

T.C.
MARMARA ÜNİVERSİTESİ
SOSYAL BİLİMLER ENSTİTÜSÜ
İŞLETME (İNGİLİZCE)
MUHASEBE VE FİNANSMAN (İNG.) ANABİLİM DALI
DOKTORA PROGRAMI

**KEY SUCCESS FACTORS FOR GLOBAL PHARMACEUTICAL
COMPANIES IN EMERGING MARKETS**

(Ph.D. THESIS)

Arda Ural

İstanbul-2014

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Tez Danışmanı: Prof. Dr. Jale Oran Sözer

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TEZ ONAY BELGESİ

İŞLETME (İNGİLİZCE) Anabilim Dalı MUHASEBE FİNANSMAN (İNGİLİZCE) Bilim Dalı DOKTORA öğrencisi ARDA URAL'ın KEY SUCCESS FACTORS FOR GLOBAL PHARMACEUTICAL COMPANIES IN EMERGING MARKETS adlı tez çalışması, Enstitümüz Yönetim Kurulunun 03.01.2014 tarih ve 2014-1/13 sayılı kararıyla oluşturulan jüri tarafından oy birliği / ~~oy çokluğu~~ ile Doktora Tezi olarak kabul edilmiştir.

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İmzası



ÖZET

Küresel ilaç ve biyoteknoloji endüstrisi 2011 yılı sonu itibariyle yaklaşık 960 milyar dolar tutarında bir hacme ulaşmış ve önceki beş yıllık dönemde ortalama yıllık % 7,8 seviyesinde bir büyüme sergilemiştir. Yeni ilaç keşfi, geliştirmesi ve pazarlaması üstüne kurulu iş modeliyle, ve 20 yıllık patent hakkının sağladığı korumayla bu endüstriyalı ve istikrarlı bir büyüme yaşamıştır. Tarihsel olarak %80 civarında brüt kâr marjı, %40-50 aralığında faaliyet marjı ve sağlıklı serbest nakit akışı sayesinde ilaç endüstrisi kârlı bir endüstri olagelmıştır.

Ancak endüstrinin büyümesini sağlayan bu ilaçların patent koruma sürelerinin son yıllarda teker teker dolmasıyla endüstri yaklaşık 125 milyar dolar civarında bir satış kaybı yaşamış, güçlü bir yeni ürün hattının olmamasından dolayı bu kaybı telaffi edememiştir. İlaç maliyetleri çoğunlukla devletler tarafından karşılandığından endüstri genellikle olumlu bir ekonomik büyüme ortamından yararlanagelmıştır. Yavaşlayan küresel ekonomiye yaşanan nüfusa bağlı artan sağlık kaynakları kullanımı, özellikle Amerika Birleşik Devletleri ve Avrupa Birliği ülkelerinde sağlığa ayrılan fonların ekonomiye oranının artmasına neden olup endüstrinin aleyhinde bir durum yaratmıştır.

Sonuç olarak ilaç şirketleri bu olumsuz piyasa koşullarının üstünden gelmek ve büyümelerini sürdürmek için yeni büyüme stratejileri arama yoluna gitmiş, vesatle gelişmekte olan, ve Türkiye'nin de dahil kabul edildiği Yükselen BRIC (Brezilya, Hindistan, Çin ve Brezilya) Pazarlarına öncelik vermişlerdir. Bu ekonomilerin, %5-10 yıllık GSYİH büyüme sergilemeleri, nüfuslarının sağlık hizmetlerine erişiminin ve ihtiyaç harcamalarının artması tüm küresel ilaç şirketleri için umut verici bir görünüm sunmuştur.

Ancak, her gelişmekte olan piyasakendine özgü sosyo-ekonomik ve politik özellikler gösterdiği dengeli piyasa da başarılı olmuş yöntemleri aynen uygulamak aynı başarıyı tekrarlamaya yeterli olmayacaktır. Bir ön literatür taraması bu araştırma konusunun incelenmediğini ortaya koymuştur. Bu tez namacı Yükselen Pazarlarda ilaç ve biyoteknoloji şirketlerinin kârlı büyümesini teminen nitel ve nicel olarak başarı etmenlerini araştırmaktır.

Niteliksel araştırma yöntemi akademik kurumlarca basılmış yayınları, düşünce tankları, yaşam bilimleri sanyidergileri, hükümetler ve yönetim

danışmanlıkfirmalarının yayınları taranması ve bahsi geçen başarılı uygulamaların saptanması şeklinde gerçekleştirilmiştir.

Retrospektif gözlemselmalianalizigerçekleştirmek amacıyla ise, küresel ölçektefaaliyet gösteren en büyük 14ilaç vebiyoteknoloji şirket verileri yatırımcılara açık kaynaklardan derlenmiş, ve endüstride yaygın olarak kullanılan finansal yaklaşım yöntemi kullanılarak ikiayrı gruptaincelenmiştir.

Sermayekârlılığı ve yatırımcılara geri dönüş değişkenleri 2009 den2011'i kapsayanüç yıllık birsüre içindedeğerlendirilmiştir. 2007-2011dönemine de bakılmakla beraber 2008ekonomik krizinin olumsuz ve tekil etkileri dolayısıyla bu dönemi kullanmaktan vazgeçilmiştir. Buçalışma, ilaç ve biyoteknolojişirketleri için bu firmaların ürün portföylerinin farklı olmasından dolayı, ayrı ayrı tekrarlanmıştır.Karşılaştırmalıçıkara gidebilmek içintakvim ve maliyillarnormalize edilmiştir.

Araştırmaya alınan ilaç ve biyoteknoloji firmaları AmerikaBirleşik Devletleri, İngiltereveyaİsviçre merkezli, dünya çapındaoperasyonları olan,yıllık satışları 20 ila61 milyar dolar aralığında ve hisseleri NYSE veya NASDAQ'ta işlem gören firmalar arasından derlenmiştir.

Yatırımcıya Geri Dönüş ve Yatırılan Sermaye Dönüşü parametrelerini belirlemek için kamuya aşık şirketlerin malikaynaklarıtoplanmış vedaha sonrakarşılaştırmalısonuç eldeedebilmek içintakvim yıllarıyla firmaların maliyillarıayarlanmak suretiylenormalize edilmiştir.

Nitel çalışma ilaç ve biyoteknoloji firmalarının Gelişmekte OlanPazarlarda yatırımcıdeğeri oluşturmak ve rekabetçi kalmak için tez kapsamında bulunan yedibaşarı faktörü aşağıda sıralanmıştır:

1. Yerli Üretim Yapabilme Kabiliyeti
2. Hızlı ve iyi ilişkilere dayanan Ruhsat ve Düzenleme Yetenekleri
3. Ticari Organizasyon ModelininYükselen Pazar Koşullarınahitabedebilmesi
4. GenişveVerimli bir Dağıtım Ağına Sahip olabilmek
5. Devlet İhalelerinde Dinamik FiyatlandırmaYetenekleri
6. Yerel Klinik Çalışma yapan düşünce liderlerini küreselKlinik Çalışma ve ürün geliştirme yapan liderlerlebutünleştirebilen bir Medikal Bölüm kabiliyeti, ve

7. Yetkin ve yetenekli yerel personele erişim, işe alma ve işte tutma becerisi.

Nicel olarak, Amerika Birleşik Devletleri'nde elde edilensatışYatırımcıya Geri Dönüş itibariylepozitif bir korelasyon gösterirkenYükselen Pazarlardaki satış geliri ilepozitif bir korelasyongörülmemiştir. Aynı örneklem için, Yatırılan Sermaye Kârlılığihemilaç ve biyoteknolojifirmalarının satış gelirleri ilepozitif bir korelasyongöstermiştir. Bu bulgular, firmaların Yükselen Pazarlara girerken Yatırımcıya Geri Dönüş açısından getiri beklememelerini ve Yatırılan Sermaye Geri dönüşübazındada mütevazıbir beklentiiçinde olmalarını ortaya koymaktadır.

ABSTRACT

The global pharmaceutical industry generated approximately \$960 billion in revenue in 2011 demonstrating a 7.8% compounded annual growth rate (CAGR) for the preceding five years. This industry, with its foundation in discovering, developing and marketing innovative medications had the benefit of patent lives-lasting around 20 years- providing sustenance for the business to grow steadily. It has been historically a profitable business with gross margins around 80% and operating margins in the range of 40-50%.

While the industry enjoyed sustained free cash flow, over the last few years, it has been challenged by the expiry of patents of its products leading to massive revenue losses estimated around \$125 billion and lack of a robust product pipeline to replace the lost revenue. Since the industry heavily relies on the governments to pay for its medicinal products, it thrives on a healthy economic mega-system. Industry's challenge was further compounded by aslowing global economy and an aging population utilizing more healthcare resources and increasing healthcare costs in developed countries, particularly in the United States and the European Union countries.

These unfavorable market conditions pushed the pharmaceutical companies to identify new strategic value levers to sustain its growth, and consequently the industry set out to expeditiously expand its footprint in the emerging markets. As the beneficiaries of the globalizing economy, the BRIC (Brazil, India, China & Brazil) bloc of countries and Turkey had offered the biggest growth platform. These economies have demonstrated a vivid GDP growth in the range of 5-10% annual growth and, thanks to an increase in access to medicine and surge in discretionary spending of their population; offer a promising outlook to all global companies. In this context, products of pharmaceutical companies are well-positioned to address healthcare needs of the growing and aging populations in the Emerging Markets.

Nonetheless, each individual emerging market demonstrates unique socio-economic and political characteristics, and even as a bloc do not present characteristics similar to developed markets due to a variety of underlying reasons.

A preliminary literature review had indicated that this research topic was not sufficiently examined leaving an opportunity to investigate. Consequently, the objective of the thesis was established to explore this non-trivial Emerging Markets growth challenge on qualitative and quantitative fronts that would link both business strategy and financial outcome aspects to the pressing dilemma of profitably growing in the Emerging Markets.

In order to perform the retrospective observational financial analysis, a total of 14 large companies operating on a global scale were identified, and investigated in two distinct groups under pharmaceutical and biotechnology company peer sets.

A shareholder value analysis framework was utilized to map out the financial levers of value generation focusing on Total Return on Shareholder Value (TRS) and Return on Invested Capital (ROIC). The relationships between the geographic revenue breakdown and the two aforementioned parameters were tested by conducting a correlation analysis.

These two parameters were collected over a three year period from 2009 through 2011. Similarly, a five year period ranging from 2007 through 2011 was also initially explored but then later discontinued since the 2008 economic downturn was identified as a disruptive confounding factor to the ability to draw meaningful conclusions.

The correlation analysis was performed separately for pharmaceutical and biotechnology companies. Pharmaceutical companies operate with a more traditional, primary care focused small molecule product portfolio whereas the biotechnology companies discover, develop and market expensive biologics products targeting specialists. Therefore, these two groups of life sciences companies were investigated in separate peer groups.

The selected pharmaceutical companies were the largest among their peers by revenue which ranged from \$20 to \$61 billion. Correspondingly, their market capitalization was also among the highest in their peer set. While these companies were headquartered in the United States, United Kingdom or Switzerland; their common stock were all traded in NYSE. Also, they all recognized revenue through

their worldwide operations that would allow to compare performance by geographic denominations. Similarly, seven largest biotechnology companies were all publicly traded in NYSE.

Company financials to determine TRS and ROIC were collected through public sources, and later normalized by adjusting their fiscal years to the calendar years to be able to draw comparative conclusions.

The qualitative study led to the identification of the following seven key success factors that the pharmaceutical and biotechnology companies need to perform exceptionally well to stay competitive in the Emerging Markets:

1. Local Manufacturing Presence
2. Building Agile Regulatory Affairs Capabilities
3. Commercial Model Addressing Emerging Market Needs
4. Broad and Efficient Distribution Network
5. Dynamic Pricing and Contracting Capabilities
6. Emerging Market Medical Affairs Capabilities Connecting Local Thought Leaders to Global Clinical Development Leaders
7. Access to and Retention of Local Talent

The quantitative analysis suggested that TRS did not show a positive correlation with the revenue booked in the Emerging Markets whereas the United States revenue showed a positive correlation. For the same sample set, the ROIC showed a positive correlation with the revenue booked by both pharmaceutical and biotechnology companies, suggesting that in the period of this study life sciences companies that enter the Emerging Markets should not expect an appreciation for their stock price while they will gain some modest returns on their invested capitals.

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TABLE OF CONTENTS

	Page
ÖZ	iii
ABSTRACT	vii
ACKNOWLEDGEMENTS	x
TABLE OF CONTENTS	xi
LIST OF ABBREVIATIONS	xiv
LIST OF TABLES	xvi
LIST OF FIGURES	xviii
INTRODUCTION	1
Objective of the Study	2
Research Questions to Be Addressed	2
Research Approach and Hypotheses	3
The Implications of the Study	3
1. BACKGROUND AND LITERATURE REVIEW	
1.1. Overview of the Global Pharmaceutical Industry	5
1.1.1. Pharmaceutical Product Discovery and Development Process	11
1.2. Trends in the Global Pharmaceutical Industry	16
1.2.1. Massive Loss of Intellectual Property Protection	17
1.2.2. Shortfall in the R&D Productivity	19
1.2.3. Need for Innovative Business Models	22
1.2.4. Healthcare Reforms	24
1.2.5. Emergence of Biosimilars	27
1.2.6. Advances in Healthcare Technology	29
1.2.7. Pressing Need for Evidence-based Decisions	30
1.2.8. Reimbursement Challenges	32
1.2.9. Supply Chain Rationalization	34
1.2.10. Cost Take-out	36

1.3.Characteristics of Pharmaceutical Emerging Markets BRIC-T	37
1.3.1. Brazil	41
1.3.2. Russia	43
1.3.3. India	44
1.3.4. China	47
1.3.5. Turkey	49
2. METHODOLOGY	52
2.1. Rationale of the Methodology	52
2.2. Sample Selection	51
2.3. Qualitative Analysis	53
2.4. Quantitative Analysis	54
3. RESEARCH FINDINGS& DISCUSSION	59
3.1. Summary of Findings	59
3.2. Qualitative Findings	64
3.2.1.Local Manufacturing Presence	64
3.2.2.Building Agile Regulatory Affairs Capabilities	65
3.2.3.Commercial Model Addressing Emerging Market Needs	66
3.2.4.Broad and Efficient Distribution Network	68
3.2.5.Dynamic Pricing and Contracting Capabilities	70
3.2.6.Emerging Market Medical Affairs Capabilities	
Connecting Local Thought Leaders to Global Clinical Development Leaders	71
3.2.7. Access to and Retention of Local Talent	72
3.3. Quantitative Findings	73
3.3.1. Pharmaceutical Company Peer SetAnalysis	74
3.3.1.1.Relationship of Revenue Source by Geography to Total Return to Shareholders - Pharmaceutical Companies	76
3.3.1.2.Relationship of Revenue Source by Geography to Return on Invested Capital - Pharmaceutical Companies	80
3.3.2. Biotechnology Company Peer Set Analysis	83
3.3.2.1.Relationship of Revenue Source by Geography to Total Return to Shareholders - Biotechnology Companies	83

3.3.2.2. Relationship of Revenue Source by Geography to Return on Invested Capital - Biotechnology Companies	89
3.4. Limitations and Recommendations	100
3.4.1. Recommendations for Further Research	100
CONCLUSIONS	102
REFERENCES	104
APPENDIX	119
Appendix 1. Economic and Business Characteristics of Countries	119
Appendix 2. Life Expectancy and Healthcare Spend Comparison of Countries	120
Appendix 3. Healthcare Characteristics and Pharmaceutical Spending Comparison	121
Appendix 4. Shareholder Value Analysis Data for Pharmaceutical and Biotechnology Companies	122
Appendix 5. Return on Invested Capital from 2009-11 for Pharmaceutical and Biotechnology Companies	125
Appendix 6. Summary of Return on Invested Capital Values by Segment	125
Appendix 7. Statistical Tables	126

LIST OF ABBREVIATIONS

AZ	Astra Zeneca
AMNOG	Act on Reform of the Market for Pharmaceutical Products
BMS	Bristol Myers-Squibb
BRIC	Brazil, Russia, India & China
CAGR	Compounded Annual Growth Rate
CMS	Center for Medicaid/Medicare Services
CRO	Clinical Research Organization
DNA	Deoxyribonucleic acid
GDP	Gross Domestic Product
GSK	Glaxo SmithKline
HIE	Healthcare Information Exchange
FCPA	Foreign Corrupt Practices Act
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
EM	Emerging Markets
EMA	European Medicinal Agency
EBIT	Earnings Before Interest and Tax
EMR	Electronic Medical Records
EHR	Electronic Health Records
HIE	Healthcare Information Exchange
NHIS-T	National Health Information System – Turkey, Saglik-Net
IRB	Institutional Review Board

NCE	New Chemical Entity
NME	New Molecular Entity
FDA	Food and Drug Administration
NICE	National Institute for Clinical Excellence
QALY	Quality-Adjusted Life Year
R&D	Research and Development
ROIC	Return on Invested Capital
SG&A	Selling, General and Administration
TRS	Total Return to Shareholders
WACC	Weighted Average Cost of Capital

LIST OF TABLES

Table 1: Ranking of Countries in terms of Size on the Global Pharmaceutical Stage

Table 2: The Effectiveness of Patents in Appropriating the Benefits from Product and Process Innovations According to Industry

Table 3: Research Spending Per New Drug Approved

Table 4: GDP and Pharmaceutical Market Growth of BRIC countries, Turkey and Developed Markets

Table 5: Stratification of Chinese Healthcare Market

Table 6: Research Questions and Methodologies

Table 7: 3-year total average revenue, 3-year average revenue source, 3-year total return on shareholders and 3-year average return on invested capital of selected pharmaceutical company

Table 8: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on shareholders of selected biotechnology company peer set

Table 9: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on invested capital of selected biotechnology company peer set

Table 10: 3-year total average revenue, 3-year average revenue source, 3-year total return on shareholders and 3-year average return on invested capital of selected biotechnology company peer set

Table 11: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on shareholders of selected biotechnology company peer set

Table 12: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on invested capital of selected biopharmaceutical company peer set

Table 13: Summary of total return to shareholders by geography by pharmaceutical and biotechnology company peer sets

Table 14: Summary of return on invested capital by geography by pharmaceutical and biotechnology company peer sets

Table 15: Summary of the overall Analysis of both Pharmaceutical and Biotechnology Company Sets with TRS and ROIC

LIST OF FIGURES

- Figure 1:** Size of Global Pharmaceutical Market
- Figure 2:** Number of Compounds in Development
- Figure 3:** Cost of Prescription Medications as part of Total Health Care Cost
- Figure 4:** Phases of Pharmaceutical Product Development
- Figure 5:** Lost Pharmaceutical Revenue due to Patent Expirations
- Figure 6:** Attrition rate of a new molecular entity through the development phases
- Figure 7:** Ratio of Approved Medicines with a Positive Return on Investment
- Figure 8:** Number of sales representative jobs between 2006 and 2011
- Figure 9:** GDP, Healthcare and Drug Spend 2012-16 Projections for Developed and Emerging Markets
- Figure 10:** US Healthcare Reform Milestones
- Figure 11:** Global Biologics Spending
- Figure 12:** Flow of Goods and Financial Transactions among Players in the U.S. Commercial Pharmaceutical Supply Chain
- Figure 13:** Household income growth in 2010-2020 in billion US dollars at 2010 constant prices for 64 countries
- Figure 14:** Growth of population volume with more than \$5,000 annual income by 2016
- Figure 15:** Healthcare spend as percentage of GDP compared to life expectancy in years for emerging and developed countries
- Figure 16:** Shareholder Value Tree Framework for a Pharmaceutical Product Company
- Figure 17:** Identified Parameters within the Shareholder Value Tree Calculated for Correlation to Test the Postulated Research Questions
- Figure 18:** Relationship between Brand Equity of Product Categories (and manufacturers) and Operating Margins
- Figure 19:** Relationship between 3-year average Total Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies
- Figure 20:** Relationship between 3-year United States Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies

- Figure 21:** Relationship between 3-year Europe Revenue to 3 year average of Total Return to Shareholders - Pharmaceutical Companies
- Figure 22:** Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies
- Figure 23:** Relationship between 3-year average Total Revenue to 3-year average return on invested capital - Pharmaceutical Companies
- Figure 24:** Relationship between 3-year-average United States Revenue to 3-year average return on invested capital - Pharmaceutical Companies
- Figure 25:** Relationship between 3-year Europe Revenue to 3-year average return on invested capital - Pharmaceutical Companies
- Figure 26:** Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average return on invested capital - Pharmaceutical Companies
- Figure 27:** Relationship between 3-year average Total Revenue to 3-year average of Total Return to Shareholders – Biotechnology Companies
- Figure 28:** Relationship between 3-year United States Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies
- Figure 29:** Relationship between 3-year Europe Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies
- Figure 30:** Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies
- Figure 31:** Relationship between 3-year Total Revenue to 3-year average return on invested capital - Biotechnology Companies
- Figure 32:** Relationship between 3-year United States Revenue to 3-year average return on invested capital - Biotechnology Companies
- Figure 33:** Relationship between 3-year Europe Revenue to 3-year average return on invested capital - Biotechnology Companies
- Figure 34:** Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average return on invested capital - Biotechnology Companies

INTRODUCTION

In an attempt to find new sources of growth, the pharmaceutical industry has placed the Emerging Markets on top of their agenda and developed initiatives with various degrees of success. However, there are many examples of growth and success that Pharma can leverage as it develops its strategies pertaining to penetrate the Emerging Markets. At present, ten of the top 20 funds over the last decade invest in developing nations. Both economic and political power is shifting to emerging markets, with the rise of the G20, and blocs like the BRIC (Brazil, Russia, India and China). The emerging markets are home to more than 70% of the world's population, 46% of its land mass, and 31% of its GDP. (Dimson, 2010)

Since the pharmaceutical market dynamics are fundamentally different in these emerging markets due to access to healthcare, reimbursement, pricing and distribution, "Big Pharma" companies need to compete with or against a class of products, labeled as "branded generics". Branded generics are generic versions of products sold either by the same manufacturer who discovered and marketed the patented drug, or by a generic manufacturer which built brand equity for the generic version of the medication, introduced right after the patent expiration of the original product. The original manufacturers aim to build upon the name recognition of the branded drug while providing a more competitive pricing point with the generic competition, while on the other end, local generic manufacturers strive to build the brand equity with support of their sales and marketing organizations.

However, the expected success had fallen way short of expectations according to a variety of industry analysts, experts and business media (Rockoff, 2012).

The objective of this thesis is to review the dynamics of the emerging markets BRIC-T (Brazil, Russia, India, China, and Turkey) and offer key success factors for global pharma companies to consider in order to create ascendancy over their competitors with a branded generics strategy when competing against local generic manufacturers, a strategy executed with very different set of rules than in developed countries.

The Objective of the Study

In today's challenging business environment the global pharmaceutical companies are operating in, the Emerging Markets offer a source of incremental growth. Nonetheless, their unique market conditions present global pharmaceutical companies a challenge since they simply cannot replicate their market expansion and development strategies that are tested and proven to be successful in mature markets of developed countries. The pharmaceutical company playbook has a wealth of tactical approaches that the industry can deploy, however it is essential to focus the resources and energy on key business drivers.

The objective of this work is to identify key success factors for the global pharmaceutical companies to consider when investing in and expanding into the emerging markets. Importantly, the study had also investigated the relationships of the financial parameters such as total return to shareholders (TRS) and return on invested capital (ROIC), and revenue generated by these pharmaceutical and biotechnology companies in the Emerging Markets.

Research Question to Be Addressed

Emerging markets offer a source of incremental growth to global pharmaceutical companies to compensate for the slowing growth in the developed markets.

Two sets of research questions were investigated, qualitative and quantitative:

Qualitative Research Question:

1. What are the key success factors for pharmaceutical and biotechnology companies to operate in the emerging markets?

Quantitative Research Questions:

1. How does the geographic breakdown of revenue correlate with the profitability as measured in (ROIC) for each pharmaceutical and biotechnology peer set?

2. How do shareholders reward pharmaceutical and biotechnology companies' investment in order to expand into emerging markets for each pharmaceutical and biotechnology peer set?
3. What strategic corporate behavioral differences exist between pharmaceutical and biotechnology companies towards emerging markets expansion?

Research Approach and Hypotheses

The methodology followed in the thesis is to identify successful identify possible hypotheses that would be applicable to the pharmaceutical set through a robust literature search, industry publications as well as interviews made by business executives in the space. The findings then were grouped and summarized to establish common themes that would be applicable to the global pharmaceutical and biotechnology companies. This was an iterative process and was repeated until certain themes shaped up, matured and ready for report out as common successful practices.

Additionally, a shareholder value analysis was performed for the leading multinational peer set of global pharmaceutical and biotechnology companies. This set represents a significant 50-60% portion of the overall market. Subsequently, correlations were calculated with their performance in the emerging markets and their financial strength with a focus on portion of revenue generated in various geographies including the emerging markets.

The Implications of the Study

Global pharmaceutical and biotechnology companies have ongoing investments implementing their strategies in BRIC-T; however, in absence of a targeted commissioned research they do not have the benefit of comparing and contrasting the outcomes of their strategy and how their strategy leads to positive return from a profitability and share-holder value creation perspectives.

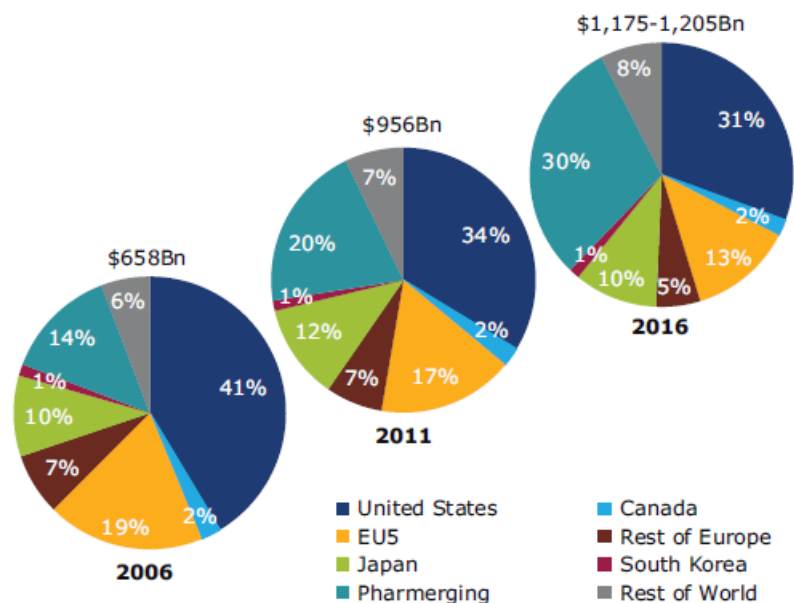
The findings of this study can serve as a framework for multinational pharmaceutical companies operating in BRIC-T to enable them to compare their operational strategy across emerging markets and may enable them to course-correct or, in the least, have the benefit of comparing the findings and recommendations to their existing strategy and its execution for cross-validation purposes.

1. BACKGROUND AND LITERATURE REVIEW

In order to provide the background for the underlying dynamics, trends and issues the pharmaceutical and biotechnology industry is facing and how the emerging markets fit in that context, a literature review was conducted.

