable costs for a wide range of diseases, our findings for the US biopharmaceutical industry call for inquiry into the deleterious impacts of the prevailing ideology that companies should be run to “maximize shareholder value”.

The MSV problem is not just an American disease. Since the late 1990s, global institutions such as OECD have been promoting the wider acceptance of the MSV ideology, thus legitimizing financialization around the world. If there is one lesson that Europeans—and the rest of the world—should be learning from this new “American challenge”, it is that MSV is destructive of innovation. The future success of the European biopharmaceutical companies to innovate within the US institutional environment depends upon their ability to maintain a home-base governance system that supports innovation and suppresses financialization.

Limitations of the research

Building on the current financialization literature, this research embarked on a qualitative inquiry to shed light on the mechanism linking the productivity paradox of the US biopharmaceutical industry with the financialization of this industry. Having adopted the *theory of innovative enterprise* as the theoretical perspective and the *social conditions of innovative enterprise* as the analytical framework, this research purposefully sampled two company cases for pursuing a comparative business history research to acquire insight into the organizational mechanisms involved. Merck was chosen as case of a long-established US company whose productive capabilities weakened as the company transformed from innovation to financialization since the 1980s. Through the analysis of Roche as a European-based company offering an alternative perspective, this research sought to place the social conditions of innovation prevailed at these companies in comparative

perspective, with the arguments for and against financialization at the forefront of the analysis.

According to the TIE perspective, even within the same institutional environment, the strategy, structure, and performance that characterizes different companies can vary significantly. Furthermore, even within the same industry innovative companies are inherently distinctive in the ways in which they transform technologies and access markets. This research offers a thorough understanding of how, why, and to what extent transitions from innovation to financialization occur in the context of two pharmaceutical companies. The thesis then examines the implications of such a transition for the productivity of the biopharmaceutical industry as part of the research agenda aspiring to reveal the mechanism linking financialization and the declining productivity of the US biopharmaceutical industry.

The selection of Roche as a European case does not necessarily mean that all the innovative companies are based in Europe. The thesis could have studied an American company that has resisted financialization although the companies based in the United States are more vulnerable to shareholder value demands than their counterparts in Europe given the distinct set of norms and governance structures under which the companies in these regions operate. In the context of the United States, an established company owned by a family or with employees interested in the long-term survival of the company could have been selected as the case for an innovative company to compare and contrast against a financialized one. Such companies do not, however, exist in the US biopharmaceutical industry.

Through the product strategy analysis of the top seven leading European biopharmaceutical companies, Chapter 5 revealed that the US institutional environment has been critical to the growth of major European biopharmaceutical companies. In addition to providing the knowledge base required for drug innovation, the US drug market, with its unregulated prices, has become a major source of European profits, especially from those innovative products developed in the United States. The US institutional environment makes the United States the most lucrative place for global drug companies to launch their innovative new therapies.

The case of Roche shows how the combination of strategic control, organizational integration, and financial commitment enabled this company to make use of the national innovation system in the United States to become a world even as Merck turned from innovation to financialization over the same time period in the same institutional environment. Also, the results of the analysis on Roche as a European case does not necessarily imply that all the European companies are innovative. The answer to this question is subject to compiling additional European company cases looking at the social conditions of innovative enterprise that prevail at those other six European companies and the relation of these social conditions to innovative performance in developing and

marketing pharmaceutical drugs. Although contributing to such an ambitious research agenda is among the purposes of this research, provide a full account of the European story and explain to what extent European companies use these high profits for innovation or, alternatively, financialization is beyond the scope of this thesis.

Future Research

Although a company case analysis is a research-intensive process, it is in fact doable to research the whole industry, case by case, using this in-depth business history approach, given that there are only a small number of companies that dominate the global pharmaceutical market. As shown in Chapter 3, the largest 10 companies accounted for about nearly half of the drug sales in the United States in 2015. An intermediate goal for analyzing the tension between innovation and financialization in the global biopharmaceutical industry is to carry out full-blown historical case studies, brought up to the present, of these 10 companies.

A longer term goal is to proceed down the list shown in Table 2 to integrate studies of the top 20 companies in the analysis. This research has strategically chosen the two cases, Merck and Roche, to begin the process of accumulating cases. This approach allows researchers to update the company case analyses in real time after developing a deep understanding on the histories of these companies. Through the process of what Lazonick dubbed as “catching up with the history”, the updates on the analyses aim to examine how the companies mitigate or succumb to the tension between financialization and innovation.

The analysis on long-established pharmaceutical companies (or Big Pharma) can be extended to mid-size companies or emerging start-ups in the field of biotechnology that aspire to become fully-integrated pharmaceutical company (FIPCO). Compiling a large set of company cases using in-depth business history approach can make immense contributions to fields such as strategy, entrepreneurial finance, technology management, innovation policy, etc. First, having adopted a financialized business model, as Lazonick and Tulum (2011) explains, young biotechnology start-up fiercely compete against large pharmaceutical companies in the labor market for scientific and managerial talent.

As explained in the earlier chapters, biotech start-ups can raise significant amount of capital through offering their stocks in the US stock market even without having biopharmaceutical products to generate revenues. Such stocks offered through what Lazonick and Tulum (2011) dubbed as product-less IPOs (PLIPOs) are in fact highly speculative. Offering through employee stock option plans (ESOPs), PLIPOs use their speculative stocks to lure talent in the labor market since they have the potential to generate significant financial returns if and when those companies successfully bring drugs to market. Despite the inherent risk in such speculative stocks, the potential for substantial financial return makes PLIPOs attractive employer in the labor market.

Increasing use of common stocks to attract and retain workers can affect the labor mobility in the extent to which they can undermines the collective and cumulative learning efforts and the economic performances of both PLIPOs and Big Pharma. As discussed in Chapter 6 through the analysis of Genentech, the financialization of the US biotech business model that gave rise to PLIPOs appears to constrain the growth of PLIPOs and subsequently undermine their efforts to become FIPCOs. Such a difficulty to transform from PLIPO to FIPCO appears to be the systematic flaw inherent in the financialized US biotech business model given that only a small number of first-generation biotech companies, i.e. Amgen, Biogen IDEC, have managed to complete such a transformation since the 1980s. Future research can evaluate this hypothesis, case by base, using in-depth business history approach, and try to explain to what extent the financialized US biotech business model has the potential to disrupt the competitive structure of the drug market given that very few PLIPOs have transformed into FIPCOs, and even fewer have developed the necessary competitive advantage over Big Pharma rivals to survive in the drug market.

REFERENCES

- Aalbers, M. B. (2008). The financialization of home and the mortgage market crisis. *Competition & Change*, 12(2), 148-166.
- Access to Medicine Foundation [AMF]. (2016). *Access to Medicine Index 2016*, November 2016. Retrieved from <https://accesstomedicineindex.org/media/atmi/Access-to-Medicine-Index-2016.pdf>
- Achilladelis, B. (1999). In R. Landau, B. Achilladelis and A. Scriabine (Eds.), *Pharmaceutical Innovation: Revolutionising Human Health* (pp. 1-147). Chemical Heritage Foundation: Philadelphia.
- Adams, C. P., & Brantner, V. V. (2010). Spending on new drug development. *Health Economics*, 19(2), 130-141.
- Akst, J. (2013). The elixir tragedy, 1937. *The Scientist*, June, 2013.
- Alafi, M. (2013). *Biotech pioneer and entrepreneur*, an oral history conducted in 2003 by Sally Smith Hughes, PhD. Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2013.
- Alberts, B. (2010). Overbuilding research capacity. *Science*, 329(5997): 1257.
- Aldridge, S., Parascandola, J., & Sturchio, J. L. (1999). *The Discovery and Development of Penicillin 1928-1945: The Alexander Fleming Laboratory Museum, London, UK, November 19, 1999: An International Historic Chemical Landmark*. American Chemical Society. Retrieved from <https://www.acs.org/content/dam/acsorg/education/whatischemistry/landmarks/fleming-penicillin/the-discovery-and-development-of-penicillin-commemorative-booklet.pdf>

- Allen, J. P. (2009). A long, hard journey: from Bayh-Dole to the Federal Technology Transfer Act. Tomorrow's technology Transfer, *Association University Technology Management (AUTM)*, Winter 2009 (1), 21-32.
- Amit, R., & Schoemaker, P. J. (1993). Strategic assets and organizational rent. *Strategic management journal*, 14(1), 33-46.
- Andersson, T., Gleadle, P., Haslam, C., & Tsitsianis, N. (2010). Bio-pharma: A financialized business model. *Critical Perspectives on Accounting*, 21(7), 631-641.
- Angell, M. (2005). *The truth about the drug companies: How they deceive us and what to do about it*. New York: Random House Trade Paperbacks.
- Arno, P. S., & Davis, M. H. (2001). Why don't we enforce existing drug price controls? The unrecognized and unenforced reasonable pricing requirements imposed upon patents deriving in whole or in part from federally-funded Research. *Tulane Law Review*, 75, 631.
- Asker, J., Farre-Mensa, J., & Ljungqvist, A. (2015). Corporate investment and stock market listing: A puzzle? *Review of Financial Studies*, 28(2), 342–390.
- Backus, S. A. (2007). Reversing Course on Reverse Payment Settlements in the Pharmaceutical Industry: Has Schering-Plough Created the Blueprint for Defensible Antitrust Violations. *The Oklahoma Law Review*, 60, 375.
- Bagherian, R. (2007). The Preserve Access to Affordable Generics Act: Will Congress's Response to Reverse Payment Patent Settlements Enhance Competition in the Pharmaceutical Market. *J. Marshall Rev. Intell. Prop. L.*, 7, i.
- Baker, D. (2004). Financing drug research: What are the issues?. *Industry Studies Association Working Papers*, WP-2008-06. Retrieved from http://isapapers.pitt.edu/88/1/2008-06_Baker.pdf
- Baldwin, C.Y., Becker, B., & Dessain, V. (2010). *Roche's Acquisition of Genentech*. HBS No. 9-210-040 [Rev. September 28, 2011]. Boston: Harvard Business School Publishing.
- Baldwin, C.Y., & Clark, K.B. (1994). Capital-budgeting systems and capabilities investments in US companies after the Second World War. *Business History Review*, 68(1), 73-109.
- Barney, J.B. (1986a). Strategic factor markets: Expectations, luck and business strategy. *Management Science*, 32: 1512–1514.
- Barney J.B. (1986b). Organizational culture: Can it be a source of sustained competitive advantage? *Academy of Management Review*, 11: 656–665.
- Bayer. (1997). Consumer Care. 100 Years Aspirin. *The unparalleled career of Aspirin*. Leverkusen: Bayer AG. Retrieved from <https://www.bayer.com/en/newsroom-aspirin-story-history.pdfx>.

- Berenson, A. (2005). Merck's New Boss Inherits a Mess. *The New York Times*, May 21. Retrieved from <http://www.nytimes.com/2005/05/21/business/mercks-new-boss-inherits-a-mess.html>
- Berenson, A. (2007). Merck agrees to settle Vioxx suits for \$4.85 billion. *The New York Times*. November 9, 2007.
- Bilanz. (2004). Fritz Gerber: Goodbye, Übervater. *Bilanz*, January 28, 2004. Retrieved from <https://www.bilanz.ch/unternehmen/fritz-gerber-goodbye-uebervater>
- Bobst, E. H. (1973). *Bobst: The Autobiography of a Pharmaceutical Pioneer*. D. McKay Company.
- Boffey, P.M. (1983). Experts criticize U.S. laboratories. *The New York Times*. July 15, 1983.
- Bogner, W. C., Thomas, H., & McGee, J. (1996). A longitudinal study of the competitive positions and entry paths of European firms in the US pharmaceutical market. *Strategic Management Journal*, 85-107.
- Booth, B., & Zemmel, R. (2004). Prospects for productivity. *Nature Reviews Drug Discovery*, 3(5), 451-456.
- Boston Consulting Group [BCG]. (2016). *Creating value through active portfolio management: The 2016 value creators report*, October 2016. Retrieved from <https://www.bcg.com/publications/collections/value-creators-2016.aspx>
- Boyer, H. W. (2001). *Recombinant DNA research at UCSF and commercial application at Genentech*. An oral history conducted in 1994 by Sally Smith Hughes, Regional Oral History Office, the Bancroft Library. University of California Berkeley.
- Bremer, H., Allen, J., & Latker, N. J. (2009). The US Bayh–Dole Act and revisionism redux. *Industry and Higher Education*, 23(5), 351-366.
- Brown, L. (2010). *Politics and health care organization: HMOs as federal policy*. Brookings Institution Press.
- Bud, R. (2005). Antibiotics, big business, and consumers: The context of government investigations into the postwar American drug industry. *Technology and Culture*, 46(2), 329-349.
- Bud, R. (2007). *Penicillin: triumph and tragedy*. Oxford University Press.
- U.S. Bureau of Labor Statistics [BLS]. (n.d.). Consumer Price Index (CPI) and Producer Price Index (PPI). Retrieved from <https://www.bls.gov/data/#prices>
- Bürgi, M., & Strasser, B. (2009). Pharma in Transition: new approaches to drug development at F. Hoffmann-La Roche & Co, 1960–1980. In V. Quirke & J. Slinn (Eds.). *Perspectives on 20th-Century Pharmaceuticals*. Oxford: P. Lang (391-432). Retrieved from <https://archive-ouverte.unige.ch/unige:16833>

- Carpenter, M., Bell, B., Glimstedt, H., & Lazonick, W. (2014). When strategies collide: the impact of financialization on the development of innovative capabilities (No. hal-01256605).
- Carpenter, M., & Lazonick, W. (2017). *Innovation, competition and financialization in the communications technology industry: 1996-2016. Innovation-fueled, Sustainable, Inclusive Growth (ISIGrowth)* Project Working Paper 08/2017.
- Carpenter, M., Lazonick, W. & O'Sullivan, M. (2003). The stock market and the innovative capability in the New Economy: the optical networking industry. *Industrial and Corporate Change*, 12(5), 963-1034.
- Casper, S., & Kettler, H. (2001). National institutional frameworks and the hybridization of entrepreneurial business models: The German and UK biotechnology sectors. *Industry and Innovation*, 8(1), 5-30.
- Carroll, J. (2013). Lilly's Lechleiter isn't budging from stand-alone \$5B R&D strategy—yet. *FierceBiotech*, October 21. Retrieved from <https://www.fiercebiotech.com/r-d/lilly-s-lechleiter-isn-t-budging-from-stand-alone-5b-r-d-strategy-yet>
- Center for Drug Evaluation and Research [CDER]. (2015). *New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products*. Retrieved from <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/default.htm>
- Centers for Medicare & Medicaid Services [CMS]. (2015). *National Health Expenditure Data, Historical*. Retrieved from <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical.html>
- Chakma, J., Sun, G. H., Steinberg, J. D., Sammut, S. M., & Jaggi, R. (2014). Asia's ascent: global trends in biomedical R&D expenditures. *New England Journal of Medicine*, 370(1), 3-6.
- Chandler, Jr., A.D. (1962). *Strategy and Structure: Chapters in the History of American Industrial Enterprise*. MIT Press.
- Chandler, Jr., A.D. (1977). *The Visible Hand: The Managerial Revolution in American Business*. Harvard University Press.
- Chandler, Jr., A.D. (1990). *Scale and Scope: The Dynamics of Industrial Enterprise*, Harvard University Press.
- Chandler, Jr., A.D. (2001). *Inventing the Electronic Century: The Epic Story of the Consumer Electronics and Computer Science Industries*. New York: Free Press.
- Chandler, Jr., A.D. (2005). *Shaping the Industrial Century: The Remarkable Story of the Evolution of the Modern Chemical and Pharmaceutical Industries*. Cambridge: Harvard University Press.
- Check, E. (2002). Bush's budget boost puts NIH on target for doubled figures. *Nature*, 415, January, 31, 2002: 459.

- Chemmanur, T. J., & Fulghieri, P. (2013). Entrepreneurial finance and innovation: An introduction and agenda for future research. *The Review of Financial Studies*, 27(1), 1-19.
- Christensen, C. M., Kaufman, S. P., & Shih, W. C. (2008). Innovation killers. *Harvard Business Review*, 86(1), 98-105.
- U.S. Centers for Medicare and Medicaid Services [CMS]. (n.d.). Office of the Actuary, *National Health Statistics Group*. Historical data. Retrieved from <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NHE-Fact-Sheet.html>;
- Cockburn, I. M. (2006). Is the pharmaceutical industry in a productivity crisis? *Innovation Policy and the Economy*, 7(2006): 1-32.
- Cockburn, I.M., & Henderson, R. (2001). Publicly funded science and the productivity of the pharmaceutical Industry. In Jaffe, A.B., Lerner, J. and Stern, S. (Eds.) *Innovation policy and the economy*. MIT Press, 2001: 1-34.
- Cohen, G. N. (1986). Four decades of Franco-American collaboration in biochemistry and molecular biology. *Perspectives in Biology and Medicine*, 29(3), S141-S148.
- Cohen, S. N. (2009). *Science, Biotechnology, and Recombinant DNA: A Personal History*. An oral history conducted in 1995 by Sally Smith Hughes, PhD. Regional Oral History Office, The Bancroft Library. University of California, Berkeley, 2009.
- Cordes, E. H. (2014). *Hallelujah moments: tales of drug discovery*. Oxford University Press.
- Cyran, R. (2014). Revival for antibiotics could spur deals. *The New York Times*, December 8. Retrieved from <https://dealbook.nytimes.com/2014/12/08/revival-for-antibiotics-could-spur-deals/>.
- Daniel, M. G., Pawlik, T. M., Fader, A. N., Esnaola, N. F., & Makary, M. A. (2016). The Orphan Drug Act: restoring the mission to rare diseases. *American journal of clinical oncology*, 39(2), 210-213.
- Danzon, P. M., Epstein, A., & Nicholson, S. (2007). Mergers and acquisitions in the pharmaceutical and biotech industries. *Managerial and Decision Economic*, 28: 307–328.
- Denning, S. (2015). Salesforce CEO Slams 'The World's Dumbest Idea': Maximizing Shareholder Value. *Forbes*, February 5, 2015. Retrieved from <https://www.forbes.com/sites/stevedenning/2015/02/05/salesforce-ceo-slams-the-worlds-dumbest-idea-maximizing-shareholder-value/#396105147883>
- Dickson, M., & Gagnon, J. P. (2004). Key factors in the rising cost of new drug discovery and development. *Nature Reviews Drug Discovery*, 3(5), 417-429.
- DiMasi, J. A. (2001). Risks in new drug development: approval success rates for investigational drugs. *Clinical Pharmacology & Therapeutics*, 69(5), 297-307.

