# POLITECNICO DI TORINO

## Corso di Laurea Magistrale in Engineering Management

Tesi di Laurea Magistrale

# Mergers & Acquisitions in Pharma Industry, Evidence from India and Italy



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|---|---|
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# Abstract

Mergers and Acquisitions are the most effective ways of accelerating the growth of companies. Pharmaceutical industries being one of the most dynamic sectors, probably see more merger and acquisition (M&A) activity than any other industry, both in the number of deals and the amount of money spent. No other industry can compare when it comes to M&As; large, game-changing deals continuously and profoundly change the competitive landscape, while smaller yet still significant transactions are an integral part the of operations of pharma companies. Pharma is a very large and complex growing part of the global economy.

This thesis is structured around the world pharma market and the competitive environment we see, India's Pharma market, its exports and Key players, the Italian pharma market and competition, Economic attractiveness of the pharma market in India. The report provides information on the growth of different Therapeutic areas and the market share of the top 10 global pharma players. This Thesis has been carried out in association with Indiogene S.A.S giving a birds-eye view of the Indian Pharma market and possible opportunities for a key Italian player.

Even though Italy is among the top 5 pharmaceutical manufacturers in Europe and one among the largest exporter of pharma products in Europe, we see a very few Italian pharma companies having their presence in India, compared with the other western pharma companies. And is also one among the largest exporter of pharma products in Europe. The findings of the research done, includes the consolidation of emerging pharma markets in the world, the trend in the growth of different therapy areas, the fastest growing diseases in the world, urging the world pharma markets to act promptly to mitigate them, the trend in the growth of generic sales and the important deals in M&A in world pharma leading to its fast growth. With respect to the potential of India's market for M&A's, the thesis gives an overview of the synergy that can be achieved owing to India's low-cost labour maximizing the returns and its fast-growing economy facilitating the pharma market growth. And of course, the challenges the M&A's must overcome in order to be successful.

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# List of Abbreviations

| | |
|---|---|
| ANDA | Abbreviated New Drug Application (USA) |
| CAD | coronary artery disease |
| CAGR | Compound annual growth rate |
| CMO | Contract manufacturing organization |
| CNS | Central nervous system |
| CRO | contract research organization |
| CV | Cardiovascular |
| EBITDA | Earnings Before Interest, Tax, Depreciation and Amortization |
| EEA | European Economic Area |
| EMA | European Medicines Agency |
| EU | Endotoxin Unit or European Union |
| FBS | fasting blood sugar |
| FDA | Food and Drug Administration |

| FFP | fresh frozen plasma |
|-----|---------------------|
| FIP | Fédération Internationale Pharmaceutique |
| GI | Gastrointestinal |
| IBEF | Indian Brand Equity Foundation |
| IFPMA | International Federation of Pharmaceutical Manufacturers Associations |
| IPI | Indian Pharmaceutical Industry |
| ISO | International Standards Organization |
| IT | Information Technology |
| M&A | Mergers and acquisitions |
| MNC | Multi National Company |
| NAFTA | North American Free Trade Agreement |
| NDA | New Drug Application (USA) |
| NPPA | National Pharmaceutical Pricing Authority |
| OTC | Over the counter medicine |

| | |
|---|---|
| PMA | Pharmaceutical Manufacturers Association |
| R&D | Research and Development |
| TA | Therapeautic Area |
| UNICEF | United Nations International Children's Emergency Fund |
| UTI | urinary tract infection |
| WBC | white blood cell |
| WHO | World Health Organization |
| WTO | World Trade Organization |
| WW | World Wide |
| YOY | Year On Year |

# CHAPTER 1: Brief Introduction of the current situation of the World Pharma market

Growth in the pharmaceutical industry will be driven by increasing wealth across the world. According to a study conducted by Torreya, the pharmaceutical industry is likely to triple in size by 2060 on an inflation-adjusted basis. Major innovations will continue to drive the size and growth of the industry with positive implications for the health of the global population. Healthcare spending in the US has gone up faster than GDP over the last 90 Years. (Torreya, October 2017)

The global pharma market was US 726 Bn $ in 2007 and grew with a CAGR of 7.2% to 1324 Bn $ in 2018E (Constant US$ growth). The world pharmaceutical market has a continuous growth, even if, in 2010, the year-on-year grow rate has declined. On a geographic basis, the world pharmaceutical market was worth an estimated 754,555 million € (852,647 million $) at ex-factory prices in 2017. The North American market (USA & Canada) remained the world's largest market with a 48.1% share, well ahead of Europe and Japan. The European market is the second largest with a 22% of the world pharma market. The Pharma market in Asia, Africa & Australia is 17% of the global pharma market and is expected to double in coming years, supported by the growth in GDP of the developing countries like India and China. The pharmaceutical market in Japan is 8% of the global market.
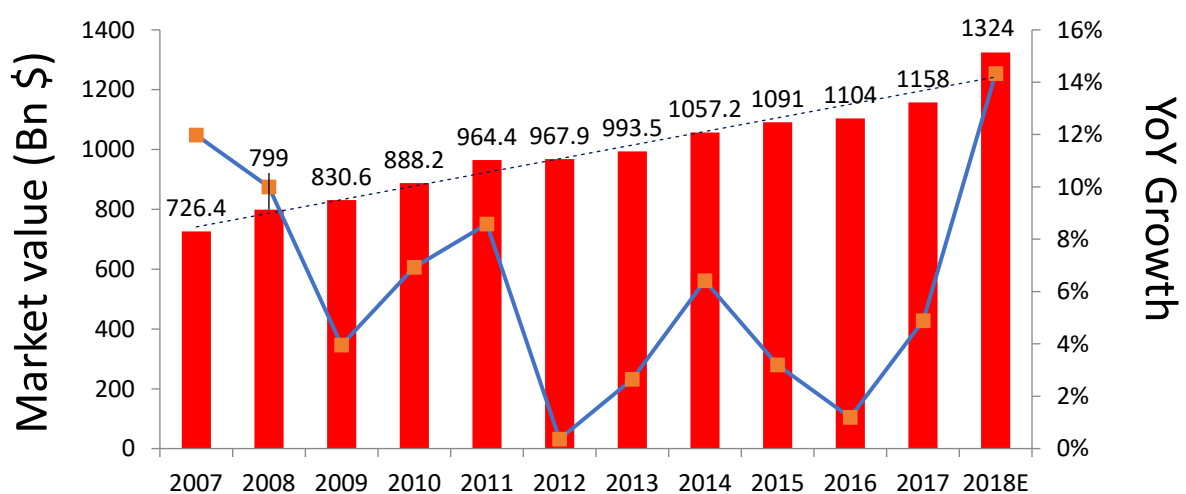


*Figure 1: Global Pharma market value from 2007 to 2018E (Bn $)*

*Source: Compiled from data of reports IMS Health, IQVIA May 2018*
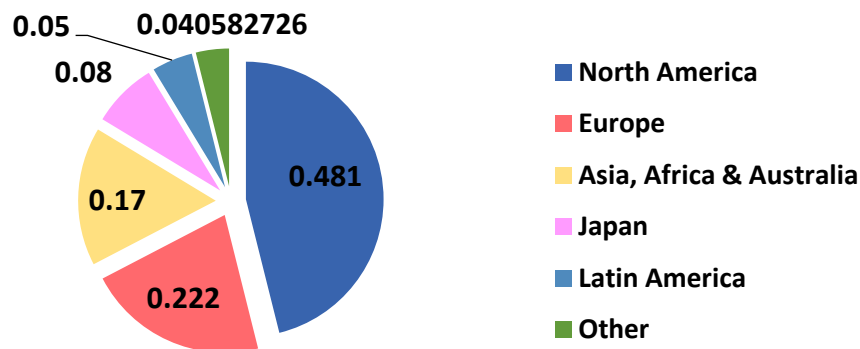
*Figure 2: Global pharma market by region 2018 (%)*

*Source: Compiled from data of reports IMS Health, IQVIA May 2018*

## 1.1 Key drivers for the growth of Pharma Industry

The factors that affect the pharmaceutical market size include disease prevalence, drug affordability, consumer attitudes, government policies and some supply-side factors:

- **Disease prevalence** is related to population size, age, genetic inheritance and behaviour (infectious disease incidence is lower where sanitation practices are better; sedentary lifestyles also encourage chronic disease)
- **Affordability** is related to income but also to drug prices
- **Consumer attitudes** include willingness to use alternative therapies or distrust of taking drugs
- **Government (and insurance company) policies** affect reimbursement and who the payer is. Other government policies determine regulation, which can be a significant barrier to the launch of new treatments
- **A major supply-side factor** is availability of an appropriate treatment, which may be a matter of quantity, as in an epidemic, or of drug discovery and development

According to a study conducted by WHO (World Health Organization) in 2018 of the 56.9 million deaths worldwide in 2016, more than half (54%) were due to the top 10 causes. Ischaemic heart disease and stroke are the world's biggest killers, accounting for a combined

15.2 million deaths in 2016. These diseases have remained the leading causes of death globally in the last 15 years, Chronic obstructive pulmonary disease claimed 3.0 million lives in 2016, while lung cancer (along with trachea and bronchus cancers) caused 1.7 million deaths. Diabetes killed 1.6 million people in 2016, up from less than 1 million in 2000. Deaths due to dementias more than doubled between 2000 and 2016, making it the 5th leading cause of global deaths in 2016 compared to 14th in 2000, Lower respiratory infections remained the deadliest communicable disease, causing 3.0 million deaths worldwide in 2016. The death rates from diarrheal diseases decreased by almost 1 million between 2000 and 2016, but still caused 1.4 million deaths in 2016. Similarly, the number of tuberculosis deaths decreased during the same period but is still among the top 10 causes with a death toll of 1.3 million. HIV/AIDS is no longer among the world's top 10 causes of death, having killed 1.0 million people in 2016 compared with 1.5 million in 2000, Road injuries killed 1.4 million people in 2016, about three-quarters (74%) of whom were men and boys (The top 10 causes of death, 2018).