1.1. Overview of the Global Pharmaceutical Industry

Over the years the pharmaceutical market worldwide revenue as measured in ex-manufacturer prices grew from \$658 billion in 2006 to a respectable \$956 billion in 2011 demonstrating a compounded annual growth rate (CAGR) of 7.8%. Assuming the projections made by Intercontinental Marketing Services (IMS), a market research company used as a standard bearer for market size assessment and projections in their latest Market Prognosis analysis in May 2012, the market is projected to grow to a range of 1,175 to 1,205 billion. Taking the midpoint 1,190 billion of this range, the IMS foresees a CAGR of 4.5% over the 2011 through 2016 period, a growth rate almost as half as the one defining the 5 year earlier period.



Source: IMS Market Prognosis, May 2012

Figure 1: Size of Global Pharmaceutical Market
(2006 through 2011 and projected through 2016)

With this stagnated outlook in the overall worldwide market it is imperative to dissect the sources of and impediments to growth. First, the developed countries, as represented by the United States, EU's Big Five (Germany, the United Kingdom, France, Spain and Italy) and Japan, which for decades have been the primary focus of pharmaceutical industry and investment will shrink from a total of 70% of the total market in 2006 to, first, 63% in 2011 and then to 54% by 2016.

The absolute size of these developed markets will not necessarily shrink but their relative contribution to growth will deteriorate, which is a major departure from a historical perspective to the industry dynamics.

Specifically, the United States market that has been the bellwether indicator of the global market for decades, will grow from \$270 billion in 2006 to \$325 billion in 2011 (CAGR of 3.8% for 2006-11) and \$370 billion in 2016 (CAGR of 2.6% for 2011-16), a rate of growth about half of the worldwide scale.

Interestingly, Japan will retain 10% of drug spending in 2016, essentially unchanged from the 2006 level. This is essentially due to the impact of the mandatory biennial price cuts expected in 2012, 2014 and 2016.

An even a more dire picture represents the outlook of the leading five European Union countries. In 2006 these five countries made up \$125 billion worth of pharmaceutical revenue, \$163 billion in 2011 (CAGR of 5.4% for 2006-11) and are projected to regress to \$155 billion in 2016 (CAGR of negative 1% for 2011-16) for the second 5-year period.

The underlying reasons for the European countries can be explained by aggressive government policies against lower pricing, increased regulatory pressure, and very unfavorable reimbursement. European governments trying to navigate the uncertain future of the European Union bloc and trying to de-risk their Southern members like Greece, Portugal, Spain and Italy through austerity and cost-containment measures are significantly cutting back their healthcare spending where pharmaceuticals are on the top of the list.

On the other side of the equation, the emerging markets as represented by a cluster of ten countries, including BRIC and Turkey among others, depict a very different and healthy outlook.

While in 2006 the emerging markets make up about only 14%, or \$92 billion, of the worldwide market, their share in the global stage is projected to grow to 20%, or \$191 billion in 2011.

Most remarkably they are projected to make up 30%, or \$357 billion, of the market, matching the size of the United States market when combined. This growth pattern will show a CAGR of 16% from 2006 to 2011 and 13% from 2011 to 2016.

Over a 10 year period the so-calledPharmerging markets will show a 10-year CAGR of 14.5% versus 2.9% for the combined US and EU5 market characteristics.

This bimodal characteristic of the market has been dubbed as a “dual-speed market” for obvious reasons with the developed countries, historically the focus are now belong to the lower growth segment and the emerging markets, mostly neglected as secondary target by global pharmaceutical companies to introduce products, now taking the spot light from the historically strong mature markets.

Another insightful perspective is to further dissect these relatively large segments of countries on a country by country analysis which Table 1 breaks down.

Table 1: Ranking of Countries in terms of Size on the Global Pharmaceutical Stage

(2005 through 2011 and projected through 2016)

2005		2011		2016	
Rank	Size \$B	Rank	Size \$B	Rank	Size \$B
1. USA	249.2	1. USA	322.0	1. USA	350-380
2. Japan	84.9	2. Japan	111.2	2. China	+1 155-165
3. France	33.3	3. China	+6 66.7	3. Japan	-1 105-135
4. Germany	33.1	4. Germany	45.0	4. Brazil	+2 42-52
5. Italy	21.3	5. France	-2 41.3	5. Germany	-1 39-49
6. UK	16.4	6. Brazil	+4 29.9	6. France	-1 32-42
7. Spain	16.1	7. Italy	-2 28.6	7. Italy	23-33
8. Canada	15.9	8. Spain	-1 22.7	8. India	+5 24-34
9. China	14.1	9. Canada	-1 22.4	9. Russia	+2 23-33
10. Brazil	11.8	10. UK	-4 21.5	10. Canada	-1 19-29

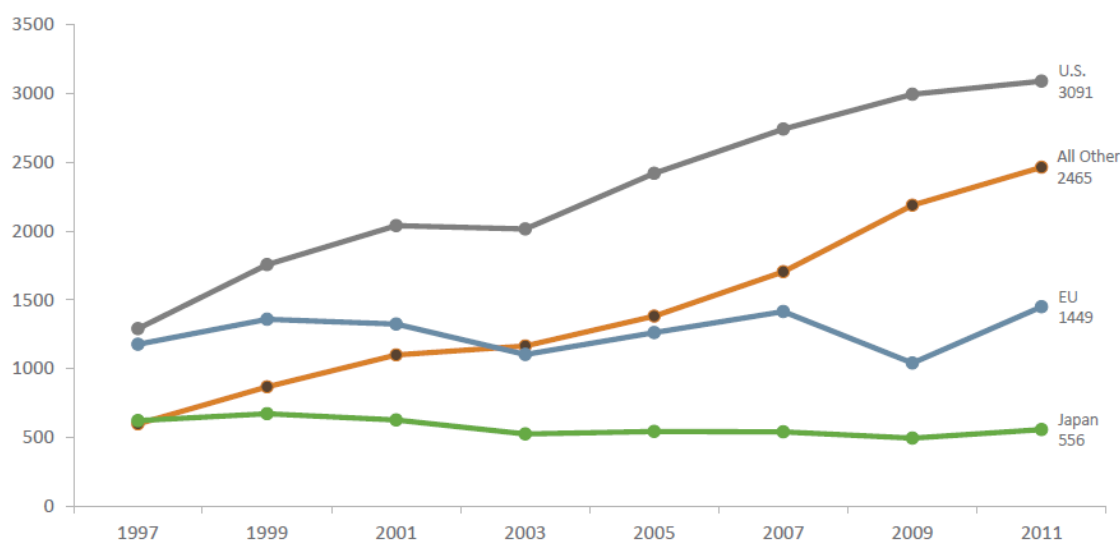
■ NA
 ■ EALA
 ■ APAC
 ▲ Placement movement
 Drops off Top 10
 Emerging Mkts

Source: IMS May 2012. Spending in US\$ with variable exchange rates.

(NA: North America, EALA: Europe, Asia and Latin America, APAC: Asia Pacific)

The immediate observation of this listing based on the latest IMS projections shows that the United States maintains its leading spot through 2016. This can be explained by the relatively sizeable R&D investment in the United States. Figure 2 breaks down the number of new compounds, candidates for development of future medications.

The United States-based institutions, government or privately-funded, generated over 3,000 compounds a number double of those that originated in the European Union and Japan combined. This innovative momentum in the United States will help maintain the United States lead with most novel therapies being introduced in the United States market pushing the market valuation to higher levels over this 10-year period. The context around the R&D will be covered later in this study to shed further light on this discussion.



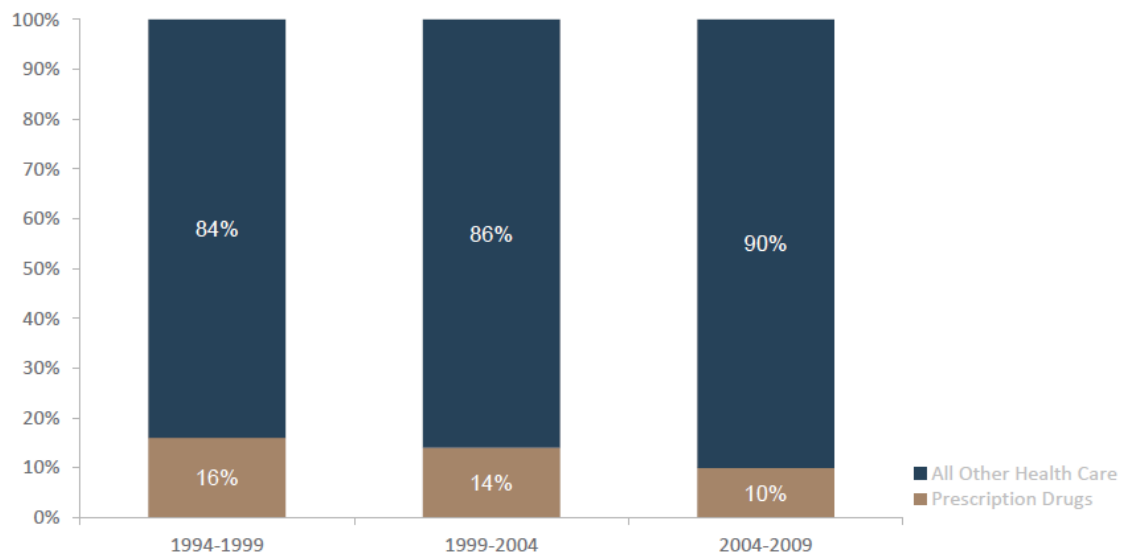
Source: Adis R&D Insight Database[†]

Figure 2: Number of Compounds in Development
(by Geographic Region, 1997–2011)

The second observation in Figure 2 is that some traditional European markets such as the United Kingdom and Spain will no longer be in the top ten worldwide markets. The abysmal European growth pattern is consistent with this cross-sectional perspective.

The third and final take-away from this analysis in Figure 2 was that the emerging markets will start dominating the top ten country list with China ranking as the world's second largest market thanks to its massive population size, aging population and healthcare reforms put in place in 2009 that would allow the rural Chinese population to access healthcare services previously not available in the settings outside of large cities. Brazil is another emerging force which is projected to become the fourth largest pharmaceutical market. Finally, India and Russia will also get to the top-ten country list due to a variety of underlying dynamics but primarily due to access to healthcare of their large populations.

Multinational companies are being challenged to understand how they can successfully compete in the emerging markets, and leverage the generics business model as an opportunity and not consider it as a risk. A few recurring strategies were observed that allow for effective penetration in the emerging markets.



Source: CMS

Figure 3: Cost of Prescription Medications as part of Total Health Care Cost
(Center of Medicare Medicaid Services, 2010)

Contrary to the conventional wisdom and perception, pharmaceutical products do not make up a large portion of healthcare expenditure. They actually comprise no more than 10% of the total healthcare cost, as the data in Figure 3 shows. The information collected by Centre of Medicare/Medicaid Services (the government body in the United States of America responsible for paying healthcare expenses including medication) has been reporting this over the decades.

There is overwhelming evidence that medications, when administered as prescribed, lower the overall healthcare cost by pre-empting more costly interventions, procedures or avoidable hospitalization and preventable re-admissions. For example, in the United States, among Medicaid beneficiaries with congestive heart failure, total healthcare costs for adherent patients were 23 percent lower than those of non-adherent patients.(Esposito et al2009)

Another study performed by diabetes patients showed that non-adherent diabetes patients were 2.5 times as likely to be hospitalized as those who followed their prescribed treatment. (Lau et al2004)

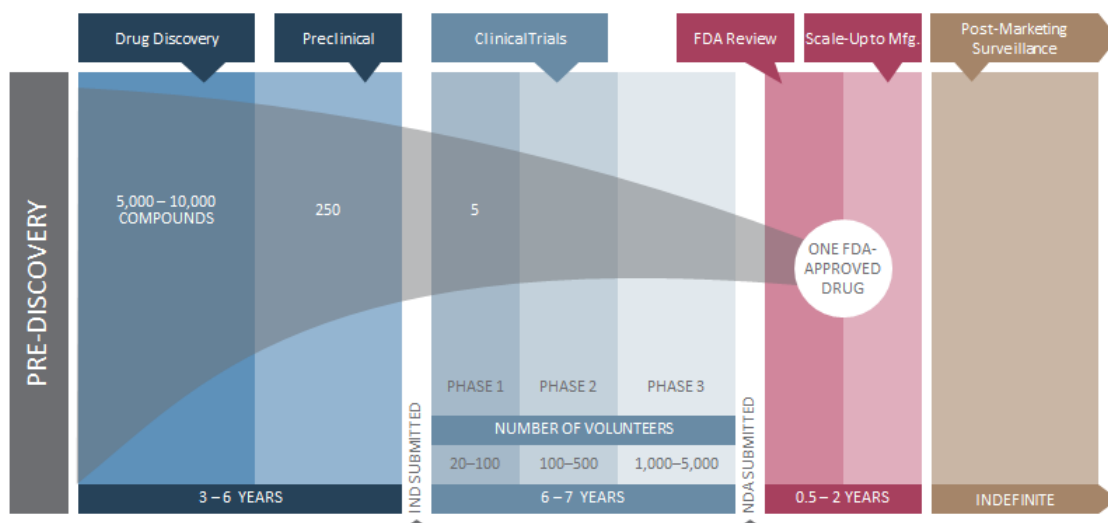
1.1.1. Pharmaceutical Product Discovery and Development Process

Pharmaceutical product discovery and development show unique characteristics when compared to other manufacturing-based industries, such as consumer goods or retail. The product development cycle is approximately 8-12 years from the ideation phase to market. This duration is an order of magnitude longer than retail product cycle, where a leading apparel manufacturer can take about 9-24 months from concept to show-room.

The high risk – high reward nature of the pharmaceutical business requires a solid intellectual property protection to justify the substantial capital expenditure necessary for a clinical development program and commercialization. Patents to protect intellectual property are typically filed as early as when a molecule demonstrates activity in the lab setting against a therapeutic target which might potentially lead to a reasonable therapeutic effect. While a typical patent in the United States and Europe can protect the original molecule for about 20 years, a relatively long (8-12 years) development timetable only allows the manufacturer about 10 years of effective exclusivity in the marketplace.

To start the protection the manufacturer typically submits the patent application to regulatory agencies when a NCE (new chemical entity) is discovered. At that point there is no proof that this molecular entity has any treatment effect of any illness or medical condition in humans.

As a result, in return of a highly risky product discovery and development undertaking the pharmaceutical manufacturer can enjoy a window of ten years with no direct competition for the same molecule. This does not preclude the competing manufacturer(s) from developing a similar product in the same class or designing other interventions to the same target molecular pathway.



Source: (PhRMA, 2007)

Figure 4: Phases of Pharmaceutical Product Development

As it would be expected for any risky product development process, there are stage-gates to retire risk along the development continuum. The phased product development process by stagewas presented and discussed below.

Research:

Basic research on functionality of molecular pathways, genes, their mutations, under- and/or overexpressions inspire scientists to establish bio-chemical interventions to modify, improve or disrupt biological functions in a pursuit of discovering medications. This research can be funded by a government entity, private enterprise or academic institutions.

At this stage, the return on investment is very dubious and uncertain making this level of investment less attractive to the private enterprise until a promising molecular intervention has shown an in vitro proof of concept in a petri dish or in a bench model in the research lab. Once the in vitro model is proven the next step is to simulate the same effect in vivo (in lab animal models).At this stage the entity that invested in the discovery can seek funding from pharmaceutical industry or private enterprise such as “angel investors”, “venture capital”, etc.(Borem et al, 2003)

Drug Discovery & Pre-clinical Research:

The next step following the discovery stage in the laboratory of the pharmaceutical company or the entrepreneur is to test the promising compound in animals. The animal studies are known as preclinical studies and are designed to detect efficacy and safety signals.

With the advancement of genetic engineering in 1990s, most common animal species to pursue these studies became transgenic mice, where a particular condition is genetically induced by blocking or accentuating a particular genomic sequence in mice's DNA. The choice of species will depend on the particular disease or condition and how closely the animal model can predict a clinical response in humans.

The protocols defining the study to be performed must be approved by IRBs (Institutional Review Boards), which are independent boards made up by medical professionals, ethicists, and scientists. For a preclinical study to proceed, an IRB must approve the clinical trial protocol, methodology and conditions upon which the animals will be treated. (Borem, 2003)

Early Stage Clinical Development (Phase I – IIa)

Assuming the tests support the a priori established hypothesis, the drug candidate will be advanced to clinical development stage involving humans and starting with healthy volunteers. This very first clinical stage is called Phase 1 development, or "first in man". The objective of the Phase 1 study is to test safety and tolerability of the new molecular entity at various dosing regimens in volunteers who do not have the condition for which the product is considered for further development.

Informed Consent must be obtained from subjects stating that they fully understand the consequences of the testing that they will undergo. The IRBs continue to get involved to approve or disapprove the study protocol before any clinical testing. They are involved in the process to ensure ethical, medical and scientific standards are adhered to. Regulatory authorities approve the clinical design, retain –and often exercise- the rights to audit the facilities, physicians and patient records.

Phase I studies can take 1-2 years due to time conducting the trial but also waiting for the interaction with regulatory and medical agencies.

Only if the molecule shows promising pharmacokinetic (what the medication does to the human body) and pharmacodynamics (what the human body does to the medication) profiles and is deemed harmless to healthy human subjects in Phase I trials, the medication candidate will start to be tested in humans with the medical condition or disease for which the product is intended to treat.

The studies in clinical development are designed to comply with what is considered a “gold standard” in clinical development and are randomized, double-blind, controlled, prospective trials.

Upon successful completion of testing in healthy human volunteers, the medicinal candidate is advanced by the sponsor to Phase 2 studies, where the drug’s efficacy will be tested for the first time in humans suffering from the particular condition the medicine was originally conceptualized. Phase 2 studies are planned in two subphases, Phase 2a and Phase 2b.

Typically in a Phase 2a study, drug manufacturer tests the dose ranging in smaller populations in fewer than 100 subjects who are afflicted by the condition for which the product candidate is intended for indication in addition to the safety and tolerability.

Late Stage Clinical Development (Phase IIb – III)

Late stage clinical development requires a control arm and several hundred if not thousands of patients. In each arm of the study pre-determined efficacy and safety will be looked for. Before the battery of studies is initiated, there will be primary and secondary endpoints to be negotiated with the regulatory agency that will ultimately sign-off on the product.

Upon identification of the sweet spots with the right balance of efficacy and tolerability in Phase 2b studies pharmaceutical developers will concentrate on end-points which will be statistically powered to show the desired outcome.

From a biostatistical study design perspective, there are two types of clinical study endpoints: primary and secondary. Consequently, the biostatistical power calculations are performed to detect significance with a p value less than 0.05 which the regulatory agencies consider to be statistically significant when compared to the placebo arm.

Placebo, also known as 'sugar pill' is a non-potent medication that resembles the active medication in the way it appears, formulated and delivered such that the neither the patient who will receive the treatment nor the clinician who will deliver it to the patient will be able to differentiate the placebo from active treatment. The use of the placebo in randomized, double-blind, controlled, prospective trials is the gold standard to measure the tolerability and efficacy of a medication.

Once the Phase 2 development is completed, pharmaceutical companies embark on very long and expensive Phase 3 clinical studies which can cost over \$100 million and take multiple years (2-5 years) depending on the end-points as discussed in Phase 2b stage of development.

The Phase 3 studies are also known as regulatory studies and, for example in the United States the FDA (Food and Drug Administration) requires two similar studies to lower the probability of a statistical chance to have an outlier effect.

One common misperception on the industry is that these clinical studies are conducted in underserved populations in the developing or emerging markets. The choice of where to perform the study is driven by multiple criteria including access to the afflicted population in sufficient numbers for an expeditious trial, competent medical centers and clinicians who can treat enrolled patients in full compliance with the study protocol.

Over the last years, in order to accelerate the long development process, the pharmaceutical industry has been increasingly on CROs (Clinical Research Organizations) to outsource its clinical development activities rather than performing it in-house.

Phase IV or Post-Approval Studies

Even after the product is approved by regulatory authorities, clinical testing will continue either to expand the usage of the product in new or existing indication(s) or as a conditional requirement to the approval granted by the regulatory authority. If a new indication is studied, the manufacturer(s) need to follow the staged phases all over again and demonstrate safety and efficacy.

The industry is also required to collect and submit drug adverse event reports in an effort to detect safety signals when the product has been exposed to millions of patients rather than thousands in the controlled environment of clinical trials with very strict inclusion and exclusion criteria

Finally, mostly triggered by hazardous and fatal adverse effects of drugs already approved and available on the market, such as Vioxx, the Congress in the United States passed the Food and Drug Administration Amendments Act of 2007. This law gave the FDA the authority to require a Risk Evaluation and Mitigation Strategy (REMS) from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks even after it is approved for general public use.

1.2.Trends in the Global Pharmaceutical Industry

In order to put the research question and its implications in the proper context, recent trends governing the pharmaceutical industry need to be put in the proper context

Summarized below are the top ten trends that are shaping the landscape within which the biopharmaceutical companies operate and make the emerging markets, especially the BRIC-T countries in scope of this research a key success factor for pharmaceutical companies to successfully operate.

1.2.1. Massive Loss of Intellectual Property Protection

When compared to industries that require similarly heavy investment in R&D, such as semi-conductors, petroleum refining, steel, computer and auto (Levin, 1977) established that pharmaceuticals ranked at the top of the list in terms of importance of patent protection for product invention and importance of patent protection for process inventions.

Table 2: The Effectiveness of Patents in Appropriating the Benefits from Product and Process Innovations According to Industry

(Source: Levin, 1977)

	<u>Petroleum Refining</u>	<u>Steel</u>	<u>Semi-conductor</u>	<u>Computer</u>	<u>Auto</u>	<u>Drug</u>
Importance of Patent Protection for Product Invention	4.33	5.10	4.50	3.43	4.50	6.53
Importance of Patent Protection for Process Inventions	4.90	3.50	3.20	3.33	4.50	4.88

Scaling Method: 1 = "not at all effective" to 7 = "very effective."

Pharmaceutical industry owes it to intellectual property that enables it to invest large sums in long-term research and development. Patents are an absolute requirement for pharmaceutical business model to succeed since the failure rates of bringing to compounds to marketplace are overwhelmingly high. It is reported (Pamolli et al, 2011) that a pharmaceutical compound has about 4% chance of making it through the regulatory approval process from the time it enters the pre-clinical development with the animal models.

Historically, the business model that the global pharmaceutical companies operated with was enabled by small molecule products, generally known as pills or tablets, with very high production margins, usually in the range of 90%. This environment, while offering high risk and high reward, worked in favor of the

pharmaceutical companies which built the so-called 'blockbuster' medicines with worldwide sales each exceeding multi-billion dollars.

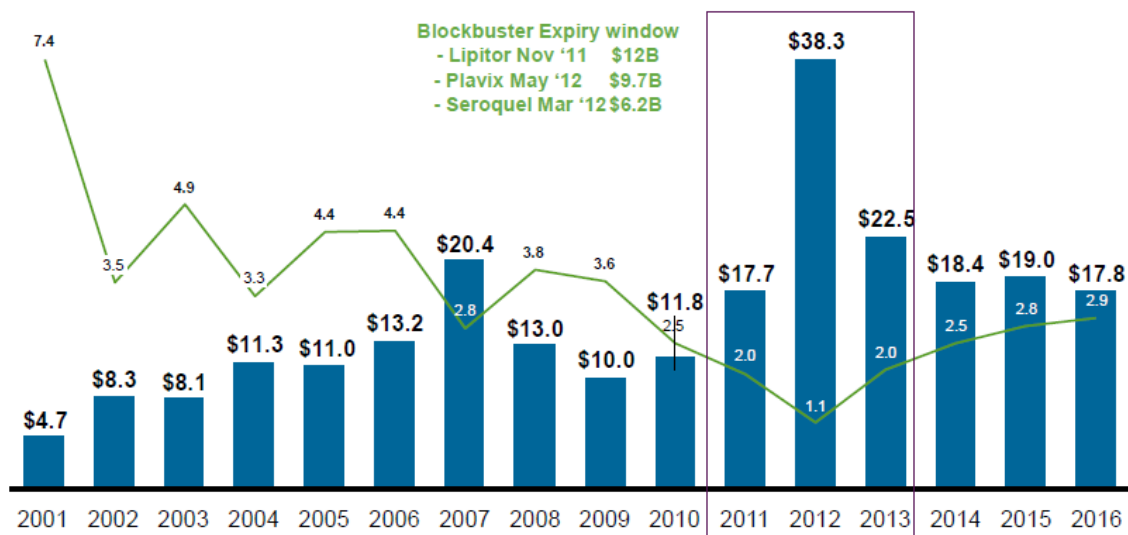


Figure 5: Lost Pharmaceutical Revenue due to Patent Expirations

(Source: IMS, 2012)

This model provided the pharmaceutical companies practically a monopoly status for the successfully developed and marketed molecules as long as the patents lasted, which is typically 20 years since the discovery of the molecule or 10-12 years in the market. It should be kept in mind, though, that in aggregate the pharmaceutical marketplace is very fragmented with the leading companies owning no more than 5-6% of worldwide value.

As the above graph shows, this model was disrupted when the marketing exclusivity of patents started expiring in early 2000s, commonly referred to as the 'patent cliff'. This trend has peaked in 2012 with many blockbuster multi-billion dollar entities losing their patents in troves and will level around 2015-16 (IMS, 2012) at a new normal when compared to early 2000s. These patent expiries will save healthcare payers in developed markets \$127 billion in the next five years, and primarily in the United States. This will be offset by \$21 billion of expected generic spending, resulting in a \$106 billion overall reduction by 2016.

The sales of a product losing patent protection can drop as much as 80% within the first month due to immediate introduction of generic products. This overnight phenomenon has a substantial and fatal impact on viability of that product's commercial sustainability. On the flip side, the generics pharmaceutical industry thrives on these trends since their business model is built on operational excellence to very inexpensively manufacture and distribute the generic copies through the local retail channels and pharmacies displacing the original medications at the point of sales.

In the United States., \$103 billion, or 44% of 2011 brandspending will shift to generics at dramatically lower prices. In other developed markets, the average brand spending exposed to generic competition will be 23%. (IMS, 2012)

It should be noted that in the short- to mid-term the industry will not be able to go back to the levels of patent expirations in 2000 to 2005, when on an annual basis approximately \$8 billion worth of products lost their protections. However, the industry has to adjust to the new plateau of 2013-2016, when on an annual basis approximately \$18 billion worth of products will be losing their patents.

According to a study commissioned by Generic Pharmaceutical Association to the market intelligence company IMS (Generic Pharmaceutical Association, 2012) the cost savings over a year period is estimated to be in the range of \$1 trillion due to novel medications replacing generic products due to patent expirations.

1.2.2. Shortfall in the R&D Productivity

Having reviewed the highly risky nature of pharmaceutical drug discovery and development it is also important to analyze the attrition rate and total costs associated with the development of a new medication.