- DiMasi, J. A. (2014). Pharmaceutical R&D performance by firm size: Approval success rates and economic returns. *American Journal of Therapeutics*, 21(1), 26-34.
- DiMasi, J. A., & Grabowski, H. G. (2007). The cost of biopharmaceutical R&D: is biotech different? *Managerial and Decision Economics*, 28(4-5), 469-479.
- DiMasi, J. A., Hansen, R. W., & Grabowski, H. G. (2003). The price of innovation: new estimates of drug development costs. *Journal of Health Economics*, 22(2), 151-185.
- Doherty, D. & Waters, R. (2010). Roche Embraces Genentech Innovation to Keep Drug Pipeline. *Bloomberg Business Week*. July 4, 2010. Retrieved from <https://www.bloomberg.com/news/articles/2010-07-01/swiss-roche-embraces-genentech-cool-to-keep-its-new-drug-pipeline-flowing>
- Donohue, J. (2006). A history of drug advertising: the evolving roles of consumers and consumer protection. *The Milbank Quarterly*, 84(4), 659-699.
- Dore, R. (2008). Financialization of the global economy. *Industrial and Corporate Change*, 17(6), 1097-1112.
- Edwards, J. (2009). Schering CEO Hassan Has \$59 Million Buyout Agreement in Merck Merger. *Moneywatch, CBS News*, March, 6, 2009. Retrieved from <https://www.cbsnews.com/news/schering-ceo-hassan-has-59-million-buyout-agreement-in-merck-merger/>
- Edwards, J. (2011). Merck "Disingenuous" for Stopping Earnings Guidance, Wall Street Says. *Moneywatch, CBS News*, February 4, 2011. Retrieved from <https://www.cbsnews.com/news/merck-disingenuous-for-stopping-earnings-guidance-wall-street-says/>
- Eisenberg, R.S. (1992). Genes, patents, and product development. *Science* 257, 903–908.
- Eisenhardt, K. M. (1989). Building theories from case study research. *Academy of Management Review*, 14(4), 532-550.
- Ernst and Young. (2015). Special recognition: André Hoffmann, Roche Holding Ltd. *EY Family Business Yearbook 2016*: 175-177.
- Ernst and Young. (2016). *Beyond Borders Global Biotechnology Report*.
- Ernst and Young. (2017). "Staying the course", Biotechnology Report 2017, Beyond Borders. Retrieved from [http://www.ey.com/Publication/vwLUAssets/ey-biotechnology-report-2017-beyond-borders-staying-the-course/\\$FILE/ey-biotechnology-report-2017-beyond-borders-staying-the-course.pdf](http://www.ey.com/Publication/vwLUAssets/ey-biotechnology-report-2017-beyond-borders-staying-the-course/$FILE/ey-biotechnology-report-2017-beyond-borders-staying-the-course.pdf).
- EvaluatePharma. (2016) *World Preview (2016) Outlook to 2022*. 9th edition.
- Evans, J. P., Meslin, E. M., Marteau, T. M., & Caulfield, T. (2011). Deflating the genomic bubble. *Science*, 331(6019), 861-862.
- Fagnan, D. E., Gromatzky, A. A., Stein, R. M., Fernandez, J. M., & Lo, A. W. (2014). Financing drug discovery for orphan diseases. *Drug Discovery Today*, 19(5), 533-538.

- Fama, E. F., & Jensen, M. C. (1983). Separation of ownership and control. *The Journal of Law and Economics*, 26(2), 301-325.
- Ferleger, L., & Lazonick, W. (1993). The Managerial Revolution and the Developmental State: The Case of US Agriculture. *Business and Economic History*, 67-98.
- Ferleger, L., & Lazonick, W. (1994). Higher education for an innovative economy: land-grant colleges and the managerial revolution in America. *Business and Economic History*, 116-128.
- Financialization. (2017). In Oxford English dictionary online. Retrieved from <https://en.oxforddictionaries.com/definition/financialization>
- Fintel, B., Samaras, A. T., & Carias, E. (2009). The thalidomide tragedy: lessons for drug safety and regulation. *Helix Magazine*.
- Firestone, R. A. (2011). Lessons from 54 years of pharmaceutical research. *Nature Reviews Drug Discovery*, 10(12), 963.
- Fiss, P. (2009). Chapter 25-Case studies and the configurational analysis of organizational phenomena. In D. Byrne & C. Ragin (Eds.), *The SAGE Handbook of Case-Based Methods* (pp. 424-440). London: SAGE.
- Flink, L. (2017). A sense of purpose, Larry Fink's annual letter to CEOs, January 24, 2017. Retrieved from <https://www.blackrock.com/corporate/en-us/investor-relations/larry-fink-ceo-letter>.
- Folkers, K.A. (1990). *Karl August Folkers*. An interview by Leon Gortler at Folkers's Summer Home, Sunapee, New Hampshire, 6 July 1990 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript # 0150).
- Food and Drug Administration (US Department of Health and Human Services) [FDA]. (2005). Sequence of Events with VIOXX, since opening of IND. Retrieved from https://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4090B1_04_E-FDA-TAB-C.htm
- Food and Drug Administration (US Department of Health and Human Services) [FDA]. (2018). List of Orphan Drug Designations and Approvals, updated January 27, 2018. Retrieved from <https://www.accessdata.fda.gov/scripts/opdlisting/oopd/>.
- Fore, J., Wiechers, I. R., & Cook-Deegan, R. (2006). The effects of business practices, licensing, and intellectual property on development and dissemination of the polymerase chain reaction: case study. *Journal of Biomedical Discovery and Collaboration*, 1(1), 7.
- Foster, J. B. (2008). The financialization of capital and the crisis. *Monthly Review*, 59(11), 1.
- Fredrickson, D. S. (1991). Asilomar and recombinant DNA: The end of the beginning. *Biomedical Politics*, 258-292.
- Freeman, R. B. (2010). It's financialization! *International Labour Review*, 149(2), 163-183.

- Freudenheim, M. (1991, Sep 12). Stock plan is offered by Merck. *The New York Times*, September 12. Retrieved from <http://www.nytimes.com/1991/09/12/business/stock-plan-is-offered-by-merck.html>.
- Freudenheim, M. (2004). Medco to Pay \$29.3 Million to Settle Complaints of Drug Switching. *The New York Times*, April 27. Retrieved from <http://www.nytimes.com/2004/04/27/business/medco-to-pay-29.3-million-to-settle-complaints-of-drug-switching.html>.
- Fried, S. (1998). *Bitter pills: Inside the hazardous world of legal drugs*. New York: Bantam.
- Froud, J., Johal, S., Leaver, A., & Williams, K. (2006). *Financialization and Strategy: Narrative and Numbers*. Routledge.
- Galambos, L., & Sewell, J. E. (1997). *Networks of Innovation: Vaccine Development at Merck, Sharp and Dohme, and Mulford, 1895-1995*. Cambridge University Press.
- Galambos, L., & Sturchio, J. L. (1998). Pharmaceutical firms and the transition to biotechnology: A study in strategic innovation. *Business History Review*, 72(02), 250-278.
- Gale, E. A. (2012). Post-marketing studies of new insulins: sales or science?. *BMJ: British Medical Journal* (Online), 344.
- Gambardella, A. (1992). Competitive advantages from in-house scientific research: The US pharmaceutical industry in the 1980s. *Research Policy*, 21(5), 391-407.
- Gambardella, A. (1995). *Science and innovation: The US pharmaceutical industry during the 1980s*. Cambridge University Press.
- Gambardella, A., Giuri, P., & Luzzi, A. (2007). The market for patents in Europe. *Research Policy*, 36(8), 1163-1183.
- Garnier, J. P. (2008). Rebuilding the R&D engine in big pharma. *Harvard Business Review*, 86(5), 68-70.
- The U.S. Government Accountability Office [GAO]. (2002). Report to Congressional Committees: Clinical Research: NIH Has Implemented Key Provisions of the Clinical Research Enhancement Act (U.S. General Accounting Office, Washington, DC) Publication GAO-02-965.
- Garraty, J.A. (1957). *Right-hand man: the life of George W. Perkins*. New York: Harper and Bros.
- Gerbin, A., & Drnovšek, M. (2013). How do university IPRs and R&D funding mechanisms affect innovation performance in the healthcare biotechnology industry? Evidence from Europe and the USA. *Periodicum Biologorum*, 115(1), 79-95.
- G-FINDER. (2015). Neglected diseases research and development: Ebola effect. *The Eight Annual G-FINDER Report, Policy Cures*. Retrieved from

<http://www.policycures.org/downloads/Y8%20GFINDER%20full%20report%20web.pdf>.

- Glaser, D. (2006). *The Bubble Chamber, Bioengineering, Business Consulting, and Neurobiology*. An oral history conducted in 2003-2004 by Eric Vettel. The Regional Oral History Office. The Bancroft Library. University of California, Berkeley, 2006.
- Gleadle, P., Parris, S., Shipman, A., & Simonetti, R. (2014). Restructuring and innovation in pharmaceuticals and biotech: The impact of financialisation. *Critical Perspectives on Accounting*, 25(1), 67-77.
- Godley, A. & Hughes, D.L. (2014). E. Merck of Darmstadt and the Origins of Industrial Research Capabilities in U.S. Pharmaceuticals at Merck & Co. Paper presented at the *Business History Conference*, Frankfurt, Germany, March 13-15, 2014.
- Goeddel, D. V. (2003). *Scientist at Genentech, CEO at Tularik*. An oral history conducted in 2001 and 2002 by Sally Smith Hughes for the Regional Oral History Office. The Bancroft Library, The University of California, Berkeley, 2003.
- Goldman Sachs, (2011). Merck & Co., Inc. at Goldman Sachs Healthcare CEO's Conference, January 6, 2011. Final transcript retrieved from <http://phx.corporate-ir.net/External.File?item=UGFyZW50SUQ9NzY4ODh8Q2hpbGRJRD0tMXxUeXBIPTM=&t=1>
- Goozner, M. (2004). *The 800 million dollar pill. The truth behind the cost of new drugs*. The University of California Press: Berkley, California
- Gortler, L. (2000). Merck in America: The first 70 years-From fine chemicals to pharmaceutical giant. *Bulletin for the History of Chemistry*, 25(1) U897-U897.
- Greene, J. A., & Podolsky, S. H. (2012). Reform, regulation, and pharmaceuticals—the Kefauver–Harris Amendments at 50. *The New England Journal of Medicine*, 367(16), 1481-1483. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4101807/>
- Guerrera, F. (2009). Welch rues short-term profit ‘obsession’. *Financial Times*, March 12, 2009.
- Harmon, F.G. & Jacobs, G. (1985). *The vital difference: unleashing the powers of sustained corporate success*. New York, NY: AMACOM.
- Haslam, C., Andersson, T., Tsitsianis, N., & Yin, Y. P. (2013). *Redefining business models: Strategies for a financialized world*. Routledge.
- Hawthorne, F. (2004). *The Merck druggernaut: The inside story of a pharmaceutical giant*. John Wiley & Sons.
- Hawthorne, F. (2006). Merck's fall from grace. *The Scientist*, 20(5).
- Hemphill, C. S., & Lemley, M. A. (2010). Earning exclusivity: generic drug incentives and the Hatch-Waxman Act. *Antitrust LJ*, 77, 947.

Herper, M. (2009). The End of Merck. *Forbes*, March 11, 2009. Retrieved from <https://www.forbes.com/2009/03/10/merck-schering-pharmaceutical-business-health-care-merck.html#36fa47232b07>

Herper, M. (2011). A decade in drug industry layoffs. *Forbes*, April 12. Retrieved from <https://www.forbes.com/sites/matthewherper/2011/04/13/a-decade-in-drug-industry-layoffs/#35dff2e16cab>

Heyneker, H. L. (2002). *Molecular geneticist at UCSF and Genentech, entrepreneur in biotechnology*. An oral history conducted in 2002 by Sally Smith Hughes, Ph.D., Regional Oral History Office, The Bancroft Library, The University of California Berkeley.

Higgins, M. J., & Rodriguez, D. (2006). The outsourcing of R&D through acquisitions in the pharmaceutical industry. *Journal of Financial Economics*, 80(2), 351-383.

Hirschler, B. (2013). Novartis CEO tempers talk of Roche stake sale. *Reuters*, January 25. Retrieved from <https://www.reuters.com/article/us-davos-novartis-roche/novartis-ceo-tempers-talk-of-roche-stake-sale-idUSBRE90O09Y20130125>

Hirschler, B. & Reid, K. (2010). Has Roche got the right medicine? *Special Report – Roche, Thomson Reuters*, September 15, 2010.

Hirschler, B., & Kelland, K. (2010). Big Pharma, Small R&D. *Thomson Reuters*, London.

Hirschmann, R. F. (2007). 1.01 Reflections of a Medicinal Chemist: Formative Years through Thirty-Seven Years Service in the Pharmaceutical Industry. *Comprehensive Medicinal Chemistry II* (1): 1-27.

Holmstrom, B., & Kaplan, S. N. (2001). Corporate Governance and Merger Activity in the US: Making Sense of the 1980s and 1990s. *National Bureau of Economic Research*, No. w8220.

Hood, L., & Perlmutter, R. M. (2004). The impact of systems approaches on biological problems in drug discovery. *Nature Biotechnology*, 22(10), 1215-1217.

Hopkins M., Crane P., Nightingale P., Baden-Fuller C. (2013). Buying Big into Biotech: Scale, Financing, and the Industrial Dynamics of UK Biotech, 1980-2009. *Industrial and Corporate Change* 22 (4): 903–52.

Hopkins, M. M., Martin, P. A., Nightingale, P., Kraft, A., & Mahdi, S. (2007). The myth of the biotech revolution: An assessment of technological, clinical and organizational change. *Research policy*, 36(4), 566-589.

Hopkins, M., & Lazonick, W. (2014). Who invests in the high-tech knowledge base? (December 4, 2014). *The Institute for New Economic Thinking Working Paper Series*, No. 14. Retrieved from <https://ssrn.com/abstract=2638091>.

Hopkins, M., & Lazonick, W. (2016). The Mismeasure of Mammon: Uses and Abuses of Executive Pay Data (October 12, 2016). *The Institute for New Economic Thinking Working Paper Series*, No. 49. Retrieved from <https://ssrn.com/abstract=2877980>.

- Hughes, S. S. (2011). Genentech: the beginnings of biotech. The University of Chicago Press.
- ICIS. (2000). Roche moves to keep Martin Ebner from board. ICIS News, April 13. Retrieved from <https://www.icis.com/resources/news/2000/04/13/109936/roche-moves-to-keep-martin-ebner-from-board/>
- Initiative for Medicines, Access & Knowledge [I-MAK], (2017). *America's overspend: How the pharmaceutical patent problem is fueling high drug prices*. Solving the drug patent problem. Excess Cost Briefing, October 2017. Retrieved from <http://www.i-mak.org/wp-content/uploads/2017/10/Excess-Costs-Briefing-Paper-FINAL-2017-10-24-with-cover-rev.compressed.pdf>.
- International Federation of Pharmaceutical Manufacturers & Associations [IFPMA]. (2017). IFPMA Facts and Figures Report, February 9, 2017. Retrieved from <https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf>.
- International Herald Tribune [IHT]. (2000). *Briefcase: Ebner shakes up Roche Holdings*, April 1. Retrieved from <http://www.nytimes.com/2000/04/01/your-money/briefcase-ebner-shakes-up-roche-holdings.html>.
- Janeway, W. H. (2012). *Doing capitalism in the innovation economy: markets, speculation and the state*. Cambridge University Press.
- Jarvis, L.M. (2008). An uphill battle. Chemical & Engineering News, April 14, 2008, 86(15): 15-20.
- Jensen, M. C. (1986). Agency costs of free cash flow, corporate finance, and takeovers. *The American Economic Review*, 76(2), 323-329.
- Jensen, M. C. (1989). Eclipse of the public corporation. *Harvard Business Review*, Sep-Oct.
- Jensen, M. C., & Meckling, W. H. (1976). Theory of the firm: Managerial behavior, agency costs and ownership structure. *Journal of Financial Economics*, 3(4), 305-360.
- Jensen, M. C., & Murphy, K. J. (1990). Performance pay and top-management incentives. *Journal of Political Economy*, 98(2), 225-264.
- Jensen, M. C. (2000). Value Maximization, Stakeholder Theory, and the Corporate Objective Function. In M. Beer and N. Nohria (Eds.), *Breaking the Code of Change* (Harvard Business School Press, Boston), pp. 37–58. Reprinted (2002) as ‘Value Maximization, Stakeholder Theory, and the Corporate Objective Function’, *Business Ethics Quarterly* 12(2), 235–256.
- Kaitin, K. I. (2010). Deconstructing the drug development process: the new face of innovation. *Clinical Pharmacology and Therapeutics*, 87(3), 356.
- Kaitin, K. I., & DiMasi, J. A. (2011). Pharmaceutical innovation in the 21st century: new drug approvals in the first decade, 2000–2009. *Clinical Pharmacology & Therapeutics*, 89(2), 183-188.