| Rank / Year | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 2000 | Coronary heart disease | Stroke | Lower respiratory infections | Chronic obstructive pulmonary disease | Diarrheal diseases | Tuberculosis | HIV/AIDS | Preterm birth complications | Trachea, bronchus, lung cancers | Road injury |
| 2010 | Coronary heart disease | Stroke | Lower respiratory infections | Chronic obstructive pulmonary disease | Diarrheal diseases | Trachea, bronchus, lung cancers | HIV/AIDS | Alzheimer disease and other dementias | Tuberculosis | Diabetes mellitus |
| 2015 | Coronary heart disease | Stroke | Chronic obstructive pulmonary disease | Lower respiratory infections | Alzheimer disease and other dementias | Trachea, bronchus, lung cancers | Diabetes mellitus | Diarrheal diseases | Road injury | Tuberculosis |
| 2016 | Coronary heart disease | Stroke | Chronic obstructive pulmonary disease | Lower respiratory infections | Alzheimer disease and other dementias | Trachea, bronchus, lung cancers | Diabetes mellitus | Road injury | Diarrheal diseases | Tuberculosis |

*Table 1: Evolution of top causes of death worldwide from 2000-2016*

*Source: Compiled from database of WHO(World Health Organization)*

- WHO finds Coronary artery disease is the top cause for most of the deaths in the world around 9.5 Mn deaths occurred in 2016 alone.

- Stroke comes second with 6Mn recorded deaths in 2016

- Deaths due to dementias more than doubled between 2000 and 2016, making it the 5th leading cause of global deaths in 2016 compared to 14th in 2000

- According to our findings Diabetes Mellitus is also rapidly increasing from below top 10 in 2000 to 5th Rank in 2016 with 1.6 Mn deaths recorded in 2016 due to Diabetes

## 1.2 Forecasts for the growth of therapeutic areas in the coming years

According to a study conducted by evaluate pharma in 2017 based on company reported data. Sales forecasts to 2024 based on a consensus of equity analysts' estimates (Anees Malik, 2018):

- Evaluate pharma finds oncology will be the dominant therapy segment in 2024 with sales reaching 233 Bn $ in 2024 and an expected CAGR of 12.2% per year

- Anti-diabetics is forecast to remain the second biggest therapy area with sales of 60 Bn $ in 2024

- The anti-rheumatic therapy area fills out the top three, with estimated 56.7 Bn $ in 2024

- The antivirals therapy space is set to see the largest decline in 2024 with a negative 0.9% CAGR. The therapy area showing the largest CAGR through 2024 is immunosuppressants with an estimated 15.7% CAGR from 2017-2024.
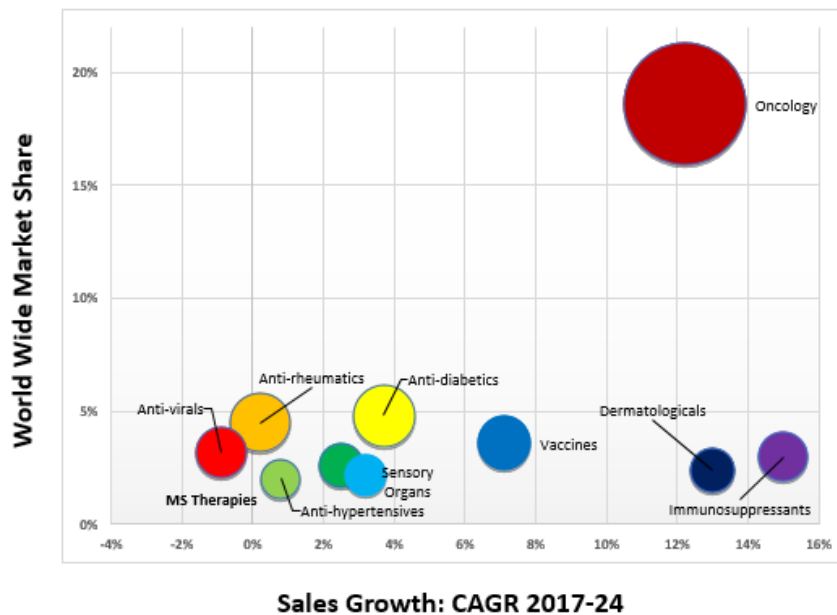
*Figure 3: Top 10 therapy areas in 2024, Market share and sales growth*

*Source: Compiled from reports of "Evaluate Pharma World Preview 2018"*

## 1.3 Worldwide growth of Prescription drug sales

Prescription drug sales CAGR for 2018 through 2024 six times that in 2011 through 2017; Orphan drug market to almost double. While prescription drug sales for 2011 through 2017 grew at a CAGR of only +1.2%, an annual CAGR of +6.4% is forecast for 2018 through 2024, with prescription drug sales expected to reach 1.2 trillion $. Growth will be driven by the continued uptake and anticipated launch of novel therapies addressing key unmet needs, as well as increasing access to medicines globally. Payer scrutiny and sales losses from genericization and biosimilar competition will act as brakes on growth. The orphan drugs sector is expected to outperform the market, almost doubling in size over 2018-2024 and peaking at 262 Bn $ in 2024, accounting for approximately 20% of prescription sales. This highlights the industry's continued move to address small groups of neglected patients with high unmet need and to benefit from traditionally reduced payer scrutiny on orphan drugs, as well as regulatory and financial incentives. Gene and cell therapies will also increasingly contribute to growth, building on the approval and launch of CAR-T therapies in 2017 and the launch of Luxturna (Spark Therapeutics), the first FDA approved gene therapy for vision loss, in 2018. However, recent industry set-backs in the immuno-oncology space with Incyte's Epacadosat failing to make a case for combination immunotherapy highlights the inherent

risk of developing novel therapies and are indicative of why diversity across the industry is healthy. Drug affordability and accessibility continue to apply downward pressure on the market with payers, including those in the USA, acting to limit prescribing options to drugs which provide enough real-world value. A continued trend will be the industry's response to this pressure in ensuring the development of value-based pricing and reimbursement approaches that de-risk healthcare budgets and clinical programs that reflect the demands of payers (e.g. outcomes data). There are also 251 Bn $ of sales at risk between 2018 and 2024, with more than 25% of these in 2023, when key patents of several biologics including Humira and Stelara will expire. However, both are still forecast to retain spots among the World's top 10 selling drugs in 2024 (Anees Malik, 2018).
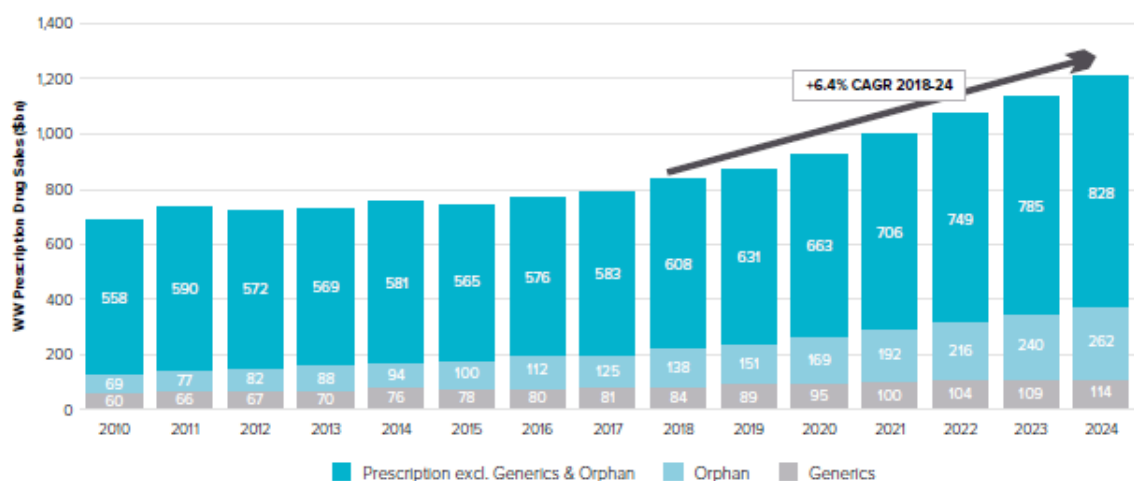


*Figure 4: Worldwide prescription drug sales (2010-2024)*

*Source: Taken from "Evaluate Pharma World Preview 2018"*

## 1.4 Worldwide market share of top 10 companies for global prescription drug sales

Top 10 companies covered 41% of the global market for prescription drugs in 2017 vs 35% in 2024; midsize innovative companies continue to make their way up the global revenue ladder. Global prescription drugs market in 2017 was about 789 Bn $(constant USD), and is estimated to go up to 1204 Bn $(CAGR +6%) following Evaluate pharma analysis (Anees Malik, 2018).