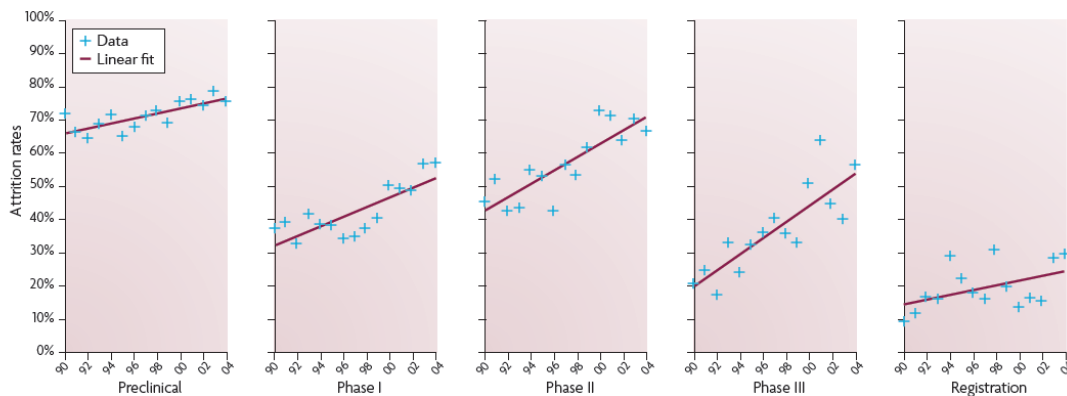


Figure 1 | Trends in attrition rates of drug development projects. Data are for projects started between 1990 and 2004 in the United States, Europe and Japan. Source: analysis of the Pharmaceutical Industry Database (BOX 1).

Figure 6: Attrition rate of a new molecular entity through the development phases (Pamolli 2011)

The end to end compounded probability of success to take a preclinical compound through the registration process and to consumers as presented by (Pamolli, 2011) and calculated hereby using the mid-range estimates can be as low as 4%.

The other and more significant observation of this trend is the consistent increase of the attrition rates over the course of the study through 2004, raising the bar on R&D productivity. Since the database used included applications through 2004, this research conjectures that the attrition rates will be higher if a new analysis would be performed. This would be due to a high number of unfavorable FDA decisions issued between 2004 and 2009 which would further lower the registration stage in the continuum highlighted in Figure 6.

Without a properly functioning R&D capability, pharmaceutical companies cannot sustain their valuations, which are typically higher than the Price to Earnings ratios of consumer goods or industrial manufacturing companies, which are relevant comparisons.

As a result, the industry is shifting its internal research and discovery efforts more heavily to external sources, such as academic institutions as a result of

technology transfer activities or start-up companies thanks to venture capital investments. On a parallel path, the industry is also supplementing their research capabilities by exploring licensing transactions more aggressively. This implication is also observed in the pattern of the industry M&A activity, while the large pharmaceutical companies shunning buying another large pharmaceutical company in order to integrate operations and fortify product pipeline but prefers, what the industry insiders call 'bolt on' acquisitions, with a smaller company that has a proven product or platform that can be easily added to the existing foundation of the "Big Pharma" company.

The cost of bringing a pharmaceutical product has been calculated as \$802 million (DiMasi, 2003), a figure widely accepted by industry experts while this estimate has its critics since the projection relies on information provided by the pharmaceutical industry (Looney, 2012) The same analysis was repeated and found that the total cost of developing a new drug was \$1.3 billion in 2006. (Vernon et al, 2009)

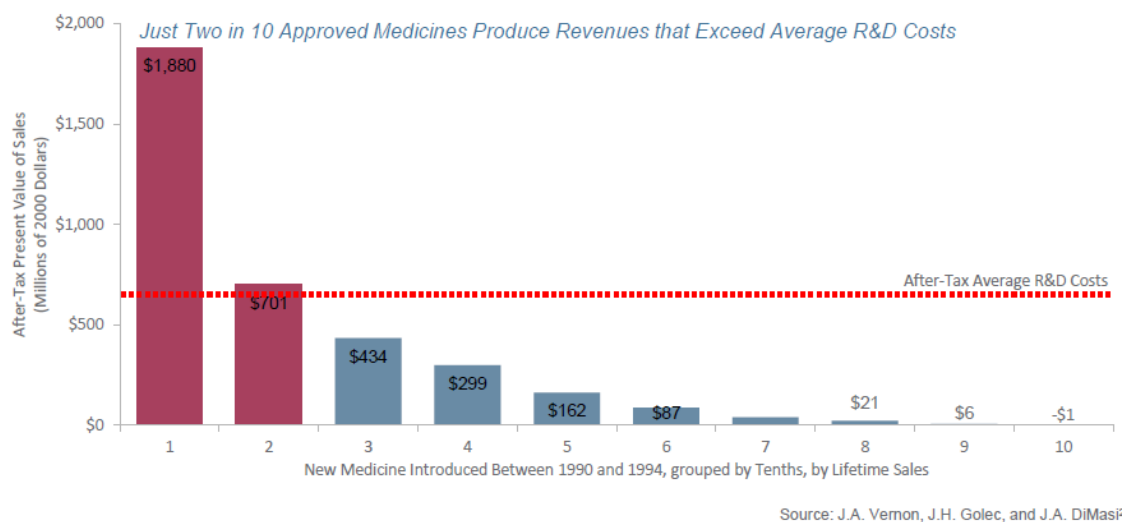


Figure 7: Ratio of Approved Medicines with a Positive Return on Investment
(Vernon et al, 2009)

This analysis in Figure 7, depicts that the revenue from only 2 of the 10 new medications can surpass the after-tax out-of-pocket costs in 2000 dollars for drugs introduced from 1990–94. Average R&D costs include the cost of the approved medicines as well as those that fail to reach approval.

Table 3: Research Spending Per New Drug Approved
(Herper, 2012)

Company	Number of drugs approved	R&D Spending Per Drug (\$Mil)	Total R&D Spending 1997-2011 (\$Mil)
AstraZeneca	5	11,790.93	58,955
GlaxoSmithKline	10	8,170.81	81,708
Sanofi	8	7,909.26	63,274
Roche	11	7,803.77	85,841
Pfizer	14	7,727.03	108,178
Johnson & Johnson	15	5,885.65	88,285
Eli Lilly & Co.	11	4,577.04	50,347
Abbott Laboratories	8	4,496.21	35,970
Merck & Co. Inc.	16	4,209.99	67,360
Bristol-Myers Squibb	11	4,152.26	45,675
Novartis	21	3,983.13	83,646
Amgen	9	3,692.14	33,229

Herper et al (2012) have used another approach and broken down the total R&D spending from 1997 through 2011 and calculated the per drug cost by dividing the total R&D figure by number of approved drugs. This analysis calculated that the total R&D spending per drug can range from \$3.7 billion to \$11.8 billion.

Regardless the precision around the estimate, the cost of developing a new drug is high and bears a major risk as illustrated in the analysis (Pomalli, 2011) reviewing the attrition rates of compounds over the course of the pharmaceutical discovery and development continuum.

1.2.3. Need for Innovative Business Models

A scan of pharmaceutical industry operating margins suggests that the industry relies on high gross product margins in the range of 80 to 90%, mostly thanks to the inelastic pricing ability enjoyed with monopolistic positions in the therapeutic areas pharmaceutical companies operate in. This ability to heavily invest in R&D as well as commercialization efforts have been the core success factor and a characteristic of the pharmaceutical companies. This characteristic differentiates pharmaceuticals from companies in other manufacturing-based industries such as consumer goods or industrials which have to work within a very narrow margin when allocating capital.

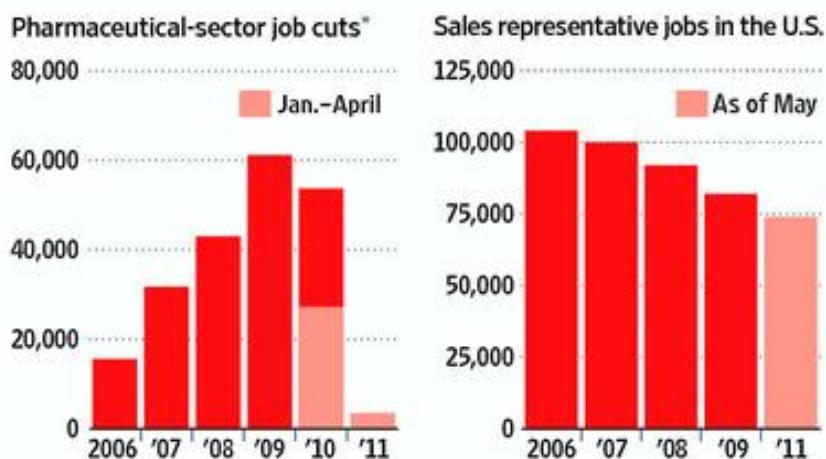
A pharmaceutical company of the last decade could clear the product through its regulatory process, make a price point decision that would garner an operating margin at 40-50% range and very aggressively market its products through a massive sales organization of several thousand representatives and marketing budgets reaching up to multiple hundreds of millions of dollars since the income statements could support such model.

The economic slowdown in 2008-09 period, among other confounding trends explained herein, however, challenged the viability and sustainability of this model since the price points come under attack by governments, which mostly pick up the tab for not only the healthcare expenses but also for pharmaceutical products.

Pharmaceuticals companies are redefining how to engage the sales representatives, the most expensive and yet most effective marketing mix item that propelled the sales of their products. There were over 100,000 representatives employed by the pharmaceutical industry in 2006, and this figure was estimated to be down to 70,000 in 2011 with further and projected to further drop. (Whalen, 2011)

Industry Downsizing

Drug companies have been cutting jobs over the past several years. A reduction in sales representatives has led to an increase in digital sales tools.



*Largely U.S.-based

Sources: Challenger, Gray & Christmas (job cuts); ZS Associates (sales representative jobs)

Figure 8: Number of sales representative jobs between 2006 and 2011(Whalen, 2011)

Access of these representatives to health care provider is getting severely regulated with some hospitals banning their presence at their facilities. Turkish government in 2010 put in effect a similar regulation with the intent to prevent taking time away from physicians who would treat a higher number of patients, if not distracted from doing so.

Finally, the ability to present content supporting the medications and/or disease state to healthcare providers is becoming increasingly challenging due to the regulated nature of the conversations pharmaceutical representatives can engage with health care providers.

The content of the documents and materials needs to be approved by several layers of internal legal counsel and external audits that require for consistency with the product label. A product label or also sometimes referred as 'package insert' lists indications, usages, side effects and risks of the products based on clinical information provided to the regulatory bodies to shape the basis of approval. In case of non-compliance the penalties can reach multiple billions of dollars as seen in two separate major settlements in the United States between the government and Pfizer and GSK. These companies now have to operate under a Corporate Integrity Agreement, which become further impediments to their operational agility.

Currently, there is no single model in the industry to designate as a successful standard to follow, but companies are still exploring with "innovation" as their key theme. This transformation from a highly leveraged P&L to one of productivity and efficiency will not happen overnight.

1.2.4. Healthcare Reforms

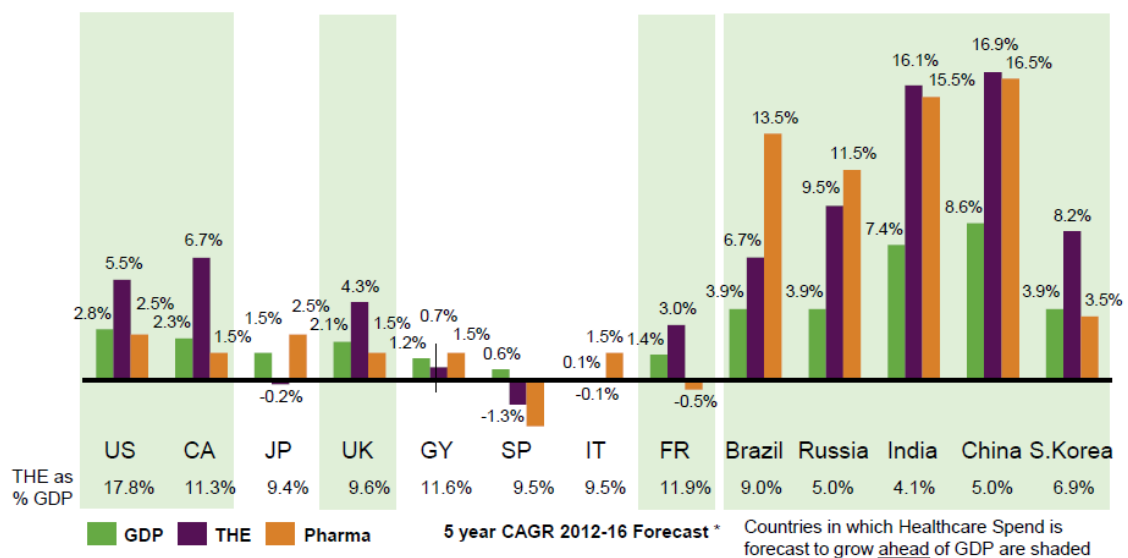
Most of the healthcare expenditure including the spending on medications is covered and reimbursed by governments, which makes government a monopsony when it comes to purchasing products and services of healthcare. The only exception

is the United States where the government pays about 40% of the healthcare spending through CMS with another additional 5% through Veterans Affairs/Department of Defense.

During the cataclysmic economic downturn of 2008-09, the governments started looking for immediate cost saving opportunities, and the healthcare expenditures, ranging from 5 to 17.8% of GDP depending on the country's healthcare system, became a convenient primary target. Several governments put a variety of healthcare reforms in place in terms of payment freezes or price claw-backs.

Especially, costs of medications present a convenient political target, despite the fact that the drug expenditure is approximately 10% of the total healthcare bill as discussed earlier.

Regardless, the administrators have realized that the growth projections for the GDP of their economies were dwarfed by the growth projections of the total healthcare spend and medication spend as illustrated in Figure 9.



* GDP Forecast is Real Growth at Constant Prices in local Currencies from (IMF Apr-12).
THE Forecast is Nominal Growth calculated from forecast change in USD Per Capita Health Spend (EIU), less forecast Population growth.(Population Reference Bureau).
Pharma Forecast is Nominal Growth (IMS Jul 2012).

Source: Accenture Research based WHO 2010, EIU Forecasts 2011, IMF Forecasts Apr 2012, Population Reference Bureau 2012.

Figure 9: GDP, Healthcare and Drug Spend 2012-16 Projections for Developed and Emerging Markets

(WHO 2010, IMS 2012)

The emerging markets, particularly Brazil, Russia, India and China clearly stand out with their GDP projections from 4.1 to 9% in 2012-19 but they also demonstrate an environment with healthcare expenditure growing at 6.7% to 17% in the same duration. Pharmaceutical spending is also mimicking the same pattern of healthcare expenses. This can be explained by the fact the percentage of healthcare spending as part of GDP is lower (around 4-5%) when compared to developed economies (with the exception of Brazil at 9%). Typical developed country has 10-17.8% of its GDP spend on healthcare.

While cost containment was one motivation, the other reason to implement health care reforms was to extend care coverage of population without access to basic healthcare services which is not unique to developed economies.

In April 2010, the Government of China announced a healthcare reform where they would spend \$124 billion over the next decade in order to bring primary care to its large rural population. (Berlin, 2010)

In the United States, the healthcare reform (Healthcare.gov, 2010) signed into law on March 23rd, 2010 offers many facets. One of its provisions is to allow 32 million uninsured individuals to be covered. It is projected that 17 million of these 32 million individuals will qualify as Medicaid beneficiary due to their lower socio-economic status. It is established (OECD, 2012) that socio-economic status is associated with lower healthcare outcomes, and thus preventive medicine and access to primary care services will help with the overall healthcare spend in the future.

The healthcare reform in the United States had provisions that spread over a 5-year window ranging from use of electronic medical records to promoting wellness. Figure 10 summarizes the breadth and complexity of activities under the reform.

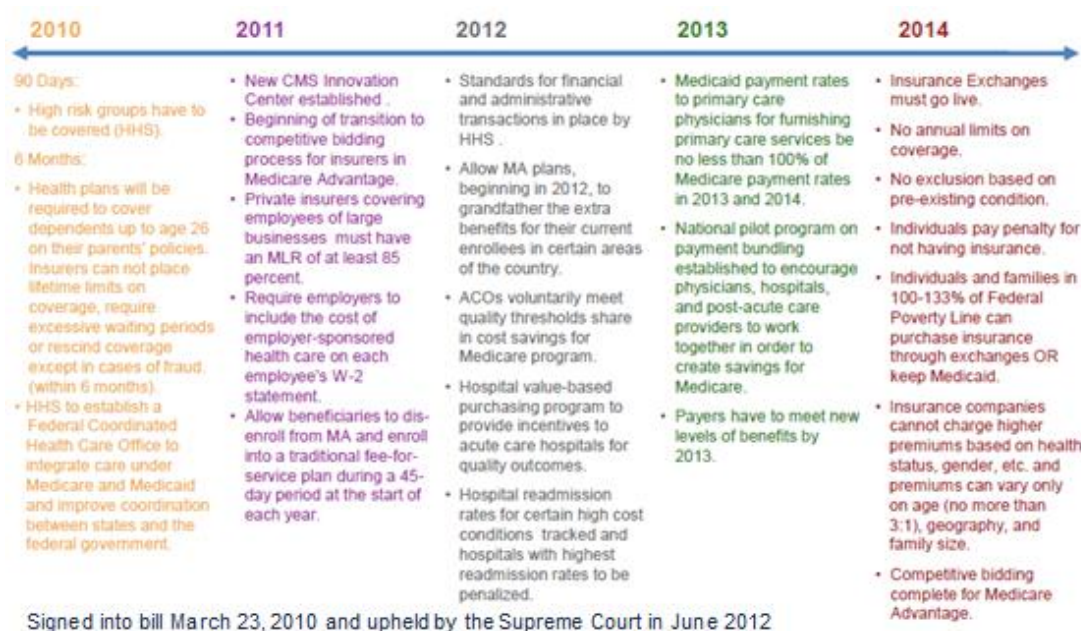


Figure 10: US Healthcare Reform Milestones
(<http://www.healthcare.gov/law/full/>, 2010)

In summary, healthcare reforms in both developed and emerging markets will continue to define the marketplace for global pharmaceutical companies.

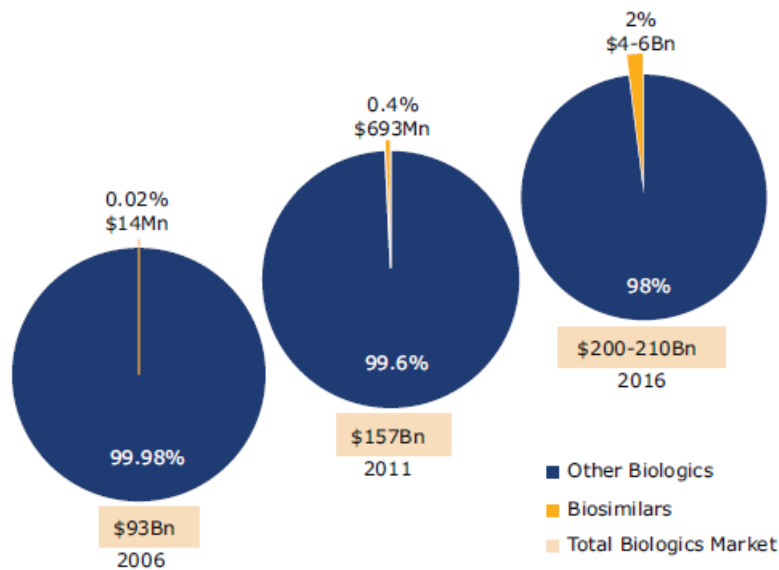
1.2.5. Emergence of Biosimilars

Another trend that needs to be taken into account is the emergence of biosimilars.

When a small molecule product loses its patent protection, copy-cat products can be offered alongside the original compound very quickly and predictably. The small molecule compound is the end-product of well-defined and replicated chemical processes. The end product can be technically identical to the original product given proper quality and process controls around the manufacturing and sourcing. (FDA, 2009)

The biological products (or biologics), however, are large molecular entities that are generated by genetically re-engineered bacteria, designed and nurtured to produce the biologically active products. Companies, with the business model to discover, develop and manufacture these types of biologic products are aptly-named as biotechnology companies.

Biologics include single identified components, whole cells, and include some forms of polymers. They can be purified from human, animal, plant or micro-organisms sources. Biologics can be produced by recombinant DNA technology or chemically synthesized. Biosimilar products are biologic products approved in a country which has an abbreviated approval process for biologic products that reference an originator biologic in the regulatory submission.



Source: IMS Consulting Group, May 2012

Figure 11: Global Biologics Spending
(IMS, 2012)

Biologics will account for an increased share of spending by 2016, as important clinical advances continue to emerge from research, and patients around the world are treated. Spending on biosimilars will increase from \$693 million in 2011 to \$4-6 billion by 2016, which represents 2% of biologics spending. (IMS, 2012)

Adoption is expected to remain modest through 2016, largely because most biologic medicines will stay protected by patents or market exclusivity in many countries.

While the market dynamics biologic medications serve are generally considered price inelastic, protected from competitive pressures and are mostly immune to patent expirations, they will come under attack from biosimilars which will exert pricing pressures on manufacturers of biologics starting beyond 2016.

1.2.6. Advances in Healthcare Technology

Healthcare is delivered along a continuum of care, where the patients' activities start with diagnostic testing, interventions by primary care providers and specialists along with other clinicians and healthcare actors such as health coaches, dieticians, and other players in the hospital acute care setting or in outpatient ambulatory care setting in numerous locations over the life time of the patient.

This state of constant disruption can easily lead to an undesirable situation where one healthcare practitioner has no access to and knowledge of what other care provider has performed on the patient or advised the patient to follow certain practices. However, it has been shown that if the care is coordinated between patients and care providers the outcomes will show improvements. (Bunting et al, 2008; Fera et al, 2009)

This intrinsic inefficiency in the healthcare system leads to two major challenges:

1. Inflated cost of care, and
2. Suboptimal patient outcomes.

Unprecedented innovation and technology-enabled new advancements are now available that will help address the interconnectivity of care providers and care coordination. A short list of these technological advancements is provided and discussed below: (Tagalicod et al, 2013),

a) Electronic Health / Medical Records (EHR or EMR)

Having patients information stored in an electronic data warehouse with access to care providers in an ethical fashion keeping patients' confidentiality will save time, lower medical mistakes and will connect the remotely located providers when caring for the same patient. Most importantly measuring the outcomes from one visit to the other will allow care providers to see the metrics of success whether their interventions are allowing the desired clinical, medical and behavioral change care providers desire for improved patient outcomes.

b) Cloud-based computing

Using remote servers to store, aggregate and share electronic health data is more cost-efficient than all healthcare facilities managing their own servers. Instead, new technologies allow health care institutions store, access, analyze and exchange the information via a 'cloud' environment.

c) Mobile Health (mHealth)

Advances in mobile technology in accessing and sharing of healthcare information by way of mobile devices such as smart phones and tablet computers led to the concept of mobility. This way, the information the health care provider needs for patient is accessible through convenient media such as tablets, iPads and phones.

d) Health Information Exchanges (HIEs)

Health information exchanges will allow the appropriate health care provider to access and receive the health records of their patients through these national (e.g., Singapore, Australia, UK) or regional (Michigan, Massachusetts, etc.) exchanges. This common platform would make it more efficient and practical for providers to access the records without trying to get through other providers who may not be immediately available and may not have the full health records when required for timely healthcare decision making.

In summary, the emergence of new technological capabilities enables healthcare processes to become more efficient and streamlined while allowing more seamless information sharing for improved care coordination and patient outcomes.

1.2.7. Pressing Need for Evidence-based Decisions

Many medications have been approved by regulatory agencies based on their effect on biomarkers but not necessarily in prevention of the catastrophic or fatal clinical endpoints. For example, a hypertension medication can be approved if it lowers the blood pressure but not necessarily by lowering the incidence of a heart

attack, which could result from high blood pressure. In this example, the blood pressure is a surrogate clinical end-point but not the actual cerebro-vascular event incidence a priori targeted to be lowered or prevented.

However, in the era of cost containment and austerity, the expectations of payers, healthcare providers and regulators are shifting from activity to outcomes with demonstrated value. The scrutiny for evidence required to demonstrate that a particular medicinal product is clinically useful has been on the increase on an unprecedented scale.

The payers are designing and enforcing financial incentives for providers that would offer rewards if the particular patient population they are managing show better health outcomes rather than the clinical activity.

NCQA (National Committee for Quality Assurance) is a non-profit organization that accredits and certifies a wide range of health care organizations based on their quality of care in the United States. Certain quality tools utilized by NCQA, such as The Healthcare Effectiveness Data and Information Set (HEDIS) is a tool now used by more than 90 percent of America's health plans to measure performance on important dimensions of care and service. (NCQA, 2012)

Altogether, HEDIS consists of 75 measures across 8 domains of care. Because so many health plans and payers collect HEDIS data, and because the measures are so specifically defined, HEDIS makes it possible to compare the performance of health (insurance) plans on a normalized basis and creates a market tool for payers and regulators to measure comparative performance of care providers.

This shift from measuring patient outcomes rather than rewarding fees based on services rendered is shaping the global healthcare eco-system in a fundamental and irreversible way.

1.2.8. Reimbursement Challenges

Historically, two key criteria; 1) safety and 2) efficacy of a particular medicinal treatment constitute the basis for regulatory approval of pharmaceutical products. In the United States, the largest pharmaceutical market in the world, the afore-mentioned dual criteria still apply to the decisions of the FDA in that regard.

However, in other developed European countries, such as in the United Kingdom, in addition to safety and efficacy criteria, the requirement of cost-effectiveness has been introduced by founding a new governing body called, National Institute for Clinical Excellence, or NICE in 1999. Since then, many European countries have been adopting the cost effectiveness to their list of requirements before granting approval to pharmaceutical companies, raising another significant challenge for the industry to surpass. As a result of this additional requirement, some treatments, that are available in the United States, have been denied approval in the United Kingdom on the basis of QALY (Quality-Adjusted Life Year), a measure of disease burden, including both the quality and the quantity of life lived. NICE has been using a range of £20,000 to £30,000 as a threshold for willingness to pay by the government for approvals. (Phillips, 2009)

Five years later in 2004, Germany also followed suit (as did France shortly thereafter) and founded IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen) which is an institute for quality and efficiency in healthcare. IQWiG is an agency that performs a similar task to that of NICE of granting reviews of safety, efficacy and cost-effectiveness.

Finally, in January 2011, Germany introduced the Act on Reform of the Market for Pharmaceutical Products (AMNOG) which has transformed the German pharmaceutical business like no law before, with significant long-term implications for the way companies develop and commercialize their products, not only in Europe (where 19 countries use Germany as the reference point for local pricing) but globally as well. Prior to 2011, pricing for new drugs was basically free at time of launch; AMNOG drastically changed the equation by introducing an administratively-complex

pricing system based on evidence of a new drug's additional benefit over established, often generic therapy. (Hager, 2012)

In the current environment, pharmaceutical companies need to balance the sense of urgency in order to gain product approval with the essential reimbursement coverage they need to secure. The current development goals focus on demonstrating clinical efficacy, but often stop short of understanding the overall health, social and economic benefits of the product. This can be a risky position to take for the pharmaceutical companies since the efficacy and safety alone are no longer sufficient to maximize the return on shareholder value in an industry –as earlier discussed- where only 2 of 10 products yield positive returns covering their R&D investment.

There are several recent examples substantiating this observation: In March, 2011 GSK and Human Genome Sciences' Benlysta –a biologic medicine- became the first new lupus therapy in more than 50 years when it gained FDA approval. (Basu, 2011) In July, Benlysta gained EMA (European Medicinal Agency) approval. Benlysta was eagerly anticipated by patients and investors alike: it was heralded as among the most important drug launches in 2011. With a price of \$35,000 a year, industry analysts expected Benlysta to reach peak sales of \$2-\$3 billion within 4-5 years. (Bennett, 2011)

However, Benlysta did not live up to these expectations and consequently, Human Genome Sciences lost 70% of its market value by December 2011 which led to a hostile takeover offer by GSK.

Despite addressing a huge unmet medical need, Benlysta faced insurmountable reimbursement hurdles in the United States and in Europe. In the United States, Medicare did not add a reimbursement code for the product for the first 9 months it was in the market, which resulted in a complicated process and doubts among prescribing physicians they would be reimbursed.