- Kantarjian, H., & Rajkumar, S. V. (2015). Why are cancer drugs so expensive in the United States, and what are the solutions? *Mayo Clinic Proceedings*, 90(4): 500-504.
- Kessel, M. (2011). The problems with today's pharmaceutical business - an outsider's view. *Nature Biotechnology*, 29(1), 27-33.
- Kesselheim, A. S., Murtagh, L., & Mello, M. M. (2011). "Pay for delay" settlements of disputes over pharmaceutical patents. *The New England Journal of Medicine*, 365(15), 1439-1445.
- Kevles, D. (1998). Diamond vs. Chakrabarty and Beyond: Political Economy of Patenting Life. In Arnold Thackray, (Eds.), *Private Science: Biotechnology and the Rise of the Molecular Sciences*, University of Pennsylvania Press.
- Kiley, T. D. (2002). *Thomas D. Kiley: Genentech Legal Counsel and Vice President, 1976-1988, and Entrepreneur*. An oral history conducted in 2000 and 2001 by Sally Smith Hughes. Regional Oral History Office. The Bancroft Library. University of California, Berkeley, 2002.
- Kinch, M. (2016). *A Prescription for Change: The Looming Crisis in Drug Development*. UNC Press Books.
- King, R.T. Jr. & Moore, S.D. (1995). Swiss Stakes: Basel's Drug Giants Are Placing Huge Bet On U.S. Biotech Firms. Roche, Sandoz, Ciba Pay Up, Seeking Breakthrough, A Strategy Some Deride. *The Wall Street Journal Europe*, November 29, 1995 S.1.
- Kleid, D. G. (2002). *Scientist and Patent Agent at Genentech*. An oral history conducted in 2001 and 2002 by Sally Smith Hughes for the Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2002.
- Knechtli, V.P. (2000). Die Rakete landete im Vorzimmer von Roche. *OnlineReports.ch*, February 27. Retrieved from <http://archiv.onlinereports.ch/2000/ebnerRocheChance.htm>.
- Kneller, R. (2005). The origins of new drugs. *Nature Biotechnology*, 23(5), 529-530.
- Kneller, R. (2010). The importance of new companies for drug discovery: origins of a decade of new drugs. *Nature Reviews Drug Discovery*, 9(11), 867-882.
- Koberstein, W. (2000). The Inner Merck. *Pharmaceutical Executive*, 20(1): 4458.
- Krippner, G. R. (2005). The financialization of the American economy. *Socio-economic Review*, 3(2), 173-208.
- Kurosawa, T. (2015). Breaking through the Double Blockade: Inter-Atlantic Wartime Communications at Roche. *Jahrbuch für Wirtschaftsgeschichte/Economic History Yearbook*, 56(1), 227-256.
- LaMattina, J. L. (2011). The impact of mergers on pharmaceutical R&D. *Nature Reviews Drug Discovery*, 10(8), 559-560.

- LaMattina, J.L. (2015). FDA Approvals 1996 vs. 2014: The Two Most Prolific Years, But Stark Differences. *Forbes Magazine*, July 7, 2011.
- Landau, B., Achilladelis, B., & Scriabine, A. (1999). Pharmaceutical taxonomy of most important drugs. In R. Landau, B. Achilladelis, & A. Scriabine (Eds.), *Pharmaceutical Innovation* (p. 298-307). Philadelphia, PA: Chemical Heritage Press.
- Langley, A. (2003). Novartis's stake In Roche fuels merger speculation. *The New York Times*, January 24. Retrieved from <http://www.nytimes.com/2003/01/24/business/novartis-s-stake-in-roche-fuels-merger-speculation.html>
- Lax, E. (1985). Banking on the biotech business. *The New York Times*, December 22. Retrieved from <http://www.nytimes.com/1985/12/22/magazine/banking-on-the-biotech-business.html?pagewanted=all>.
- Lax, E. (2004). *The Mold in Dr. Florey's Coat*. New York: Henry Holt & Co.
- Lazarus, D. (2014). What's behind the huge price jump for some generic drugs? *Los Angeles Times*. October 20. Retrieved from <http://www.latimes.com/business/la-fi-lazarus-20141021-column.html>.
- Lazonick, W. & Hopkins, M. (2016). Corporate Executives Are Making Way More Money Than Anyone Reports. *The Atlantic*, September 15. Retrieved from <http://www.theatlantic.com/business/archive/2016/09/executives-making-way-more-than-reported/499850/>.
- Lazonick, W., & March, E. (2011, January). The rise and demise of Lucent Technologies. In Business History Conference. Business and Economic History On-line: Papers Presented at the BHC Annual Meeting (Vol. 9, p. 1). Business History Conference.
- Lazonick & Prencipe (2005). Dynamic capabilities and sustained innovation: strategic control and financial commitment at Rolls-Royce plc. *Industrial and Corporate Change*, 14(3), 501-542.
- Lazonick, W. & Shin, J.S. (2018). *Predatory Value Extraction: How the looting of the business enterprise became the US norm and how sustainable prosperity can be restored*. Book manuscript, January 2018.
- Lazonick, W. & Tulum, Ö. (2011). US biopharmaceutical finance and the sustainability of the biotech business model. *Research Policy*, 40(9), 1170-1187.
- Lazonick, W. (1991). What Happened to the Theory of Economic Development? Cambridge: Harvard University Press.
- Lazonick, W. (2001). *The Us Industrial Corporation and" the Theory of the Growth of the Firm."* INSEAD.
- Lazonick, W. (2002). Innovative enterprise and historical transformation. *Enterprise and Society*, 3(01), 3-47.
- Lazonick, W. (2005). *The innovative firm* (pp. 29-55). Oxford University Press: New York.

- Lazonick, W. (2007). The US stock market and the governance of innovative enterprise. *Industrial and Corporate Change*, 16(6), 983-1035.
- Lazonick, W. (2009). *Sustainable prosperity in the new economy? Business organization and high-tech employment in the United States*. New York: Upjohn Institute.
- Lazonick, W. (2010). The Chandlerian corporation and the theory of innovative enterprise. *Industrial and Corporate Change*, 19(2), 317-349.
- Lazonick, W. (2011). From innovation to financialization: how shareholder value ideology is destroying the US Economy. *The Handbook of the Political Economy of Financial Crises*, 491-511.
- Lazonick, W. (2013a), Financialization of the US Corporation: What Has Been Lost, and How It Can Be Regained, *Seattle University Law Review*, 36, 857-909.
- Lazonick, W. (2013b). The Theory of Innovative Enterprise: Methodology, Ideology, and Institutions In C. Bina, J.K. Moudud, P.L. Mason (Eds.), *Alternative Theories of Competition*. London: Routledge.
- Lazonick, W. (2014a). Profits without Prosperity. *Harvard Business Review*, 92(9), 46-55.
- Lazonick, W. (2014b). Innovative enterprise and shareholder value. *Law and Financial Markets Review*, 8(1), 52-64.
- Lazonick, W. (2015). Stock Buybacks: From Retain-and-Reinvest to Downsize-and-Distribute," Center for Effective Public Management, Brookings Institution", April 2015, pp. 10-11. Retrieved from <http://www.brookings.edu/research/papers/2015/04/17-stock-buybacks-lazonick>
- Lazonick, W. (2017). The value-extracting CEO: How executive stock-based pay undermines investment in productive capabilities. *Structural Change and Economic Dynamics* (In Press).
- Lazonick, W. (2018). The Functions of the stock market and the fallacies of shareholder value. In C. Driver and G. Thompson (Eds.), *What next for corporate governance?* Oxford University Press, 2018: 117-151.
- Lazonick, W., & O'Sullivan, M. (2000). Maximizing shareholder value: a new ideology for corporate governance. *Economy and Society*, 29(1), 13-35.
- Lazonick, W., & Prencipe, A. (2005). Dynamic capabilities and sustained innovation: strategic control and financial commitment at Rolls-Royce plc. *Industrial and Corporate Change*, 14(3), 501-542.
- Lazonick, W., & Sakinç, M. E. (2010). Do financial markets support innovation or inequity in the biotech drug development process?. In Workshop on *Innovation and Inequality: Pharma and Beyond*, Scuola Superiore Sant'Anna, Pisa, Italy, May (pp. 15-16).
- Lazonick, W., & Teece, D. J. (Eds.). (2012). *Management Innovation: Essays in the Spirit of Alfred D. Chandler, Jr.* Oxford University Press.

- Lazonick, W., & Tulum, Ö. (2011). US biopharmaceutical finance and the sustainability of the biotech business model. *Research Policy*, 40(9), 1170-1187.
- Lazonick, W., Hopkins, M., Jacobson, K., Sakinç, M.E., & Tulum, Ö. (2017). U.S. Pharma's Financialized Business Model. *The Institute for New Economic Thinking Working Paper No. 60* (Rev.), September 8, 2017.
- Lazonick, W., Moss, P., Salzman, H., & Tulum, Ö. (2014). Skill Development and Sustainable Prosperity: Collective and Cumulative Careers versus Skill-Biased Technical Change, *The Institute for New Economic Thinking Working Group on the Political Economy of Distribution Working Paper No. 7*, December 2014.
- Lazonick, W., & Tulum, Ö. (2015). Global tax dodging just one part of Pfizer's corrupt business model," appeared as blog pieces at *The Institute for New Economics Thinking and Huffington Post*, December 3, 2015.
- Leaver, A., & Montalban, M. (2010). Sanofi-Aventis and the complexity of capitalist organization. *Competition & Change*, 14(1), 1-22.
- Lehoux, P., Daudelin, G., Williams-Jones, B., Denis, J. L., & Longo, C. (2014). How do business model and health technology design influence each other? Insights from a longitudinal case study of three academic spin-offs. *Research Policy*, 43(6), 1025-1038.
- Lehoux, P., Miller, F. A., Daudelin, G., & Urbach, D. R. (2015). How venture capitalists decide which new medical technologies come to exist. *Science and Public Policy*, 43(3), 375-385.
- Lehrman, S. (1992). Cetus: a collision course with failure. *The Scientist*, 6(2), 1.
- Levy, C.J. (1993). Drug maker reshuffles at the top. *The New York Times*. September 22, 1993. Retrieved from <http://www.nytimes.com/1993/09/22/business/company-news-drug-maker-reshuffles-at-the-top.html>
- Ley, T. J., & Rosenberg, L. E. (2005). The physician-scientist career pipeline in 2005: build it, and they will come. *The Journal of the American Medical Association*, 294(11), 1343-1351.
- Light, D.W. (2009). Global drug discovery: Europe is ahead. *Health Affairs*, 28(5), w969-w977.
- Light, D.W. (2017). Debunking The Pharmaceutical Research 'Free Rider' Myth: A response To Yu, Helms, And Bach. *Health Affairs Blog*, June 2, 2017. Retrieved from <https://www.healthaffairs.org/do/10.1377/hblog20170602.060376/full/>
- Light, D.W., & Warburton, R.N. (2005a). Extraordinary Claims Require Extraordinary Evidence. *Journal of Health Economics*, 24, 5: 1030-1033.
- Light, D.W., & Warburton, R.N. (2005b). Setting the Record Straight in the Reply by DiMasi, Hansen, and Grabowski." *Journal of Health Economics*, 24, 5: 1045-1048.
- Lindsay, M. A. (2003). Target discovery. *Nature Reviews Drug Discovery*, 2(10), 831-838.

- Lipton, M. (2015). Some thoughts for boards of directors in 2016. *Harvard Law School Forum on Corporate Governance and Financial Regulation*, December 9. Retrieved from <https://corpgov.law.harvard.edu/2015/12/09/some-thoughts-for-boards-of-directors-in-2016/>
- Loftus, P. (2011a). New Pfizer, Merck CEOs take different tacks on research costs. *Dow Jones News Service*, February 3, 2011.
- Loftus, P. (2011b). Merck CEO: Spending on research crucial for Long-term success. *Dow Jones News Service*, July 15, 2011.
- Loise, V., & Stevens, A. J. (2010). The Bayh-Dole Act turns 30. *Science Translational Medicine*, 2(52), 52cm27-52cm27.
- Long, H. (2015). America's problem: 'quarterly capitalism'? *CNN Money*, August 29, 2015. Retrieved from <http://money.cnn.com/2015/08/20/investing/quarterly-capitalism-hillary-clinton/index.html>
- Love, J., & Hubbard, T. (2007). The Bid Idea: Prizes to Stimulate R&D for New Medicines. *Chicago-Kent Law Review*, 82(3): 1519-1554.
- Magdoff, H., & Sweezy, P.M. (1987). *Stagnation and the financial explosion*. NYU Press.
- Malerba, F., & Vonortas, N.S. (Eds.). (2009). *Innovation networks in industries*. Edward Elgar Publishing.
- Matloff, N. (2013). Are Foreign Students the 'best and the Brightest'? Data and Implications for Immigration Policy. *Economic Policy Institute*, Briefing Paper #356, February 28, 2013.
- Marcoulides, G.A., & Heck, R.H. (1993). Organizational culture and performance: Proposing and testing a model. *Organization Science*, 4(2), 209-225.
- Maugh II, T.H. (2005). Leo Sternbach, 97; Invented Valium, Many Other Drugs. Los Angeles Times. October 01, 2005.
- Maxwell, J. A. (1996). Applied social research methods series, Vol. 41. *Qualitative research design: An interactive approach*. Thousand Oaks, CA: Sage Publications.
- Mc Namara, P., & Baden-Fuller, C. (2007). Shareholder returns and the exploration-exploitation dilemma: R&D announcements by biotechnology firms. *Research Policy*, 36(4), 548-565.
- Meadows, M. (2006). Promoting safe and effective drugs for 100 years. *FDA Consumer Magazine*, 40(1). Retrieved from <https://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/ucm2017809.htm>
- Merck Annual Report [MAR]. (1963). *Merck & Co., Inc. 1963 Annual to Stockholders*. Retrieved from ProQuest Historical Annual Reports

Merck Annual Report [MAR]. (2016). *Merck & Co., Inc. 2016 Annual Report*. Retrieved from ProQuest Business Collection. Web. 22 Mar. 2016.

Middleton, F.A. (2002). *First Chief Financial Officer at Genentech, 1978-1984*. An oral history conducted in 2001 by Glenn E. Bugos. Regional Oral History Office. The Bancroft Library, The University of California, Berkeley, 2002.

Milberg, W. (2008). Shifting sources and uses of profits: Sustaining US financialization with global value chains. *Economy and Society*, 37(3), 420-451.

Miller, H. I., & Henderson, D. R. (2007). Governmental influences on drug development: striking a better balance. *Nature Reviews Drug Discovery*, 6(7), 532-539.

Mirowski, P. (2011). *Science-Mart: Privatizing American Science*. Harvard University Press.

Montalban, M., & Sakinç, M.E. (2013). Financialization and productive models in the pharmaceutical industry. *Industrial and Corporate Change*, 22(4), 981-1030.

Moses, H., Matheson, D. H., Cairns-Smith, S., George, B. P., Palisch, C., & Dorsey, E. R. (2015). The anatomy of medical research: US and international comparisons. *The Journal of the American Medical Association*, 313(2), 174-189.

Mowery, D. C., Nelson, R. R., Sampat, B., & Ziedonis, A. A. (1999). The effects of the Bayh-Dole Act on US university research and technology transfer: An analysis of data from Columbia University, the University of California, and Stanford University. *Research Policy*, 29, 729-40.

Mukunda, G. (2014). The price of Wall Street's power. *Harvard Business Review*, 92(6), 70-78.

Mullard, A. (2014). An audience with...: John Reed. *Nature Reviews Drug Discovery*, 13(3), 170-172.

Munos, B. (2009). Lessons from 60 years of pharmaceutical innovation. *Nature Reviews Drug Discovery*, 8(12), 959-968.

Nash, D. B. (2009). R&D Redux. *Pharmacy and Therapeutics*, 34(4), 174.

National Institutes of Health [NIH]. (2016). National Institutes of Health Budget. Retrieved from <https://www.nih.gov/about-nih/what-we-do/budget>

National Institutes of Health [NIH]. (2017a). A Short History of the National Institutes of Health, Office of NIH History. Retrieved from <https://history.nih.gov/exhibits/history/index.html>

National Institutes of Health [NIH]. (2017b). Impact of NIH Research, Our Society. Retrieved from <https://www.nih.gov/about-nih/what-we-do/impact-nih-research/our-society>

Nature. (2011). Fix the PhD. Editorial, *Nature*, 472 (April 21): 259–260.