- In 2017 the Top 10 companies:
    - Pfizer was market leader with 5.8% (45.4Bn $) of total sales

6

- Novartis & Roche followed with 5.3% each of the total sales
- Johnson & Johnson had a market share of 4.4 %
- Top 10 companies covered 41% of the market

- In 2024 the top 10 companies
  - Novartis is predicted to replace Pfizer as the market leader with 4.4% (53.2Bn $) of total sales
  - Pfizer is predicted to be second with a 4.3% of the market share
  - Roche is estimated to be third largest company with a market share of 4.2 %
  - Top 10 companies are estimated to covered 35% of the market
- According to the evaluate pharma study amongst the top 20, Celgene has the highest CAGR, the company is expected to go from 21st in 2017 to 13th in 2024 based on revenue expansion in oncology and immunology
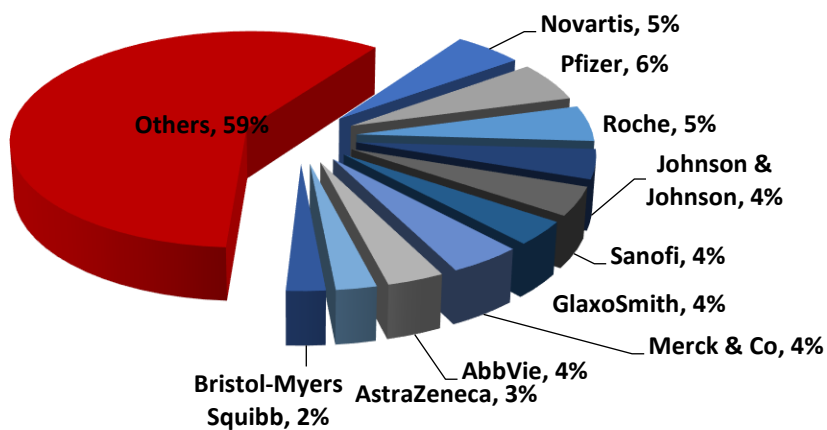


*Figure 5: Market share in the prescription drugs sales 2017 (%)*

*Source: Compiled from reports of "Evaluate Pharma World Preview 2018"*
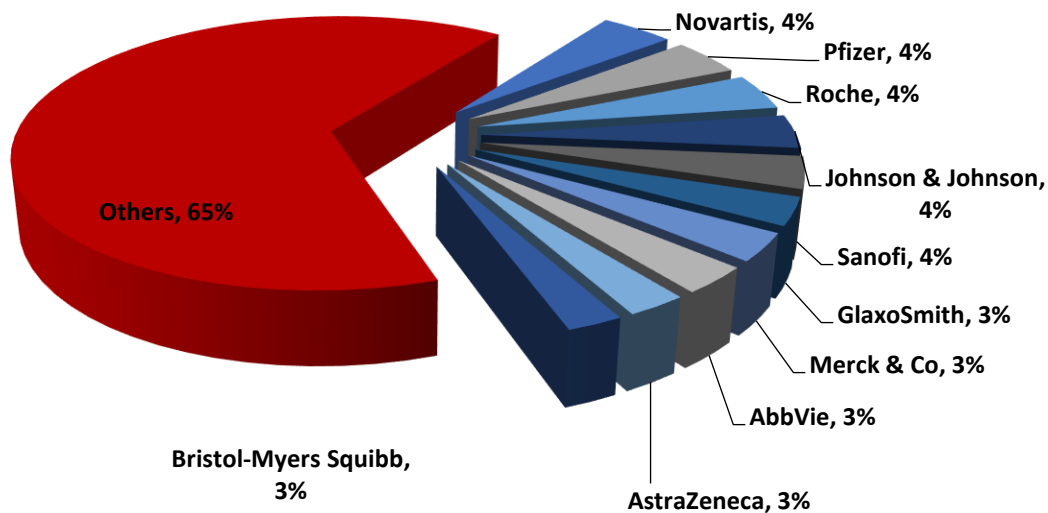
*Figure 6: Market share in the prescription drugs sales 2024F (%)*

*Source: Compiled from reports of "Evaluate Pharma World Preview 2018"*

## 1.5 Categorizing worldwide market share of global prescription drug sales based on Geography

### 1.5.1 Considering top 15 firms based on revenues

Pfizer is market leader with 6% of M/S. Top 15 companies cover 54% of the global market; 8 firms within the Top 15 come from USA. Global Prescription pharma market in 2017 was about 789 Bn $ (constant USD), following Evaluate Pharma analysis.

Within the Top 15 companies:

- Pfizer is market leader with 5.8% of sales
- Novartis and Roche follow with 5.3% each of market share
- J&J has 4.4%, Sanofi has 4.3%
- Glaxo smith, AbbVie and Gilead with 3.6%,3.5%and 3.3% respectively.
- Top 15 companies cover 54% of the market

Analysing revenues of these 15 top players by nationality:

- 8 of the top 15 firms are US, representing 53% of total 15's sales
- Switzerland and UK have each 2 top players within the top 15, covering respectively 17% and 15% of sales
- France, Denmark and Germany have 1 player each, with 7% of revenues

As we can infer from the data there is neither Italian nor Indian companies in the top 15 even though India has 3rd largest drugs production by volume and 13th by volume, and the Italian pharmaceutical industry is second in Europe for production volume (both in absolute and per capita terms), and Italy also Exports a major chunk of the pharmaceutical produce. Among foreign-owned companies in Italy, pharma ranks top for investments and export overall value.
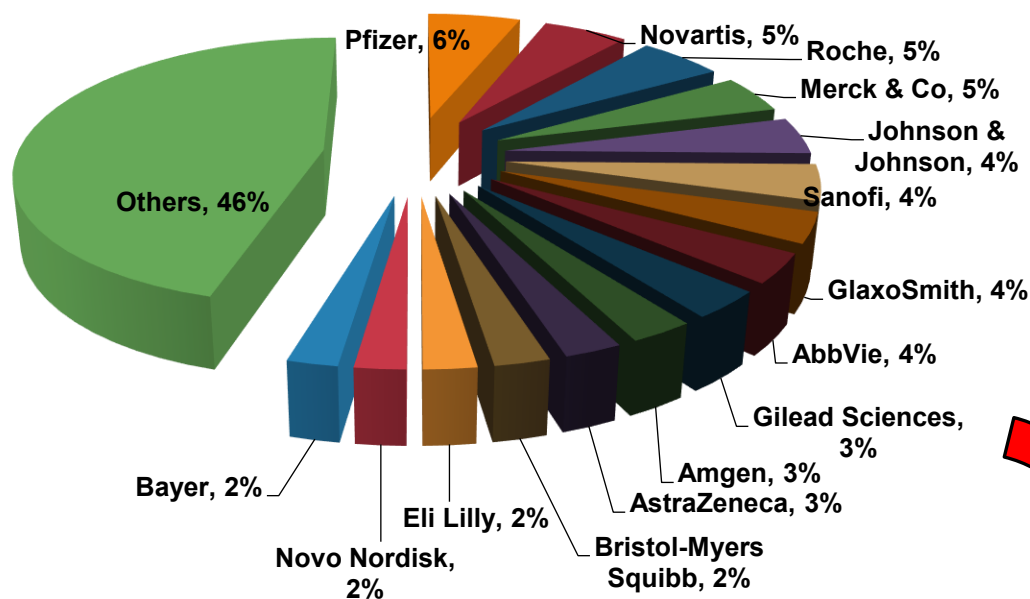


*Figure 7: Market share in the world prescription pharma market w.r.t companies in 2017 (789 Bn $, constant USD)*

### 1.5.2 Considering top 30 firms based on revenues

Analysing the data of the top 30 world's biggest pharmaceutical companies based on 2017 revenues, we found that there were neither Italian nor Indian companies in the Top 30. Referring to the data in the fig we can infer the below comments:

- Top 30 companies Generated 731 Bn $ sales in 2017

- 44% of them coming from US companies that have 26.9 Bn $ revenues on average

- 14% of top 30 companies are from Switzerland and have the highest revenues level on average (51.8 Bn $).

- No Italian nor Indian companies within the Top 30 firms
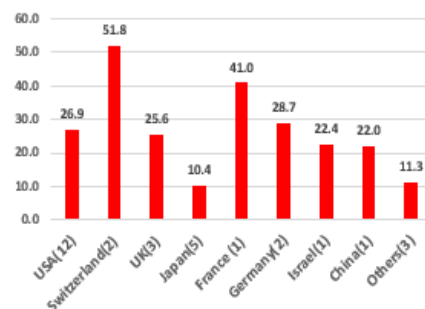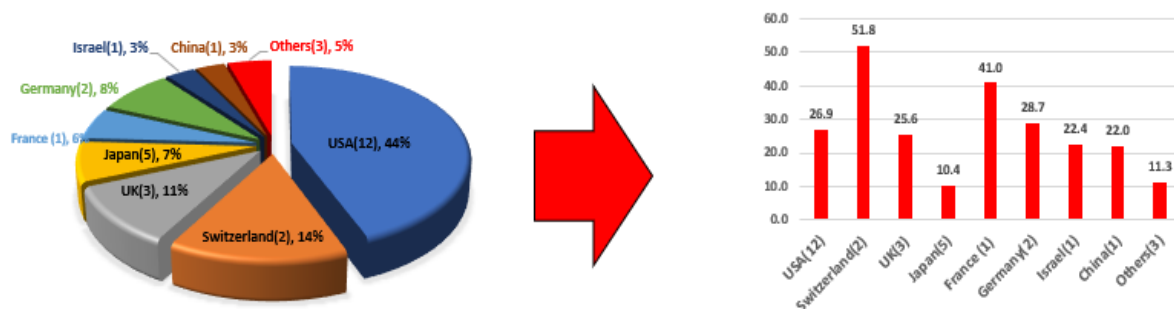