Similarly in Europe, despite the regulatory authorities, specifically, European Medicinal Agency, had approved the drug, individual countries decided not to pay for

it. United Kingdom's NICE recommended against covering the drug because the authorities were not convinced the medication worked markedly better than an existing product being used off-label for lupus.

Even while patient advocacy and professional organizations protested the agency was acting outside its purview, NICE pointed to a lack of comparative efficacy data and determined that Benlysta did not represent "good value for money." Similarly, Germany's IQWiG recommended against the drug, citing, "No additional benefit documented."

1.2.9. Supply Chain Rationalization

The pharmaceutical supply chain is the means through which prescription medicines are delivered to patients. Pharmaceuticals originate in manufacturing sites; are transferred to wholesale distributors; stocked at retail, mail-order, and other types of pharmacies; subject to price negotiations and processed through quality and utilization management screens by pharmacy benefit management companies (PBMs); dispensed by pharmacies; and ultimately delivered to and taken by patients.

There are many variations on this basic structure, as the players in the supply chain are constantly evolving, and commercial relationships vary considerably by geography, type of medication, and other factors.

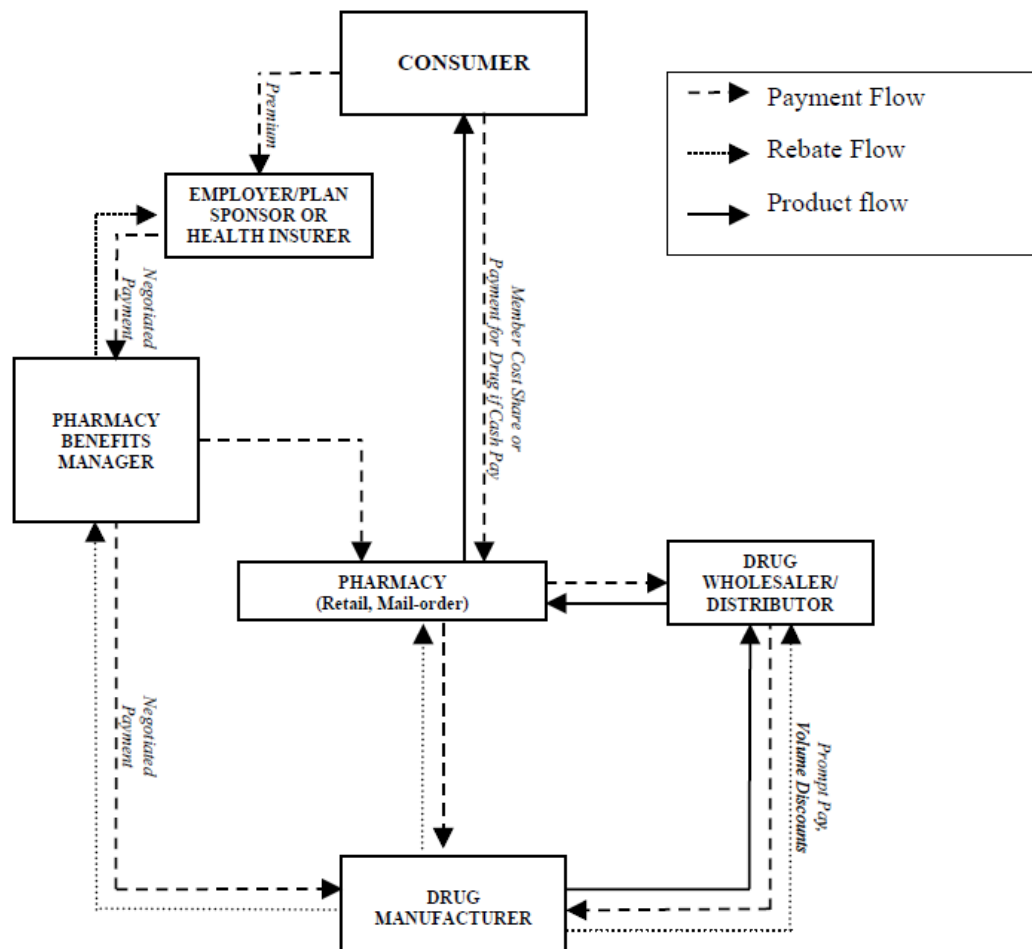


Figure 12: Flow of Goods and Financial Transactions Among Players in the U.S. Commercial Pharmaceutical Supply Chain
(Health Strategies Consultancy, 2005)

Figure 12 is a graphic depiction of flow of goods and corresponding financial transactions among players in the United States. There are many variations outside of the United States where PBMs are replaced by direct contracting between pharmaceutical manufacturers and wholesalers or large pharmacy chains.

A relatively few large, multinational firms comprise the bulk of the brand pharmaceutical manufacturing industry today. The 10 largest pharmaceutical corporations, as measured by their revenue in the United States, typically accounted for almost 60 percent of total turnover.

While Pharmaceutical manufacturers have the most influence over pharmaceutical prices, assessing expected demand, future competition, and projected marketing costs to establish the wholesale acquisition cost (WAC), which is the baseline price at which wholesale distributors purchase drug products. Discounts and rebates may be applied, based on market share, volume, and prompt payment.

The trends discussed herein also put pressure on pharmaceutical companies to rationalize these processes through Enterprise software. Another important factor is the plant architecture which pharmaceutical manufacturers constantly seek to optimize by identifying lower cost and lower tax countries (such as Ireland and Puerto Rico) or trade zones to manufacture and globally distribute their products.

1.2.10. Cost Take-out

The expensive and vast infrastructure of a global pharmaceutical company has been established over past decades based on the dynamics of the business model explained above. This model relies on a healthy throughput of novel and differentiated pharmaceutical products which can be priced at points to deliver historically high margins. With the slowdown in the R&D productivity, inability of pricing at attractive levels compounded with lower reimbursement rates the payers and governments are willing to pay, are forcing the pharmaceutical companies to cut their cost structure at unprecedented levels. (Hansen et al, 2009)

The industry initially attempted to realize cost savings by attacking the SG&A line, in particular direct sales representatives which was an easy target since there no longer were enough products to promote to health care providers. However, that line item alone cannot fully help address the issue at satisfactory levels.

Consolidating facilities and global operations by avoiding duplicate geographic services are also a major source of cost cutting. Specifically, the companies eliminated country-level resources and consolidated those resources and functions such as Finance and HR regionally, which helped eliminate several management ranks in the country organizations.

Additionally, employment of enterprise resource management systems including the ones built by software firms such as SAP or Oracle helped optimize these processes once defined and streamlined. These systems also provide end-to-end visibility to any key performance indicator that the particular enterprise deems strategic and enables the leadership to make necessary adjustments in a timely fashion.

All of these underlying fundamentals and trends placed the Emerging Markets, that are traditionally have been a secondary growth focus and an after-thought for product launch priorities in the spot-light, which is investigated and explained next.

1.3. Characteristics of Pharmaceutical Emerging Markets BRIC-T

While the global pharma market growth has slowed from 9.1% in 2003 to 4.1% in 2010, successful pharmaceutical companies have shifted their focus to obtaining growth in the emerging markets. IMS research suggests that 70% of pharmaceutical growth in the next 5 years will come from the emerging pharmaceutical markets, also dubbed as “phamerging markets”. (IMS, 2012)

While the exact definitions of the emerging pharmaceutical markets vary, the emerging markets are nations experiencing periods of high business growth and industrialization. Given the issues and challenges the pharmaceutical industry is facing, the emerging markets nations present a unique opportunity for investment in today’s global marketplace. (Looney, 2010)

Table 4: GDP and Pharmaceutical Market Growth of BRIC countries, Turkey and Developed Markets
(World Bank 2011, IMS 2012)

Country	GDP Growth (2010)	Pharma Market Growth (CAGR 2011-2015)
China	10.4%	19-22%
Brazil	7.5%	10-13%
Russia	4.0%	11-14%
India	8.8%	14-17%
Turkey	9.0%	10-13%
United States	3.0%	0-3%
EU5 (Germany, France, Italy, Spain, UK)	1.4%	1-4%

Another characteristic of the underlying growth of the emerging markets is the strength of their consumer purchasing power. According to a survey published by Oxford Economics (2010), 57% of the global growth in 2010-2020 will be generated by the consumers in the emerging markets with a 5.4% CAGR when compared to the developed economies demonstrating a CAGR of only 2.0% in the same time period.

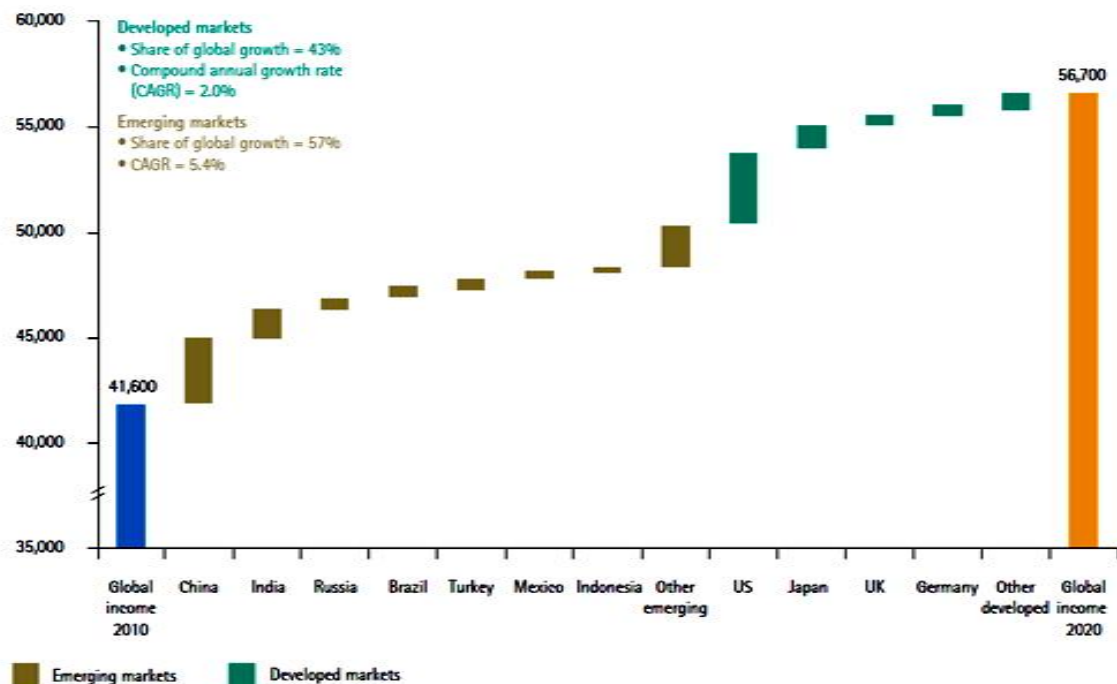


Figure 13: Household income growth in 2010-2020 in billion US dollars at 2010 constant prices for 64 countries
(Oxford Economics 2010)

Finally, another perspective to keep in mind when exploring the emerging markets is the volume growth of the population with over \$5,000 annual income. For example, China stands out with over 300 million people, a population equal to that of United States, shifting the dynamics towards the emerging markets.

Interestingly, Turkey's almost entire population is considered above this threshold placing Turkey more towards the developed nations than the emerging ones, similar to Mexico.

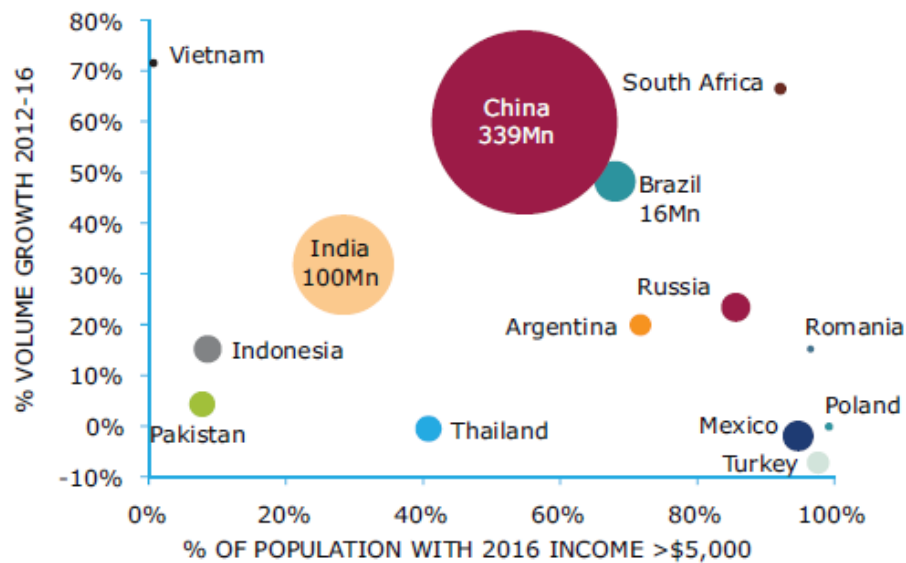


Figure 14: Growth of population volume with more than \$5,000 annual income by 2016

(IMS 2012, Economist Intelligence Unit, 2012)

Although there are certainly specific variations between the individual countries, some general trends have driven growth in the emerging markets. First, a growing middle class with greater spend ability.

A very important observation when comparing developed markets with the emerging ones is the life expectancy and percentage of GDP spent on healthcare as Figure 14 depicts. The developed markets typically spend between 11-17% of their GDP on healthcare and in return receive a life expectancy averaging over 75 years.

Emerging markets, on the other hand, spend around 3-6% of their GDP on healthcare and their population showing a life expectancy between 65-75 years, depending on the country. As the consumer spending increases and governments apply healthcare reforms the emerging markets group as highlighted with the red oval will migrate over to the developed markets' location.

Another conclusion one can draw from Figure 15 is that the developed markets would need to curb their spending since it is not sustainable for these economies to

pay an 'innovation premium' in order to take risks for highly uncertain investments in developing new technologies or medications.

It should be remembered that branded or plain generics are more prevalent in the emerging markets further dragging down the total cost of healthcare.

This disequilibrium will over time disappear or at least will lessen as the global markets become integrated while the emerging economies will start building healthcare infrastructure leading to a greater percentage spend of their GDP to healthcare.

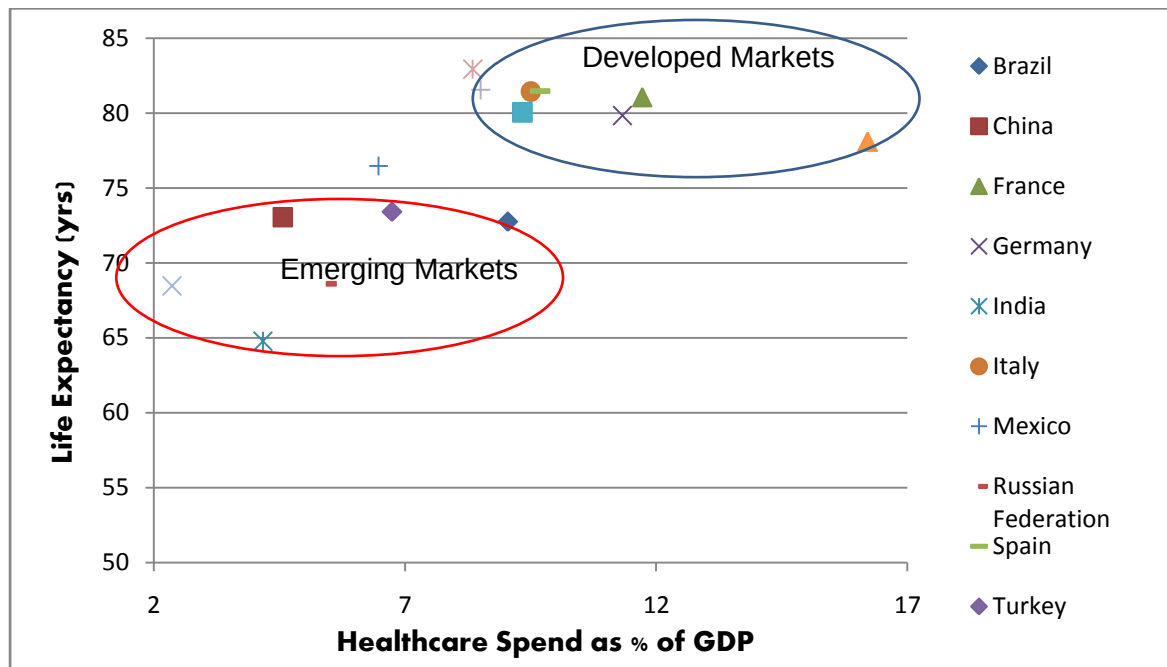


Figure 15: Healthcare spend as percentage of GDP compared to life expectancy in years for emerging and developed countries
(Calculated using data from World Bank, OECD, 2011)

Although some common characteristics are shared amongst emerging markets, it is important to understand each market as there are ways to leverage multiple approaches based on shared macro-economic and healthcare driven dynamics. Successful multinational pharmaceutical companies will tailor their strategy for each individual market.

In summary, China is and will remain by far the biggest of the emerging markets, with a projected growth of \$63B in pharmaceutical market and 1.3 billion in population over the next five years. A second tier consists of Brazil, Russia, and India which is projected to grow \$10B in the same period. Turkey is also a fast-growing market of particular interest to the multinational pharmaceutical company. With this background, each market is examined separately.

1.3.1. Brazil

Brazil is the fifth most populous country in the world with over 190 million inhabitants, however there is a great disparity between middle and lower classes that represents varying levels of access to healthcare services and pharmaceutical products. Public health insurance is available to Brazilian people whereas 90% of the population is covered to have reimbursed access to healthcare services. (WHO, 2012) It should be noted that there is a high out of pocket burden on the individuals. On a relative basis, Brazil's population has greater access to healthcare than most other emerging markets which is crucial for growth (Agarwal 2012).

The Brazilian pharmaceutical market is valued at \$22.9 billion, and by 2015, experts expect pharmaceutical sales to reach \$38.5 billion. (IMS, 2012) This double-digit growth in the last few years is due to largely from population growth and increasing access to healthcare with the growing GDP and disposable income of the middle-class. (Ingold et al, 2010)

There are about 300 pharmaceutical companies operating in Brazil which is an indication of the fragmented nature of this marketplace (Lakkis, 2012) and fierce competition on price and prominent prevalence of generics business (Barra et al, 2011).

By value of sales, the multinational pharmaceutical companies control 75% of the pharmaceutical market. While the public health insurance exists, there are high out of pocket costs which shift the demand towards generic products (Wagner, 2011).

However, Brazilians face high out of pocket costs and there is a great disparity between the middle and lower class (IMS, 2012). Accordingly, the Brazilian government has placed a great emphasis on the use of generics in order to reduce costs, spurring much competition amongst manufacturers. The government emphasis on cost containment has favored local companies over multinationals. Local companies compete fiercely over distribution and promotion(Focus Reports, 2007).

Pharmacists tend to have a large influence on the consumer during the final stage of purchase (Pomerantz,2011). Localization has also been a key element of the Brazilian pharmaceutical market. Most multinational companies prefer local manufacturing to access the market easily and also supply other Latin American countries using Brazil as a production platform. Access to manufacturing talent is relatively easier than in other countries in the region.

In an effort to build market position quickly, pharmaceutical companies choose to access Brazil market quickly through collaborations and joint ventures in addition to organically growing their revenue. As recent examples, in October of 2010, Pfizer acquired 40% stake in Laboratorio Teuto Brasileiro, a local generics company with an option to buy more share.

Another similar example of a "Big Pharma" company to enter the market through a joint venture agreement in order to quickly establish a market position is Merck's agreement with Supera Farma in February 2012 to commercialize branded generics in Brazil.

In addition, R&D opportunities are growing with the increased occurrence of government joint-venture investments with universities.

With a large and diverse population, Brazil plays an important role in the development and delivery of a growing number of drugs. From 2007 to 2011, clinical trials in the country nearly doubled.Because of a complicated regulatory environment and potentially a 17-step process, study approval in Brazil can take three years (Salama, 2011).

1.3.2. Russia

With over 140 million inhabitants, Russia is the ninth most populous country in the world. The Russian pharmaceutical market, estimated at \$13.6 billion in 2011, has also experienced high double digit growth in recent years. Factors contributing to growth include increased government healthcare and private insurance options, and positive developments in the reimbursement system. (IMS, 2012)

The general health of the Russian population is relatively poor, with a high prevalence of smoking and chronic disease which put cardiovascular illnesses as the leading cause of death. It should be noted that cardiovascular diseases, while still critical, are replaced by more pressing disease categories such as diabetes, oncology, hepatitis C among others in the Western Democracies due to ample and inexpensive medications to lower high blood pressure and control hypercholesterolemia. (WHO, 2009)

In addition, it is widely believed that the physician training and resulting knowledge tends to be mediocre when compared to Western standards, although it is improving through increased emphasis on core education.

Moscow and St. Petersburg are considered two metropolitan hubs for healthcare services with more access to care while the rest of the country does not enjoy similar level of access, a pattern that can also be observed in China and India.

Prices of pharmaceutical products and healthcare services tend to be high in Russia, and most consumers deal with high out of pocket expenses for visits to healthcare facilities and drug purchases. There is a high propensity to purchase brand-name products due to trust in quality and brand equity. (Focus Reports, 2011)

Politics also play a key role in the Russian pharmaceutical marketplace – there is a great amount of government influence over drug prescribing and powerful lobbies show favor to local manufacturers over multinational pharmaceutical companies. (S&P Industry Survey)

Another major issue that the multinational companies need to manage in operating in Russia is the implicit business practices which are inconsistent with the Western standards and compliance. There are several laws such as the FCPA (Foreign Corrupt Practices Act) in the United States and similar EU policies and laws that put pressure on multinationals to operate very carefully. (Isherwood, 2012)

These laws hold the global pharmaceutical companies liable if any monetary compensation changed hands in an unlawful manner even if the transactions occur through third parties and agents unbeknownst to the senior management in the global headquarters. As a result, it is not uncommon to have a high turnover rate of senior management as a result of a scrutiny of local business engagement practices.

With a vast geographic footprint, there is a high level of distributor influence in Russia, and a network of regional formularies.

1.3.3. India

India is the second most populous country in the world with over 1.1 billion inhabitants; however, with an estimated \$12.3 billion in annual pharmaceutical sales, India's per capita healthcare spending is well below that of other emerging markets countries. Approximately 25% of the Indian population mainly in urban environments has access to healthcare as defined in the Western setting. Traditional medicine is widely practiced in the rural areas. (Plunkett Report, 2011)

Currently only 10% of Indians are covered by health insurance. Private medical services dominate the market, with 70% of hospitals privately owned and 80% of healthcare expenditures coming from private sources. There are high end hospital chains, such as Apollo, servicing at somewhat comparable quality levels to hospitals in developed countries. They constitute about 2-5% of the total healthcare providers in the country. Still the access to health insurance is also very low with only 10% of population is covered. An expensive oncology medication treatment, major orthopedic or cardiac surgery can be a traumatic economic burden to the average Indian family due to lack of a broad medical insurance coverage. (Plunkett Report, 2011)

However, India does have a growing middle class and emerging rural markets, along with an improving medical infrastructure. Since this issue has been a historical political sore wound, recently in 2012, Indian government issued a mandate to provide a much larger safety net for its populace similar to what Government of China did in 2010. Economically, there is increasing competition in the region between India and China and as a result the governments do not wish to fall behind in their level of work force competitiveness, which is one other way of interpreting the universal health care move of India. (Tempest, 2006)

An important recent development in India is the establishment of Intellectual Property Rights. While these laws are being passed, there is still a lack of consistent enforcement thereof. (Watal, 2000) This lenient enforcement has resulted in a prevalence of copycat generic drugs and low cost biosimilars within the Indian pharmaceutical market. Although recent progress has been made, Indian patent laws are still not as powerful as most developed countries. (Financial Express, 2006)

The Indian pharmaceutical market is hugely fragmented and dominated by local companies, with Ranbaxy leading the way in terms of revenue. More than 10,000 firms control 70% of the market, many of them local generic producers. The branded generics market encompasses hundreds if not thousands of brands. Physicians have a heavy influence in selection of brand choice (Singal et al 2011).

There is a highly fragmented distributor network and marketplace especially due to the vast size of markets and consumers outside of cities. Due to its proximity to other surrounding Asian markets and existing strong engineering talent base coupled with the cost to manufacture a drug in India is an attractive value proposition to MNCs. (Sennik, 2011)

Although there still are challenges to entering the Indian market, multinationals have flocked to India and have begun setting up manufacturing facilities at a fraction of the cost of the Western markets. (Bhadoria et al 2010)

The cost of manufacturing a drug in India currently represents about 40 percent of costs borne by pharmaceutical companies working in developed countries, with substantial savings in land acquisition, construction, labor and operations. (FocusReports India, 2011)

The pharmaceuticals industry has traditionally been dominated by companies in developed markets. But deregulation and new production processes have allowed new players to gain leadership in the generics market. India's leading pharmaceutical players have taken advantage of the opportunities presented by deregulation and patent expiration through innovative approaches to process design.

Traditionally, pharmaceutical industry R&D has been a slow process, but in India the adoption of reverse pharmacology has provided production efficiency gains and helped manufacturers to test generic drugs more quickly and increase the speed to market. The ability to bring relevant products quickly to market at low price points has been instrumental for domestic players in shaping the Indian market on their terms. (Taneja, 2009)

While 15 of the world's top 20 pharmaceutical companies have an active presence in India, domestic players supply 90 percent of bulk drugs in the country. Domestic companies are also rapidly expanding sales in advanced formulations and specialty medicines. In response, foreign multinationals are aggressively pursuing joint ventures with Indian players. These ventures are designed to gain immediate access to the Indian market. For example, in 2011 Merck wanted to gain fast access to Indian market and entered in a joint venture agreement with India's Sun Pharma. (Staton 2011)

Bayer HealthCare, as another example, launched a joint venture with Cadila, one of India's largest privately held pharmaceutical companies. The strategic objective of these joint ventures go beyond India and are also designed to establish a new base for expansion into other and adjacent emerging market territories using India as the launching pad.

In 2009, GSK, the world's third-largest pharmaceutical company, signed an agreement with India's Dr. Reddy's to develop and market selected products across emerging markets.

Building on the strength of their domestic position and the advantages of joint ventures with multinational players, Indian companies are expected to grow exports nearly 20 percent this fiscal year, to \$12 billion. They will supply nearly 50 percent of the world's bulk drug requirement. (The India Brand Equity Foundation, 2012)

The United States remains the largest export destination, followed by the United Kingdom, Germany, South Africa and Russia. In coming years, however, Indian firms anticipate significant growth in exports to emerging economies. A recent study forecasts that by 2020, seven emerging markets—Brazil, China, India, Indonesia, Mexico, Russia and Turkey—will account for one-fifth of international pharmaceutical sales. (IMS, 2012)

As new markets develop in emerging economies, Indian players and their joint-venture partners may hold an advantage. They can apply their domestic experience to new geographies and innovate at home before scaling across global markets. Success in these markets will play a critical role in determining the future growth prospects of even the largest companies. Pfizer estimates that 75 percent of pharmaceutical sales growth over the next five years will come from emerging markets. (Staton, 2011)

1.3.4. China

The sheer opportunities presented by the Chinese market nearly outweigh the rest of the emerging markets combined. (Zifferblatt, 2011) China is the most populous country in the world and reached the enviable second largest economy position in 2012. Pharmaceutical sales totaled \$41.1 billion in 2010 and rapid growth near 20% is expected in the next few years.