- Neilan, T. (2004). Merck Pulls Vioxx Painkiller From Market, and Stock Plunges. *The New York Times*, September 30. Retrieved from
www.nytimes.com/2004/09/30/business/merck-pulls-vioxx-painkiller-from-market-and-stock-plunges.html?mcubz=0
- Nesi, T. (2008). *Poison Pills: The Untold Story of the Vioxx Drug Scandal*. New York: St. Martin's Press.
- New York Community Trust (n.d.). *George W. Merck 1894 to 1957, Memorialized by The George W. Merck Fund*, New York, NY. Retrieved from
<http://www.nycommunitytrust.org/Portals/0/Uploads/Documents/BioBrochures/George%20W.%20Merck.pdf>
- The New York Times. (1919). Offer \$3,500,000 Merck & Co. Stock. *The New York Times*, August 1, 1919. Retrieved from
<https://timesmachine.nytimes.com/timesmachine/1919/08/01/98290827.html>
- Nicholson, C.V. (2011). Roche's bloc of heirs lose majority vote after one bolts. *The New York Times*, March 25. Retrieved from
<https://dealbook.nytimes.com/2011/03/25/roches-bloc-of-heirs-lose-majority-vote-after-one-bolts/?mtrref=www.google.com&gwh=EC89D9D4F38EA9541A90BE1310FCD9D9&gwt=pay>
- Nightingale, P., (2000). Economies of scale in experimentation: knowledge and technology in pharmaceutical R&D. *Industrial and Corporate Change* 9: 315 –359.
- Nightingale, P., & Martin, P. (2004). The myth of the biotech revolution. *Trends in Biotechnology*, 22(11): 564-569.
- Norman, B., & Karlin-Smith, S. (2016). The one that got away: Obamacare and the drug industry. *Politico Magazine*, July 13, 2016. Retrieved from
<https://www.politico.com/story/2016/07/obamacare-prescription-drugs-pharma-225444>
- Olson, E. (2001). In surprise, Novartis gets a 20% stake in Roche. *The New York Times*, May 8. Retrieved from <http://www.nytimes.com/2001/05/08/business/in-surprise-novartis-gets-a-20-stake-in-roche.html>
- O'Sullivan, M. (2000). The Innovative Enterprise and Corporate Governance. *Cambridge Journal of Economics*, 24, 4: 393–416.
- Office of Technology Assessment [OTA]. (1993). *Pharmaceutical R&D: Costs, Risks, and Rewards*, US Congress, OTA-H-522. US Government Printing Office, Washington, DC, 1993.
- Palley, T. (2007). Financialization: What It Is and Why It Matters, *The Levy Economics Institute*, Washington DC, Working Paper (No. 525).
- Pammolli, F., Magazzini, L., & Riccaboni, M. (2011). The productivity crisis in pharmaceutical R&D. *Nature Reviews Drug Discovery*, 10(6), 428-438.

- Paul, S. M., Mytelka, D. S., Dunwiddie, C. T., Persinger, C. C., Munos, B. H., Lindborg, S. R., & Schacht, A. L. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nature Reviews Drug Discovery*, 9(3), 203.
- Penrose, E. T. (1959). *The Theory of the Growth of the Firm*. Fourth Edition (2009), Oxford University Press.
- Perkins, T. J. (2002). *Kleiner Perkins, venture capital, and the chairmanship of Genentech, 1976-1995*. An oral history conducted in 2001 by Glenn E. Bugos. Regional Oral History Office. The Bancroft Library. University of California, Berkeley, 2002.
- Peyer, H. C. (1996). *Roche: A company history, 1896-1996*. Editiones Roche.
- Pharmaceutical Research and Manufacturers of America [PhRMA]. (2016). *2015 Annual Membership Survey*. Retrieved from <http://phrma-docs.phrma.org/sites/default/files/pdf/annual-membership-survey-results.pdf>
- Pisano, G. P. (2006). *Science business: The promise, the reality, and the future of biotech*. Harvard Business Press.
- Pisano, G. P. (2015). You need an innovation strategy. *Harvard Business Review*, 93(6), 44-54.
- Pisano, G. P. (2017). Toward a prescriptive theory of dynamic capabilities: connecting strategic choice, learning, and competition. *Industrial and Corporate Change*, 26(5), 747-762.
- Pollack, A. (1990). Taking the crucial next step at Genentech. *The New York Times*. January 28, 1990.
- Pollack, A. (2010). Awaiting the genome payoff. *The New York Times*, June 14.
- Pollack, A. (2015). Drug goes from \$13.50 a tablet to \$750, overnight. *The New York Times*, September 20.
- Pollack, R. (1982). Biologists in Pinstripes. *The Sciences*, 22(7), 35-37.
- Public Citizen Congress Watch. (2001). *Rx R&D Myths: The Case Against the Drug Industry's R&D 'Scare Card'*. Public Citizen, Washington, DC, 2001.
- Quinn, R. (2013). Rethinking antibiotic research and development: World War II and the penicillin collaborative. *American Journal of Public Health*, 103(3), 426-434.
- Quirke, V. M. (2014). Targeting the American Market for Medicines, ca. 1950s–1970s: ICI and Rhône-Poulenc Compared. *Bulletin of the History of Medicine*, 88(4), 654.
- Quirke, V. M. (2004). War and change in the pharmaceutical industry: A comparative study of Britain and France in the twentieth century. *Entreprises et histoire*, (2), 64-83.
- Quirke, V., & Gaudillière, J. P. (2008). The era of biomedicine: science, medicine, and public health in Britain and France after the Second World War. *Medical History*, 52(04), 441-452.

- Raab, G. K. (2003). *G. Kirk Raab: CEO at Genentech, 1990-1995*. An oral history conducted in 2002 by Glenn E. Bugos, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2003.
- Rabinow, P. (1996). *Making PCR: A Story of Biotechnology*. The University of Chicago Press.
- Rabitschek, J. H., & Latker, N. J. (2005). Reasonable Pricing-A New Twist for March-in Rights Under the Bayh-Dole Act. *The Santa Clara High Technology Law Journal*, 22, 149.
- Rafols, I., Hopkins, M. M., Hoekman, J., Siepel, J., O'Hare, A., Perianes-Rodríguez, A., & Nightingale, P. (2014). Big pharma, little science?: A bibliometric perspective on Big Pharma's R&D decline. *Technological Forecasting and Social Change*, 81, 22-38.
- Rahm, D. (1989). Federal Efforts to Enhance US International Competitiveness: The Encouragement of Domestic Cooperation. *Policy Studies Journal*, 18(1), 89-99.
- Reingold, J. (1995). Mercky Waters, *Financial World*, January 17, 1995, pp. 28-29.
- Reinhold, R. (1981). Drugs that promise help but not profit reside in limbo. *The New York Times*, March 17, 1981.
- Relman, A. S., & Angell, M. (2002). America's other drug problem. How the drug industry distorts medicine and politics. *The New Republic*, December 16, 2002, 27-36.
- Research!America [R!A]. (2018, January). Mission & History. Retrieved from <http://www.researchamerica.org/about-us/mission-history>
- Riggs, A. D. (2006). *Arthur D. Riggs: City of Hope's Contribution to Early Genentech Research*. An oral history conducted by Sally Smith Hughes. Berkeley: Regional Oral History Office, Bancroft Library, University of California.
- Robbins-Roth, C. (2001). *From alchemy to IPO: the business of biotechnology*. Basic Books.
- Robinson, J. [Jeffrey]. (2001). *Prescription games: money, ego and power inside the global pharmaceutical industry*. London: Simon and Schuster.
- Robinson, J. [Judith]. (2001). *Noble conspirator: Florence S. Mahoney and the rise of the National Institutes of Health*. Washington D.C.: The Francis Press.
- Roche Historical Achieve, (n.d.). *Traditionally Ahead of Our Time*, Roche Historical Achieve, F. Hoffmann-La Roche Ltd, Basel
- Rosen, W. (2017). *Miracle Cure: The Creation of Antibiotics and the Birth of Modern Medicine*. Penguin.
- Roy, A. S. (2012). Stifling new cures: the true cost of lengthy clinical drug trials. *Manhattan Institute for Policy Research*, 5.

- Roy, V., & King, L. (2016). Betting on hepatitis C: how financial speculation in drug development influences access to medicines. *British Medical Journal*, 354, i3718.
- Ruhli, E., & Sachs, S. (1999). Case study. The Novartis mega-merger: an intra-organizational evolutionary perspective. *Strategic Change*, 8(4), 217.
- Rutter, W.J. (2005). *William J. Rutter: Co-Founder and Chairman, Chiron Corporation*. An oral history interview conducted by Sally Smith Hughes in 2004 and 2005, Oral History Center of the Bancroft Library, The Bancroft Library, University of California, Berkeley, 2015.
- Salvatore, S. & Davies, K. (2006). Merck President Touts Technology Benefits. *Bio-IT World*, March 14. Retrieved from <http://www.bio-itworld.com/issues/2006/march/merck/>
- Sarett, L.H. (1990). *Lewis Hastings Sarett*. An oral history interview by Leon Gortler at Viola, Idaho, September 6, Oral History Transcript # 0149. Philadelphia: Chemical Heritage Foundation.
- Scannell, J. W., & Bosley, J. (2016). When quality beats quantity: decision theory, drug discovery, and the reproducibility crisis. *PLoS One*, 11(2), e0147215.
- Scannell, J. W., Blanckley, A., Boldon, H., & Warrington, B. (2012). Diagnosing the decline in pharmaceutical R&D efficiency. *Nature Reviews Drug Discovery*, 11(3), 191-200.
- Schacht, W. H. (2012). *Federal R&D, drug discovery, and pricing: insights from the NIH-university-industry relationship*. DIANE Publishing. Retrieved from <https://www.fas.org/sgp/crs/misc/RL32324.pdf>
- Scheinberg, H. (1981). Drugs and profit. *The New York Times*, March 24.
- Scherer, F. M. (2011). R&D Costs and Productivity in Biopharmaceuticals. *Faculty research working paper series*, John F. Kennedy School of Government, Harvard University.
- Schmeck, H.M. (1984). Strange alliance: legions of bacteria created to serve man. *The New York Times*, January 3. Retrieved from <http://www.nytimes.com/1984/01/03/science/strange-alliance-legions-of-bacteria-created-to-serve-man.html>
- Schrage, M., & Henderson, N. (1984). Biotech becomes a global priority. *Washington Post*, December 17.
- Schuhmacher, A., Gassmann, O., & Hinder, M. (2016). Changing R&D models in research-based pharmaceutical companies. *Journal of Translational Medicine*, 14(1), 105.
- Schumpeter, J. A. (1939). *Business cycles* (Vol. 1, pp. 161-74). New York: McGraw-Hill.
- Schumpeter, J.A. (1942). *Capitalism, Socialism, and Democracy*, Harper, third edition (1950), p. 106.

- Seawright, J., & Gerring, J. (2008). Case selection techniques in case study research: A menu of qualitative and quantitative options. *Political Research Quarterly*, 61(2), 294-308.
- Seitel, F. P., & Doorley, J. (2012). *Rethinking reputation: How PR trumps marketing and advertising in the new media world*. Macmillan.
- Sheehan, J. C. (1982). *The enchanted ring: the untold story of penicillin*. Cambridge, Mass.: MIT Press
- Shleifer, A. and Vishny, R. W. (1997). A Survey of Corporate Governance. *The Journal of Finance*, 52: 737-783.
- Sidders, B., Brockel, C., Gutteridge, A., Harland, L., Jansen, P. G., McEwen, R., Michalovich, D. & Woodwark, M. (2014). Precompetitive activity to address the biological data needs of drug discovery. *Nature Reviews Drug Discovery*, 13(2), 83-84.
- Simons, J. (2004). Merck's man in the hot seat critics blame CEO Ray Gilmartin for getting the drug giant into its present mess. He thinks he's the one to get it out. *Fortune Magazine*, February 23,
- Slaughter, S., & Rhoades, G. (1996). The emergence of a competitiveness research and development policy coalition and the commercialization of academic science and technology. *Science, Technology, & Human Values*, 21(3), 303-339.
- Smaglik, P. (1997). NIH research funding reality fails to keep pace with rhetoric. *The Scientist*, 11(22), 1.
- Southwick, K. (1988). Ah, innovation! The pipeline to success. *HealthWeek* 17(223).
- Spelsberg, A., Prugger, C., Doshi, P., Ostrowski, K., Witte, T., Hüsgen, D., & Keil, U. (2017). Contribution of industry funded post-marketing studies to drug safety: survey of notifications submitted to regulatory agencies. *British Medical Journal*, 356, j337.
- Starr, P. (1983). *The Social Transformation of American Medicine*. New York, NY: Basic Books; 1983.
- Steen, K. (2014). *The American Synthetic Organic Chemicals Industry: War and Politics, 1910-1930*. UNC Press Books.
- Steffen, J. (2012). Tadeusz Reichstein: The Alchemist of Vitamin Science. *Sight and Life Magazine*, 26(3), 44-90.
- Stephan, P. E. (2012). *How economics shapes science* (Vol. 1). Cambridge, MA: Harvard University Press.
- Stevens, A. J. (2004). The enactment of Bayh-Dole. *The Journal of Technology Transfer*, 29(1), 93-99.
- Stevens, A. J., Jensen, J. J., Wyller, K., Kilgore, P. C., Chatterjee, S., & Rohrbaugh, M. L. (2011). The role of public-sector research in the discovery of drugs and vaccines. *New England Journal of Medicine*, 364(6), 535-541.

- Stockhammer, E. (2010). Financialization and the global economy. *Political Economy Research Institute Working Paper*, 242.
- Sturchio, G., & Galambos, L. (2011). The German Connection: Merck and the Flow of Knowledge from Germany to the United States. 2011. Retrieved from <http://www.thebhc.org/sites/default/files/sturchioandgalambos.pdf>.
- Sturchio, J. L. (1991). *Values and visions: A Merck century*. Rahway, NJ: Privately published.
- Swanson, R. A. (2001). *Robert A. Swanson: Co-founder, CEO, and Chairman of Genentech, Inc., 1976–1996*. An oral history conducted in 1996 and 1997 by Sally Smith Hughes, Regional Oral History Office. The Bancroft Library. University of California, Berkeley.
- Swinney, D. C., & Anthony, J. (2011). How were new medicines discovered? *Nature Reviews Drug Discovery*, 10(7), 507-519.
- Swissinfo.ch. (2001). Swiss investment guru attacks Roche board. *Swissinfo.ch*, April 3, 2001. Retrieved from <https://www.swissinfo.ch/eng/swiss-investment-guru-attacks-roche-board/1970684>
- Tagliabue, J. (2000). Roche: Drug Giant Stubbing Its Toes. *The New York Times*, October 1. Retrieved from <http://www.nytimes.com/2000/10/01/business/roche-drug-giant-stubbing-its-toes.html>
- Tagliabue, J. (2001). Europeans' rallying cry: One share, one vote. *The New York Times*, June 10. Retrieved from <http://www.nytimes.com/2001/06/10/business/europeans-rallying-cry-one-share-one-vote.html>
- Taylor, M. (2011). Reform the PhD system or close it down. *Nature News*, 472(7343), 261-261.
- Teece, D.J. (1982). Towards an economic theory of the multiproduct firm. *Journal of Economic Behavior & Organization*, 3(1), 39-63.
- Teece, D.J. (2009). *Dynamic capabilities and strategic management: Organizing for innovation and growth*. Oxford University Press on Demand.
- Teece, D.J., Pisano, G., & Shuen, A. (1997). Dynamic capabilities and strategic management. *Strategic management journal*, 18(7), 509-533.
- Teitelbaum, M. S. (2008). Structural disequilibria in biomedical research. *Science*, 321(5889), 644-645.
- Teitelbaum, M. S. (2014). *Falling behind? Boom, bust, and the global race for scientific talent*. Princeton University Press.
- Temin, P. (1979). Technology, regulation, and market structure in the modern pharmaceutical industry. *The Bell Journal of Economics*, 429-446.

Temin, P. (1980). *Taking your medicine: drug regulation in the United States*. Cambridge, Mass.: Harvard University Press.

The Economist. (1997). Mercky waters. *The Economist*, May 22. Retrieved from <http://www.economist.com/node/369820>

The Economist. (2002). The acceptable face of capitalism? *The Economist*, Dec 14. Retrieved from <https://www.economist.com/node/1491753>.

Tishler, M. (1983). *Max Tishler*. An interview by Leon Gortler and John A. Heitmann at the Library at Wesleyan University, 14 November 1983, Oral History Transcript # 0008. Philadelphia: Chemical Heritage Foundation.

Tobbell, D. (2011). *Pills, power, and policy: the struggle for drug reform in cold war America and its consequences* (Vol. 23). University of California Press.

Todd, S. (2009). Hoffman La Roche planning to leave Pharma. *The Star-Ledger*, June 29. Retrieved from http://www.nj.com/business/index.ssf/2009/06/hoffman_la_roche_planning_to_1.html

Todd, S. & Jones, S. (2012). Roche will close Nutley plant, shed nearly 1,000 jobs. *The Star-Ledger*, June 27. Retrieved from www.nj.com/news/index.ssf/2012/06/roche_will_close_nutley_campus.html

Tone, A. (2008). *The age of anxiety: A history of America's turbulent affair with tranquilizers*. Basic Books.