*Figure 9: Revenues and (n.) by nationality (Top 30 tot. 731 Bn $ 2017) – figure on left and  Figure 10: Revenues on average (Bn $ 2017) – figure on right.*

*Source: Analysis at Indiogene*

### 1.5.3 Considering Top 31st to 120 firms based on revenues

Analysing the data of the top 31st to 120 of world's biggest pharmaceutical companies based on 2017 revenues, we found that there were 11 Indian and 8 Italian companies are present in in the rank from 31th to 120th pharma firms (group tot. sales of 182 Bn $). Referring to the data in the fig we can infer the below comments:

- China has the largest presence with 29 companies generating 31% of the sales of this group, with 2.0 Bn $ revenues on average

- Japan follow with 14 firms and 18% of this group's total revenues (2.3 Bn $ on average)

- India generated 10% of total sales, with 11 firms present in the positions between 31th and 120th and 1.7 Bn $ revenues on average

- Italy has 8 companies in this rank generating 7% of the sales with revenues on average of 1.5 Bn $, similar to India
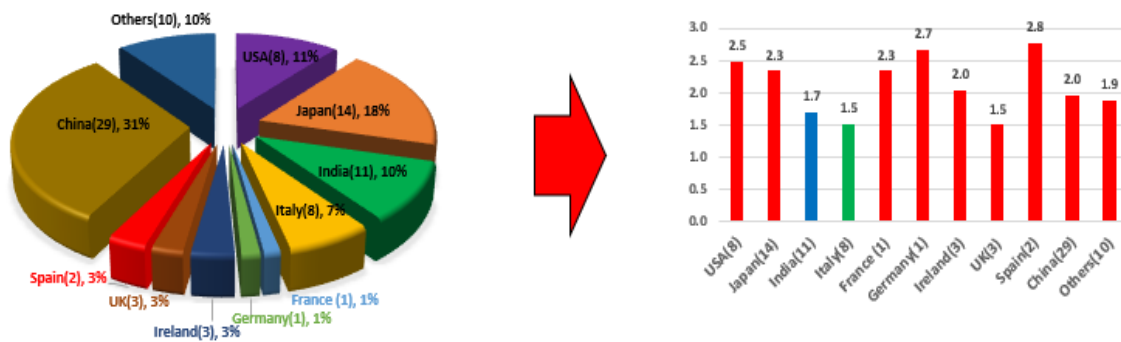


*Figure 11: Revenues and (no.) by nationality (Tot. 180 Bn $ 2017) – figure on left, Figure 12: Revenues on average (Bn $ 2017) – figure on right.*

Source: Analysis at Indiogene.

## 1.6 Global medicine spending growth by region and product type

The total volume of medicines consumed globally will increase by about 3% annually through 2021, only modestly faster than population and demographic shifts, but driven by very different factors around the world. Spending on medicines will grow by 4–7%, primarily driven by newer medicines in developed markets and increased volume in pharmerging markets. Developed markets will offset increased costs from new medicines with the use of generics, and a greater focus on pricing and access measures, while pharmerging markets will struggle to live up to promised access expansions made when their economic outlooks were stronger. According to a report by IMS the total spending on the medicines is estimated to go up to 1455-1485 Bn $ by 2021, the tables below show the spending and growth by region and product type (QuintilesIMS, 2016):

- In which the original brands contribute 56% of the total market share, in developed countries 69% is the contribution of original brands whereas its only 22% in Pharmerging countries

- 78% of pharmerging markets spending on products other than the original from the inventors or marketers of a medicine, compared to 69% of developed market spending going to those originators
- Global medicine spending and growth will be driven by divergent patterns over the next five years. Developed markets will balance a substantial surge in spending on new medicines with cost controls, a focus on pricing and transparency across markets and the impact of patent expires at $170 billion (1/3rd greater than in the last five years)

| Spending 2021 US $ | Original Brands | Non-Original Brands | Unbranded | Other products | Total Bn $ |
|---|---|---|---|---|---|
| Global | 56% | 22% | 12% | 10% | 1,455–1,485 |
| Developed | 69% | 14% | 12% | 5% | 975–1,005 |
| Pharmerging | 22% | 42% | 14% | 22% | 315–345 |
| Rest of World | 51% | 27% | 8% | 14% | 130–160 |

*Table 2: Spending by region and Product type*

| 2017–2021 CAGR Constant US $ | Original Brands | Non-Original Brands | Unbranded | Other Products | Total |
|---|---|---|---|---|---|
| Global | 3–6% | 9–12% | 3–6% | 3–6% | 4–7% |
| Developed | 3–6% | 13–16% | 1–4% | 0–3% | 4–7% |
| Pharmerging | 4–7% | 7–10% | 8–11% | 5–8% | 6–9% |
| Rest of World | 2–5% | 4–7% | 3–6% | 3–6% | 3–6% |

*Table 3: CAGR of spending and growth by product type*

## 1.7 Number of Important M&A deals in Pharma and Biotech sector from 2013 – 2017

The pharmaceutical industry's contributions to global health and economic development make it one of the most important commercial sectors in the world. In particular, the biopharma and biotech sectors have experienced a steady growth during the last decade, driven by the rise in global healthcare expenditures (which now account for 10.5% of the total GDP), the increasingly aging population and the prevalence of chronic and communicable diseases. Additionally, M&A activity has played a fundamental role in such an industry: indeed, acquisitions in these sectors are highly linked to the business strategy of pharma companies. For the former, M&A activity is crucial, as it ensures incumbents to grow or leverage on the acquired target's R&D knowledge by diversifying or replenishing their pipeline of products in order to remain competitive on the market. Moreover, acquisitions constitute efforts by leading pharmaceutical companies to compensate for the lack of new discoveries. Despite the steady growth that the industry has experienced overtime, the M&A deal volume and value in the biotech and pharma subsectors has been at its lowest levels over the last two years. As shown in the graph below, overall deal volume has declined since the beginning of 2016, with megadeals such as the acquisitions of Actelion Pharmaceuticals (Q1 2017) and C.R. Bard (Q2 2017) accounting for most of the spikes in value throughout 2017.Between The years 2013-2017 saw a high level of M&A activity in the Pharma and Biotech industry: deal volumes, the number of deals and average multiples are still at very high level as compared to the past.

- In 2013 the total no of deals was close to 226 the total deal valuation stood close to 79.6 Bn $

- In 2014 the total no of deals marginally Increased to 229 but total deal valuation more than doubled to 219 Bn $

- 2015 saw 290 deals but total deal valuation stood at 190 Bn $

- The total no of M&A deals went down to 200 in 2016 and the deal valuation was about 104 Bn $

- In the first 8 months of 2017 saw deals close to 122 worth 70 Bn $
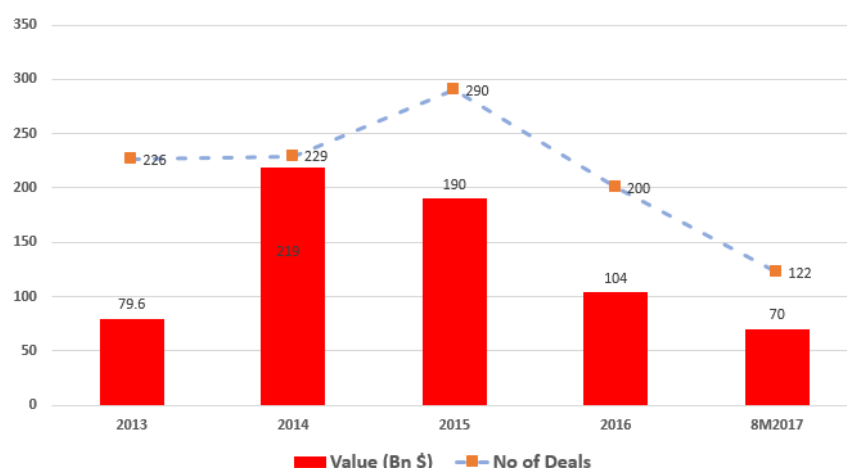
*Figure 13: M&A transaction from 2013-2017*

*Source: Compiled from data of "Evaluate Pharma Vantage 2018"*

### 1.7.1 Segmentation of M&A acquirers, Targets in 2017 by countries and segment breakdown of the deals happened in various pharma segments

In this thesis I have tried to categorize the M&A activity into acquirers and targets in order to understand better the buy side activity and the sell side activity based on the geography and I have also tried to further classify the M&A deals by segment so that there is a clear understanding of which sub sector of the pharma industry the is showing more growth.