China is currently experiencing rapid expansion in total GDP and healthcare spend accelerated by urbanization, access to healthcare and recent healthcare reform. (Beckett, 2012)

The China healthcare market is stratified in terms of urban and rural, Eastern costal area and inland. The Chinese pharmaceutical market can essentially be segmented into three tiers as generally and consistently agreed by researchers:

Table 5: Stratification of Chinese Healthcare Market

Tier 1	Handful of megacities along the eastern coastline of China and their adjacent areas, such as Beijing, Shanghai and Guangzhou.
Tier 2	Large, medium and small size cities along the eastern coastline, Southwest China and Central China.
Tier 3 and below	Medium and small size cities in inland China and counties in the vast rural areas of China.

Affluence varies sharply across these tiered markets as well as the level of education and technology literacy. As a result, Tier 1 market is the most mature market segment of China and tends to be most receptive to Western ideas and innovation. Tier 3 and below markets are less mature and more dispersed, hence much more ill-prepared for centralized information and analytic focused types of changes.

Much focus has been placed on Tier-1 cities, however, Tier-2 cities comprise more than one-third of the pharmaceutical market, with sales doubling since 2000. The pharmaceutical market contains over 5,000 Chinese firms, who control 70% of the market. Multinational corporations account for the remaining 30% market share. Pharmaceutical sales have doubled in tier-2 cities since 2000, which account for one third of the market. (IMS, 2012)

The strong influence of the Chinese government and the uncertainty around future healthcare reforms make China a very complex market for the multinational pharmaceutical to operate in. Currently, there is a large gap between policy change at

the national level and the actual implementation and enforcement of the policies at the provincial and local levels. (Berlin et al, 2010)

The government is currently implementing a \$124 billion healthcare stimulus package with the intent to provide healthcare to nearly 90% of the Chinese population with an emphasis on inclusion of rural areas within the healthcare coverage. (Berlin et al, 2010)

Importantly, there is a massive migrant population of 200 million Chinese workers who tend to be temporarily employed as seasonal workers in larger cities only to return to their rural settings consistent with agricultural labor needs. (China FocusReports, 2010)

There currently is a lack of a primary care system in China resulting in hospitals acting as the primary care provider. The Chinese Ministry of Health is currently targeting “profit seeking” activities at hospitals, especially focusing on profits from drug sales. (China FocusReports, 2010)

Similarly, physicians currently receiving a monthly commission based on sales may be affected by the Ministry of Health pressures. The Chinese government has also created an Essential Drug List (EDL) which has reduced pricing on many western drugs. Many hospitals and pharmacies are restricted to providing only generic products from the EDL.(Plunkett Report, 2011)

1.3.5. Turkey

With a population of nearly 75 million and a median age of 29.3, Turkey is the 18th most populous country and is ranking as the 16th largest economy in the world. Therefore, the Turkish market provides a great deal of potential and growth for pharmaceutical industry. (World Bank, 2010)

Situated between Europe and Asia, Turkey's pharmaceutical market is valued at \$10.5 billion with an expected growth rate of 8.1% in the next four years. The market is highly fragmented, with nearly 300 local pharmaceutical companies and over 50 multinational pharmaceutical companies in the marketplace. The top 20 companies control 70% of the market share, with the top 10 MNCs controlling 40% of the market. (IMS, 2012)

The government has a great deal of influence in the Turkish healthcare and pharmaceutical markets. The government funding accounts for 73% of the total healthcare spending.

In addition, there has recently been a great deal of change in the healthcare system in Turkey, namely the Health Transformation System. As such, nearly 98% of the population receives health coverage via social security or government health insurance. As part of these reforms, there has also been a recent implementation of a nationwide network of family doctors. Access to family doctors is becoming increasingly difficult.

The implementation of a national electronic health record infrastructure National Health Information System of Turkey (NHIS-T / Saglik-Net) was a favorable factor that would allow the care providers track treatment outcomes and associated cost elements to help improve the quality of care. (Dogac, 2011)

The Turkish government presents challenges to pharmaceutical companies in the form of strict pricing measures and a challenging regulatory environment. The government has focused on bringing down the costs of drugs. Generic brands are emphasized and higher discounts are also passed to innovative drugs. Pricing continues to decrease as cost-cutting measures increase. Turkish government has been utilizing a reference pricing system which takes the average of a quota of 5 lower-price countries in the European Union system.

There is a great deal of obstacles a pharmaceutical company must face to comply with Turkey's regulatory laws. Companies must be registered in Turkey to

obtain market authorization. In addition, there is a significant backlog in the registration process – typically 18 to 36 months. (Kretschmer, 2011)

There is a great amount of distributor influence on the marketplace.

Turkey has begun accession talks with the European Union. This resulted in a substantial flow of foreign direct investments and other forms of international attention into the country. As a result, the Turkish economy has been ranked 52nd out of 103 countries according to a recently released Business Competitiveness Index from the World Economic Forum. (World Economic Forum, 2011)

2. METHODOLOGY

The research methodology was determined following a robust literature review including academic and industry sanctioned sources as well as interviews with senior executives from global pharmaceutical companies and thought leaders in the pharmaceutical industry.

2.1. Rationale of the Methodology

Due to the complex nature of the research question that comprises of both qualitative strategic perspectives and the need to identify quantitative patterns, a hybrid and complementary research methodology was determined. The benefits of this hybrid approach was to demonstrate not only some quantitative pattern that may or may not ground itself to the industry real-live perspectives in absence of real world experience. The findings that were identified in the end of both qualitative and quantitative analyses were also attempted to be cross-linked to create the ability for a more robust set of conclusions and recommendations.

2.2. Sample Selection

Publicly available financial data gathered from 14 global pharmaceutical and biotechnology companies' public investor disclosures were collected. The companies were selected based on their size and geographic footprint to ensure sufficient presence across the geographies in which they booked revenue.

Certain companies though generating large revenues were excluded since they were not publicly traded and therefore did not report their earnings with granularity to allow for such an analysis. Additionally, companies with divisions in non-pharma operations such as agricultural business were excluded since the market and investor sentiment would not be objectively reflected in their market value.

Finally, since some companies do not report their earnings consistent with the calendar year, the data was normalized to ensure that the fiscal and calendar years properly overlap to be able to draw consistent conclusions. A high level data set is summarized in the Appendix.

Table 6: Research Questions and Methodologies

Research Questions	Methodology
1. What are the key success factors for pharmaceutical and biotechnology companies to operate in the Emerging Markets?	<u>Qualitative</u> Interviews Industry Journals Review Academic Journals Review
1. How does the geographic breakdown of revenue correlate with the profitability as measured in (ROIC) for each pharmaceutical and biotechnology peer set? 2. How do shareholders reward pharma and biotech companies' investment in order to expand into Emerging Markets for each pharmaceutical and biotechnology peer set? 3. What strategic corporate behavioral differences exist between pharmaceutical and biotechnology companies towards Emerging Markets expansion?	<u>Quantitative</u> For each Pharmaceutical and Biotech set of companies non-parametric statistical Spearman's correlation analysis of TRS and separately of ROIC with the three year average revenue generated Globally, in the US, in the EU and Emerging Markets from 2009-2011

2.3. Qualitative Analysis

On the qualitative front the research question:

What are the key success factors for pharmaceutical and biotechnology companies to operate in the Emerging Markets?

was asked and addressed through a qualitative methodology that built upon literature review which included work published by academic institutions, academic journals, think tanks, life sciences industry journals, governments and management consulting firms that are actively conducting cross-life sciences industry research., as well as qualitative interviews, and comparative secondary market research.

An adaptive approach was embraced when conducting the qualitative research in which the in-person interviews built upon the knowledge and insights acquired up to that point. Interviews were performed by key thought leaders and executives of the

pharmaceutical and biotechnology who have Profit and Loss accountabilities as well as strategic oversight to their companies' capital allocation decisions.

Consequently, the qualitative interviews and comparative secondary market research helped identify successful strategic elements which led to the identification of seven themes based on prominence and frequency of mention.

2.4. Quantitative Analysis

Concerning the quantitative front, the thesis postulated the following three research questions:

1. How does the geographic breakdown of revenue correlate with the profitability as measured in (ROIC) for each pharmaceutical and biotechnology peer set?
2. How do shareholders reward pharma and biotech companies' investment in order to expand into Emerging Markets for each pharmaceutical and biotechnology peer set?
3. What strategic corporate behavioral differences exist between pharmaceutical and biotechnology companies towards Emerging Markets expansion?

An ensuing comparative retrospective observational financial analysis built upon this qualitative foundation to ensure that the identified strategies were financially accretive and deliver fiscal value-added when implemented both from a profitability perspective, as well as shareholder value generation perspective for both pharmaceutical and biotech company sample sets.

Since the absolute number of global pharmaceutical companies and biotechnology companies with sizeable operations across the geographies including the emerging markets is limited, a non-parametric statistical analysis methodology was selected.

Testing for statistical significance of the selected parameters was performed using SPSS software tool and the results are listed in Appendix 7.

A comparative shareholder value analysis of leading pharmaceutical companies was conducted to specifically focus on exploring the relationship of the reported revenue of the selected top 8 pharmaceutical companies and the ROIC (Return on Invested Capital) with a 3 and 5 year time frame to incorporate the negative one-time effect of the global economic slowdown.

The relationship of ROIC and Revenue generated outside of the United States including Europe and the Emerging Markets are presented in Section 3.

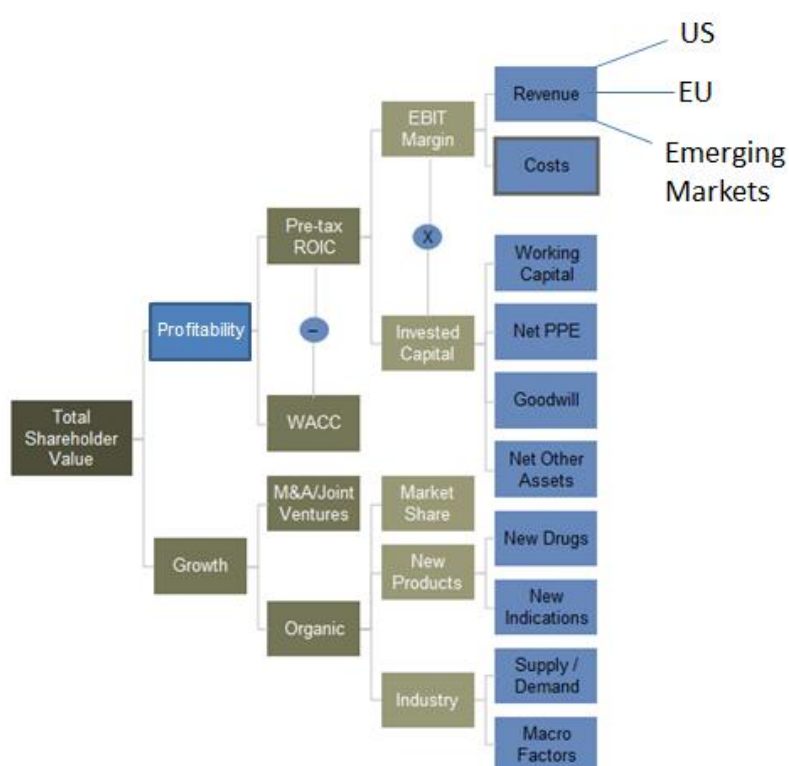


Figure 16: Shareholder Value Tree Framework for a Pharmaceutical Product Company

For a biopharmaceutical enterprise, the shareholder value tree framework is especially useful and broadly utilized since it focuses on profitable growth comprising of two fundamental qualities that drive the shareholder value.

The strategic financial tree also ties the revenue generated in a particular geography to ROIC and/or TSV which will help address the aforementioned research questions.

The shareholder value tree de-composes these two key performance indicators into branches and with the following definitions.

Profitability:

A measure to generate sustainable profitability as a result of Pre-Tax ROIC less weighed average cost of capital (WACC).

Return on invested capital (ROIC):

ROIC is equal to Earnings Before Interest & Taxes (EBIT) divided by Invested Capital. At a high level, ROIC is a way to measure how efficiently the company uses the cash it invests in its operations – whether that cash comes from loans or cash it generates from its ongoing operations.

Another way looking at ROIC is the amount of profit that a business generates for every dollar invested in its ongoing operations.

Weighted Average Cost of Capital (WACC):

A company's assets are financed by either debt or equity. WACC is the average of the costs of these sources of financing, each of which is weighted by its respective use in the given situation. By taking a weighted average, the analysts can see how much interest the company has to pay for every dollar it finances.

Earnings Before Income and Tax (EBIT) Margins:

The EBIT margin can be calculated by EBIT divided by net revenue. Investors use EBIT margin to see how earnings of the company grow from year to year. Since EBIT does not include interest or tax, it shows how the firm operates. Interest has no bearing on the firm's operation and the effective tax rate can vary from year to year. Therefore, EBIT may be more accurate than net income in determining operational efficiency.

Working Capital

Working capital is the difference between current assets minus current liabilities. Working capital measures how much in liquid assets a company has available to build its business. The number can be positive or negative, depending on how much debt

the company is carrying. In general, companies that have a lot of working capital will be more successful since they can expand and improve their operations. Companies with negative working capital may lack the funds necessary for growth.

Net Property Plant and Equipment:

Balance Sheet amount of Gross Property Plant and Equipment (PPE) minus the accumulated depreciation gives one the net property plant and equipment value. Watching the net PP&E of a company can tell you if they are spending enough capital to replace the assets that run the business. When PP&E is continually declining (meaning capital expenditures are less than depreciation) it is a general indication that the business is not maintaining itself over the long run.

Goodwill:

Goodwill is defined by the surplus of the purchase price over a company's acquired assets. The goodwill value shown on a company's books is periodically revised based upon an updated valuation of the company's future prospects.

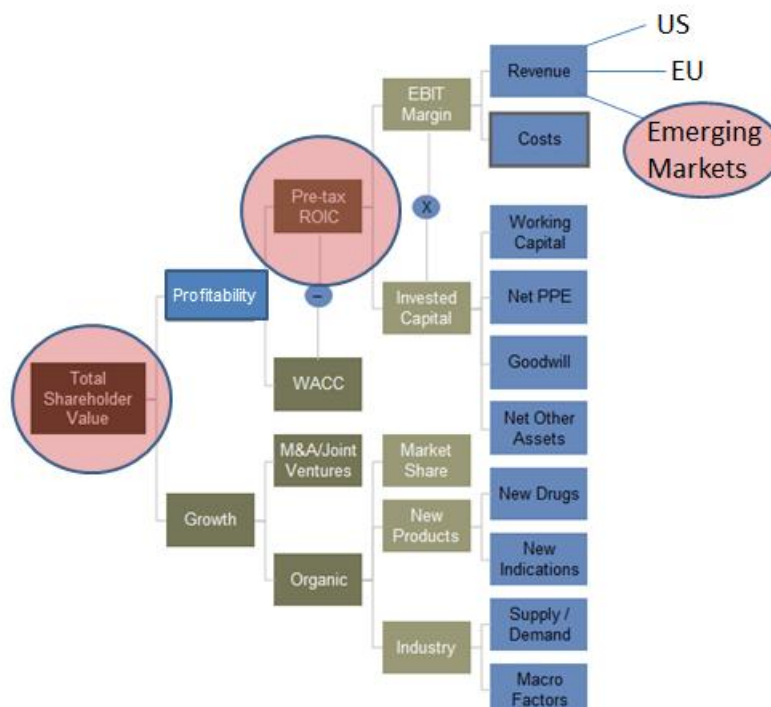


**Figure 17: Identified Parameters within the Shareholder Value Tree
Calculated for Correlation to Test the Postulated Research Questions**

The hypotheses postulated were tested by calculating the correlation between the following parameters as also indicated in the Figure 17.

1. Total Shareholder Value and the Emerging Markets Revenue for the 3-year period from 2009 to 2011
2. Pre-tax ROIC and the Emerging Market Revenue for the 3-year period from 2009 to 2011

These sets were both investigated for Pharmaceutical and Biotech company sets in two distinct and separate groups to be able to draw meaningful comparisons.

3. RESEARCH FINDINGS& DISCUSSION

The qualitative study led to the identification of the following seven key success factors that the pharmaceutical and biotechnology companies need to perform exceptionally well to stay competitive in building shareholder value in the Emerging Markets:

1. Local Manufacturing Presence
2. Building Agile Regulatory Affairs Capabilities
3. Commercial Model Addressing Emerging Market Needs
4. Broad and Efficient Distribution Network
5. Dynamic Pricing and Contracting Capabilities
6. Emerging Market Medical Affairs Capabilities Connecting Local Thought Leaders to Global Clinical Development Leaders
7. Access to and Retention of Local Talent

3.1. Summary of Findings

These findings were examined in both qualitative and quantitative terms to provide a holistic perspective as to what success factors multinational pharmaceutical companies need to follow.

Figure 18 depicts the summary of our findings visually but it is helpful to describe the product categories identified:

Branded Pharmaceutical Products:

These products are novel, patent protected medications that typically address an unmet need and have a better pricing flexibility to the extent allowed by the reimbursement scheme of the payers. This product category historically has been the core focus area of pharmaceutical enterprise since it has a higher margin that allows for SG&A investment while protected by patents. In this analysis, both small molecules and biologics are combined under this category while there is a clear distinction in how they are manufactured and priced. Small molecules are the pills and tablets that generally represented the product portfolio of pharmaceutical companies.

On the other hand, the biologics are manufactured by genetically engineered bacterial cells that are designed to generate the large molecular entity with the desired therapeutic effect on human organism. The manufacturing of biologics requires an investment over \$100 million in capacity and thus are priced significantly higher due to their cost that. They are delivered through injection or infusion.

Branded Generics:

Historically, pharmaceutical companies had the challenge of enforcing intellectual property rights in emerging markets as their economies became more globally integrated. De facto, "Big Pharma" had to compete against generic versions of its own medications that are otherwise protected in developed countries. Couple that with the lower percentage disposable income and the governments' inability to afford novel medications at developed country pricing, led to the emergence of a new segment called branded generics. These are exactly same molecules as the branded products that are no longer protected by the patent –or were never protected due to lack of enforcement of patent laws.

Branded generics are now broadly recognized as a reality and a key product category for any company to operate in the emerging markets (Dunham, 2010).

The difference that makes the branded generics a viable option is their brand equity built over decades with physicians and consumers. Branded generics can be manufactured and promoted by the original manufacturer (such as Sandoz for Novartis or Winthrop for Sanofi, etc.) or by local manufacturers who over time adapted the sales and marketing prowess of multinationals and potentially beat them in their own game.

These findings indicate that, in the emerging markets winning with branded generics is a key skill set that pharmaceutical companies typically do not possess. They have developed and improved commercialization techniques over years in the mature market environment of developed economies with established processes which do not apply to the emerging market environment. Some examples of companies that offer these products include Genentech/Roche, Amgen, BMS, Pfizer Oncology, etc.

Pure Generics:

Once the patent exclusivity expires, any pharmaceutical manufacturer in compliance with Good Manufacturing Procedures can file with regulatory authorities and get approval for the molecular entity which is no longer protected by patent. The fact that the molecular entity is priced and manufactured as a commodity shifts the key business capability to succeed from a R&D and Commercial prowess to one of process efficiency characterized with attaining high-volume manufacturing efficiency at low cost. Attaining economies of scale in order to reach cost efficiencies is a key critical success factor.

A representative example of such pharmaceutical manufacturer includes Teva which has over years built a global supply network through organic and inorganic growth. Similarly, local manufacturers such as Abdi Ibrahim, Bilim Ilac in Turkey, Dr. Reddy in India, many in China will supply the generic equivalents of once patent protected products at a fraction of the original price points.

Over the Counter (OTC):

In most of the countries, regulatory authorities allow certain medications with large safety margins to be sold in pharmacies without a need of a doctor's visit or a written prescription. This category of products comprises of cough and cold remedies, allergies and pain management. These products are mostly not reimbursed by payers or private health plans.

The benefits of having OTC products from a healthcare perspective is easy and fast access to medication without the need of seeking an appointment from a physician and lowering healthcare costs due to the fact that the patient is paying for the medication out of pocket. These products can be generally advertised to public depending on local government practices and marketing and supply chain capabilities require the agility and competitiveness mostly demonstrated by typical consumer goods companies.

It is also common that OTC products are directly promoted to pharmacies and retail point of sales by an OTC company sales force to attain competitive advantage and promote demand.

Private Labels Brands:

Another category of pharmaceutical products are private label brands, which is a concept similar to consumer goods in which a retailer commissions a subcontractor or manufactures the OTC products at its own manufacturing facility, and sells the product under the store's name. In this sense, the retailer will assume manufacturing risk in exchange of moving the privately labeled product from its own shelves generating higher profit since the margins are generally higher than in the case of OTC products.

However, the retailer needs to have built compelling brand equity which should motivate the consumer to choose the private label brand over another OTC product.

Manufacturers who supply retailers with private label products include Perrigo and Watson. In emerging markets, such as Russia, where consumer demonstrate a strong propensity to purchase a brand, retailers such as 36.6, Rigla and A5 all pursue private label products leveraging their strong brand equity.

Figure 18 maps the relationship of the brand equity of the product categories described above in relation to the operating margins in an illustrative fashion.

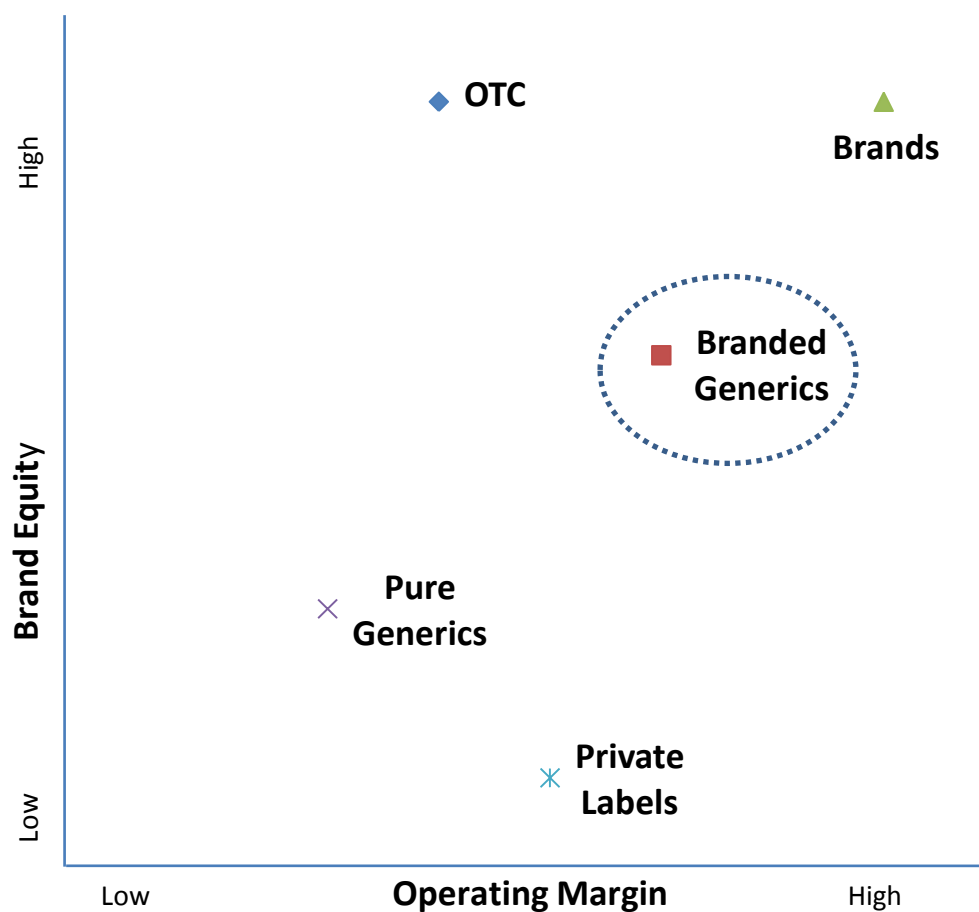


Figure 18: Relationship between Brand Equity of Product Categories (and manufacturers) and Operating Margins
(Personal interviews, 2010-11)

Branded Generics still offer a healthy 60-85% gross product margin allowing a meaningful amount of promotion spend while still commanding favorable brand equity. The provider trusts the branded generic similar to the novel medications since they have been in use for a long time, in some cases for decades, and there is an element of intrinsic trust in quality and the company that sells them.

If instead of operating margin the relationship using gross margins were mapped, these categories could not be discriminated, since the absolute cost of manufacturing of small molecules are very similar to each other with the exception of biologics as previously explained.

3.2. Qualitative Findings

Through literature review including both academic and industry sources as well as interviews with life sciences company practitioners, and based on prominence and frequency of mentions, seven key factors were identified which can be considered to be elements of a successful strategy for pharmaceutical companies when devising their emerging markets expansion strategy.

A key to winning in the emerging markets is a strong understanding the local market. Emerging markets is not one market, but distinct markets that have different market segments with different needs. Multinational corporations must realize that they can't effectively compete in the emerging markets when their management is located thousands of miles away. The key to an effective strategy is truly understanding the market and customer base. Successful pharmaceutical manufacturers have taken steps to localize each emerging market, including setting up Emerging Market specific business units and having local operations within the countries they are competing in.

Successful multinational companies have been also known to create partnerships with local companies who tend to have greater expertise in the local market and may have greater support from the local government. (Wall, 2011) Bayer HealthCare, for example, recently launched a joint venture with Cadila, one of India's largest privately held pharmaceutical companies. But these ventures are also designed to establish a new base for expansion into other emerging markets. In 2009, GSK, the world's third-largest pharmaceutical company, signed an agreement with India's Dr. Reddy's to develop and market selected products across emerging markets.

3.2.1. Local Manufacturing Presence

In developed markets, supply chain is a function that at best operates via a central command center to have visibility of the entire portfolio around the world. The multi-national corporation, using a refined S&OP process and enabled by ERP systems, can allocate capital, acquire raw material, optimize the manufacturing architecture and move inventory without using undue cash.

The above reality is somehow twisted in an emerging market setting. Supplying the market cheaply and quickly is an important success factor in the emerging markets that will ensure that the 'shelves' in the pharmacies are stocked and are done so by constantly moving smaller quantities. Given the fact that accounts receivable is a major stumbling block in all of the emerging markets, the agility of the supply chain is of critical importance.

Having a local manufacturing and distribution center is a requirement to gain entry to some of the emerging markets countries. Some governments require in-country operations to gain access to the market at all. Other countries, such as Brazil, make it very difficult for companies to compete without local operations by imposing import duties or tariffs to keep prices competitive in face of local competition. There is also an additional benefit in the form of lower production costs in-line with local regulation and specific packaging requirements. Finally, local manufacturing will qualify for some tax advantages. This advantage has been the primary reason for pharmaceutical companies to invest in Puerto Rico and Ireland.

Similarly, emerging market governments favor local manufacturing for job creation and knowledge transfer. However, there is a general skepticism about the intentions of such incentives, since the pharmaceutical companies may tend to believe that ultimately their Intellectual Property will leak into the local manufacturers.

3.2.2. Building Agile Regulatory Affairs Capabilities

For Branded Generics, the function of regulatory affairs in the emerging market setting around the branded generics is structurally different than the one in developed markets. Typically, the regulatory affairs function plays the role to provide guidance about a new product's labeling process to optimize the ability to promote the product post-approval.