Tribble, S.J. & Lupkin, S. (2017). The Orphan Drug Machine - Drugmakers Manipulate Orphan Drug Rules To Create Prized Monopolies. Kaiser Health News, January 17, 2017. Retrieved from <https://khn.org/news/drugmakers-manipulate-orphan-drug-rules-to-create-prized-monopolies/>

Udenfriend, S. (1995). Camelot in Nutley, NJ - Roche Institute of Molecular Biology remembered. *The Scientist*, 9 (21): 12.

Ugolik, K. (2015). MIT's Andrew Lo touts megafund to tackle cancer, rare diseases. *Institutional Investor*, October 26, 2015. Retrieved from <https://www.institutionalinvestor.com/article/b14z9ypfg10q6q/mits-andrew-lo-touts-megafund-to-tackle-cancer-rare-diseases>

UK Department of Health. (2012). The Pharmaceutical Price Regulation Scheme, *Eleventh Report to Parliament*, February 2012: 30.
Note: Subsequent PPRS reports do not provide these data.

United States Census Bureau [USCB]. (2012). Statistics of U.S. Businesses (SUSB), *Data on 2012 SUSB Annual Data Tables by Establishment Industry*. Retrieved from <https://www.census.gov/data/tables/2012/econ/susb/2012-susb-annual.html>.

Vagelos, P. (1991). Are Prescription Drug Prices High? *Science*, 252(5009): 1080-1084. Retrieved from <http://www.jstor.org/stable/2876283>

- Vagelos, P. R., & Galambos, L. (2004). *Medicine, science and Merck*. Cambridge University Press.
- Vagelos, P. R., & Galambos, L. (2006). *The moral corporation: Merck experiences*. Cambridge University Press.
- Välikangas, L. (1995). Upon the shoulders of giants. *Iryo To Shakai*, 5(1), 58-118.
- Valle, F., & Gambardella, A. (1993). ‘Biological’ revolution and strategies for innovation in pharmaceutical companies. *R&D Management*, 23(4), 287-302.
- van Thiel, G. J., & van Delden, J. J. (2008). Phase IV research: innovation in need of ethics. *Journal of Medical Ethics*, 34:415-416.
- Varmus, H. (2009). *The art and politics of science*. WW Norton & Company.
- Vettel, E. J. (2006). *Biotech: The countercultural origins of an industry*. University of Pennsylvania Press.
- Ward, A. (2015, Sep 21). Roche scion André Hoffman on benefits of family ownership. *The Financial Times*, September 21, 2015.
- Weber, J. (1991). Offering employees stock options they can't refuse. *Business Week*, October 7.
- Weber, J. (1993). Suddenly, no heir is apparent at Merck. *Business Week*, July 26.
- Weber, J. (1996). Merck’s Mr. nice guy with a mission. *BusinessWeek*, November 25.
- Weber, J., Byrne, J., McNamee, M., & McWilliams, G. (1994). Merck Finally Gets its Man. *BusinessWeek*, June 27: 22-25.
- Weissbach, H. (1987). The Roche institute of molecular biology. *BioEssays*, 7(6), 243-245.
- Weissbach, H., Witkop, B. (2003). Sidney Udenfriend, 1978-1999. A Biographical Memoir by Herbert Weissbach and Bernhard Witkop, *Biographical Memoirs*, Volume 83 (271), Washington D.C.: The National Academies Press.
- Wernerfelt, B. (1984). A resource-based view of the firm. *Strategic management journal*, 5(2), 171-180.
- Werth, B. (1994). *The billion-dollar molecule: The quest for the perfect drug*. Simon and Schuster.
- Werth, B. (2014). *The Antidote: Inside the World of New Pharma*. Simon and Schuster.
- Wilkins, M. (2009). *The history of foreign investment in the United States, 1914-1945* (Vol. 43). Harvard University Press.
- Willens, R. (2009). Merck’s “Unusual” Deal Moves Beyond Taxes. *CFO.com – An Argyle Company*, Mar. 16, 2009. Retrieved from http://www.cfo.com/article.cfm/13312058/1/c_2984354?f=rsspage.

Wokasch, M.G. (2010). *Pharmaplasia*. Wokasch Consulting, LLC, Madison, Wisconsin: Privately Published.

Wright, R. (1996). How Zantac became the best-selling drug in history. *Marketing Health Services*, 16(4), 24.

Wyden, R., Grassley, C., & Hatch, O. G. (2015). The Price of Sovaldi and Its Impact in the U.S. Health Care System, Committee on Finance, United States Senate, December 1, 2015. Retrieved from <http://www.finance.senate.gov/ranking-members-news/wyden-grassley-sovaldi-investigation-finds-revenue-driven-pricing-strategy-behind-84-000-hepatitis-drug>

Yin, R. K. (2003). *Case study research design and methods third edition*. Applied social research methods series, 5. Sage Publications.

Yu, N., Helms, Z., & Bach, P. (2017). R&D costs for pharmaceutical companies do not explain elevated US drug prices, *Health Affairs Blog*, March 7. Retrieved from <https://www.healthaffairs.org/do/10.1377/hblog20170307.059036/full/>

Zeller, C. (2004). North Atlantic innovative relations of Swiss pharmaceuticals and the proximities with regional biotech arenas. *Economic Geography*, 80(1), 83-111.

Zweigenhaft, R. L., & Domhoff, G. W. (2007). Women in the power elite. In B.A. Arrighi (Ed.) *Understanding Inequality: The Intersection of Race/Ethnicity, Class, and Gender* (p. 201-207), Lanham, Maryland: Rowman & Littlefield Publishers, Inc.

Wall Street Journal [WSJ]. (1993). Roche raises \$702 million in U.S. offer. *The Wall Street Journal*, September 9, 1993.

APPENDICES

Appendix 1: Summary in Slovenian language / Daljši povzetek disertacije v slovenskem jeziku

Institucionalno okolje v Združenih državah Amerike (v nadaljevanju ZDA) omogoča edinstvene prednosti za razvoj in komercializacijo farmacevtskih zdravil. Vlada ZDA prek Nacionalnih inštitutov za zdravje (ang. National Institutes of Health, v nadaljevanju NIH) zagotavlja več kot 30 milijard dolarjev na leto za podporo raziskavam s področja znanosti o življenu, ki se izvajajo prek dobro vzpostavljene mreže vladnih, neprofitnih, univerzitetnih in bolnišničnih raziskovalnih laboratorijev. Pogoji privabljajo talentirane posameznike iz celega sveta za študij na ameriških univerzah in nadaljevanje kariere v vladnem, neprofitnem, univerzitetnem ali korporativnem okolju. Pravni sistem v ZDA spodbuja prenos raziskav financiranih iz zveznega proračuna v podjetja, katerim nato omogoča podelitev 20-letne patentne zaščite za odkritje novih zdravil. Poleg tega lahko biofarmacevtska podjetja na podlagi zakona iz leta 1983 (Orphan Drug Act of 1983) v primeru zdravil za zdravljenje redkih in genetskih bolezni pridobijo 7-letno ekskluzivno pravico za trženje zdravila od trenutka, ko Uprava ZDA za hrano in zdravila (angl. Food and Drug Administration, v nadaljevanju FDA) zdravilo odobri. Ta podjetja lahko koristijo tudi številne različne vrste subvencij na zvezni, državni in lokalni ravni namenjenih za raziskave.

Poleg omenjenih ugodnosti za financiranje inovacij na področju farmacevtskih zdravil so ZDA edina večja država, ki ne regulira cen farmacevtskih zdravil, ki so v splošnem v ZDA vsaj dvakrat večje kot v ostalih razvitih državah (Lazonick et al., 2017). Trg farmacevtskih zdravil v ZDA je največji na svetu, pri čemer vladne agencije plačujejo več kot 40 odstotkov teh izdatkov. Visoke cene zdravil in ekonomije obsega zagotavljajo biofarmacevtskim podjetjem velike dobičke, ki jih lahko namenijo za odkrivanje novih zdravil. Največja biofarmacevtska podjetja v ZDA, ki so vključena v S&P 500 Index, tako porabijo približno 16 odstotkov prihodkov za raziskave in razvoj [R&D] (Lazonick et al., 2017).

Kljub nacionalni ureditvi naklonjeni inovacijam pa obstajajo številne trditve, da je v farmacevtski panogi v ZDA prisotna kriza produktivnosti (Garnier, 2008; Munos, 2009; Paul et al., 2010; Pammolli et al., 2011; Scannell et al., 2012; Rafols et al., 2014; Gleadle et al., 2014; Scannell & Bosley, 2016; Kinch, 2016). Cilj raziskave je dvojen. Prvič, ta preučuje obstoječe dokaze, da je mogoče razlago za omenjeni paradoks iskati v financializaciji farmacevtske panoge ZDA. S preučevanjem zgodovinskih podatkov in izvajanjem poglobljene analize na ravni podjetij raziskava omogoča boljše razumevanje mehanizmov, ki povezujejo upočasnitev produktivnosti raziskav in razvoja v farmacevtski panogi s financializacijo pred tem inovativnih farmacevtskih podjetij iz ZDA. Raziskava se nato osredotoča na preučevanje dokazov, ki bi kazali na to, da so manj-financializirana evropska biofarmacevtska podjetja, ki so podvržena cenovni regulaciji na svojih domačih trgih, povečala svoje inovacijske sposobnosti z izkoriščanjem ogromne baze znanja ZDA in prodajo svojih proizvodov v ZDA po visokih, nereguliranih cenah.

Z vidika teorije Williama Lazonicka o inovativnem podjetju (angl. Theory of the innovative enterprise, v nadaljevanju TIE) raziskava v svojem kontekstu povzema definicijo inovativnosti kot spremjanje tehnologij in trgov zaradi (A) ustvarjanja zdravil višje kakovosti in (B) nižjih stroškov (C) z namenom zadovoljevanja zdravstvenih potreb potrošnikov na trgu farmacevtskih proizvodov. Čeprav je prisotno splošno prepričanje o obstoju "inovacijske krize" oziroma "krize inovativnosti" v farmacevtski panogi, obstajajo številne, pogosto konkurenčne teorije, ki želijo pojasniti izvor tega problema. Takšne teorije so kategorizirane na podlagi treh tematik: (1) teorije, ki se osredotočajo na vprašanja, ki izhajajo iz omejitve na področju znanosti in tehnologije; (2) teorije, ki se ukvarjajo z vlogo regulative in vladnih intervencij; in (3) teorije, ki obravnavajo vprašanja povezana z upravljanjem inovativnosti.

Znotraj prve skupine teorij obstajajo argumenti, ki se osredotočajo na razkorak med znanjem v znanosti in tehnologiji ter odkrivanjem zdravil. Nekateri komentarji se tako osredotočajo na omejitve pri razvoju in uporabi učinkovitih strategij ocenjevanja zdravil, na primer Booth & Zemmel, (2004); Lindsay, (2004); Swinney & Anthony, (2011); Sidders et. al., (2014) medtem ko ostali poudarjajo pomen prizadevanja za premagovanje kompleksnosti sistemsko biologije (Hood & Perlmutter, 2004) in potrebo po obdelavi poplave informacij, ki izhaja iz t.i. "genomskega mehurčka" (angl. genomic bubble) (Pollack, 2010; Evans et al., 2011). Druga skupina razlag krize produktivnosti povezuje padajočo učinkovitost raziskav in razvoja z regulativnim pristopom Uprave ZDA za hrano in zdravila (FDA) med procesom odobritve zdravila, saj naj bi ta podaljšal trajanje kliničnih preiskusov (Dickson & Gagnon, 2004; Miller & Henderson, 2007; Kaitin & DiMasi, 2011). Po navedbah tega korpusa literature rast potrošnje za raziskave in razvoj kaže na povečano stopnjo strogosti pri odobritvah FDA. Ta se je pokazala po umiku proizvodov zaradi varnostnih razlogov v prvih letih po letu 2000 in tako obstaja trditev, da previdnejši pristop FDA, ki je bil sprejet po teh dogodkih, ovira inovacije biofarmacevtskih podjetij (Kaitin, 2010; Roy, 2012).

Tretja skupina argumentov o zmanjševanju učinka inovacijskih naporov v povezavi z industrijskimi zdravili se osredotoča na upravljanje farmacevtskih podjetij in investicije proizvodnih virov v raziskave in razvoj (v nadaljevanju R&R). V obdobju post-genomike (ang. post-genomics) so se R&R skoncentrirale na neraziskana področja kompleksnih terapij za onkološke in nevrodegenerativne bolezni. Prizadevanja so bila usmerjena v doseganje ciljev z visokimi donosi (nagradami), ampak so utrpela precejšnje izgube glede na kompleksnost osnovnih bioloških sistemov (Munos, 2009; Pammolli et al., 2011; Swinney & Anthony, 2011; Scannell et. al, 2012). Tretja skupina argumentov pravi, da bi lahko bolj strateški pristop k managementu raziskav in razvoja znotraj velikih farmacevtskih podjetij, privadel do učinkovitejših rezultatov s sodelovanjem zunanjih inovacijskih mrež in doseganjem večjega medorganizacijskega partnerstva z daljšim časovnim obdobjem (Munos, 2009; Pisano, 2015).

Znotraj tretje skupine nastaja poseben korpus literature, ki se ukvarja z načini razvijanja in uporabe proizvodnih virov v farmacevtskih podjetjih. Ta literatura ponuja prepričljive dokaze o vlogi financializacije farmacevtskega poslovnega modela v ZDA v sedanji krizi produktivnosti. Dobički, ki izhajajo iz uspeha podjetja pri ustvarjanju inovativnih proizvodov in vlaganje dobičkov z namenom povečevanja inovacijskih kapacetet podjetja zagotavljajo finančne temelje za nadaljnjo rast podjetja. Z vidika inovativnega podjetja, bo zasledovanje dobičkov brez kakršnihkoli drugih namenov z veliko verjetnostjo ogrozilo socialne razmere v inovativnem podjetju. Poleg tega se bo povečal pomen ekstrakcije vrednosti nad ustvarjanjem nove vrednosti in s tem vzpodbudilo nastanek bolezni produktivnosti poznane kot financializacija prek različnih panog, vključno s farmacevtsko (Lazonick, 2013a & 2017; see also Baldwin & Clark, 1992; Christensen et al., 2008; Lazonick & Tulum, 2011). Literatura s področja financializacije tudi kaže na to, da je prevelika odvisnost panoge od modela temelječega na t.i. "izdelkih preboja" (angl. blockbuster) za vzdrževanje dobičkonosnosti spodbudila strateške managerje k neutemeljenim stavam na podlagi novih tehnologij brez ustvarjanja potrebnih baz znanja, ki bi poganjalo takšne naložbe in ustvarjalo uspešne proizvode (Nightingale & Martin, 2004; Froud et al., 2006; Hopkins et al., 2007; Lazonick & Sakinç, 2010; Kessel, 2011; Montalban & Sakinç, 2013; Haslam et al., 2013; Gleadle et al., 2014).

Z vidika financializacije disertacija "izziva" argumente osredotočene na stroškovni vidik, ki zaznavajo vzrok neučinkovitosti farmacevtskih inovacij kot zunanji dejavnik upravljanja in organizacije farmacevtske panoge. Na podlagi ogrodja TIE disertacija raziskuje ali krizo učinkovitosti povzročajo zunanji dejavniki ali je ta globoko zakoreninjena v farmacevtskih organizacijah. Na podlagi okvirja socialnih razmer v inovativnem podjetju (angl. social conditions of innovative enterprise, v nadaljevanju SCIE), disertacija preučuje kako se lahko inovativno podjetje sooča z omejitvami, ki naj bi jih ustvarjala tehnologija in trgi z namenom preoblikovanja tehnologij in dostopa do trgov v njihovo lastno korist.

Študija identificira pojav "financializacije" kot niz novih organizacijskih ciljev in vrednot upravljanja, kjer cilj doseganja kapitalske učinkovitosti izključno za maksimiranje vrednosti premoženja delničarjev (angl. maximizing shareholder value, v nadaljevanju MSV) izpodriva ostale cilje in vrednote, ki prinašajo koristi širši bazi deležnikov. V kontekstu farmacevtske panoge v ZDA disertacija pojasnjuje kako je financializacija prinesla delničarjem oziroma lastnikom večje donose na finančne zaslужke ustvarjene na podlagi izboljšane produktivnosti v "realnem gospodarstvu", legitimizirala zahteve lastnikov po izplačilu korporativnih sredstev, omogočila, da je MSV postal norma v korporativnem upravljanju ter prispevala k trajajoči krizi inovativnosti.

Kot je podrobneje pojasnjeno v četrtem poglavju, predstavlja ZDA idealno okolje za nekatera biofarmacevtska podjetja, ki se osredotočajo na razvoj učinkovitih novih terapij z zdravili, ki lahko povzročijo "razbitje" trga in v zameno privedejo do precejšnjih finančnih donosov. ZDA lahko prav tako predstavlja idealno okolje za tiste, ki se zanimajo za vlaganje v programe razvoja zdravil, ki bi lahko vodila do višjih in hitrejših donosov tudi

brez razvoja visoko inovativnih novih zdravil ali sploh brez razvoja kakršnihkoli zdravil. Ko število podjetij v zadnji skupini enkrat preseže število podjetij v prvi, se celotna panožna usmeritev spremeni na način, da začne nagrajevati delničarje (lastnike) na račun drugih deležnikov kot so pacienti, davkoplačevalci ali zaposleni v takih podjetjih.