By referring the Data in graphs, we can infer the following points:

- US remained the most active country, both as an acquirer and acquisition target. US companies were acquirers in 31% of total global M&A deals, followed by Chinese (11%) and UK companies (6%)

- In terms of acquisition targets, the US constituted 36% of total global M&A activity, followed by China (9%) and the UK (6%)

- Pharma prescription and biotech have been active segments in the last 12 months, accounting for 23% and 21% of total global M&A activity respectively

- Pharma generics and outsourcing services accounted for 18% and 22% of total global M&A activity respectively
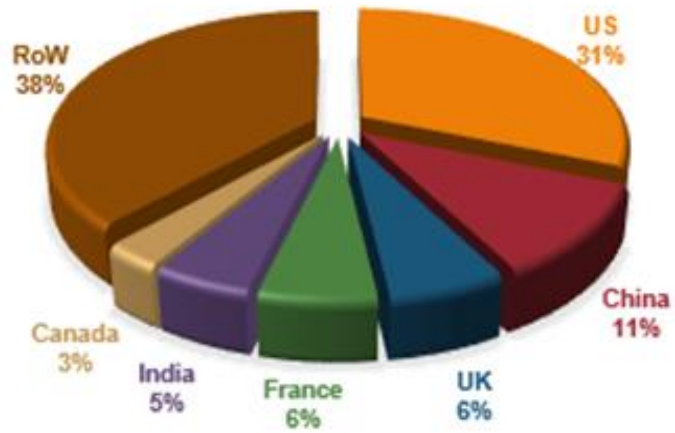
*Figure 14: M&A (International and National) Acquirer by Country (Oct 2016 – Sep – 2017)*

*Source: Compiled from data of "Clearwater International 2017"*
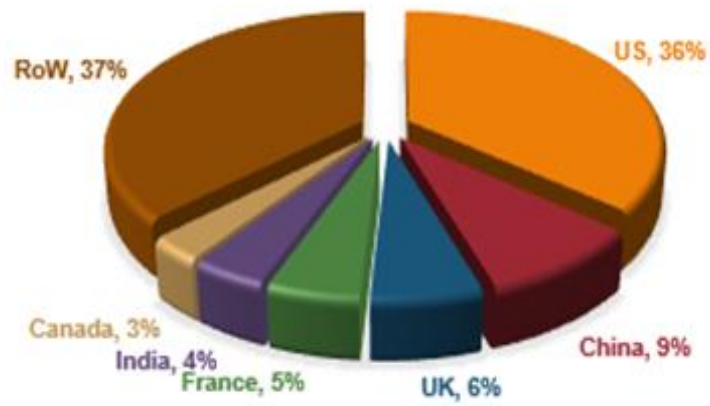


*Figure 15: M&A (International and National) targets by Country (Oct 2016 – Sep 2017)*

*Source: Compiled from data of "Clearwater International 2017"*
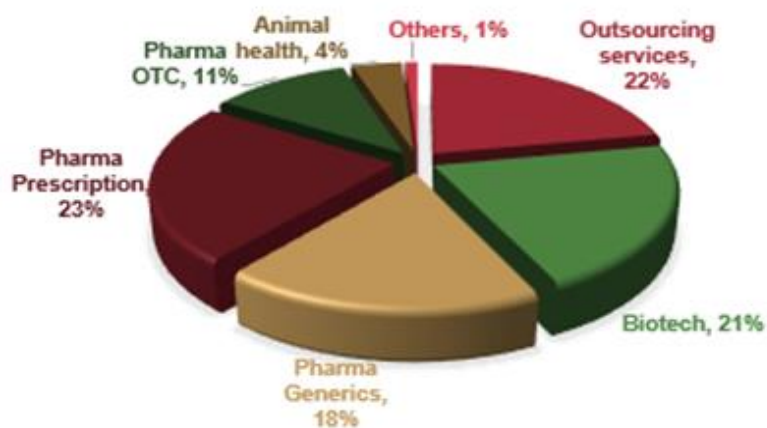
*Figure 16: Deals by segment (Oct 2016 – Sep 2017)*

*Source: Compiled from data of "Clearwater International 2017"*

### 1.7.2 Top 10 Key M&A deals happened in 2018

Just the top 10 deals completed and/or announced by biotech's and pharma's so far this year—and highlighted on this list—added up to $170.2 billion, whether they are deals involving two drug developers, or a drug developer and a company that applies a technology for a biomedical purpose, as is the case with two of those top 10 transactions. All the details of the deals is shown in the below table

| Announcement Date | Acquirer | Target | Deal Value (Bn USD) | Rationale |
|---|---|---|---|---|
| Sep-16 (Completed in May -18 ) | Bayer | Monsanto | 63 | U.S. Justice Department announced that Bayer agreed to sell $9 billion in assets to BASF in return for conditional approval. The assets included Bayer's canola, soybean, and vegetable seed businesses, as well as its Liberty herbicide business, all of which compete with Monsanto products. |
| May -18 | Takeda Pharmaceutical | Shire | 60.50 | Expected to close in the first half of 2019 |
| Jan-18 | Sanofi | Bioverativ | 11.6 | Expanded Sanofi's portfolio in specialty care and was intended to strengthen the rare disease presence it established seven years ago. |
| Jan-18 | Celgene | Juno Therapeutics | 9.0 | Expanded the buyer's presence in cancer therapeutics by catapulting Celgene into the thick of the scramble to develop CAR (chimeric antigen receptor) T-cell and TCR (T-cell receptor) treatments. |

| | | | | |
|---|---|---|---|---|
| Apr-18 | Novartis | AveXis | 8.7 | Expanded both Novartis' neuroscience portfolio and its presence in gene therapy with a promising candidate for spinal muscular atrophy (SMA). |
| Jan-18 | Celgene | . Impact Biomedicines | 7.0 | Consisted of $1.1 billion upfront, up to $1.4 billion tied to achieving regulatory approvals, and up to $4.5 billion tied to achieving sales in any four consecutive calendar quarters of between $1 billion and $5 billion, according to Celgene. |
| Jan-18 | Sanofi | Ablynx | 4.9 | The acquisition, announced January 29, was designed to expand Sanofi's R&D pipeline and rare blood disorders portfolio with a late-stage candidate and its underlying technology based on therapeutic proteins, or Nanobodies. |
| Jun-18 | Roche | Foundation Medicine | 2.4 | Roche's growing interest in personalized oncology treatments as well as diagnostics. Roche will expand its majority stake in Foundation Medicine into full ownership of the cancer-focused molecular diagnostics developer through the deal, which is expected to close in the second half of this year. |
| Feb-18 | Roche | Flatiron Health | 1.9 | This was one of three deals over the past year through which Roche signaled its intent to grow in personalized medicine and oncology. The other two were the planned $2.4 billion merger with Foundation Medicine (see below) and the $1.7 billion acquisition of targeted cancer therapeutics developer Ignyta, completed February 8. |
| May-18 | Eli Lilly | Armo BioSciences | 1.6 | The acquisition, announced May 10, expanded Lilly's immuno-oncology pipeline with AM0010 (pegilodecakin), a Phase III pancreatic cancer candidate that is also being developed to treat other solid tumors. |

*Table 4: CAGR of spending and growth by product type*

*Source: Compiled from data of "GEN news 2018"*

# CHAPTER 2 Brief introduction of the current situation of the Indian pharma market

## 2.1 An overview of the India's Economy, its challenges, opportunities, and Impact

India is the world's fourth-largest economy. It produced $9.4 trillion in goods and services in 2017. But it has a long way to go to beat the top three: China, with a production worth $23.1 trillion; the European Union, with $19.9 trillion; and the United States, with $17.4 trillion.

On June 26, 2017, President Trump met with Indian prime minister Narendra Modi. They discussed increasing the number of H-1B visas for Indian immigrants and the number of U.S. arms. American business leaders want India to reduce protectionist policies that give

domestic companies an unfair advantage. This would help U.S. companies compete in pharmaceuticals, entertainment, and consumer electronics. The Trump Organization wants to double its real estate holdings in India.

On May 16, 2014, India elected Modi as prime minister. By doing so, it rejected 60 years of leadership by the party led by Mahatma Gandhi. Mr. Modi, a successful businessman, promised to reduce bureaucracy and regulation, greenlight infrastructure projects and simplify the tax code.

Modi must streamline the government bureaucracy that has so far raised the cost of foreign direct investment. For example, he has talked about ending "tax terrorism." He promised to rationalize India's complicated tax regimes and support the introduction of a Goods and Services Tax. This would bring greater predictability to India's business climate.

In 2014, Modi promised to boost trade with the United States. Modi said he would level the playing field for U.S. companies by reducing policies that favor Indian manufacturing and intellectual property. This could help U.S. pharmaceutical companies, Hollywood, and consumer electronics.

India has a mixed economy. Half of India's workers rely on agriculture, the signature of a traditional economy. One-third of its workers are employed by the services industry, which contributes two-thirds of India's output. The productivity of this segment is made possible by India's shift toward a market economy. Since the 1990s, India has deregulated several industries. It's privatized many state-owned enterprises, and opened doors to foreign direct investment (AMADEO, 2019).

### 2.1.1 India's strengths

India is an attractive country for outsourcing and a cheap source of imports. Its economy has these five comparative advantages:

- The cost of living is lower than in the United States. Its gross domestic product per capita is $7,200, half that of China or Brazil. This is an advantage because Indian workers don't need as much income since everything costs less.
- India has many well-educated technology workers.

- English is one of India's official languages. Many Indians speak it. This, combined with the high level of education, attracts U.S. technology and call centers to India. For example, an Indian call center employee only costs $12 per hour. That's almost half the American counterpart of $20 an hour. According to the Technology Manufacturing Corporation, more than 250,000 call center jobs, as a result, were outsourced to India and the Philippines between 2001 and 2003.
- India's 1.3 billion people come from a wide range of economic and cultural backgrounds. This diversity can be a strength or a challenge. Socioeconomic status is largely determined by geography. India's three main regions each have distinct class and education divisions. Annually, 11 million people leave the rural areas to live in the cities. Most of them are young and educated. They seek a higher quality of life.

These comparative advantages mean great opportunities for American business. Foreign direct investment in Indian companies has the potential to be very profitable. The Indian middle class is almost 250 million people. That's bigger than the U.S. middle class. It will continue to drive India's consumer spending and economic growth.

In addition to FDI, India has seen more than 100 initial public offerings in the last 18 months. Private equity funding grew in 2012 and 2013, a trend that is expected to continue. Energy, health care, industry, and materials have been the top four sectors. While inbound mergers and acquisitions deals have declined in the last year, outbound deals have increased substantially in the emerging markets in the Middle East, Asia, Africa and South America. These deals are driven by depressed valuations due to the recent recession. In March 2016, Mr. Modi dedicated $1.5 billion in funding and tax breaks to boost high-tech startups. The program will streamline patent applications and investments. That should double India's new startups to 11,500 in the next five years.