In the emerging markets, the ability to accelerate the go-to-market capability by moving the branded generic application through multiple bureaucratic hurdles is a key capability that the regulatory affairs personnel must master. The level of relationships

is immensely important and it is not unusual to see many former government officials and/or regulators to join the ranks of the local or multi-national companies. In the context of the emerging market realities, multi-nationals who play in the branded generic space should have a very solid regulatory affairs function to have a smooth and agile go-to-

3.2.3. Commercial Model Addressing Emerging Market Needs

While the number of sales reps in the United States is down to 70,000 from its peak of 120,000 around 2004, pharmaceutical companies are actually expeditiously adding to their sales ranks in key emerging markets since they wish to participate in market growth.

In absence of intellectual property protection, pharmaceutical companies in the emerging markets heavily rely on their ability to extend and the frequency of their reach to the providers reminiscent of the market dynamics in the United States in 90s where the size of the sales organization was a major success factor to gain market prominence. From an emerging market provider perspective sales force is still considered a major source of education about managing the condition for which the products are sold.

While the access to information and guidelines over the internet to some extent tempers the value-add providers will get from an in-person interaction with a sales representative there are cultural elements of relationship that cannot be discounted. Furthermore, the personal interaction is key as branded generics begin building brand equity. As the product moves through its life cycle and the brand equity is established, Pharmaceutical companies can reassess the best way to leverage the sales force interaction.

Emerging markets pose untested challenges to “Big Pharma” sales model which historically focused on its representatives’ reach of physicians and the frequency upon which the representatives called on medical professionals. However, these metrics no longer apply when –such as in China- the industry needs to call on one million medical

doctors. Introducing novel reach methodologies including digital content and reach via mobile devices virtually (O’Riordan, 2011) is reported to be a successful model with a positive return on investment.

Importantly, sales representatives hold on to their knowledge of their territories and established relationships with providers even as they move from one company to the other.

The fully loaded cost of a sales rep, on the other hand, is increasing ahead of the market growth in relation to market supply/demand dynamics. “Big Pharma” companies can apply skills and capabilities such as sales analytics and sales effectiveness they are maturing in the developed markets, to create a competitive edge versus local manufacturers. Having said that, local manufacturers also have access to same services raising the bar on level of competition. Local manufacturers are also quickly catching up on the learning curve by acquiring talent trained by multinational companies and mimicking and improving upon their processes. Additionally, continuing sales training is a key way to keep the selling capabilities sharp while using these training programs as a talent retention tool.

Finally, some of the selling practices that are no longer condoned in the developed markets, such as giving away trinkets or questionable consulting agreements, are prevalent and important in the emerging market selling environment. It will be important to monitor how these practices evolve in emerging markets.

The research identified certification and training programs as effective tools for pharmaceutical companies to build their presence in the emerging markets. By educating their customers on their products and the diseases, they raise awareness and generate new revenue opportunities in markets with less understanding of Western medicine. Multinational corporations may create training regimens to “certify” physicians in the use of their product. For example, Novo Nordisk created a certification program for their insulin products in rural India.

In summary, the research concludes that the commercial model which can efficiently coordinate the marketing, sales force, pricing and tendering capabilities remains to be the most effective success factor in the emerging market landscape and the multi-national companies can stay competitive by applying their sales effectiveness and analytics capabilities and providing local talent with continuing training.

3.2.4. Broad and Efficient Distribution Network

In the developed markets, retail pharmacies typically play the role of medicine dispensation. A relatively recent phenomenon, triggered by incentives of the recent healthcare reform in the United States, encourages pharmacists to get out behind the counter and play a consultative role to the patients about how they should take medicine and underline the importance of adherence. In the United States, big pharmacy retail chains such as CVS and Walgreens increasingly are changing their business models to apply these operational principles.

In all five emerging markets researched, the role of pharmacists has been historically different than the role they play in developed countries.. Pharmacists can be active care providers and are mostly trusted by consumers more than physicians.. If the consumer is willing to pay out of pocket, they can offer for-prescription remedies. This is even true for pharmacy staff with no medical training. They play a very influential role on what medication to dispense, even if there is prescription as the pharmacist suggests and in many cases decides which generic product to dispense if there is an option available.

If the patient cannot afford the branded original product due to its relatively higher price, the pharmacist is observed to offer the 'next best' product, a branded generic supplied by a local manufacturer, following the pattern outlined in Figure 17. If the consumer is restrained up to a ceiling price, he/she at least goes home with 'a' prescription of the same molecule or a 'me too' product. Multinationals should look to connect, educate, train and incentivize the pharmacists to dispense the novel product, or at least their branded generic, transcending their engagement beyond the typical sales transactional.

While there are certain benefits of having a trained pharmacist intervene in the medication regimen, especially for chronic conditions such as hypertension or diabetes, it is not uncommon that the pharmacist assistants to play that role as well. Economically, branded generics can be more profitable to pharmacists, since they typically have better payment terms –unlike a multi-national company that has to report out their A/P terms on a quarterly basis.

Another strategy to employ is for pharmaceutical companies to determine the most effective way to reach their distribution networks. For example, in China it is currently very tough for pharmaceutical sales reps to meet physically with doctors due to high patient load, time pressures, and a variety of other factors. Companies are focusing on ways to reach doctors through digital channels such as internet and email.

Understanding these dynamics cannot be easy for a multi-national company trained in a developed market. And unless these dynamics are understood and an appropriate mitigation plan(s) are developed the battle to occupy the emerging market will be uphill.

A critical factor for creating an effective distribution network strategy in the emerging markets is ensuring that multinationals understand their customers (consumers) needs – credit, supply predictability, and/or assurance that this is a genuine (not counterfeit) product.

As the multi-nationals invest in entering the emerging markets, they need to fully synchronize their operational principles with the realities of these countries. This vignette summarizes one such example; one multi-national disposable medical device company that wanted to significantly expand their distribution capabilities in India took a tour of a wholesaler market in New Delhi. The key question the company wanted to answer was whether they can access this lower priced segment of the growing Indian market with no institutionalized healthcare system and a significant rural population that has no access to care. As the company officials continued their tour of the wholesale market it was evident that the operational dynamics were very different than originally hypothesized.

There were close to 3,000 'wholesalers' in this cramped marketplace each comprised of a storefront of less than 2-3 feet facing the alleys of the labyrinthine market. The 'inventory' was made of the boxes sitting on the shelf with an ability to trade certain goods with each other at prices that differ of a fraction of a dollar. The officials also saw a major activity of card boxes of the sold medical supplies being 'recycled'.

In the interviews, when the officials inquired about the recycling activity they found out that sometimes the wholesalers made the money on recycling the card boxes and not on the product that they once contained. It was all about a speedy turnover –sometimes multiple times the inventory in a .day- which is a mind-boggling speed when compared to wholesalers in developed markets

3.2.5.Dynamic Pricing and Contracting Capabilities

Pharmaceutical companies also need to understand the generic drug markets in emerging markets countries. Many emerging market countries have strict pricing measures enforced by the government and a consumer base with low income levels that favors generic drugs

In most emerging markets and even some developed markets, the tendering process is an important area of focus for multinational pharmaceutical companies. Implementing effective contracting capabilities is a strategy that may assist in winning the branded generics game.

Currently, the tendering process in the emerging markets tends to be low tech and reactive rather than proactive. Many relationships with key customers are developed informally and policy changes result in delayed reactions. Many markets simply use Microsoft Excel as a tool to track historical bid prices. The decision makers do not readily have access to data or tools to drive actionable insight. In order to compete with local players such as Ranbaxy and Dr. Reddy's in India, multinational corporations need to view tendering/contracting as a commodities game, not a brand game.

The tendering process for off-patent products has the additional complexity of dealing with generic competitors whose price points are generally not known. Preparing multiple bidding scenarios, as part of the “Crafting the Offer” phase of the process can help prepare for the potential inconsistencies of a customer with low influence on price.

With significant pricing pressure for off-patent drugs, offering a portfolio discount strategy can be a valuable way to sell both patent and off-patent drugs. Global pharmaceutical companies can gain market share and potentially create positive prescribing spillover for the off-patent drugs, which is often difficult to do in a low transparency market.

Given the lower margins of off-patent products, profitability is driven through high-volume sales. Tenders, which are the main source for high-volume sales opportunities, gain even larger importance in the overall commercial plan. Thus, identifying the tenders, through investment in 3rd party aggregating services or in establishing data-sharing relationships with distributors is essential to finding tendering opportunities.

3.2.6. Emerging Market Medical Affairs Capabilities Connecting Local Thought Leaders to Global Clinical Development Leaders

Recent news about Merck investing around \$1.5 billion in an R&D facility in China is another milestone for “Big Pharma” entrenching themselves to the emerging markets landscape. These moves can be construed in two ways:

- 1) Getting access to an educated workforce to crank up discovery functions at a lower cost and,
- 2) Establishing the company as a ‘net investor’ in the emerging market to be able to play that card when dealing with the local governments which are almost always the monopolies in the market in absence of a healthy ‘commercial insurance’ segment.

Another development in the recent years is to enroll an increasingly larger patient population from emerging markets to help with the speed of patient recruitment which has become an operational obstacle for clinical stage development.

Due to lower treatment rates in emerging markets, the propensity to find more eligible patients has been attracting drug developers to these geographies to perform Phase III clinical trials which also can help speed up the approval process with the regulatory authorities by claiming that the submission package contains local population outcomes data.

These moves can enhance the image of the “Big Pharma” company in the eyes of the local providers as a progressive and innovative company that supplies quality products.

However, the cost and benefit need to be weighed in carefully since many other factors play into that perception including, nationalistic protectionism to invest in local technologies, irreverence of government officials in light of their pricing, payment and coverage decisions under the pressure of containing their healthcare costs under control.

3.2.7. Access to and Retention of Local Talent

Since both multi-national companies and local branded generic manufacturers heavily invest in emerging markets, the war for talent is a key success factor. It is a counter-intuitive notion especially when the unemployment rates hovered around 9% in the United States and in the double-digits in some European countries, such as Spain and Italy.

This pervasive demand for talent makes the cost of hiring and remuneration of the individuals with the right skill sets disproportionately expensive and in some cases reverses the net immigration to developed markets. For example, over the last few years, more Turks migrated from Germany to Turkey leaving the net immigration on a negative number in many decades.

Talent acquisition costs are also steadily increasing bringing a fully-loaded cost of a pharma sales rep in China to a level closer in the United States. In some Eastern-European countries and Russia, it is a common practice to hire physicians who can earn multiples of their government-paid salary when compared to their healthcare provider jobs.

Social work was another way for pharmaceutical companies to build their brand in emerging markets. Contributing to the local economy or infrastructure goes a long way towards building goodwill and winning over a customer base that recognizes your brand and attracting talent.

Continuing education, training and having a sustainable career path in a multi-national company remain very important to local talent; however, this edge is being lost to local branded generic manufacturers. The local branded generic manufacturers used to attract talent once they complete their initial training and gain hands-on multi-national commercialization experience, but they can also offer similar perks and career paths as well.

In general, rates of attrition were uncharacteristically high in the Emerging Markets since companies also do not shy away from attracting talent already trained by competition.

3.3. Quantitative Findings

The quantitative portion of this study investigated the relationship of two financial metrics to the geographic source of revenue generated. Two variables, the return to total shareholders and ROIC, were selected, consistent with Figure 16, as two key measures of strong performance for any corporation.

The revenues recognized in the United States, Europe and the Emerging Markets –to the extent they were reported- were investigated in order to identify potential relationships between the geographic source of the revenue and the quality of earnings

to shareholders. This relationship would provide quantitative insights in order to identify the role Emerging Markets plays in generating shareholder value and profitability as measured in ROIC.

The specific period to investigate was determined to range from 2009 through 2011, and hence excluded the 2008 data, with the foreknowledge that the massive economic downturn in the 2008-09 period would confound the findings. Therefore, this exclusion eliminated the one-time significant market event.

While the three year period from 2009 through 2011 was used the study averaged out the three years to avoid year to year variations. Additionally, a mid-point was selected to represent all variables analyzed. This further eliminated –to an extent– a potential one time impact of the share price which could be due to non-operating results, such as a law suit or an FDA decision that could have material impact on the stock performance.

Finally, since both pharmaceutical and biotechnology companies represent life sciences business in aggregate, they were included in the peer set. However, these two segments were analyzed separately since they behave differently and have different valuations dynamics, as established earlier in this study. As a result, these two sets are analyzed separately to seek findings in isolation and protecting the analysis from confounding effects of either segment to the other.

3.3.1. Pharmaceutical Company Peer Set Analysis

The following seven companies were selected to represent the pharmaceutical peer set. These companies were the largest by revenue ranging from \$20 to \$61 billion and correspondingly in market capitalization. Some of these companies are headquartered in the United States, United Kingdom or Switzerland; however, they are all traded in NYSE and recognize revenue through their worldwide operations.

These companies are listed below in alphabetical order.

1. AstraZeneca (AZ)

2. Bristol Myers-Squibb (BMS)
3. Glaxo SmithKline (GSK)
4. Merck
5. Novartis
6. Pfizer
7. Sanofi

Table 7: 3-year total average revenue, 3-year average revenue source, 3-year total return on shareholders and 3-year average return on invested capital of selected pharmaceutical company

	3 year (2009-11) Avg Revenue (MM)	3 year (2009-11) average revenue source			3 year (2009-11) TRS	3 year (2009-11) average ROIC
		US Rev.	Europe Rev.	ROW Rev.		
Sanofi	\$31,026	30.5%	38.2%	31.3%	7.7%	11.3%
AZ	\$33,221	42.1%	30.5%	27.4%	2.0%	34.8%
BMS	\$19,845	64.3%	18.1%	17.6%	14.9%	30.1%
GSK	\$27,928	33.8%	32.3%	33.9%	4.6%	34.5%
Merck	\$40,487	46.4%	28.2%	16.3%	7.4%	10.3%
Novartis	\$51,152	32.8%	38.7%	28.5%	0.6%	16.0%
Pfizer	\$61,250	42.2%	24.7%	33.1%	6.9%	14.5%

The companies listed above typically do not report the revenue they recognize in the Emerging Markets explicitly. Further, the exact composition of and definition of the emerging market vary from one company to the other depending on the set of countries they chose to include in the business portfolio.

For example in the recent years, Merck designated Japan as an emerging market while Japan was generally accepted to be a developed market and World's third largest economy. The emphasis Merck's leadership made in that statement was more symbolic to underscore the fact that they expect growth from Japan as though it is a BRIC country.

Also, depending on the operating model some companies may choose to include South Korea in the emerging markets, while this country demonstrates characteristics of a Western Economy.

3.3.1.1. Relationship of Revenue Source by Geography to Total Return to Shareholders (TRS) -Pharmaceutical Companies

Before discussing the impact of the individual geographic segments, first the relationship of total worldwide revenue is compared to the 3-year average of total shareholder value from 2009-11.

It is interesting to observe in Figure 19 that the worldwide total revenue of the selected pharmaceutical companies did not show a positive impact ($R^2 = 0.2152$) on their ability to generate shareholder value. One can hypothesize that in that period, the investors were concerned about patent expirations, an industry threat which was established earlier in this study.

The other explanation that can be hypothesized here was that the extra non-value added infrastructure and headcount cost –representative of the blockbuster business model of early 2000s - did not bode well for the large cap pharmaceutical product peer set depicted here. It should be recalled that this was a period of pharmaceutical companies undergoing massive lay-offs and targeting cost cuts.

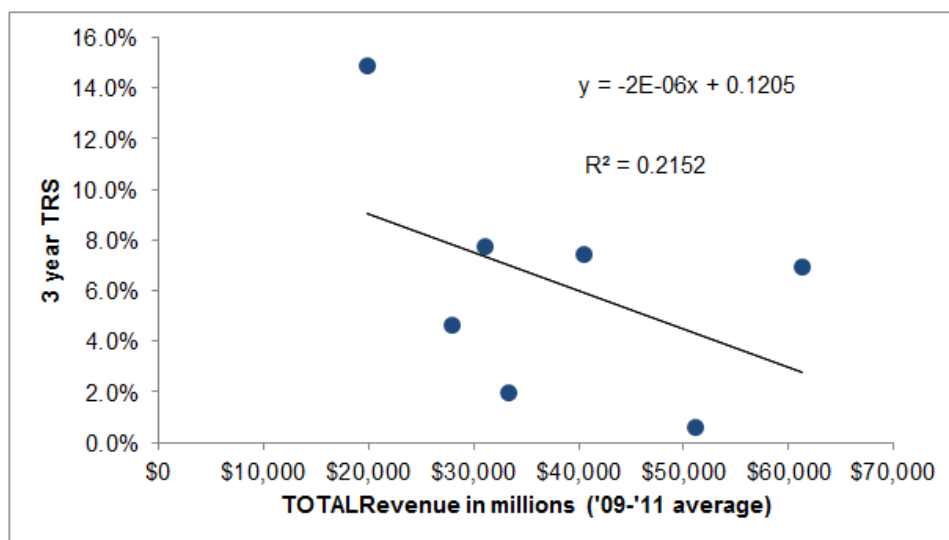


Figure 19: Relationship between 3-year average Total Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies

Another hypothesis tested as shown in Figure 20 was the impact of the United States revenue to the total shareholder value over the 3-year period. The correlation here is a relatively strong one with ($R^2 = 0.5748$).

As described earlier in this study, the relatively flexible pricing in the United States market and the ability of setting the price higher allow pharmaceutical companies to increase their profitability which can lead to increased TRS.

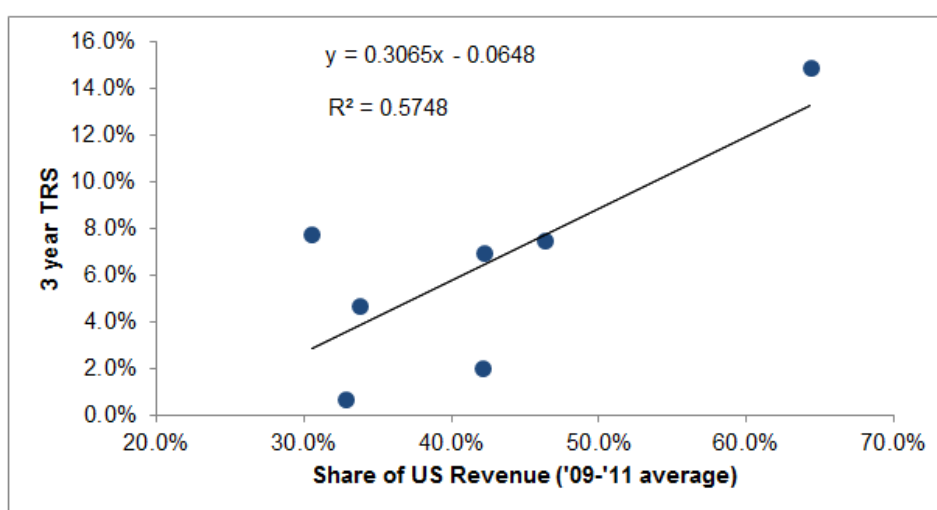


Figure 20: Relationship between 3-year United States Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies

The flip side of this observation was the trends in the markets outside of the United States and especially Europe as shown in Figure 21. The relationship clearly showed that a higher percentage of sales revenue generated in Europe did not lead to improved total shareholder value.

During this period Europe was still undergoing its recovery with governments under significant fiscal pressure to fund their very basic operational activities and desperate for resources for investments.

As pharmaceuticals were almost always purchased and paid for by governments in a monopsony, European governments applied pricing and reimbursement controls, therefore lowering the attractiveness of revenue generated in Europe due to lower profitability.

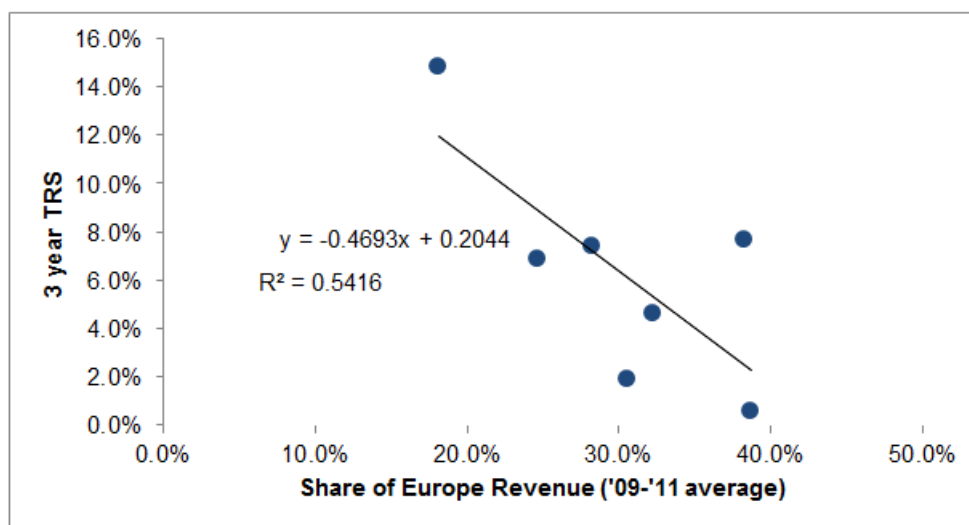


Figure 21: Relationship between 3-year Europe Revenue to 3 year average of Total Return to Shareholders - Pharmaceutical Companies

An interesting finding of this analysis is the percentage of revenue recognized in the rest of the world including the BRICs. It should be noted, as shown in Figure 21, that Emerging Markets still made up 15% to 35% of “Big Pharma” company revenues and they might not have had enough weight in the revenue mix to impact the total return.

However, one would have expected that the more your revenue originated from within the BRICs, whereas there was high single digit to low double-digit pharmaceutical market growth, one would expect that shareholders would value the quality of those earnings more and factor that into the share price.

This should –however- be interpreted in conjunction with the ROIC analysis for emerging markets in in Figure 25.

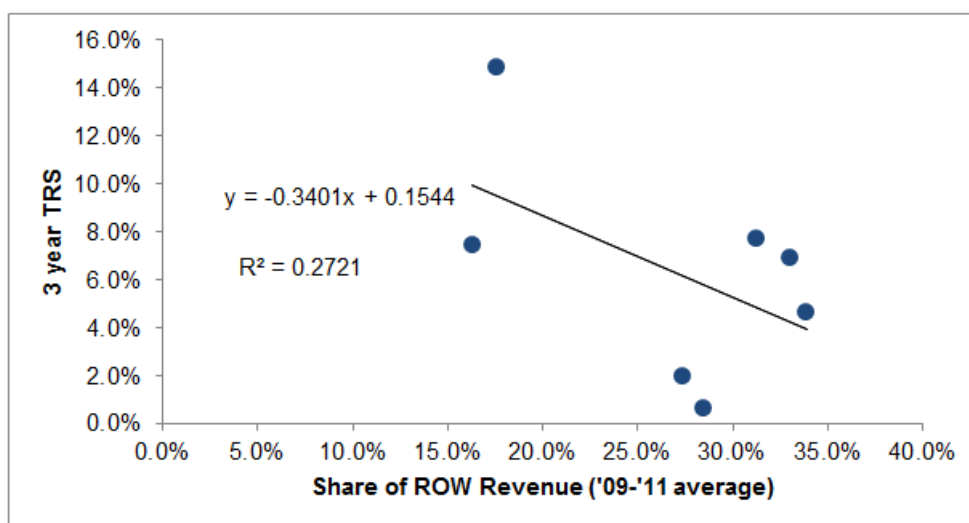


Figure 22: Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average of Total Return to Shareholders - Pharmaceutical Companies

The summary of the correlation co-efficients for 3-year total revenue by geography in comparison to the total shareholder value in the same period was listed in Table 8.

Table 8: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on shareholders of selected biotechnology company peer set

<i>(2009-11 Average)</i>	Pharmaceutical Companies
	vs. 3 Year TRS (R^2 Values)
Total Revenue	0.2152
US Revenue	0.5748
EU Revenue	0.5416
ROW Revenue	0.2721

The take-away from this portion of the analysis was that the TRS in the 2009-2011 period was negatively correlated to the size of the revenue of the pharmaceutical

companies and that the revenue recognized in the United States showed a better indication for shareholder value appreciation than the revenue recognized in Europe and the Rest of World including BRIC-T countries.

3.3.1.2. Relationship of Revenue Source by Geography to Return on Invested Capital - Pharmaceutical Companies

The ROIC is widely recognized as a core indicator of profitability as also was established in Figure 16. Hence, ROIC was investigated for the selected seven pharmaceutical companies in order to explore the relationship of size and geographic break up with the ROIC.

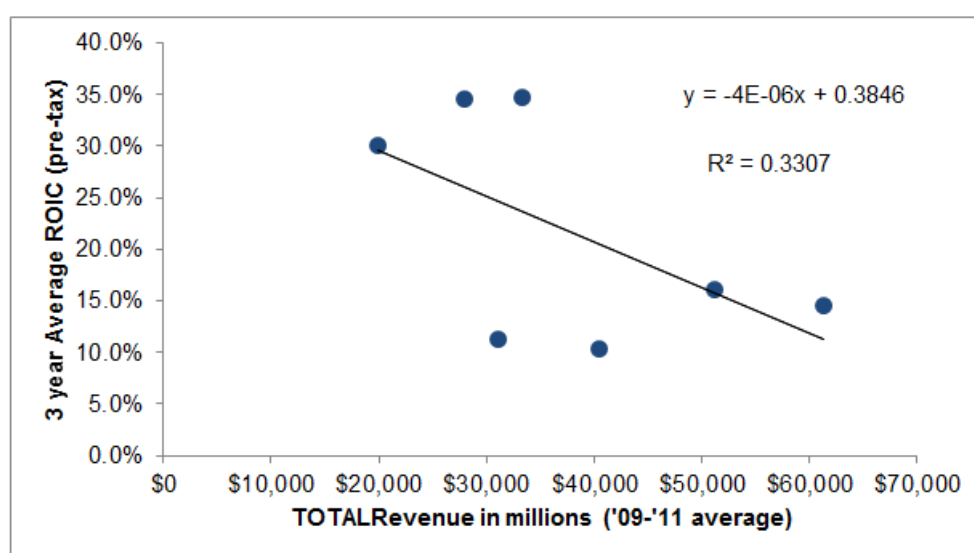


Figure 23: Relationship between 3-year average Total Revenue to 3-year average return on invested capital - Pharmaceutical Companies

As shown in the above Figure 22 the total revenue of the pharmaceutical company was inversely proportional to the ROIC of over the same period of 2009-2011. This finding was similar to the TRSAs in Figure 18. The analysis showed that the size of the pharmaceutical company in the sample set did not positively affect the return shareholders enjoyed over the duration of the period.