Vse korporacije se soočajo s pritiskom oziroma razpetostjo med inovativnostjo in financializacijo. Podjetje mora vlagati v ustvarjanje vrednosti v kolikor želi razvijati visokokakovostne, nizko-stroškovne dobrine in storitve, ki mu omogočajo ustvarjanje prihodkov na trgih proizvodov in mu prinašajo zadostne dobičke, da nastane in preživi kot inovativno podjetje. Toda, ko podjetje enkrat postane uspešno in inovativno, bodo žeeli udeleženci v podjetju, vključno z zaposlenimi, davkoplačevalci in financerji, ki so prispevali k procesu ustvarjanja vrednosti, "izvleči" nekaj ali vso povečano vrednost, ki jo je inovacijska usmerjenost podjetja omogočila. Ta "ekstrakcija" vrednosti bo nagradila delavce, davkoplačevalce in financerje za njihove prispevke k ustvarjanju vrednosti. Toda, če bodo iz podjetja "izvlekli" preveč vrednosti, lahko s tem ogrozijo finančno sposobnost podjetja kot aktivnega podjetja – vključno s finančno sposobnostjo podjetja za naslednje investicije v novo generacijo inovativnih proizvodov.

Dilema med inovativnostjo in financializacijo postane precej bolj problematična, kadar se podjetje upravlja zaradi finančnih interesov, ki posedujejo moč na podlagi katere lahko zase iz podjetja "izvlečejo" veliko več vrednosti kot so jo sami prispevali v procesu ustvarjanja vrednosti. In v institucionalnem okolju, v katerem prevladuje ideologija, da mora biti podjetje upravljan z namenom "maksimiranje vrednosti premoženja delničarjev", to predstavlja natanko to, kar se je zgodilo v ZDA (Lazonick & O'Sullivan, 2000; Lazonick, 2017; Lazonick, 2018; Lazonick & Shin, 2018). Izvršni direktorji korporacij, bankirji z Wall Street-a in managerji hedge skladov predstavljajo tiste, ki so pridobili koristi iz ogromnih distribucij korporativnega denarja delničarjem v obliki odkupa lastnih delnic in denarnih dividend, kjer so njihovi finančni zaslužki v povsem neproporcionalnem razmerju z njihovimi prispevki v procesu ustvarjanja vrednosti v podjetju.

Tako v ZDA kot v Evropi se biofarmacevtska podjetja soočajo s pritiskom med inovativnostjo in financializacijo in tu lahko tista podjetja, ki so upravljana z namenom ustvarjanja inovacij najbolje izkoristijo ogromen nacionalni inovacijski sistem, ki obstaja v ZDA. Skozi analizirane primere podjetij disertacija pokaže pomen socialnih razmer v inovativnem podjetju pri podpiranju procesa inoviranja in izogibanju financializaciji. Na podlagi argumenta, da je financializacija farmacevtskega poslovnega modela v ZDA resnični krivec za zmanjševanje produktivnosti v farmacevtskih podjetjih ZDA, disertacija podrobno pojasnjuje zakaj in kako so se biofarmacevtska podjetja v ZDA preusmerila od inoviranja k financializaciji v kontekstu podjetja Merck. Na primeru podjetja Roche ta raziskava pojasnjuje kako se vzpostavijo socialne razmere za inoviranje, ki onemogočajo financializacijo in omogočijo inovativnost z namenom ustvarjanja večje produktivnosti.

Za preučevanje tako pomembnega ekonomskega pojava, kako lahko določeni akterji v gospodarstvu "izvlečejo" oziroma pridobijo vrednost brez prispevanja k procesu inoviranja skozi katerega se ta vrednost ustvarja, ta disertacija povzema ogrodje Lazonickove Teorije inovativnega podjetja (TIE) kot ekonomske teorije, s katero je mogoče pojasniti procese skozi katere se ustvarja vrednost. Šele tako lahko bralec razume povezavo med akterji, ki prispevajo k ustvarjanju vrednosti in tistimi akterji, ki izvršujejo moč za pridobivanje vrednosti.

Inovativno podjetje se vključuje v skupno in kumulativno učenje ob soočanju z negotovostjo. Vprašanje, ki se tu pojavi je, kako lahko delo ljudi, skupno v določenem trenutku v času in kumulativno skozi čas, prispeva k procesu ustvarjanja vrednosti in rasti podjetja? Lazonick trdi, da morajo biti v inovativnem podjetju strategija, organizacija in finance previdno zasnovane in implementirane, da se lahko podjetje sooča z negotovimi, skupinskimi in kumulativnimi značilnostmi inoviranja (Lazonick & O'Sullivan, 2000). Inovativnost je negotova: pri vlaganju v inovativnost ni noben donos zagotovljen, zato je potrebna strategija dodeljevanja sredstev za inovativne investicijske projekte. Inovativnost je kolektivna: inoviranja se ni mogoče lotiti samostojno ampak zahteva veliko napora za organizacijsko učenje od posameznikov z različnimi sposobnostmi in odgovornosti. Inovativnost je kumulativna: inoviranja ni mogoče izvesti vsega od enkrat ampak ta zahteva neprestano učenje in za to namenjena finančna sredstva, da se lahko akumulira znanje za ustvarjanje visokokakovostnih proizvodov in se tako zavzame večji obseg trga ter se lahko izkoriščajo ekonomije obsega (Lazonick, 2015b).

S pomočjo ogrodja TIE se Lazonick osredotoča tako na socialne razmere v inovativnem podjetju (SCIE), strateško kontrolo, finančno zavezanost in organizacijsko povezovanje kot na gospodarske institucije, zadolžene za upravljanje, zaposlovanje in investiranje, ki lahko omogočijo ali zavirajo inovativno podjetje. V farmacevtskem podjetju, ki želi optimizirati vrednost za svoje lastnike z alociranjem resursov na podlagi pristopa, ki temelji na zmanjševanju delovne sile in distribuciji prihodkov podjetja (angl. *downsize-and-distribute*), lahko najvišji izvršni direktorji odložijo investicije v transformativne raziskovalne ideje, ki zahtevajo dolgoročne spodbude za učenje. Prav te zahtevajo strateško kontrolo, organizacijsko povezovanje in finančno zavezanost in se posledično težje "prodajo" kratkoročnim investitorjem, ki pričakujejo krčenje raziskav in razvoja na račun povečanja zaslužkov.

Po mnenju Lazonicka (2017) inovativno podjetje postane financializirano, če in ko odločitve vodstva o alokaciji proizvodnih virov postanejo vodene z namenom ustvarjanja koristi skupine ljudi, vključno s samim vodstvom, ki precej presegajo njihov prispevek k procesu ustvarjanja vrednosti. Primarna način tega, kar bi se lahko poimenovalo "plenilska ekstrakcija vrednosti" (angl. "predatory value extraction"), predstavlja distribucija delničarjem ne samo v obliki dividend ampak tudi (kar je še bolj pomembno) v obliki odkupov lastnih delnic. Lazonick trdi, da takšen plenilski način alokacije resursov izhaja iz prevladujoče ideologije korporativnega upravljanja, to je maksimiranja vrednosti

premoženja delničarjev (MSV), ki temelji na neoklasični teoriji tržnega gospodarstva. Glede na ideologijo MSV predstavljajo delničarji edine ekonomske akterje, ki sprejemajo tveganja in so tako edini akterji, ki imajo spodbudo za alociranje resursov glede na njihove najbolj učinkovite alternativne možnosti uporabe.

Lazonick kritizira takšno stališče na podlagi trditve, da delavci ponujajo svoje spremnosti in napor zato, da omogočijo podjetju ustvarjanje proizvodov iz katerih sledijo prihodnji prihodki, in na ta način prevzamejo tveganje, da prihodnja zaposlitev in pričakovano plačilo ne bosta sledila, bodisi zaradi neuspešne strategije inoviranja, bodisi zato, ker "korporativni" plenilec "izvleče" vrednost, ki so jo delavci pomagali ustvariti. Podobna situacija je lahko v primeru, ko vladne agencije ali gospodinjstva kot davkopalčevalci oskrbujejo podjetje s fizično infrastrukturo in človeškim znanjem in na ta način prav tako sprejemajo tveganje, saj obstaja možnost, da korporativni dobički na podlagi katerih podjetja plačujejo davke gospodinjstvom mogoče ne bodo sledili ali bodo korporacije mogoče prepričale politike v znižanje davčne stopnje.

Istočasno pa delničarji, zaradi katerih se glede na MSV podjetje sploh upravlja, sprejemajo zelo malo tveganja, saj preprosto kupujejo in prodajajo delnice na likvidnem delniškem trgu in prodajajo svoje delnice z nizkimi transakcijskimi stroški kadarkoli se za to odločijo. Poleg tega MSV, izhajajoč iz neoklasične teorije tržnega gospodarstva, nima teorije o tem kako se "najbolj učinkovite alternativne možnosti uporabe" ustvari. Torej, kot teoriji, ki legitimizira ekstrakcijo vrednosti s strani tistih, ki najmanj prispevajo k procesu ustvarjanja vrednosti, MSV-ju manjka teorija ustvarjanja vrednosti.

Kvalitativna analiza v tej disertaciji, kot je pojasnjeno v drugem poglavju, v veliki meri izhaja iz Lazonickovega dela (1991, 2002, 2013b, 2017) in ogrodja socialnih razmer v inovativnem podjetju (SCIE). Tretje poglavje predstavlja strategijo raziskovanja razvito na podlagi Lazonickove metodologije zgodovinskega preoblikovanja (2002) vodene s pomočjo ogrodja TIE. Takšna metodologija je omogočila tej raziskavi globinsko ocenjevanje gospodarske uspešnosti podjetja na podlagi sistematične analize treh ključnih organizacijskih konceptov, opredeljenih kot SCIE.

Lazonick (2009) povzema način alokacije resursov, ki je potreben za inovativnost kot "obdrži-in-reinvestiraj" (angl. "retain-and-reinvest"): podjetje obdrži svoj denar in ljudi ter ponovno investira v proizvodne zmogljivosti, zlasti v delovno silo. Toda v določeni točki v svoji zgodovini, se lahko način podjetja s katerim alocira resurse, spremeni iz "obdrži-in-reinvestiraj" v "zmanjšaj-in-razdeli"; podjetje zmanjša obseg delovne sile (z odpuščanjem, rezni v plače in outsourcanjem) in razdeli korporativni denar med delničarje. Preoblikovanje iz načina "obdrži-in-reinvestiraj" v način "zmanjšaj-in-razdeli" predstavlja preoblikovanje iz inovativnosti v financializacijo. Glede na to, da je prehod iz inovativnosti v financializacijo do neke mere specifičen za vsako podjetje, obstaja potreba po preučevanju vodilnih podjetijih v farmacevtski panogi v ZDA z namenom ugotavljanja kdaj se podjetja preusmerijo od inovativnosti k financializaciji.

S tem, ko se socialni odnosi znotraj glavnih farmacevtskih podjetij v ZDA spreminjajo iz inovacijske na financializacijsko stran, se vodstvene prioritete spreminjajo na način, da v končni fazi postane alokacijska strategija "zmanjšaj-in-razdeli" glavni managerski cilj z namenom maksimiranja vrednosti premoženja lastnikov. Z uporabo metodologije zgodovinskega preoblikovanja, ki omogoča globinske študije inovativnega podjetja skozi daljše časovno obdobje, je primerjalna analiza v tej raziskavi na primeru dveh izbranih različnih farmacevtskih podjetij uspešno ujela, kako so se socialne razmere, ki vplivajo na inoviranje, spremajale skozi čas.

Za identifikacijo uveljavljenih biofarmacevtskih podjetij, ki so predstavniki podjetij v dveh kategoričnih skupinah, je uporabljena namenska metoda vzorčenja. Za ta podjetja je tako značilno, da povzemajo izrazito različne poslovne modele (Eisenhardt, 1989): Old Economy Business Model (OEBM) in New Economy Business Model (NEBM) (Lazonick, 2005). Seawright & Gerring (2008) pri analizi primerov z majhnimi vzorci identificirata sedem splošno poznanih namenskih metod vzorčenja: tipične, raznolike, skrajne, deviantne, vplivne, najbolj podobne in najbolj različne. Vsaka metoda ima določene posebne prednosti in pomanjkljivosti, ki služijo različnim raziskovalnim potrebam in ciljem, odvisno od odnosov, ki se preučujejo med ključnimi spremenljivkami. Za namen raziskave oziroma prispevku k hipotezi o financializaciji sta bili med prvimi dvajsetimi farmacevtskimi podjetji izbrani dve podjetji, ki predstavljata tipična, odstopajoča in ekstremna primera. Vsak primer je analiziran glede na kontekst v odnosu do ustreznega preučevanega obdobja v svoji evolucijski poti.

Analiza v tretjem poglavju pokaže, da je velikost populacije podjetij v farmacevtski panogi v ZDA, če upoštevamo vrednost prodaje posameznega podjetja, relativno majhna. Velik delež trga z zdravili na recept v ZDA (v vrednosti 330 milijard ameriških dolarjev) namreč obvladuje relativno majhno število farmacevtskih podjetij, ki izvirajo tako iz ZDA kot iz Evrope. Vrednost prodaje prvih petnajstih podjetij je tako v letu 2015 predstavljala skoraj tri četrtine celotne prodaje zdravil v ZDA, medtem ko je ostalo vrednost ustvaril preostanek populacije (EvaluatePharma, 2016). Vrednost prodaje farmacevtskih proizvodov je v prvih petih podjetjih (pri čemer je vključeno podjetje Roche kot edino iz Evrope) znašala 29 odstotkov celotne vrednosti prodaje v ZDA. Med prvih deset podjetij so bila uvrščena podjetja Merck & Co., Novartis in Sanofi-Aventis iz Evrope kot tudi Roche, njihova prodaja pa je znašala 51 odstotkov. Vrednost prodaje prvih petnajstih podjetij, vključno s podjetjem GlaxoSmithKline in AstraZeneca iz Evrope, je znašala skupno 66 odstotkov celotne vrednosti prodaje. Vrednost prodaje prvih dvajsetih podjetij pa 76 odstotkov celotne vrednosti prodaje zdravil v ZDA v letu 2015. Samo vrednost prodaje podjetij Roche in Merck & Co. je tako skupno predstavlja skoraj 10 odstotkov celotne vrednosti prodaje zdravil v ZDA.

Za namen raziskave sta bila tako strateško izbrana dva primera podjetij, Merck in Roche. S pristopom "zgodovinskega preoblikovanja", ki omogoča posodabljanje analize primerov podjetij, lahko raziskovalci razvijejo poglobljeno razumevanje zgodovine teh podjetij.

Skozi proces, ki ga je Lazonick označil kot "približevanje oziroma spoznavanje zgodovine" (angl. catching up with the history), je namen teh posodobitev analize preučevanje načina, kako se podjetja soočajo z ali popuščajo pod pritiskom med inovativnostjo ali financializacijo. Disertacija je sprožila ta dolgoročni raziskovalni projekt na temo inovativnih farmacevtskih podjetij s primerjalnega vidika, s preučevanjem ameriškega podjetja Merck in švicarskega podjetja Roche. V primeru ZDA sem se odločil za Merck & Co. (prej poimenovano Merck Sharp & Dohme) zaradi njegove zgodovine, saj je v začetku 90-ih let imelo visoko inovativen poslovni model pod vodstvom izvršnega direktorja Roya Vangelosa. Z njegovo upokojitvijo pa je sredi 90-ih let podjetje naredilo nenadno spremembo od inovativnosti k financializaciji.

Kot navaja analiza, ki so jo izvedli Lazonick et al. (2017), je 459 podjetij uvrščenih v Indeks S&P 500 (z njihovimi delnicami se je javno trgovalo od leta 2006 do 2015) razdelilo 90 odstotkov svojih dobičkov delničarjem. Lazonick (2017) je takšno finančno obnašanje poimnenoval kot "v veliki meri legalizirano pljenjenje ameriških korporacij" (angl. largely legalized looting of the US business corporation). Financializacija farmacevtske industrije v ZDA tako očitno predstavlja ekstremen primer financializacije, ki sicer na splošno prizadene ameriške korporacije. Glede na isto raziskavo, so bili dejansko skoraj vsi dobički (99%), ki jih je v istem obdobju od 2006 do 2015 želo 18 farmacevtskih podjetij, razdeljeni delničarjem v obliki denarnih dividend in odkupov lastnih delnic.

Za institucionalno okolje farmacevtske panoge v ZDA je značilno, da lahko in tudi pogosto podpira inovativna podjetja. Še bolj ugodne spodbude (najboljše v svetovnem merilu) pa ponuja trg farmacevtskih proizvodov v ZDA v primeru postavljanja cen proizvodov, kar je brez primerjave, ko je govora o postavljanju visokih cen zdravil. Tako biofarmacevtska podjetja v ZDA zahtevajo visoke cene zdravil za financiranje svoje porabe za raziskave in razvoj. Toda, glede na to, da je znesek, ki so ga podjetja razdelila delničarjem znašal 516 milijard dolarjev in tako presegal 465 milijard dolarjev, ki so jih podjetja poročala kot znesek namenjen raziskavam in razvoju, je očitno, da so ta podjetja izkoriščala visoke cene zdravil za ohranjanje visokih dobičkov in cen delnic svojih podjetij.