### 2.1.2 India's challenges

India's Prime Minister Modi is up against India's bloated government bureaucracy. That makes the execution of any fiscal or monetary policy difficult. In August 2015, he was blocked from passing a bill to acquire land to promote infrastructure. He has also not been able to produce a bill to create a uniform goods and services tax.

U.S. monetary policy has hurt India's economy. When the Federal Reserve began its quantitative easing program, the lower interest rates strengthened the value of the dollar. This caused the value of India's rupee to fall. The resulting 9.6 percent inflation forced India's central bank to raise its interest rates. This action slowed India's economic growth, resulting in mild stagflation in 2013. In the second quarter, it had 9.6 percent inflation and 0 percent GDP growth. Inflation was caused by a declining rupee. Slow growth came from contractionary monetary policy to stem inflation. By 2017, inflation had slowed to 3.6 percent.

Investors backed off from India and other emerging markets when the U.S. Federal Reserve began tapering its quantitative easing program. When the dollar rose 15 percent in 2014, it forced the value of the rupee and other emerging market currencies down. Raghuram Rajan was the governor of the Reserve Bank of India, the nation's central bank. He raised interest rates to keep the currency strong and head off inflation.

### 2.1.3 India's foreign relations

The United States is one of India's biggest military allies, and China is one of its biggest economic partners. In 2006, the United States agreed to defy the Nuclear Non-Proliferation Treaty by allowing full civil nuclear cooperation with India. This is despite India's violations of the treaty. They exploded nuclear devices and did not put its program under the International Atomic Energy Agency's safeguards.

India wants to be treated like the official five nuclear powers: United States, Russia, Britain, France and China. The United States wants India to cap its production of fissile material, which consists of highly enriched uranium and plutonium. But India has refused. India plans to increase its warheads from 50 to 300 by 2010.

This bending-the-rules for India looks bad to U.S. allies that agreed to refrain from building nuclear capacity: South Korea, Taiwan, Brazil, Argentina, South Africa, Ukraine, Kazakhstan and Japan. The agreement was part of an overall increase in the business relationship between American companies and India. The United States and India should place greater importance on military cooperation, including joint defense exercises and counterterrorism efforts.

China and India are two of the world's largest and fastest growing economies. Because of their tight economic partnership, the countries are often called Chindia. China and India have complementary economies. India has raw materials; China has manufacturing. India has high-tech; China has the businesses and consumers to use them.

They also have long-standing trade disputes stemming from their common borders and China's friendliness with India's enemy, Pakistan. There are few airline routes and many visa delays. These disputes will not be solved by one friendly trade agreement. Fortunately, both realize the potential advantages of a partnership. A trade agreement is a good first step toward a "Chindia" of some sort.

With one-third of the world's people, Chindia could be a tremendous economic powerhouse in the global economy. It could also be a threat to the balance of power in that region. It is in the United States' best interest to maintain its alliance with India. That will offset the growing power of China in the region.

## 2.2 Population dynamics in India and Implications for Economic growth

Demographic change in India is opening up new economic opportunities. As in many countries, declining infant and child mortality helped to spark lower fertility, effectively resulting in a temporary baby boom. As this cohort moves into working ages, India finds itself with a potentially higher share of workers as compared with dependents. If working-age people can be productively employed, India's economic growth stands to accelerate. Theoretical and empirical literature on the effect of demographics on labor supply, savings, and economic growth underpins this effort to understand and forecast economic growth in India. Policy choices can potentiate India's realization of economic benefits stemming from demographic change. Failure to take advantage of the opportunities inherent in demographic change can lead to economic stagnation. Global population grew at roughly 2% per annum from 1960-2000, a level that is unsustainable in the long term, as it translates into population doubling every 35 years. India's population is currently growing at a rate of 1.4% per year, far surpassing China's rate of 0.7%. The differential between India and China will result in India surpassing China with respect to population size in less than 20 years.

The below graphs illustrate the comparative growth of the populations of India and China from the period 1960-2017 and population breakdown based on the different age groups. The population in India has grown significantly from 450 Mn in 1960 to 1339 Mn in 2017, nearly reaching China and ranking second by population Worldwide. In 2017 66% of the total population was in the working age group (15-64years). The median age of the country is just 24 years.
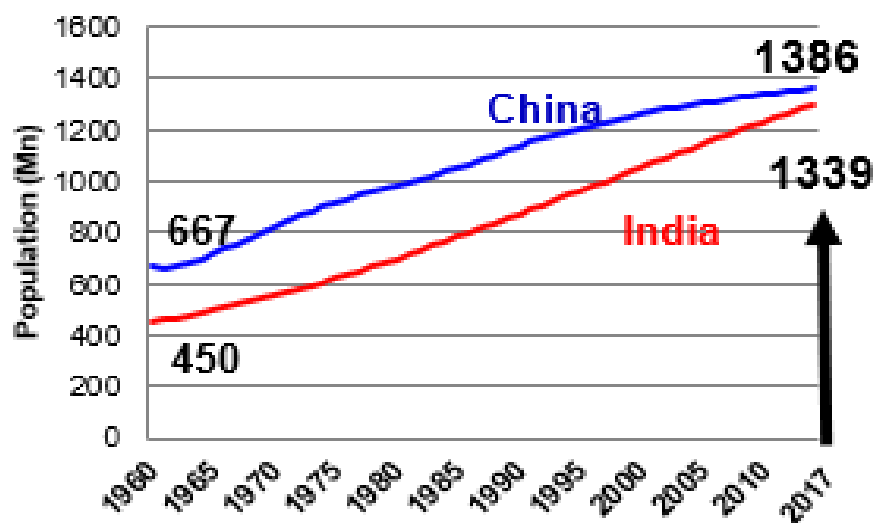


*Figure 17: Indian Population 1960-2017*
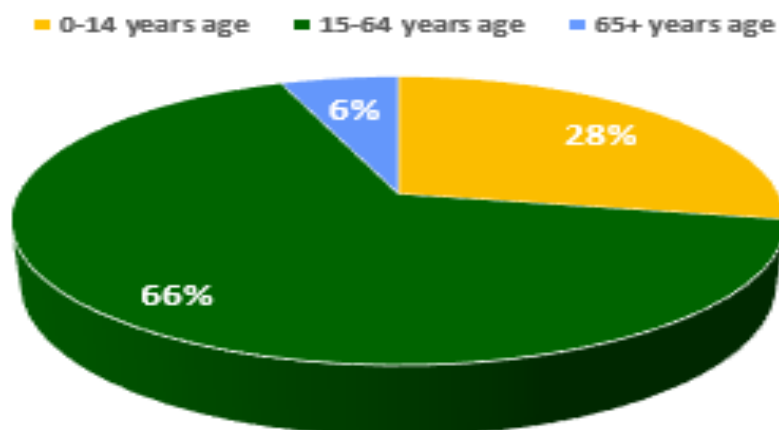
*Source: Compiled from database of world bank and Statista*

India's rapid economic growth has set the stage for fundamental change among the country's consumers. The same energy that has lifted hundreds of millions of Indians out of desperate poverty is creating a massive middle class centered in the cities. A new study by the McKinsey Global Institute (MGI) suggests that if India continues its recent growth, average household incomes will triple over the next two decades and it will become the world's 5th-largest consumer economy by 2025, up from 12th now. Along the way, spending patterns will shift significantly as discretionary purchases capture a majority of consumer spending. India's potential should make it a high priority for most consumer goods businesses, but to succeed in this complex market they must overcome major challenge. The below graphs illustrate the Poverty headcount ratio at the national poverty lines from 2000-2018 and the other graph illustrates the Indian population evolution by income bracket from 1998-2016. As you can see the income has grown significantly:

- Poverty headcount ratio at national poverty lines passed from 45% in 2004 to 5% in 2018, according to the estimates as you can see there is a gradual and consistent decrease in the poverty headcount ratio from 2000-2018
- High- and medium-income brackets (more than 30,000$ per year and between 6 and 30,000$ per year respectively) increased a lot, from 20% of total Indian population in 1998-99 to 68% in 2015-16
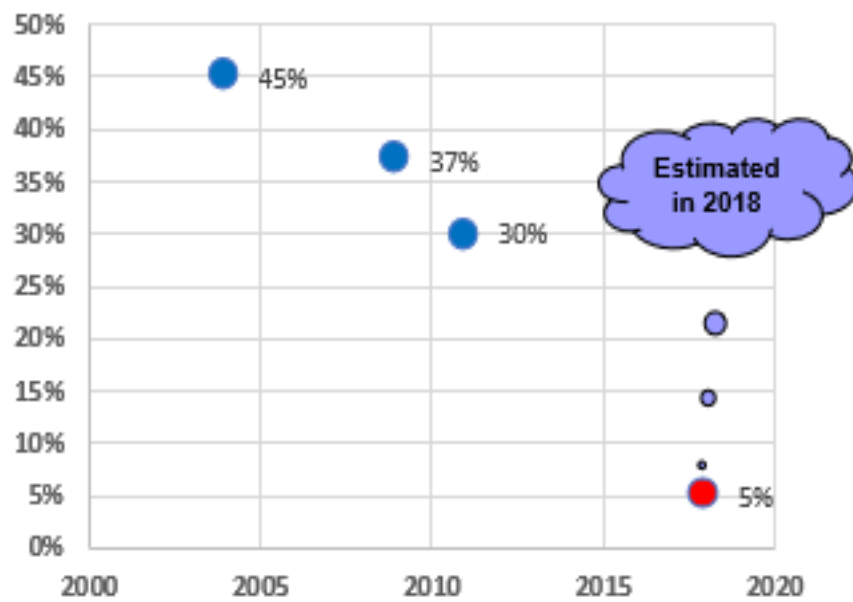
*Figure 19: Poverty headcount ratio at national poverty lines (percentage of population)*