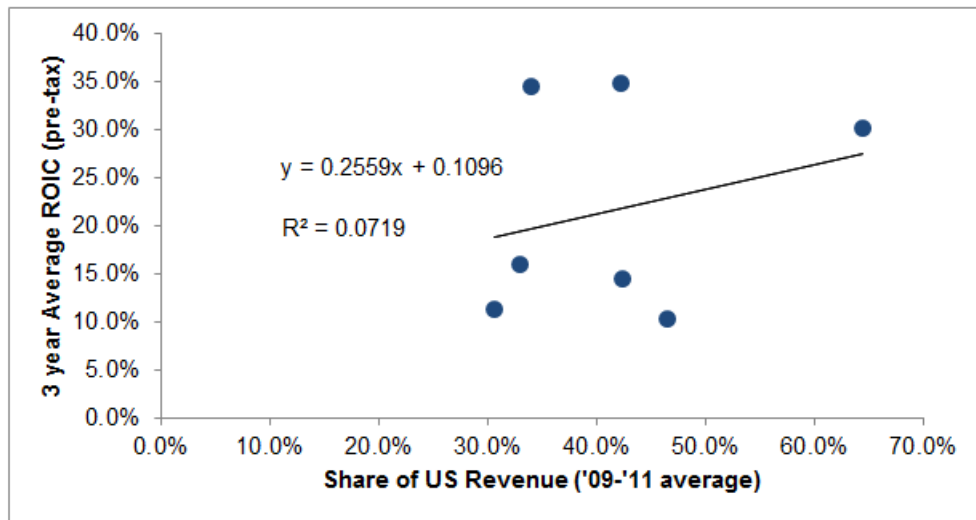


Figure 24: Relationship between 3-year-average United States Revenue to 3-year average return on invested capital - Pharmaceutical Companies

The relationship of the percentage of total revenue as generated in the United States was also analyzed as shown in Figure 24. Consistent with the outcome in Figure 19, the revenue generated in the United States shows a positive correlation with the ROIC over the 2009-2011 period.

This again underscored the observation that the quality of earnings in the United States for a pharmaceutical company due to higher profitability driven by ability to enjoy less price elastic regulatory environment.

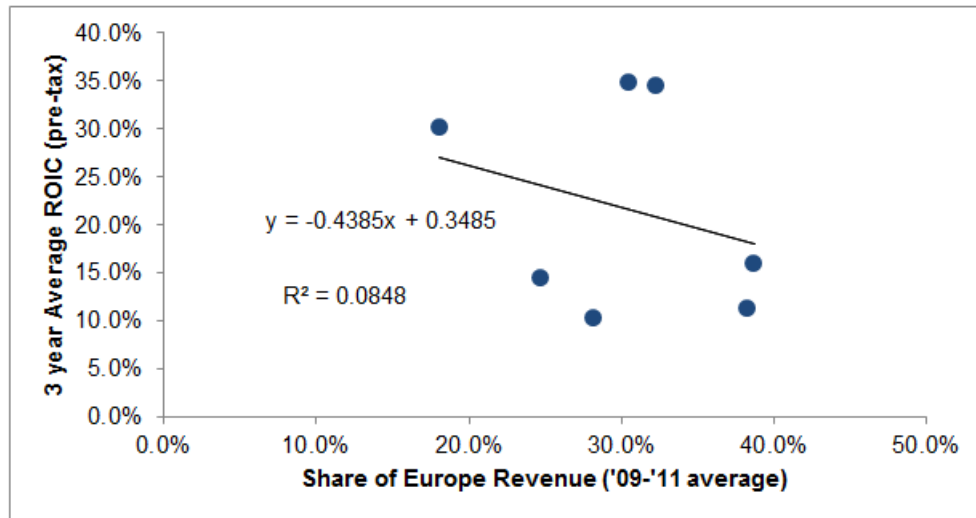


Figure 25: Relationship between 3-year Europe Revenue to 3-year average return on invested capital - Pharmaceutical Companies

Similarly, the relationship of the percentage of total revenue as generated in the Europe was also analyzed and shown in Figure 25. Interestingly, and consistent with the outcome in Figure 21, the revenue generated in Europe showed an inverse relationship with the ROIC over the 2009-2011 period. This again underscores the observation that the quality of earnings in the European Union countries was not as accretive as in the United States.

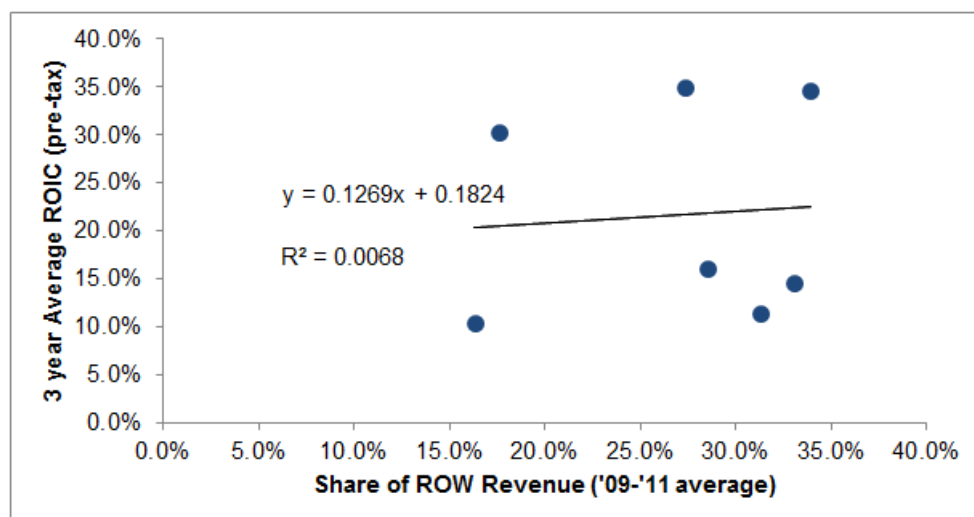


Figure 26: Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average return on invested capital - Pharmaceutical Companies

Investigating the rest of the world including BRIC-T countries, the analysis was summarized in Figure 26. Interestingly, the revenue generated in the rest of the world did not show either a positive or negative effect to the ROIC in the study period.

Table 9: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on invested capital of selected biotechnology company peer set

<i>(2009-11 Average)</i>	Pharmaceutical Companies
	vs. ROIC (R^2 Values)
Total Revenue	0.3307
US Revenue	0.0719
EU Revenue	0.0848
ROW Revenue	0.0068

The coefficients of the correlations are summarized in Table 9 and should be interpreted in the collective context of the Figures 23, 24, 25 and 26.

In summary of this subsection, one might argue that this geographic source was not as strong as a contributor to the ROIC unlike the high quality revenues earned in the United States but showed a stronger contribution than the sales originated from Europe.

3.3.2. Biotechnology Company Peer Set Analysis

The following companies were selected to represent the biotechnology peer set. These seven companies are the largest by revenue and correspondingly in market capitalization:

1. Amgen
2. Biogen Idec
3. Celgene
4. Genentech (known as Roche outside of the United States)

5. Gilead
6. Regeneron
7. Vertex

It should be noted that biotechnology segment is a very dynamic one comprising of companies heavily concentrated on one or two products' performance and do not typically have an broad portfolio of products that helps with revenue diversity. Therefore, the individual product news flow can affect their share price that leads to significant fluctuations and variability depending on the date of the data cut. The companies down-selected possess multiple products with a billion dollar revenue strength and have demonstrated long-term sustainability to stay in business and value generation for their shareholders.

It should also be noted that these companies, with the exception of Roche/Genentech are all based out of the United States market. The Basel, Switzerland based Roche, in fact, after having acquired Genentech, a California based biotechnology company, abandoned its name in the United States market and started using Genentech due to very strong brand equity of Genentech being associated to be the leading company in the biotechnology set.

Most importantly, for the purposes of this study, they have not significant revenues generated outside of the United States with the exception of Vertex.

Table 10: 3-year total average revenue, 3-year average revenue source, 3-year total return on shareholders and 3-year average return on invested capital of selected biotechnology company peer set

	3 year (2009-11) Avg Revenue (MM)	3 year (2009-11) average revenue source			3 year (2009-11) TRS	3 year (2009-11) average ROIC
		US Rev.	Europe Rev.	ROW Rev.		
Biogen	\$3,486	51.1%	30.2%	18.7%	32.2%	24.8%
Gilead	\$7,782	53.1%	8.0%	38.9%	-7.2%	59.8%
Roche	\$46,352	34.3%	35.8%	29.9%	-0.7%	32.1%
Vertex	\$552	100.0%	0.0%	0.0%	3.0%	-36.3%
Amgen	\$15,092	77.4%				15.8%
Regeneron	\$428	85.4%	14.6%	0.0%	44.5%	-28.2%
Celgene	\$3,719	61.3%	33.7%	5.0%	6.9%	18.5%

Excluded as European revenues not available

Excluded as ROW revenues are unable to be determined

These companies typically do not report the revenue they recognize in the Emerging Markets explicitly. Further, the definition of the emerging market varies from one company to the other. In fact, Amgen does not even break down their international sales by other continents. Some of these companies also license out their revenues outside of the United States to allow the large-cap pharmaceutical companies to leverage their infrastructure for regulatory, medical affairs, marketing and sales to pull through their products.

3.3.2.1. Relationship of Revenue Source by Geography to Total Return to Shareholders - Biotechnology Companies

First the relationship of the total shareholder return of biotechnology companies to their investors were examined in relevance to the size of their overall revenue globally booked and then these revenues were broken down by geographic area as collected and publicly reported.

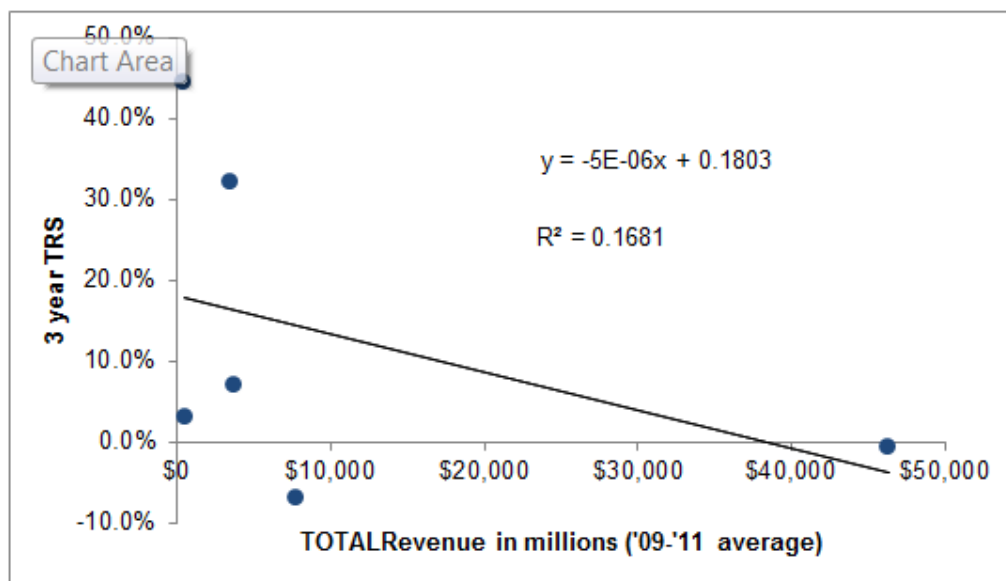


Figure 27: Relationship between 3-year average Total Revenue to 3-year average of Total Return to Shareholders – Biotechnology Companies

The first analysis in Figure 27 shows the relationship of total revenue of these biotech companies to the total shareholder value generated over the 2009 and 2011 period.

It was interesting to observe that, similar to the pharmaceutical company set, there was a negative correlation of the total revenue to value the shareholders received. In summary, the biotechnology company size did not immediately translate to value generation. Next, the geographic break up of this revenue was explored.

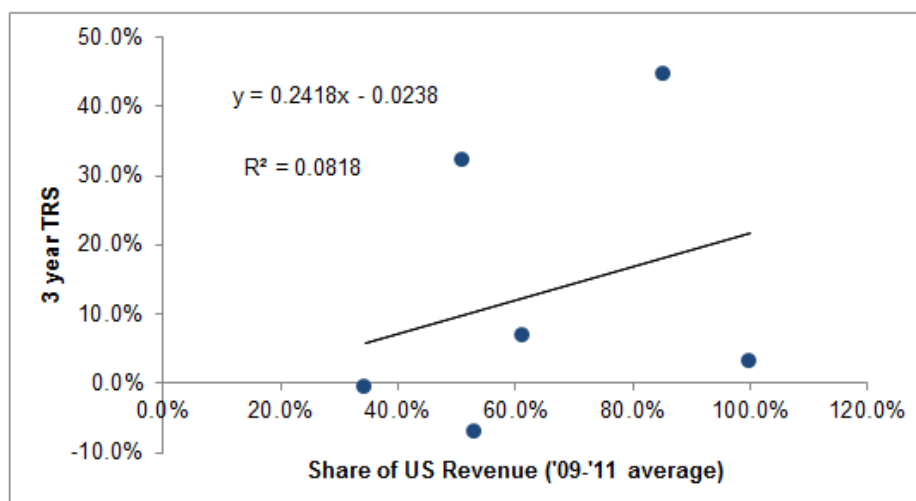


Figure 28: Relationship between 3-year United States Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies

The first analysis in Figure 28, showed the relationship of the revenue generated in the United States of the selected biotech companies to the total shareholder value generated over the course of 2009 and 2011 period. The relationship showed a positive correlation between the degree of shareholder value generated and the portion of revenue recognized in the United States.

It should be noted that unlike the pharmaceutical set, biotechnology companies have in aggregate a higher portion of their revenues emanating from their domestic market. It was interesting to observe that, similar to the pharmaceutical company set, there was a negative correlation of the total revenue to value the shareholders received.

In summary, the biotechnology company size did not immediately translate to value generation. Next, the geographic break up of this revenue was explored.

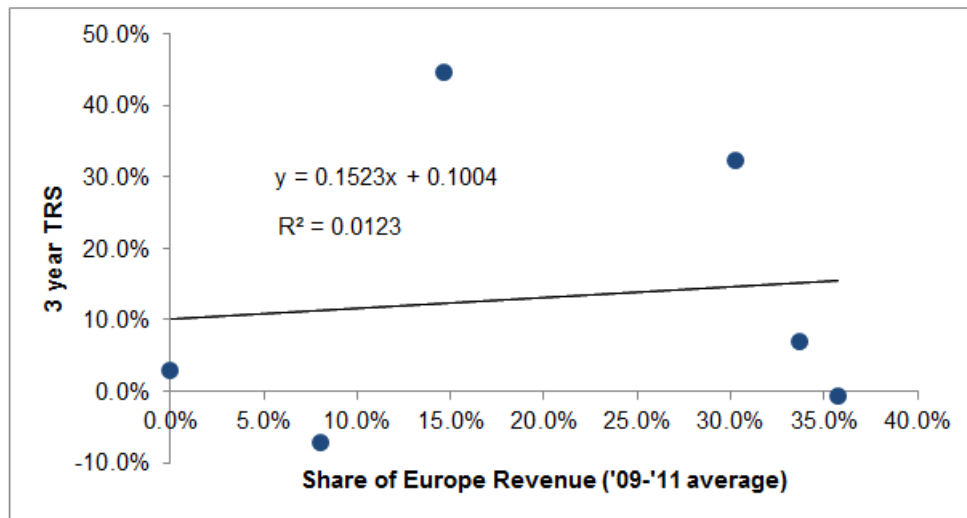


Figure 29: Relationship between 3-year Europe Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies

The analysis in Figure 29, showed the relationship of European revenue of these biotech companies to the total shareholder value generated over the course of 2009 - 2011 period.

Unlike the findings for the pharmaceutical set, it was interesting to observe a more positive correlation to the shareholder value generation in Europe. One may deduce that, shareholders put more value on biotechnology companies' ability to extract value outside of the United States (their domestic market) since they might see this as an opportunity to incremental revenue in a developed geography.

However, the relationship is weaker than the revenue generation capability in the United States.

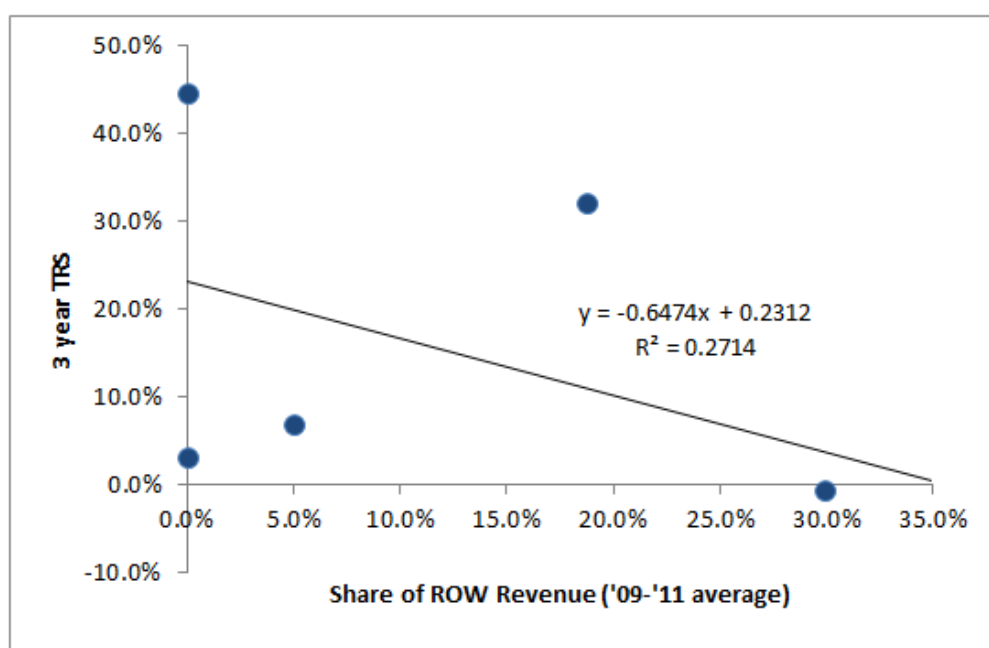


Figure 30: Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average of Total Return to Shareholders - Biotechnology Companies

Finally, Figure 30 plots the relationship of total revenue generated out of the rest of the world these biotech companies to the total shareholder value generated over the course of 2009- and 2011 period.

It was an interesting observation that, similar to the pharmaceutical company set, there was a negative correlation of the total revenue to value the shareholders received. In summary, the biotechnology company size did not immediately translate to value generation.

Table 11: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on shareholders of selected biotechnology company peer set

(2009-11 Average)	Biotechnology Companies
	vs. TRS (R^2 Values)
Total Revenue	0.1681
US Revenue	0.0818
EU Revenue	0.0123
ROW Revenue	0.2714

The take-away from this portion of the analysis is that the TRS in the 2009-2011 timeframe was negatively correlated to the size of the revenue of the biotechnology companies.

Further, the revenue recognized in the United States and to an extent in Europe showed a better indication for shareholder value appreciation than the revenue recognized in the Rest of World including BRIC-T countries.

An interim conclusion in absence of the broader picture enabled by the analysis can be that the shareholder value generation was more appreciated for biotechnology companies in developed markets than the emerging markets.

3.3.2.2. Relationship of Revenue Source by Geography to Return on Invested Capital - Biotechnology Companies

The ROIC was a core indicator of profitability as established in Figure 16. The relationship of the ROIC and source of revenue was investigated for the selected seven biotechnology companies in order to deduce insights pertaining to biotechnology company financial performance.

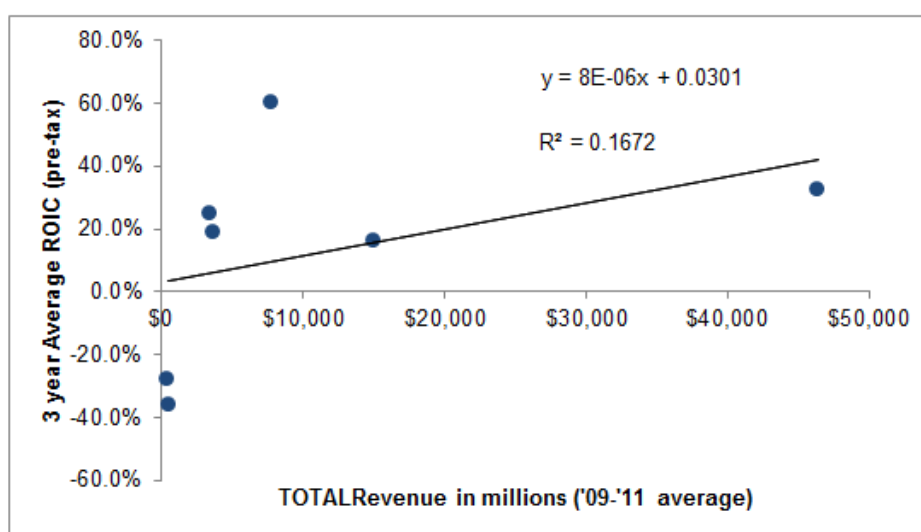


Figure 31: Relationship between 3-year Total Revenue to 3-year average return on invested capital - Biotechnology Companies

The change in average 3 year ROIC showed a positive correlation with the total revenue of the biotechnology company peer set as shown in Figure 31.

However, the R was too small (0.1672) to conclude that this relationship was strong enough. It should be noted that the two companies in the peer set, Regeneron and Vertex, had negative ROIC, and therefore skewed the overall set.

While these companies were highly valued by the shareholders due to their product pipeline strength and was demonstrated in the TRS comparisons with the revenue, the same conclusion could not be drawn for the ROIC relationship.

This observation should not have come as a surprise for some of the biotechnology companies with the future value was defined by the promise the investors expect from the research pipeline rather than the established commercial operation of a large pharmaceutical company.

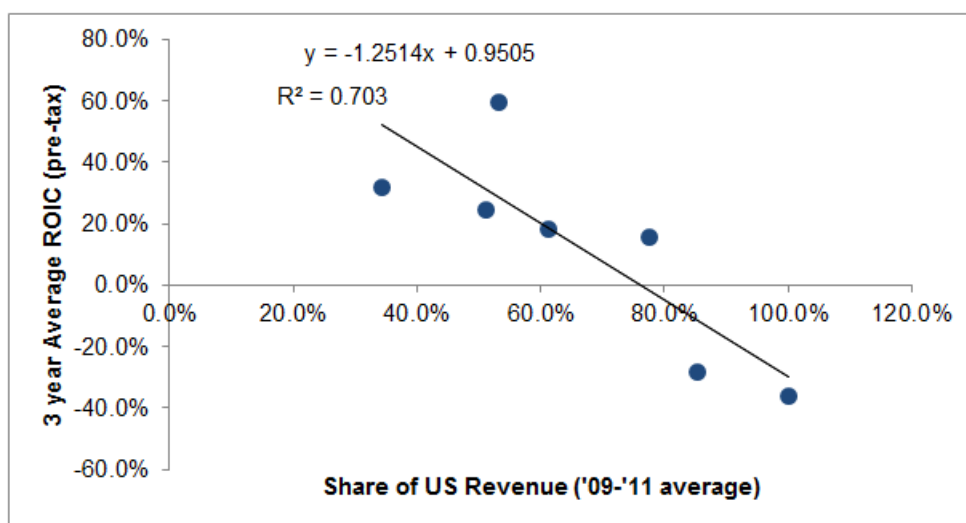


Figure 32: Relationship between 3-year United States Revenue to 3-year average return on invested capital - Biotechnology Companies

The ROIC when compared to the breakdown of the geographic revenue, as depicted in Figure 32, showed a negative and statistically significant relationship with the revenue generated in the United States. Appendix 7 lists the results of the statistical test conducted.

Interpreting the findings in Figure 32, one might conclude here that the biotechnology companies, which did not diversify their source of revenue beyond the United States did not generate higher ROIC.

Hence, an interim conclusion could be that expansion into markets segments and geographic territories beyond the United States could translate into a higher ROIC.

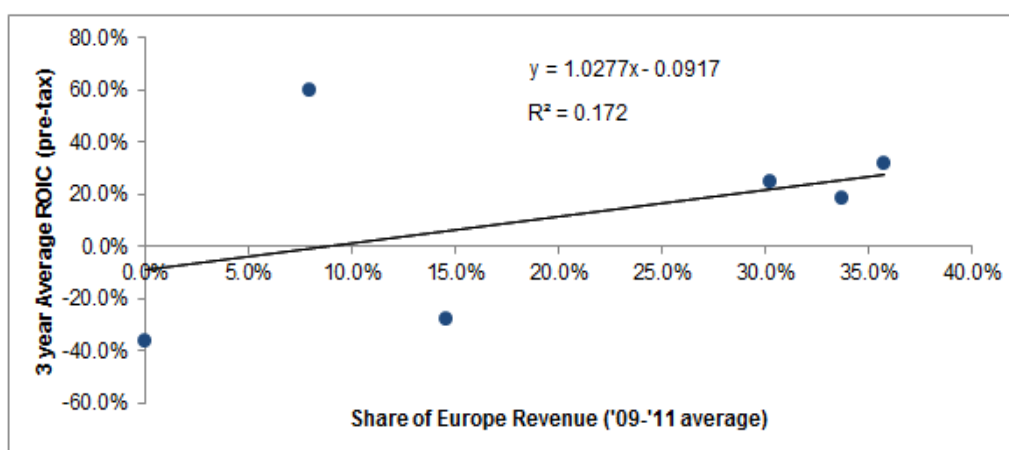


Figure 33: Relationship between 3-year Europe Revenue to 3-year average return on invested capital - Biotechnology Companies

Building on the preceding interim explanation, a similar observation was made in the Figure 33 that plotted the relationship of the share of revenue generated in Europe with the ROIC. One could deduce that the directionally, the higher the share of the revenue of a biotechnology company, the higher ROIC could be expected, though the R is relatively small (0.1720).

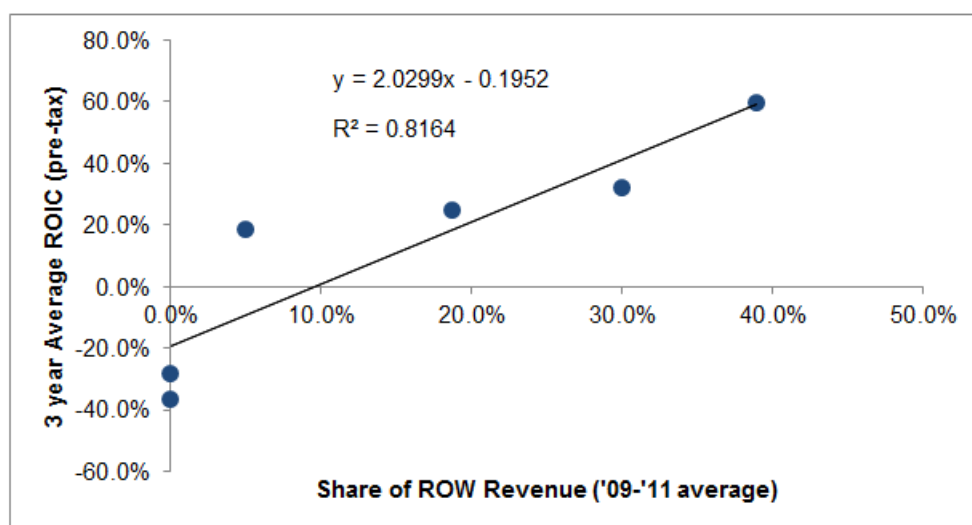


Figure 34: Relationship between 3-year Emerging Market/Rest of the World Revenue to 3-year average return on invested capital - Biotechnology Companies

Finally, the relationship of the share of revenue generated in the rest of the world including the markets labeled as emerging markets was shown in Figure 34. This correlation factor was found to be significant in the statistical analysis conducted and provided in Appendix 7.

One might conclude that biotechnology companies with revenues generated in these emerging geographies generated higher ROIC, rewarding the diversified business model over one that was more highly concentrated in the United States.

Table 12: Summary of Correlation co-efficients for 3-year total average revenue by geography when compared to 3-year total return on invested capital of selected biopharmaceutical company peer set

<i>(2009-11 Average)</i>	Biotechnology Companies
	vs. ROIC (R^2 Values)
Total Revenue	0.1672
US Revenue	0.7030
EU Revenue	0.1720
ROW Revenue	0.8164

In summary, the take-away from the section examining the relationship between ROIC and source of revenue by geography could be that the ROIC typically correlated to a large revenue size, especially when generated outside of the United States. It could imply that the diversification in geographic source of revenue tended to have a positive impact on the profitability as measured by ROIC.