Četrto poglavje analizira spremembe, ki so se zgodile v institucionalnem okolju ZDA in so dejansko spodbudile prehod ameriških farmacevtskih podjetij iz inovativnosti v financializacijo. Ta se manifestira na različne načine in s spreminjačim vplivom na gospodarsko uspešnost. Kakorkoli, obstajajo določene značilnosti financializacije, ki jih je mogoče opazovati v organizacijah, ki povzamejo financializirano poslovni model. Lazonick (2009) je skoval izraz "poslovni model nove ekonomije" (angl. New Economy Business Model, v nadaljevanju NEBM), ki naj bi se nanašal na tista podjetja, ki so povzela financializirani poslovni model. Od 80-ih let je NEBM nadomestil "poslovni model stare ekonomije" (angl. Old Economy Business Model, v nadaljevanju OEBM), ki je ustvaril temelje za veliko ekspanzijo ameriškega gospodarstva v večjem delu 20. stoletja.

Razpoložljivost špekulativnih trgov v ZDA je omogočila rast biotehnoloških podjetij "nove ekonomije" v 80-ih in 90-ih letih. Prav ta špekulativna narava delniškega trga v ZDA je tista, ki pogosto spodbuja tako biotehnološke start-upe, kot tudi najbolj tvegana podjetja brez kakršnikoli proizvodov na trgu k ustvarjanju stalnih tokov prihodkov od proizvodov, z namenom zbiranja velikih vsot kapitala od borznih trgovcev skozi prve javne ponudbe delnic podjetja (angl. initial public offerings, v nadaljevanju IPOs). Lazonick in Tulum (2011) poimenujeta takšna biotehnološka podjetja nove ekonomije kot "prva javna ponudba delnic podjetja brez proizvodov" (angl. product-less initial public offerings, v nadaljevanju PLIPO), ko pojasnjujeta kako je obstoj špekulativnih trgov omogočil širitev pojava PLIPOV. Prvi podjetji, ki sta se posluževali takšnega načina in predstavljata ikone prvih javnih ponudb delnic biotehnoloških podjetij sta bili Genentech in Cetus v zgodnjih 80-ih letih in tako predstavljata predhodnika številnim drugim biotehnološkim start-upom, ki so sledili podobni poti z namenom pridobivanja kapitala na špekulativnih trgih.

Z zanašanjem na kombinacijo financiranja s strani NIH in štekulativnih PLIPOV za odkrivanje novih zdravil in razvoj so uveljavljena biofarmacevtska podjetja svoje lastne t.i. "hišne" R&R zmogljivosti, prepustila nazadovanju (Higgins & Rodriguez, 2006; Hirschler & Kelland, 2010; LaMattina 2011; Mirowski, 2011, poglavje 5). Velika biofarmacevtska podjetja so postala še večja s tem, ko sta na primer Merck in Pfizer prevzela druga uveljavljena podjetja z namenom pridobivanja dostopa do dokazanih "izdelkov preboja" oziroma "blockbusterjev" s preostalim patentnim obdobjem. Nato v imenu MSV prevzemnik namesto ustvarjanja lastnih sposobnosti za odkrivanje zdravil iz pripojenega podjetja izčrpa denar k delničarjem (Montalban & Sakinç, 2013; Lazonick & Tulum, 2015; Lazonick et al., 2017). Od poznih 90-ih let so bili tako nameni velikih farmacevtskih podjetij za vključevanje v ustvarjanje lastnih kapacitet in učenje ogroženi zaradi izstopa tehničnega in vodstvenega osebja, ki je želelo poskusiti svojo srečo v PLIPO segmentu farmacevtske panoge. To pa je še bolj spodbudilo zagovornike idej v velikih farmacevtskih podjetjih, ki trdijo, da je njihov lastni uspeh odvisen od spodbujanja cen delnic in s tem od uporabe delniških opcij za tekmovanje pri iskanju talentov na trgu.

Kot že pojasnjeno v četrtem poglavju, institucionalno okolje ZDA s svojo podporo inovacijam na področju farmacevtskih izdelkov zagotovo omogoča razvoj inovativnim podjetjem. Od 80-ih let je mnogo ameriških farmacevtskih podjetij ustvarilo inovativna zdravila. Toda s tem, ko so večja biofarmacevtska podjetja (omenjena v tretjem poglavju) prevzela nadzor nad velikim številom zdravil, ki so se uvrščala med t.i. izdelke preboja, in postala bolj financializirana, so njihovi pristopi k alociranju resursov ogrozili inovacije in razvoj novih zdravil. Razliko med inovativnostjo in financializacijo je mogoče najti v poslovni praksi, kjer biofarmacevtska panoga v ZDA predstavlja odličen primer. Peto poglavje opisuje kako se je dolgo uveljavljeno ameriško podjetje Merck od 80-ih let spremenjalo od inovativnega do financializiranega podjetja in pri tem pod vplivom ideologije MSV zlorabilo institucionalno okolje ZDA.

Lazonick (2014) trdi, da lastni odkupi delnic, ki se izvajajo kot ponovni nakupi lastnih delnic na odprttem trgu, nimajo konstruktivne vloge pri izboljšanju produktivnosti ampak predvsem veliko uničajočih posledic. Tako je prav stopnja sredstev, ki jih podjetja alocirajo za nakup lastnih delnic in se lahko razlikuje od podjetja do podjetja v spektru od nič do večkratnika lastnih neto dohodkov tista, ki predstavlja najbolj jasen kazalnik za merjenje ali oziroma do kakšnega obsega je podjetje financializirano. Osnovni namen lastnih odkupov delnic predstavlja spodbujanje cene delnice in glavni akterji, ki imajo koristi od tega so izvršni direktorji podjetja, katerih plačilo pretežno temelji na delnicah (Lazonick, 2015b; Hopkins & Lazonick, 2016).

Kot je razvidno iz analize v petem poglavju, so si izvršni direktorji v Merku od 90-ih let ustvarili precejšnje zasluge na račun realiziranih delniških opcij. To poglavje tudi kaže, kako so prioritete managerjev postavile in uveljavile strategijo alociranja resursov "zmanjšaj-in-razdeli" kot prvi cilj, ki naj bi ga zasledovali managerji. Ta je bil legitimiziran na podlagi ideologije MSV s tem, ko se je od 90-ih let strateška kontrola znotraj podjetja spremnjala od inovativnosti k financializaciji. Analiza tudi kaže, da so v istem obdobju inovacijske zmogljivosti podjetja upadle, ko se je podjetje Merck spremnjalo od inovativnega k financializiranemu podjetju.

Po Lazonickovem mnenju (2002) se organizacijsko povezovanje nanaša na niz odnosov, ki spodbujajo skupino posameznikov znotraj podjetja k sodelovanju v skupnih in kumulativnih učnih procesih. Stopnja, do katere organizacijsko povezovanje vodi do inovativne produktivnosti, je odvisna od tega, kako uspešno socialni odnosi v podjetju privabljajo posamezni, da svoje spremnosti in napore usmerijo skupno in kumulativno na najbolj usklajen in produktiven način. Kot je pojasnjeno v petem poglavju, je kolektivna želja, da bi postali najbolj inovativno farmacevtsko podjetje na svetu, spodbujala zaposlene v Merku do 90-ih let. Od takrat pa je cena delnice podjetja Merck vplivala na plačo večine zaposlenih, saj kot značilnost podjetij "nove ekonomije" v splošnem (in kot pokaže Lazonick (2017)), lahko na ceno delnice vplivajo špekulacije in manipulacije, kot tudi inovativnost.

Ko se cena delnice podjetja znatno poveča, lahko delniške opcije omogočijo precejšen dodatni zasluge zaposlenim, ki jih posedujejo. V primeru podjetja Merck se pokaže, da je uporaba delniških opcij kot oblika plačila zaposlenim povečala razkorak med izvršnim direktorjem in ostalimi zaposlenimi, kar je značilnost financializiranega podjetja. Način spodbujanja raziskovalnega osebja na podlagi možnih zaslukov z delniškimi opcijami namesto možnosti varne zaposlitve in kariere, je prispevala k zlomu "kariera z enim podjetjem" (angl. "career-with-one-company" (CWOC)), saj je povečanje mobilnosti delovne sile povzročilo odliv delavcev v R&R iz velikih farmacevtskih podjetij v PLIPO.

S tem, ko podjetje Merck ni uspelo uvesti inovacij, delno zaradi razpada organizacijskega učenja kot posledice povečane menjave delovne sile, si je prizadevalo ohranjati prihodke s priključitvami in prevzemi, ki bi lahko tem uveljavljenim podjetjem omogočilo nadzor nad

preizkušenimi zdravili, ki jim je običajno preostala večletna patentna zaščita. Ta strategija konsolidacije je v splošnem privedla do velikih odpuščanj zaposlenih, kar je nadalje ogrozilo in mogoče tudi uničilo organizacijsko povezovanje. V nasprotju z močnim poudarkom, ki ga je podjetje v zadnjih letih dajalo uspešnosti gibanja cene delnice, primer podjetja Merck raziskuje omejeno vlogo, ki jo je imel delniški trg pri financiranju rasti podjetja v nedavni zgodovini. Prav tako raziskuje posledice za prihodnost podjetja zaradi odločitve o dokončanju izplačila več kot 60 milijard dolarjev delničarjem od leta 2010. V tem obdobju je namreč podjetje prav tako porabilo čez 40 milijard dolarjev za prevzem dolgoletnega tekmeца kot sredstvo za izboljšanje slabih rezultatov prodaje in razvoja proizvodov.

Kot že opisano v četrtem poglavju, je bilo institucionalno okolje v ZDA ključno za rast velikih evropskih farmacevtskih podjetij. Poleg zagotavljanja baze potrebnega znanja za inovacije na področju zdravil, je ameriški trg zdravil, s svojimi nereguliranimi cenami, postal glavni vir evropskih dobičkov, še posebej od tistih inovativnih proizvodov razvitetih v ZDA. Zaradi svojega institucionalnega okolja so ZDA najbolj donosna lokacija, kjer lahko globalna biofarmacevtska podjetja lansirajo svoja inovativna zdravila. Vprašanje, ki se tu pojavi je, do kakšnega obsega ta podjetja uporablajo te dobičke za inoviranje ali alternativno za financializacijo. Za odgovor na to vprašanje je potrebno pogledati socialne razmere, ki prevladujejo v teh evropskih podjetjih in povezavo teh socialnih razmer z uspešnostjo inoviranja pri razvoju in trženju farmacevtskih zdravil.

Na podlagi trditve, da je financializacija farmacevtskega poslovnega modela v ZDA resnični krivec za zmanjševanje produktivnosti ameriških farmacevtskih podjetij, peto poglavje podrobnejše razлага zakaj in kako se je podjetje Merck & Co spreminkalo od inovativnosti k financializaciji. To poglavje tudi obravnava osnovne vzroke za odločitev podjetja Merck za opustitev poti inovacijsko usmerjene rasti v zadnji polovici 90-ih let in posledice, ki so jih ti managerski ukrepi imeli na podjetje, ki je v prejšnjem desetletju spodbujalo svojo produktivnost in beležilo znatno gospodarsko rast.

V petem poglavju so predstavljeni argumenti o financializaciji glavnih farmacevtskih podjetij v ZDA kot so Merck & Co. Značilnosti financializirane farmacevtske panoge v ZDA predstavljajo idealno okolje za nefinancializirano podjetje, ki je pripravljeno reinvestirati svoje dobičke v razvoj zdravila in ustvarjanja inovacij. To bi tako lahko veljalo za evropska biofarmacevtska podjetja, ki so podvržena cenovni regulaciji na svojih domačih trgih, v kolikor bi lahko izkoristila ogromno bazo znanja v ZDA in prodajla svoje proizvode v ZDA po visokih, nereguliranih cenah.

Temeljna hipoteza, ki se ocenjuje s primerjalno analizo primerov podjetij v tej disertaciji, je, da bodo v okoljih, ki se pogosto označujejo kot "socialna tržna gospodarstva" evropska biofarmacevtska podjetja manj izpostavljena vplivu ideologije MSV in bodo na ta način manj izpostavljena uničajočim vplivom na inovativnost. Namen šestega poglavja je raziskati delovanje in uspešnost glavnih farmacevtskih podjetij v Evropi, ki so zelo aktivna

v razvoju in prodaji zdravil v ZDA, z namenom pridobivanja vpogleda v veljavnost hipoteze "inovativnost ali financializacija". Umeščanje podatkov o tržnih deležih največjih proizvajalcev zdravil, torej Roche (Švica), Novartis (Švica), GlaxoSmithKline (Združeno kraljestvo), AstraZeneca (Združeno kraljestvo), Sanofi-Aventis (Francija), Bayer (Nemčija) in Merck KGaA (Nemčija) v globalni kontekst, pokaže pomen ohranjanja inovativnosti za globalno konkurenčnost v farmacevtski panogi.

Kot je navedeno v šestem poglavju, je 49 odstotkov prihodkov, ki jih je največjih sedem evropskih proizvajalcev zdravil ustvarilo na podlagi proizvodov lansiranih v 80-ih letih, izhajalo iz zdravil, ki so bila prvotno odkrita oziroma je večje raziskovalno delo v povezavi z njimi potekalo v Švici ali Nemčiji. Prihodki od zdravil s poreklom v ZDA so predstavljeni samo 24 odstotkov celotnih prihodkov od proizvodov lansiranih v 80-ih letih. Razmerje prihodkov, ki so temeljili na prodaji proizvodov s poreklom iz ZDA se je z uvedbo novih generacij biokemičnih proizvodov v 90-ih letih hitro povzpelo iz 24 odstotkov na 58 odstotkov. V enem desetletju so tako proizvodi s poreklom iz ZDA začeli predstavljanje zelo pomemben del celotne prodaje farmacevtskih izdelkov.

Analiza v šestem poglavju razkriva pomen ZDA ne samo kot pomembnega proizvodnega trga, ki je bil glavni gonalni dejavnik dobičkonosne rasti, ampak tudi kot osrednje točke preoblikovanja organizacijskih zmogljivosti na način, da so te lahko omogočale premagovanje ovir, ki so izhajale iz spreminjačih tržnih in tehnoloških pogojev. Najvišje uvrščeni evropski proizvajalci zdravil so danes tudi najuspešnejši igralci na globalnem trgu zdravil, ki tudi vodijo "dirko" v farmacevtskih inovacijah. Tisti, ki so omogočili doseganje takšne uspešnosti danes, morajo pazljivo preiskovati vire inovacijskih sposobnosti v preteklosti.

V sedmem poglavju so analizirane socialne razmere za inovacije zdravil na primeru podjetja Roche. To je bilo identificirano kot eno najbolj produktivnih farmacevtskih podjetij na svetu, ki kaže značilnosti inovativnega podjetja. Skozi sistematično analizo podjetja Roche sedmo poglavje ponuja vpoglede v načine na katere je mogoče doseči, s sposobnostmi in spodbudami strateških managerjev vključenih v proces inoviranja, z inovacijami vodenim rast.

Kot je razloženo v tretji sekciji, ki analizira finančno obvezo kot socialne razmere inovativnega podjetja v Rocheju, je "intimno razmerje", ki ga družini Hoffmann in Oeri več ali manj vzdržujeta že skoraj stoletje, omogočilo preživetje podjetja skozi različne katastrofalne svetovne dogodke, industrijske krize ali turbulentne čase na svetovnih trgih. Dejansko predstavlja Roche eno izmed redkih podjetij, ki mu je uspelo obdržati svoje tradicije, korporativno identiteto in neodvisen značaj z izogibanjem kakršnikoli večji združitvi z drugim farmacevtskim podjetjem za vsako ceno.

Sedmo poglavje s preučevanjem edinstvene strukture lastništva, ki jo je Roche ohranjal v preteklem stoletju, pojasnjuje, kako so sposobnosti in spodbude strateških managerjev

ostale nespremenjene, kar je omogočalo podjetju strateško osredotočanje na izboljšanje inovativne produktivnosti tudi potem, ko je industrijsko gospodarstvo v ZDA, kjer so bile skoncentrirane R&R operacije podjetja, postajalo vedno bolj financializirano. Natančneje, sedmo poglavje pojasnjuje, da je, s spodkopavanjem socialnih razmer inovativnega podjetja, ekstrakcija vrednosti s strani finančnih interesov v ZDA omogočila "zunanjemu" podjetju Roche pridobitev dostopa do dragocenih tokov znanja v ZDA, ki bi jih bilo drugače veliko težje pridobiti.

Trenutno se zdi, da je podjetje Roche najmanj financializirano in najbolj produktivno izmed velikih proizvajalcev zdravil. Podjetje Roche je s sprejetjem visoko osredotočene strategije rasti sprejelo visoko tvegano odločitev za inoviranje znanstveno zahtevnih posebnih zdravil, s katerimi bi zajeli najbolj donosne segmente trga zdravil kot so onkologija, protivnetne in nalezljive bolezni. V kolikor se bo ta izkazala za uspešno, bo Roche pridobil pomembno konkurenčno prednost pred svojimi tekmeci, saj se vsi soočajo s strašno konkurenco na trgu zdravil majhnih molekul za katere so značilni padajoči dobički.

V podjetju Roche je zadržani dobiček vedno predstavljal glavni vir za naložbe v proizvodne vire. V skrbi zaradi redčenja delnic so se v Rocheju odločili za uporabo zadržanih dobičkov in izdajo dolžniških instrumentov za financiranje prejšnjih prevzemov kot tudi največji prevzem Genentech-a v letu 2000. Zgodovinsko gledano, so se v Rocheju odločali samo za operativne prilagoditve za nadomeščanje stroškov ekspanzije kapitalskih odhodkov, s prihranki ustvarjenimi skozi prestrukturiranje prejšnjega programa, v nasprotju z velikimi financializiranimi farmacevtskimi podjetji kot je Merck, kjer so takšne prihranke denarja iz organizacijskega prestrukturiranja, razdelili, kot je bilo pojasnjeno v prejšnji sekciiji.