*Source: Compiled from data in the reports of  BNP Paribas, Banca Mondiale, NCAER, Prometeia, FMI,Statista*
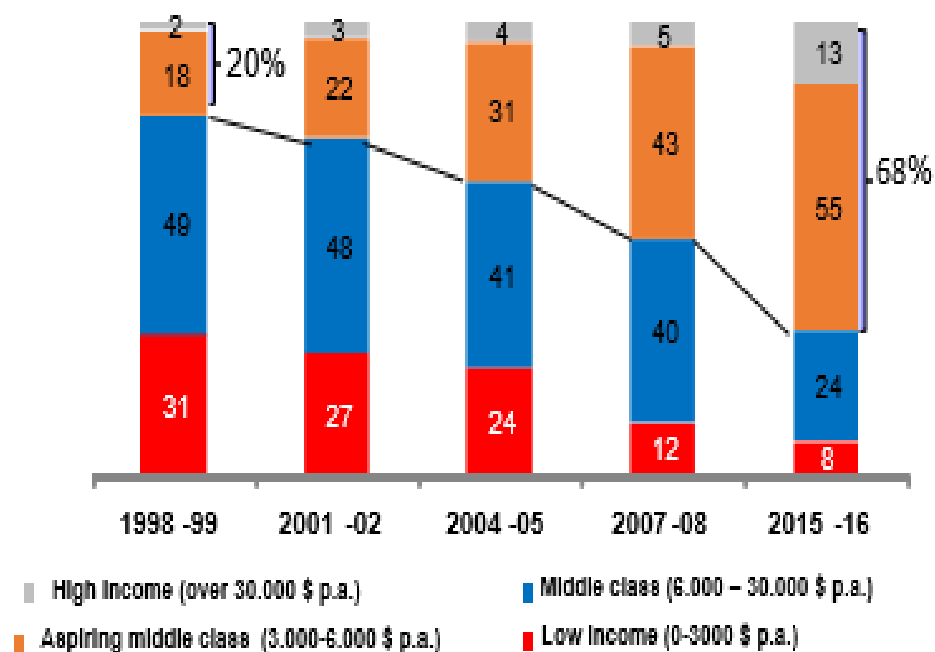


*Figure 20: Indian population evolution by income bracket 1998-2016 (percentage of total)*

*Source: Compiled from data in the reports of BNP Paribas, Banca Mondiale, NCAER, Prometeia, FMI, Statista*

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## 2.3 Macro Economic Factors and Economic Attractiveness of India and impact of economic conditions on mergers & acquisitions activity in international markets:

There are two methods of investing that a firm can choose when it comes to foreign direct investments (FDI). The first method is called "greenfield investment," in which the investor seeks to establish new facilities and operations in the foreign country in hopes of new cash flows from the market expansion. The second method is to acquire an existing, already operating firm in the foreign country through an M&A transaction. It is essential to perceive this basic distinction between the two forms of FDI when it comes to understanding international M&A activity.

In their study, they addressed two main questions, which are, why a company decides to invest in a foreign country and what makes a country so appealing that it attracts foreign investors. These questions are important because they involve the existence and generation of FDI inflows and outflows. The study arrived at intriguing conclusions. First, the size of the economy is "positively correlated with all series of inward and outward investment." This conclusion is intuitive, since when an economy grows larger, more companies will be competing consequently, at a certain point in a company's cycles of growth, provided that it continually prospers, the company will have to look across the border for new opportunities that would potentially facilitate more growth for its business. On the other hand, a big economy often goes hand in hand with an appealing market, which attracts international investors who hunger for market expansion. Second, surprisingly, economic growth is not so much necessarily correlated with attracting FDI in the form of M&A as it is with greenfield investments. The study found that a fast-growing industry appeals to investors that are interested in building 3 new facilities and operations in said country, hence greenfield investments. As for outward FDI, it prompts domestic companies to invest abroad in M&A transactions. Third, as the study concluded, financial development is also crucial to cross-border M&A activity. These findings are important to investors that are interested in forecasting the volume of international M&A as well as policy makers that try to stimulate growth in such sector.

Now let's have a look at the Macro Economic factors of India (Refer the Graph below). India's GDP (at market price) in 2018 is expected to be 2,8 Trillion $, making it the 3rd. largest economy in Asia and among the top 10 WW economies,

- In 2011 Indian GDP was at around 1224 Bn $. It has more than doubled to 2848 Bn $, in a decade (2018)

- As economic reforms picked up pace, India's GDP grew five-fold to 2848 Bn $, in 2018

- More specifically, India's GDP trend shows:

    - In 2008 GDP went down at 1224 Bn $, at -1% compared with 2007

    - Then, in 2009, there was an important recovery, continued until 2011

    - GDP decreased again, from 1832 Bn $, in 2011 to 1827 in 2012

    - In 2015 there has been another important increase of 11% vs 2013

    - From 2016 to 2017 there has been a substantial increase of 15%

    - From 2017 to 2018 the Indian GDP is estimated to increase by 9% to 2848

- India's GDP annual growth rate in 2018 is expected at 9% compared to China's 6,8%, making it the fastest growing among the large economies economy

    - The World Bank has projected a robust growth rate of 7.5% for 2019 and 2020

    - China's GDP growth rate has been slowing down from 2016-18 as its economy is wracked by multiple economic concerns, ranging from a slowdown in demand to capital outflows due to a depreciating
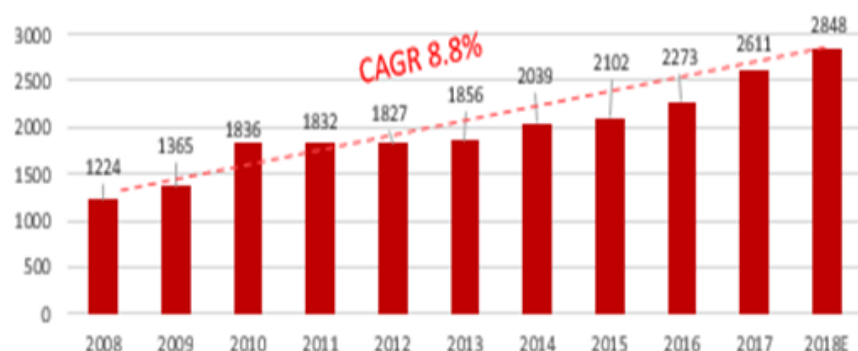
*Figure 21: India's GDP at market prices 2008-2018E (Bn $)*

*Source: Compiled from database of world bank and Statista*
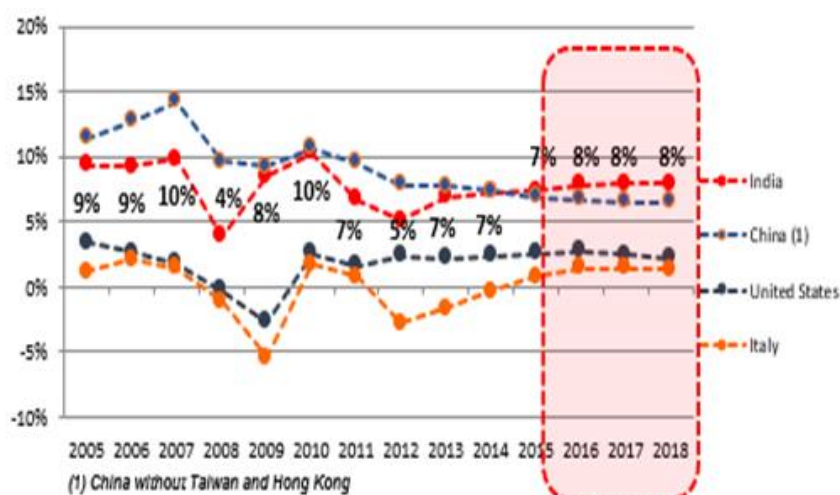


*Figure 22: India's GDP annual growth rate 2005-2018 (percentage)*

*Source: Compiled from database of world bank and Statista*

The World Economic Forum's Global Competitiveness Index 4.0 is a composite indicator that assesses the set of factors that determine an economy's level of productivity - widely considered as the most important determinant of long-term growth. The GCI 4.0 framework is built around 12 main drivers of productivity -- Institutions, Infrastructure; Technological readiness; Macroeconomic context; Health; Education and skills; Product market; Labor market; Financial system; Market size; Business dynamism; and Innovation. The World Economic Forum forecasts that India will attain 40° position in the global

competitiveness index, among 137 countries in the World Economic Forum's (WEF), sustained by increasing domestic demand and attributable to the momentum initiated by the election in 2014 of pro-Business Narendra Modi.