In this period, the projected investment risk tied to ongoing and impending patent exclusivity losses as well as lack of R&D productivity leaving a gap in the pipeline, overshadowed the premium paid for the worldwide revenue growth. While, in this period, there is a strong emphasis in expansion into the emerging markets by the pharmaceutical C-suite in communicating their strategy to the investor community, the investors continued to reward company management based on their US sales performance.

The earnings booked in the United States are considered high quality revenues. The period examined is concurrent with the reforms in the European Union countries where the governments had been curbing their healthcare spending in order to help balance their budgets under duress. This presented a major downward adjustment of pharmaceutical pricing leading to lower profitability due to increased pressures for coverage and reimbursement of therapeutic entities. Consequently, the lack of correlation with the European Union revenue may be explained by the lowered profitability of that revenue stream provides. The earnings in the Emerging Markets –in the least- did not lead to value dilution. Growth in BRIC-T markets in the period helped mitigate the lower profitability leading to

Since biotechnology companies typically introduce their first and follow-on pipeline products first in the United States, the commercial and therapeutic class risks are mitigated early on, at which point the investors observe and consequently reward the performance. As discussed earlier, the biotechnology companies are deriving their revenues predominantly from the developed countries and especially the United States. Since the share of the revenue contribution coming from the Emerging Markets is relatively small the investor community did not show a particular interest in the performance of biotechnology companies in the Emerging Markets.

Another perspective to keep in mind is that the biotechnology companies may - and do- engage in licensing agreements with the established pharmaceutical companies that would allow the pharmaceutical company to carry their products in the emerging markets, an strategic decision that would keep the biotechnology companies' management focus on R&D and the United States commercial arena, rather than dealing with the diverse landscape of the Emerging Markets fraught with variety of regulatory and policy challenges.

The strategic importance of generating revenue in the Emerging Markets is more critical for the biotechnology company set for profitability purposes than the pharmaceutical company set in the period investigated. The perspective offered above regarding the biotechnology companies outlicensing their revenue to other companies in the Emerging Markets could also play a role in this observation since the biotechnology company will recognize only the license fee under other income without the operational expenses and investment in building infrastructure. This could explain the high ROIC as shown in the above analysis.

During the literature search an abundance of publication and articles concerning the pharmaceutical business in industry journals were encountered but only a handful of articles in peer review academic journals ranging over 10 years. Since the field is moving so rapidly, and the industry is in a stage of unprecedented transformation, one believes that this thesis will uniquely bridge the knowledge base gap between the academic literature and industry.

While the shareholder value generation has been looked at in the context of mergers and acquisitions in the pharmaceutical industry, exploring the role in shareholder value generation in regards to emerging markets expansion strategies has not been studied. (Fishman, 2007, Grewal, 2008; MacDonald 2010; Skrepnek 2002)

The emphasis on mergers and acquisitions in the period from 90s through 2005 can be explained by the phase the industry had gone through with several major friendly mergers and hostile takeovers such as Glaxo SmithKline, Pfizer/Warner

Lambert, Pfizer/Pharmacia, Pfizer/Wyeth, Merck/Schering Plough, etc. (Malik, 2009; Ornaghi, 2009)

Since the emerging markets rose as one of the key growth areas that every single major pharmaceutical company is pursuing, emphasis on the combination of emerging markets, pharmaceutical industry and strategies to succeed for pharmaceutical companies will elucidate some of the current operating practices in an academic framework.

For both pharmaceutical and biotechnology companies, as summarized in Table 13 the only variable that showed a positive correlate to TRS was revenue recognized in the United States.

A neutral effect was observed for the sales in Europe for biotechnology companies. All other variables showed a negative effect on total shareholder value.

Table 13: Summary of total return to shareholders by geography by pharmaceutical and biotechnology company peer sets

Total Return to Shareholders	Pharmaceutical	Biotechnology
Overall Revenue	-	-
US Revenue	+	+
Europe Revenue	-	0
ROW/EM Revenue	-	-

As regards to the ROIC, biotechnology companies showed a better relationship overall, as summarized in Table 14 below.

Based on this analysis with a limited scope, one could argue that biotechnology companies had better capital appreciation opportunities to expand overseas which would demonstrate a higher positive correlation with the ROIC.

Table 14: Summary of return on invested capital by geography by pharmaceutical and biotechnology company peer sets

Return on Invested Capital	Pharmaceutical	Biotechnology
Overall Revenue	-	+
US Revenue	+	-
Europe Revenue	-	+
ROW/EM Revenue	0/+	+

In regards to pharmaceutical company peer set, the growth in the United States and to an extent growing into the rest of the world (the portion includes the emerging markets and the BRIC-T) had a favorable correlation effect.

Table 15: Summary of the Overall Analysis of both Pharmaceutical and Biotechnology Company Sets with TRS and ROIC

	Total Return to Shareholder (TRS)			Return on Invested Capital (ROIC)		
Pharmaceutical	A	WW	(-)	B	WW	(-)
		US	(+)		US	(+)
		EU	(-)		EU	(-)
		EM	(-)		EM	(0/+)
Biotechnology	C	WW	(-)	D	WW	(+)
		US	(+)		US*	(-)
		EU	(0)		EU	(+)
		EM	(-)		EM*	(+)

* shows statistical significance using non-parametric Pearson's analysis

A. Pharmaceuticals: Total Return to Shareholder (TRS) vs. Revenue

TRS of the big pharmaceutical company set was negatively correlated to the size of the revenue. However, the revenue recognized in the United States showed a better indication for shareholder value appreciation than the revenue recognized in Europe and the Rest of World including BRIC-T countries.

In this period, the projected investment risk, caused by patent exclusivity losses and low R&D productivity, overshadowed any willingness to reward the industry for global revenue growth. While, in this period, there is a strong emphasis in expansion into the emerging markets by the pharmaceutical C-suite in communicating their strategy to the investor community, the investors continued to disproportionately reward the company stock price according to their US sales performance.

Over the 2009-2011 period, the total return to shareholders of the big pharmaceutical company sample was negatively correlated to the size of the revenue. However, the revenue recognized in the United States showed a better indication for shareholder value appreciation than the revenue recognized in Europe and the Rest of World including BRIC-T countries.

B. Pharmaceuticals: Return on Invested Capital (ROIC) vs. Revenue

Similar to the relationship between the TRS and the revenue, the ROIC of pharma companies also did not show a positive correlation with the pharma company worldwide revenue. Revenue generated in the United States showed a positive and strong contribution towards higher ROIC, however, revenue generated in the European Union countries did not show a similar effect, and were not correlated to higher ROIC numbers. Interestingly, Emerging Market revenues showed a flat to modest performance which was better than the European Union countries. However, they were less favorable than the ROIC to revenue correlation when compared to the similar parameters in the United States pertaining to the ROIC.

The earnings booked in the United States are considered high quality revenues. The period examined is concurrent with the reforms in the European Union countries where the governments had been curbing their healthcare spending in order to help balance their budgets under duress. This presented a major downward adjustment of

pharmaceutical pricing leading to lower profitability due to increased pressures for coverage and reimbursement of therapeutic entities. Consequently, the lack of correlation with the revenue obtained in the European Union may be explained by the lowered profitability of that revenue stream provides. The earnings in the Emerging Markets –in the least- did not lead to value dilution. Growth in BRIC-T markets in the period helped mitigate the lower profitability leading to

C. Biotechnology: Total Return to Shareholder (TRS) vs. Revenue

Over the 2009-2011 period, the TRS of biotech companies showed negative correlation with the size of the revenue. The revenue recognized in the United States and to an extent in Europe showed a better indication for shareholder value appreciation than the revenue recognized in the Rest of World including BRIC-T countries. Biotech companies derive most of their enterprise value from the promise of their pipeline and this hypothesis was confirmed. An interim conclusion in absence of the broader picture enabled by the analysis can be that the shareholder value generation is more appreciated for biotechnology companies in the developed markets than the Emerging Markets.

Since biotechnology companies typically introduce their first and follow-on pipeline products first in the United States, the commercial and therapeutic class risks are mitigated early on, at which point the investors observe and consequently reward the performance. As discussed earlier, the biotechnology companies are deriving their revenues predominantly from the developed countries and especially the United States. Since the share of the revenue contribution coming from the Emerging Markets is relatively small the investor community did not show a particular interest in the performance of biotechnology companies in the Emerging Markets. Another perspective to keep in mind is that the biotechnology companies may -and do- engage in licensing agreements with the established pharmaceutical companies that would allow the pharmaceutical company to carry their products in the Emerging Markets, an strategic decision that would keep the biotechnology companies' management focus on R&D and the United States commercial arena, rather than dealing with the diverse landscape of the Emerging Markets fraught with variety of regulatory and policy challenges.

D. Biotechnology: Return on Invested Capital (ROIC) vs. Revenue

ROIC was generally positively correlated to revenue size, especially when generated outside of the United States including both the European Union and the Emerging Markets. It could imply that the diversification in geographic source of revenue tended to have a positive impact on the profitability as measured by ROIC.

The strategic importance of generating revenue in the Emerging Markets is more critical for the biotechnology company set for profitability purposes than the pharmaceutical company set in the period investigated. The perspective offered above regarding the biotechnology companies outlicensing their revenue to other companies in the Emerging Markets could also play a role in this observation since the biotechnology company will recognize only the license fee under other income without the operational expenses and investment in building infrastructure. This could explain the high ROIC as shown in the above analysis.

3.4. Limitations and Recommendations

The limitations of this thesis and recommendations to potentially address these in future research are addressed below.

The financial analysis considering shareholder value assessment was not a dynamic analysis but an average of a three year time period. The nature of the analysis conducted was observational and retrospective. Size of the sample did not allow use of parametric statistical analysis and non-parametric Pearson's methodology was utilized. Consistent with the volatility of the publicly traded securities of the pharmaceutical, and especially of those representing the biotechnology companies, the analysis did not have a predictive power for the future.

The references rely more on publications that were sourced from professional and industry authors due to paucity of peer-reviewed publications in academic journals about the subject of this study. While this clearly indicates that this thesis would fill a gap in the academic literature, it could also be highlighted as a limitation that future research ought to take into account.

3.4.1. Recommendations for Further Research

Now that the immediate Emerging Market countries had been already reached out by MNCs, there is a new wave of emerging markets comprising of Indonesia, Malaysia and several sub-Saharan African countries such as South Africa and Nigeria. Starting in 2020 and beyond these countries could be expected to become the new destinations and strategic emphasis of global pharmaceutical and biotechnology companies.

All of these countries already attract some limited amount of foreign direct investment and will over time become the new emerging markets as the current BRIC countries mature. This maturation could be expected to go in sync with their political democratization process.

Finally, through the mergers and acquisitions mentioned in the earlier section, the pharmaceutical companies started marketing a significant amount of biologics products which would over time challenge the repeatability of this study since the two peers sets would converge in their characteristics. Therefore, a follow on study might want to also test the behavior of the combined peer set.

CONCLUSIONS

The qualitative and quantitative analyses conducted herein investigated the topic what success factors exist for biopharmaceutical companies in expanding in the emerging markets including BRIC-T, and how this expansion related to these companies abilities to generate shareholder value and ROIC in the period from 2009 through 2011.

The qualitative assessment based on a robust literature analysis deriving content from both academic and industry publications revealed seven success factors listed below and explained in sections from 3.2.1 through 3.2.7.:

1. Local Manufacturing Presence
2. Building Agile Regulatory Affairs Capabilities
3. Commercial Model Addressing Emerging Market Needs
4. Broad and Efficient Distribution Network
5. Dynamic Pricing and Contracting Capabilities
6. Emerging Market Medical Affairs Capabilities Connecting Local Thought Leaders to Global Clinical Development Leaders
7. Access to and Retention of Local Talent

These findings were also put in the context of how the shareholder value was generated and ROIC had performed.

A. Pharmaceuticals: TRS vs. Revenue

TRS of the big pharmaceutical company set was negatively correlated to the size of the revenue. However, the revenue recognized in the United States showed a better indication for shareholder value appreciation than the revenue recognized in Europe and the Rest of World including BRIC-T countries.

B. Pharmaceuticals: ROIC vs. Revenue

Similar to the relationship between the TRS and the revenue, the ROIC of pharma companies also did not show a positive correlation with the pharma company

worldwide revenue. Revenue generated in the United States showed a positive and strong contribution towards higher ROIC, however, revenue generated in the European Union countries did not show a similar effect, and were not correlated to higher ROIC numbers. Interestingly, Emerging Market revenues showed a flat to modest performance which was better than the European Union countries. However, they were less favorable than the ROIC to revenue correlation when compared to the similar parameters in the United States pertaining to the ROIC.

C. Biotechnology: TRS vs. Revenue

The TRS of biotech companies showed negative correlation with the size of the revenue. The revenue recognized in the United States and to an extent in Europe showed a better indication for shareholder value appreciation than the revenue recognized in the Rest of World including BRIC-T countries. Biotech companies derive most of their enterprise value from the promise of their pipeline and this hypothesis was confirmed. An interim conclusion in absence of the broader picture enabled by the analysis can be that the shareholder value generation is more appreciated for biotechnology companies in the developed markets than the Emerging Markets.

D. Biotechnology: ROIC vs. Revenue

ROIC was generally positively correlated to revenue size, especially when generated outside of the United States including both the European Union and the Emerging Markets. It could imply that the diversification in geographic source of revenue tended to have a positive impact on the profitability as measured by ROIC.

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APPENDIX

Appendix 1. Economic and Business Characteristics of Countries

Total Population millions)*	Urban Population*	GDP Growth*	GDP Cap
313.85	82%	1.7%	\$
81.31	74%	3.1%	\$
63.05	80%	0.7%	\$
65.63	85%	1.7%	\$
127.37	67%	-0.7%	\$
47.04	77%	0.7%	\$
61.26	68%	0.4%	\$
138.08	73%	4.3%	\$
79.75	70%	8.5%	\$
205.72	87%	2.7%	\$
1,343.24	47%	9.2%	\$
1,205.07	30%	7.2%	\$

* World Factbook 2012

transparency International - 2011 Corruption Perception

Appendix 2. Life Expectancy and Healthcare Spending Comparison of Countries

Country Name	Life Expectancy at Birth (2009)	Healthcare Spend as Percentage of GDP (2009)
Brazil	72.76	9.05
China	73.06	4.57
France	81.07	11.72
Germany	79.84	11.33
India	64.78	4.17
Italy	81.44	9.51
Mexico	76.47	6.47
Russian Federation	68.60	5.44
Spain	81.48	9.69
Turkey	73.42	6.74
United Kingdom	80.05	9.34
United States	78.09	16.21
Indonesia	68.47	2.36
Japan	82.93	8.35
South Africa	51.61	8.51
Australia	81.54	8.51

(World Bank, OECD, 2011)

Appendix3. Healthcare Characteristics and Pharmaceutical Spend Comparison

Total Healthcare Expenditure per Capita (\$USD)**	Healthcare Expenditure as % of GDP**	Total Pharmaceutical Expenditure (\$USD, billions)***
\$ 990	9.0%	\$ 29.9
\$ 221	5.1%	\$ 66.7
\$ 4,691	11.9%	\$ 41.3
\$ 4,668	11.6%	\$ 45.0
\$ 54	4.1%	\$ 14.3
\$ 3,248	9.5%	\$ 28.6
\$ 4,065	9.5%	\$ 111.2
\$ 525	5.1%	\$ 15.7
\$ 2,883	9.5%	\$ 22.7
\$ 678	6.7%	\$ 12.0
\$ 3,503	9.6%	\$ 21.5
\$ 8,362	17.9%	\$ 322.0

book 2012

- The Global Use of Medicines: Outlook Through 2016 (Appendix

Appendix 4.Shareholder Value Analysis Data for Pharmaceutical and Biotechnology Companies

Revenue by Geographic Location for Pharmaceutical and Biotechnology Companies(in alphabetical order)

Break up of Revenues	2009	2010	2011
Amgen			
US	11,421	11,636	11,985
International	3,221	3,417	3,597
Sum	14,642	15,053	15,582

Break up of Revenues	2009	2010	2011
AZ			
US	14,777	13,727	13,426
Western Europe	9,252	9,168	8,501
Canada	1,203	1,510	1,604
Japan	2,367	2,617	3,064
Other Established ROW	853	1,049	1,233
Established ROW	4,423	5,176	5,901
Emerging Europe	1,091	1,165	1,244
China	811	1,047	1,261
Emerging Asia Pacific	780	890	968
Other Emerging ROW	1,670	2,096	2,290
Emerging Markets	4,352	5,198	5,763
Sum	32,804	33,269	33,591

Break up of Revenues	2009	2010	2011
Biogen			
US	1,638.00	1,744.40	1,954.80
Europe	913.7	1,090.70	1,163.30
Germany	374.8	362.4	377.5
Asia	47.9	69	88.7
Other	178.5	203.6	251.8
Sum	3,152.90	3,470.10	3,836.10

Break up of Revenues	2009	2010	2011
BMS			
United States	11,867	12,613	13,845
Europe	3,625	3,448	3,667
Japan, Asia Pacific and Canada	1,522	1,651	1,862
Latin America, Middle East and Africa	843	856	894
Emerging Markets	753	804	887
Other	198	112	89
Sum	18,808	19,484	21,244

Break up of Revenues	2009	2010	2011
Celgene			
Other	50	170	410
Europe	908	1,267	1,571
US	1,732	2,189	2,861
Sum	2,690	3,626	4,842

Break up of Revenues	2009	2010	2011
Gilead			
US	3,599	4,224	4,608
Dev Europe	2	3	3
Rest Europe	603	665	579
Other	432	555	652
Total non US	3,412	3,725	3,777
Sum	7,011	7,949	8,385

Break up of Revenues	2009	2010	2011
GSK			
USA	10,315	9,345	8,687
Europe	9,696	9,091	8,271
Emerging	4,078	5,023	5,323
Asia Pacific	1,418	1,614	1,793
Japan	1,418	2,155	2,318
Other	1,079	1,164	995
Sum	28,004	28,392	27,387

Break up of Revenues	2009	2010	2011
Merck			
United States	14,401	20,226	20,495
Europe, Middle East and Africa	7,326	13,497	13,782
Japan	2,452	3,768	4,835
Other	3,249	8,496	8,935
Sum	27,428	45,987	48,047

Break up of Revenues	2009	2010	2011
Novartis			
Switzerland	604	608	726
United States	14,254	16,893	19,225
Germany	4,035	3,999	4,362
Japan	3,545	4,288	5,281
France	2,355	2,460	2,848
Other	19,474	22,376	26,124
Sum	44,267	50,624	58,566

Break up of Revenues	2009	2010	2011
Pfizer			
United States	21,540	28,855	26,933
Developed Europe	12,586	16,345	16,297
Developed Rest of World	8,097	10,008	11,091
Emerging Markets	7,046	11,849	13,104
Sum	49,269	67,057	67,425

Break up of Revenues	2009	2010	2011
Roche/Genentech			
Switzerland	499	464	507
European Union	16,219	14,596	12,815
– of which Germany	3,320	2,970	2,595
Rest of Europe	1,568	1,630	1,486
Europe	18,286	16,690	14,808
United States	17,208	16,446	14,133
Rest of North America	948	1,051	1,047
Latin America	2,940	3,397	3,115
Japan	5,036	4,718	4,314
Rest of Asia	3,166	3,591	3,616
Africa, Australia and Oceania	1,467	1,580	1,498
Sum	49,051	47,473	42,531

Break up of Revenues	2009	2010	2011
Sanofi			
Western Europe	9,793	8,997	9,130
US	9,426	8,968	9,957
Emerging	7,356	9,075	10,133
– of which E. Europe	2,266	2,612	2,666
Other	2,731	3,344	4,169
–of which Japan	1,844	2,225	2,865
Sum	29,306	30,384	33,389

Appendix 5. Return on Invested Capital from 2009-11 for Pharmaceutical and Biotechnology Companies

Company Name	2009	2010	2011	ROIC (2009-11 Avg)
Celgene	16.4%	17.0%	22.0%	18.5%
Amgen	13.6%	16.2%	17.5%	15.8%
AZ	34.6%	37.6%	32.1%	34.8%
Biogen	28.8%	25.3%	20.2%	24.8%
BMS	35.0%	30.3%	25.2%	30.1%
Gilead	36.5%	67.6%	75.3%	59.8%
GSK	34.9%	35.7%	33.0%	34.5%
Merck	13.5%	8.7%	8.6%	10.3%
Novartis	14.5%	17.0%	16.6%	16.0%
Pfizer	14.5%	14.0%	14.9%	14.5%
Regeneron	-42.6%	-25.1%	-16.8%	-28.2%
Roche	35.1%	32.9%	28.2%	32.1%
Sanofi	10.7%	10.1%	13.0%	11.3%
Vertex	18.0%	-60.5%	-66.3%	-36.3%

Appendix 6. Summary of Return on Invested Capital Values by Segment

Segment	Biotech	Pharma
ROIC Avg	15%	23%

Appendix 7. Statistical Tables

WWR & TRS Pharma

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,429
		Sig. (2-tailed)	.	,176
		N	7	7
	TRS	Correlation Coefficient	-,429	1,000
		Sig. (2-tailed)	,176	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,500
		Sig. (2-tailed)	.	,253
		N	7	7
	TRS	Correlation Coefficient	-,500	1,000
		Sig. (2-tailed)	,253	.
		N	7	7

USR & TRS Pharma

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,429
		Sig. (2-tailed)	.	,176
		N	7	7
	TRS	Correlation Coefficient	,429	1,000
		Sig. (2-tailed)	,176	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,429
		Sig. (2-tailed)	.	,337
		N	7	7
	TRS	Correlation Coefficient	,429	1,000
		Sig. (2-tailed)	,337	.
		N	7	7

EUR & TRS Pharma

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,429
		Sig. (2-tailed)	.	,176
		N	7	7
	TRS	Correlation Coefficient	-,429	1,000
		Sig. (2-tailed)	,176	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,571
		Sig. (2-tailed)	.	,180
		N	7	7
	TRS	Correlation Coefficient	-,571	1,000
		Sig. (2-tailed)	,180	.
		N	7	7

ROW & TRS Pharma

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,429
		Sig. (2-tailed)	.	,176
		N	7	7
	TRS	Correlation Coefficient	-,429	1,000
		Sig. (2-tailed)	,176	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,571
		Sig. (2-tailed)	.	,180
		N	7	7
	TRS	Correlation Coefficient	-,571	1,000
		Sig. (2-tailed)	,180	.
		N	7	7

WWR & ROIC Pharma

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,200
		Sig. (2-tailed)		,624
		N	7	7
	ROIC	Correlation Coefficient	-,200	1,000
		Sig. (2-tailed)	,624	
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,300
		Sig. (2-tailed)		,624
		N	7	7
	ROIC	Correlation Coefficient	-,300	1,000
		Sig. (2-tailed)	,624	
		N	7	7

USR & ROIC Pharma

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,048
		Sig. (2-tailed)		,881
		N	7	7
	ROIC	Correlation Coefficient	,048	1,000
		Sig. (2-tailed)	,881	
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,000
		Sig. (2-tailed)		1,000
		N	7	7
	ROIC	Correlation Coefficient	,000	1,000
		Sig. (2-tailed)	1,000	
		N	7	7

EUR & ROIC Pharma

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,048
		Sig. (2-tailed)	.	,881
		N	7	7
	ROIC	Correlation Coefficient	-,048	1,000
		Sig. (2-tailed)	,881	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,000
		Sig. (2-tailed)	.	1,000
		N	7	7
	ROIC	Correlation Coefficient	,000	1,000
		Sig. (2-tailed)	1,000	.
		N	7	7

ROW & ROIC Pharma

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,143
		Sig. (2-tailed)	.	,652
		N	7	7
	ROIC	Correlation Coefficient	,143	1,000
		Sig. (2-tailed)	,652	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,214
		Sig. (2-tailed)	.	,645
		N	7	7
	ROIC	Correlation Coefficient	,214	1,000
		Sig. (2-tailed)	,645	.
		N	7	7

WWR & TRS Biotech

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,524
		Sig. (2-tailed)	.	,099
		N	7	7
	TRS	Correlation Coefficient	-,524	1,000
		Sig. (2-tailed)	,099	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,643
		Sig. (2-tailed)	.	,119
		N	7	7
	TRS	Correlation Coefficient	-,643	1,000
		Sig. (2-tailed)	,119	.
		N	7	7

USR & TRS Biotech

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,143
		Sig. (2-tailed)	.	,652
		N	7	7
	TRS	Correlation Coefficient	,143	1,000
		Sig. (2-tailed)	,652	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,286
		Sig. (2-tailed)	.	,535
		N	7	7
	TRS	Correlation Coefficient	,286	1,000
		Sig. (2-tailed)	,535	.
		N	7	7

EUR & TRS Biotech

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,000
		Sig. (2-tailed)	.	1,000
		N	7	7
	TRS	Correlation Coefficient	,000	1,000
		Sig. (2-tailed)	1,000	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,126
		Sig. (2-tailed)	.	,788
		N	7	7
	TRS	Correlation Coefficient	,126	1,000
		Sig. (2-tailed)	,788	.
		N	7	7

ROWR & TRS Biotech

			Revenue	TRS
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,411
		Sig. (2-tailed)	.	,210
		N	7	7
	TRS	Correlation Coefficient	-,411	1,000
		Sig. (2-tailed)	,210	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,556
		Sig. (2-tailed)	.	,195
		N	7	7
	TRS	Correlation Coefficient	-,556	1,000
		Sig. (2-tailed)	,195	.
		N	7	7

WWR & ROIC Biotech

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,429
		Sig. (2-tailed)	.	,176
		N	7	7
	ROIC	Correlation Coefficient	,429	1,000
		Sig. (2-tailed)	,176	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,643
		Sig. (2-tailed)	.	,119
		N	7	7
	ROIC	Correlation Coefficient	,643	1,000
		Sig. (2-tailed)	,119	.
		N	7	7

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USR & ROIC Biotech

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	-,810*
		Sig. (2-tailed)		,011
		N	7	7
	ROIC	Correlation Coefficient	-,810*	1,000
		Sig. (2-tailed)	,011	
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	-,893**
		Sig. (2-tailed)		,007
		N	7	7
	ROIC	Correlation Coefficient	-,893**	1,000
		Sig. (2-tailed)	,007	
		N	7	7

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

EUR & ROIC Biotech

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,390
		Sig. (2-tailed)		,224
		N	7	7
	ROIC	Correlation Coefficient	,390	1,000
		Sig. (2-tailed)	,224	
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,505
		Sig. (2-tailed)		,248
		N	7	7
	ROIC	Correlation Coefficient	,505	1,000
		Sig. (2-tailed)	,248	
		N	7	7

ROWR & ROIC Biotech

			Revenue	ROIC
Kendall's tau_b	Revenue	Correlation Coefficient	1,000	,926**
		Sig. (2-tailed)	.	,005
		N	7	7
	ROIC	Correlation Coefficient	,926**	1,000
		Sig. (2-tailed)	,005	.
		N	7	7
Spearman's rho	Revenue	Correlation Coefficient	1,000	,964**
		Sig. (2-tailed)	.	,000
		N	7	7
	ROIC	Correlation Coefficient	,964**	1,000
		Sig. (2-tailed)	,000	.
		N	7	7

** . Correlation is significant at the 0.01 level (2-tailed).