Primer podjetja Roche tako kaže, da so tista evropska biofarmacevtska podjetja, ki so bila zaščitena pred vplivom ideologije MSV v svojih matičnih državah, boljše pozicionirana in bi lahko izkoristila institucionalno okolje ZDA za izboljšanje svojih inovativnih sposobnosti. Podjetje Roche je bilo uspešno pri izgradnji ključnih kompetenc v posebnih zdravilih, saj je podjetje vztrajno izvajalo svoje ambiciozne inovacijske programe, ki jih delno podpira institucionalno okolje ZDA, ki je zelo spodbudno za inovacije. Najpomembnejše kompetence iz ZDA so v podjetju Roche pridobili s prevzemom podjetja Genentech, vendar so te kompetence obrodile sadove šele po tem, ko je Rocheju uspelo vzpostaviti red v hitro razkrajajoči Genentechovi organizaciji, ki je bila posledica globokih finančnih težav podjetja.

Kot je podrobneje opisano v sedmem poglavju, načini s katerimi so v Rocheju uspeli doseči stabilnost v Genentechu, kažejo, kako lahko spremembu v strateški kontroli izboljša produktivnost z implementacijo organizacijskega povezovanja in finančnih obvez potrebnih za podporo inovacijskemu procesu. Z združevanjem podjetniških spretnosti in inovacijskih sposobnosti podjetja Genentech z upravljalstvo in finančno stabilnostjo

podjetja Roche, kot tudi preživetvenimi sposobnosti slednjega, je imelo Roche-Genentech partnerstvo, globoko produktiven vpliv na ameriško in svetovno farmacevtsko panogo.

Med pričakovanimi teoretičnimi prispevki disertacije je predvsem zapolnitev vrzeli v sedanji literature, ki ponuja le zelo omejen vpogled v mehanizme, ki povezujejo financializacijo in zmanjšano inovativno produktivnost. Tako teoretični kot metodološki problemi povezani z ekonomsko analizo industrijske organizacije zmanjšujejo interes za raziskovanje takšnih mehanizmov. Prav tako obstaja splošno pomanjkanje empiričnih podatkov o tem, kako financializacija vpliva na socialne razmere v inovativnem podjetju in ogroža produktivnost inovacijskega procesa znotraj inovativnega podjetja. Uporaba najbolj ustreznega teoretičnega ogrodja in metodologije predstavlja ključen element in trenutno je mogoče dostopati do zelo podrobnih in uporabnih podatkov v elektronski obliki iz številnih virov. Z uporabo ogrodja TIE, ki ga je razvil Willam Lazonick in metodologije zgodovinskega preoblikovanja, je ta raziskava poskušala najbolje izkoristiti takšne podatke v kvalitativni in kvantitativni obliki, zbranih iz tako primarnih kot sekundarnih virov.

Uporabnost ugotovitev, ki izhajajo iz ekonomske analize uporabljenе v tej raziskavi presegajo znanstvene prispevke k literaturi. Analiza v tej raziskavi lahko zakonodajalcem oziroma regulatorjem, zainteresiranim za financializacijo industrije v ZDA, Evropi ali drugod, zagotovi vpogled v značilnosti financializiranega poslovnega modela. Zakononodajalci oziroma regulatorji lahko pridobijo razumevanje o tem, katera podjetja se poskušajo soočati s pritiskom oziroma dilemo med inovativnostjo in financializacijo, kako lahko podjetja zmanjšajo pritiske, ki jih povzroča financializacija in kako lahko vlade pomagajo podjetjem pri izogibanju povzemanja financializiranega poslovnega modela.

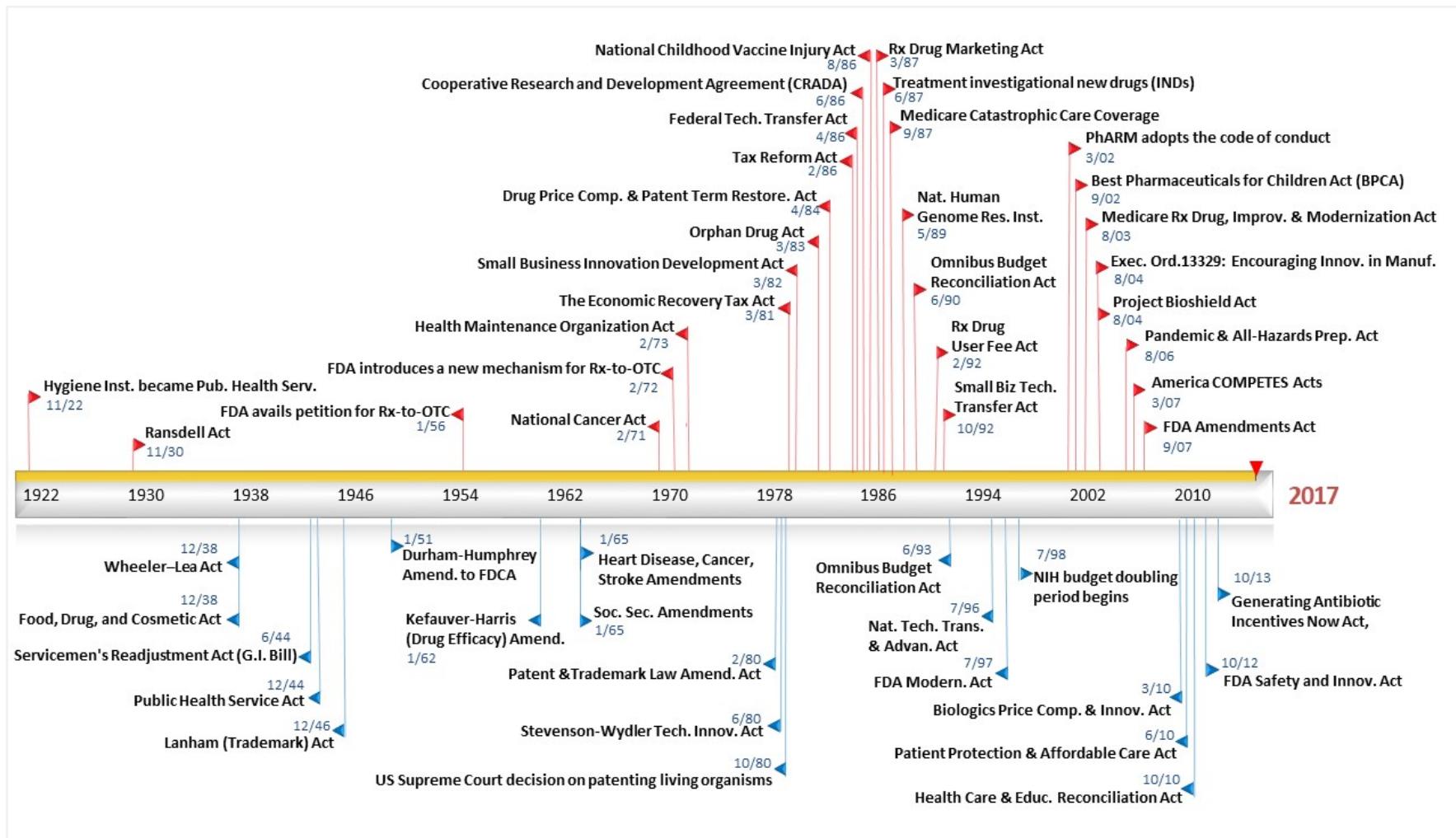
Nasprotniki regulacije za nadzor cen farmacevtskih proizvodov v ZDA pogosto trdijo, da je glavni razlog zakaj imajo ZDA nekatere od najbolj inovativnih farmacevtskih podjetij ta, da lahko ljudje zaslužijo z inoviranjem zdravil in so tako visoko motivirani, da lahko nadaljujejo z inovacijami. Čeprav je bilo to do 90-ih let do neke mere res, ta raziskava kaže, da je težko trditi, da tržno okolje spodbuja podjetja k inovacijam ampak so ta precej bolj motivirana za spodbujanje (dvigovanje) cen zdravil in za ekstrakcijo (kratkoročnega) monopolnega dobička. V tej disertaciji je zgodovinska ocena farmacevtske panoge v ZDA pokazala, da je bil vodilni poslovni model v ZDA, ki se je odražal v visoki stopnji panožne produktivnosti, prvenstveno skoncentriran na ustvarjanja novih inovativnih zdravil. Ta inovativni poslovni model je konec končev usmerjal podjetja k ustvarjanju vrednosti za deležnike in še posebej za paciente, ki nujno potrebujejo nova inovativna zdravila. Zgodovinski pregled podjetja Merck je pokazal, da je bil v času, ko je podjetje uživalo napredek v produktivnosti, prevladujoči poslovni model inovacijsko orientiran in je zahteval precejšnja vlaganja za pridobitev in razvoj potrebnih organizacijskih sposobnosti za inoviranje novih zdravil.

Kot je bilo prikazano na primeru podjetja Merck model alokacije "zmanjšaj-in-razdeli" v bistvu izstopa kot najpomembnejši dejavnik, ki spodbuja naraščajoče neravnovesje med

inovativnostjo in financializacijo v farmacevtskih podjetjih in tako prispeva k naraščajoči neenakosti pri distribuciji finančnih zaslužkov v podjetjih in gospodarstvu kot celoti. Raziskava v tej disertaciji kaže, da financializirani poslovni model, ki prevladuje v farmacevtski panogi v ZDA, potrebuje spremembo v korporativnem upravljanju, da bi lahko ameriška podjetja ponovno vrnili na pot alokacijske strategije "obdrži-in-reinvestiraj".

Obnova inovacijskih poslovnih modelov farmacevtske panoge v ZDA zahteva spremembe norm, ki presegajo tako meje panoge kot ZDA. Svetovne institucije, kot je OECD, so promovirale širše sprejemanje ideologije MSV in spremljajočih financializiranih korporativnih strategij upravljanja. Dokazi navedeni v disertaciji so pripomogli k razkrivanju nevarnosti ideologije MSV. Evropejci bi se tako morali odreči ideologiji vrednosti premoženja delničarja s priznavanjem inovativnega potenciala in realnosti modela vrednosti deležnika. Prihodnji uspeh evropskih farmacevtskih podjetij za boljšo uporabo institucionalnega okolja ZDA je v končni fazi določen z njihovo sposobnostjo vzdrževanja domače baze za katero so značilne institucije, ki lahko zavirajo sile financializacije.

Appendix 2: Timeline of major policy changes affecting the biopharmaceutical industry in the US



Source: Own illustration developed based of the review of major policies

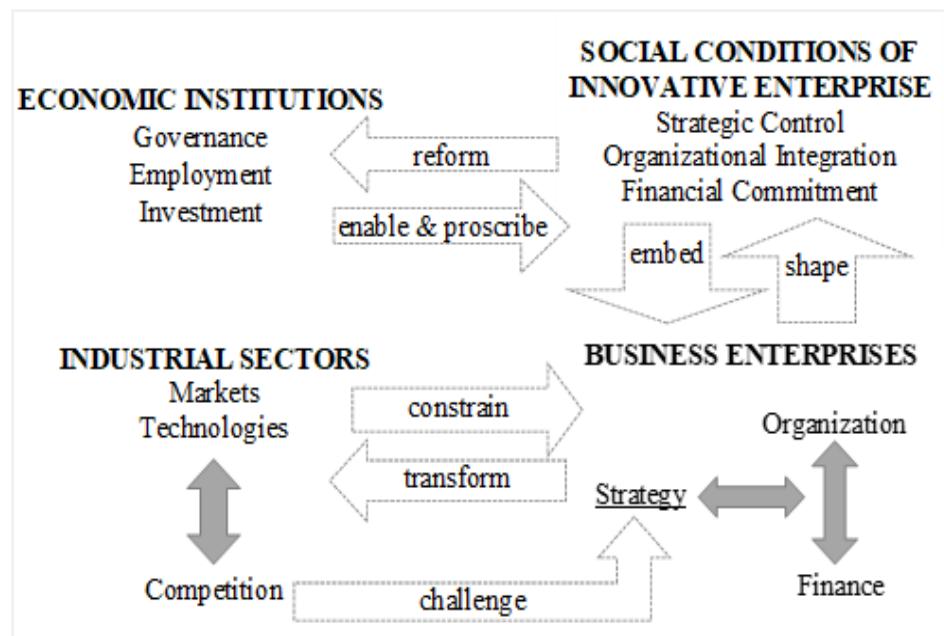
Appendix 3: Comparing “the theory of innovative enterprise” (TIE) and the “innovating firm” vs. the theory of market economy (TME) and the “optimizing firm”

OCCURRED IN THE FORM OF	Root-causes		
		TME	TIE
Diminishing productivity of R&D (declining # of NMEs/NBLs by \$ invested on R&D)	Market-side	<ul style="list-style-type: none"> * Strict FDA safety and efficacy guidelines increase drug failure rates, the length of approval process and the overall cost of drug development * Interventionist policies diminish the efficiency of R&D investments and drive up drug development costs 	<ul style="list-style-type: none"> * A profit-driven innovation strategy targets “one-size-fits-all” types of blockbuster drugs for chronic diseases, geared towards high-income patient groups and targeting these types of “high-risk/high-reward” projects increases the drug development cost and leads to a higher failure rate * Placing more emphasis on the development of follow-on (me-too) drugs as opposed to first-in-class, truly novel therapies; this type of product strategy requires greater focus on SM&D activities and drives companies to engage in more non-R&D operations and increase overheads * Blockbusters and follow-on drugs are subject to greater regulatory scrutiny to prove efficacy; however, NMEs or NBLs are eligible for a priority review process for fast-track-approvals
	Tech-side	<ul style="list-style-type: none"> * The body of new knowledge is not growing fast enough to enable the discovery of new generations of therapies * As government support for research and training programs continues to decline, the knowledge-base in medical science diminishes * BP’s sluggish and bloated R&D programs underperform compared to those of small biotech firms in terms of R&D efficiency * Markets can perform better in terms of improving the efficiency of capital invested in R&D by identifying productive firms and investing in their R&D programs; Thus the companies with the most efficient R&D – big pharma – should spend less on R&D and return disgorged cash to the market and shareholders 	<ul style="list-style-type: none"> * The <i>downsize-and-distribute</i> resource allocation regime means less capital invested in projects that are risky and long-term in nature and that require more investment in basic research; vertical disintegration means outsourcing certain functions * Big pharma increases its use of equity to acquire companies with innovative products * There are less incentives for the executives of <i>optimizing-firms</i> to invest in alternative drug development * As the internal capabilities for drug development continue to diminish, big pharma becomes more dependent on external partners * Since the <i>retained-and-reinvest</i> mode of resource allocation is challenged by TME’s MSV ideology, business organizations are withdrawing from research and focusing on development and commercialization

# of patient groups with unmet medical needs (new therapies for rare and tropical diseases; & diminishing accessibility of innovative new therapies due to high pricing)	Market-side	<ul style="list-style-type: none"> * The increase in costs of pharmaceuticals is insignificantly low as a proportion of overall healthcare costs * Despite this “insignificant” increase, innovation by drug companies is bringing overall healthcare cost down by reducing enormous healthcare costs associated with hospitalization; it contributes to the growth in economic productivity. Innovation improves the length and quality of human life and reduces significant economic costs stemming from loss of work * High drug prices, determined by the value offered in terms of cost-savings, are justifiable 	<ul style="list-style-type: none"> * Revenues from potential therapies in rare or tropical conditions can simply be inadequate to justify big pharma’s expanding SM&D operations, * Such a size of operation is a by-product of the blockbuster-driven business model * In “optimizing-firms” resource allocation decisions on R&D programs are driven by projected market opportunities * No one can predict the market outcome of a project unless engaged in learning, hence the prevailing resource allocation models within optimizing-firms
	Tech-side	<ul style="list-style-type: none"> * Markets (not firms) fails to address unmet medicinal needs * There are simply no economic incentives for firms to engage in research for those rare or tropical diseases; * A pharmaceutical business enterprise is a profit-seeking entity not a charity * The increasing length of FDA approval process reduces a product’s time in the market under patent protection to recoup ever-growing investments on R&D * At the end of patent life, a product’s revenues quickly drop due to generic competition * High drug prices are necessary to sustain the innovation process for future lifesaving therapies 	<ul style="list-style-type: none"> * The profit-driven innovation strategy makes many rare, tropical, antibacterial or complex diseases unattractive targets * Innovation embodies market uncertainty but even an investment in R&D for rare diseases can pan out well, the industry’s history is full of examples of this phenomenon * The MSV ideology often discourages executives from allocating resources to this type of blue-sky research programs which used to be the norm during the OEBM era

Source: Adapted from Lazonick (2009, p. 17). *Sustainable prosperity in the new economy? Business organization and high-tech employment in the United States.* WE Upjohn Institute. Lazonick 2009, p. 17

Appendix 4: Conceptual framework for analyzing the evolution and influence of the social conditions of innovative enterprise in a national context



*Source: Reprinted from Lazonick, W. (2013b, p. 29). *The theory of innovative enterprise: A foundation of economic analysis*. The Academic Industry Research Network Working Paper WP#13-0201 (Rev. 2015).*