- The countries had sunk in this competiveness index to 71 in 2014-15 given the poor pre-election situation
- In 2006-07 India had reached 41° position, sinking gradually to 2014-15

As per the World Economic Forum forecasts (World Economic Forum, 2017), India leads the region in all other areas of competitiveness except for health, education and skills, where Sri Lanka boasts the highest healthy life expectancy (67.8 years) and the workforce with the highest amount of schooling (9.8 years). The score improves across most pillars of competitiveness particularly for example from 2016 to 2017:

- The development of a country wholly depends on the availability of its infrastructural facilities. Infrastructure plays a vital role in the improvement of the country's standard of living. It also plays an important role in contributing to a higher rate of economic growth. In infrastructure India is 66th, up two from the previous year
- The World Economic Forum's Networked Readiness Index (NRI), also referred to as Technology Readiness, measures the propensity for countries to exploit the opportunities offered by information and communications technology (ICT) and the usage of ICT among these stakeholders. India's Technological readiness was 107th, up three from the previous year, reflecting recent public investments in these areas.
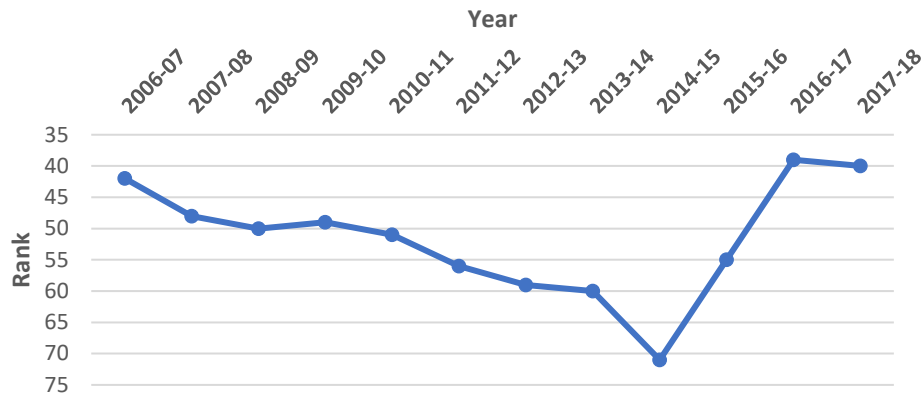
*Figure 23: Global Competitive Index rank*

*Source: World Economic Forum, "Global Competitiveness Index 2017-2018",*
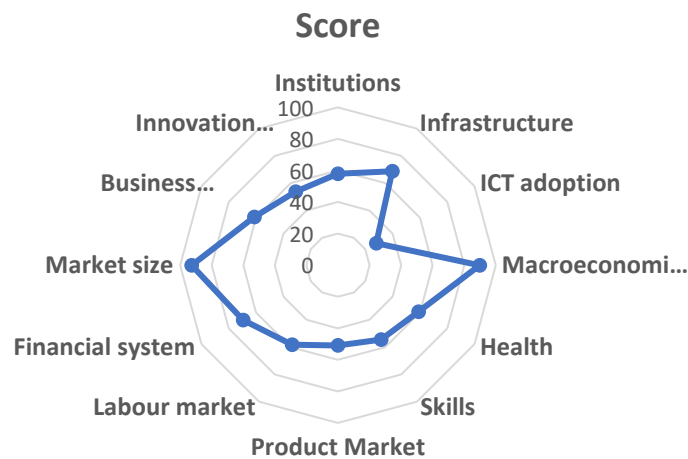


*Figure 24: Performance overview of India*

*Source: World Economic Forum, "Global Competitiveness Index 2017-2018",*

## 2.4 An introduction to Indian pharmaceutical Industry

The chapter provides a description and relevance of the industry selected for the research area of mergers and acquisitions as a strategy for global expansion. The Pharmaceutical Industry has been investigated for developing the model of global expansion through cross border mergers and acquisition. The industry specificity helps us in limiting the extraneous effects which would have impacted our study on the strategic tool of mergers and acquisitions. The section briefly details the growth statistics of the Indian pharmaceutical

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industry with respect to the global markets. The study also outlines the direction of growth of the Indian pharmaceutical firms with reference to the current business model. The impact of the change in the Indian intellectual property protection legislations on the growth model of the industry have been discussed in the third section of the chapter. The study also explores the value adding activities leading to the "discovery" capability for a pharmaceutical firm.

### 2.4.1 Evolution of the Indian pharmaceutical Industry

The Indian pharmaceutical industry has grown rapidly over the last few decades. Prior to 2005, the Indian regulatory system recognised only process patents. This helped build a firm foundation for the strong and competitive domestic pharmaceutical industry. During this phase, the prevalent price control mechanisms helped companies deliver medicines at affordable prices, to patients across India. The different phases that the Indian pharmaceutical industry has gone through, during the pre-patent (till 2005) and post-patent (post 2005) regimes are as follows (Life Sciences & IT Knowledge Banking (LSIT), 2015).

#### 2.4.1.1 Pre-patent regime (Before 2005)

Process patents helped the Indian pharmaceutical sector flourish, amid a fast-growing generics industry. During this regime, multinational companies (MNCs) were reluctant to directly introduce new products in India. Domestic companies leveraged this situation, by re-engineering these products and marketing them in India.

#### 2.4.1.2 Indian Patent Act, 1970

The Indian Patent Act aimed at encouraging domestic players to manufacture drugs and ensure self-sufficiency in medicines. The Act granted patents, based on the process of manufacturing, as against the global practice of granting patents based on the new drug alone. As a result, several Indian players began manufacturing products, based on the same bulk drug, yet through different processes. This strengthened domestic players' process chemistry skills and increased their expertise in developing low-cost generic drugs.

*2.4.1.3 Drug Price control order (DPCO), 1970*

The DPCO governed prices of all bulk drugs and formulations, to ensure widespread availability of medicines, at reasonable prices. Together, the Indian Patent Act and the DPCO, significantly influenced the structure and growth pattern of the domestic pharmaceutical industry.

*2.4.1.4 Decline in share of MNCs*

Introduction of these regulations caused great dismay among MNCs, who were left with little incentive to introduce new products in India. They shifted their focus towards vitamins, cough preparations, NSAIDs (pain killers) and eventually built up a strong brand equity in these products. Hence, it is not surprising that the share of multinationals in total production of formulations began to decline after 1970.

*2.4.1.5 Growth of small-scale units*

At the same time, the number of domestic small-scale units increased rapidly, due to following reasons:

- Low-entry barriers
- Abundant availability of bulk drugs
- Numerous incentives, such as waiver of price control on drugs produced by them, offered to SSIs
- A vast, geographically dispersed market

Additionally, several large producers began outsourcing production to small units (under the loan licensing scheme) to contain costs, which further encouraged growth of SSIs.

Some of the major outcomes were:

- Spread of research know-how
- Bulk drug production increases
- Market share of multinationals continued to slide
- Indian players leveraged the opportunity to widen their exports

- Increased investments

In line with its commitments to the WTO, the Indian Government passed an ordinance to introduce the product patent regime w.e.f. January 2005. This aided the integration of India into the global pharmaceutical market and rendered duplicating of post-1995 patented drugs illegal. While this discouraged process re-engineering of products patented post 1995, the amendment aimed at gradually enhancing confidence of large global players on Indian companies.

In 2005, the Indian pharmaceutical industry witnessed a series of regulatory developments, ranging from the implementation of value added tax (VAT), shift from excise duty levy to an MRP-based levy system and Schedule M implementation to recognize the product patent regime. While implementation of the VAT and shift in the excise duty regime had short-term implications, the implementation of Schedule M (compliance with tenets of cGMP) and adherence to the product patent regime will have medium and long-term implications, respectively.

### 2.4.1.6 Enactment of product patent regime

India entered the product patent regime on January 1, 2005. This marked the end of a protectionist era and better integrated India with the global pharmaceutical market. While the earlier process patent regime helped the Indian pharmaceutical industry develop into a world-class generics industry, the product patent regime aimed at encouraging new drug discoveries over the long-term.

Traditionally, pharmaceutical MNCs had maintained a low-key presence in the Indian market, due to the absence of product-based patents and rigid price controls. Hence, the recognition of product patents will gradually boost confidence levels, placed by large global players on India.

From January 2005 till date, India has seen a handful of patented product launches. The launch of patented products in India has been slow as innovators are taking their time, to seek clarity on data protection, patenting of derivatives and pre- and post-grant opposition.

While not much has changed on this front, MNC's approach towards the domestic market is slowly changing.

### 2.4.1.7 Rising focus on exports

India gained a foothold on the global arena, with innovatively-engineered generic drugs and active pharmaceutical ingredients (API). The country now seeks to become a major player in outsourced clinical research and the contract research and manufacturing services (CRAMS) segments. India has the highest number of manufacturing facilities (332 sites) approved by the US Food and Drug Administration (US FDA). Further, in 2011, one-third of all Abbreviated New Drug Applications (ANDA) approved by the US FDA, belonged to Indian companies.

### 2.4.1.8 Implementation of schedule M

The mandate issued to small-scale pharmaceutical units, necessitated compliance with the Schedule M norms. Schedule M of the Drugs and Cosmetics Act outlines various requirements for manufacturing good quality drugs and pharmaceuticals, by applying cGMP.

### 2.4.1.9 Affixing of prices by NPPA

The Government fixed prices of nine commonly used drugs, in cases where it was noticed that companies have increased prices for no legitimate reason. As a result, pharmaceutical companies will no longer be able to increase medicine prices, at their discretion. Major companies were asked to revise drug prices to levels fixed by the National Pharmaceutical Pricing Authority (NPPA). The regulator directed companies to make relevant changes in their maximum retail prices (MRPs). Drugs, which have come under the scanner, cater to major therapeutic areas, such as diabetes, cardiovascular, allergies and infections.

### 2.4.1.10 Drug law

In 2013, the Drug Controller General of India (DCGI) reviewed the rationality of fixed dose combinations (FDCs) available in the market. Based on the review, the regulator issued directives for withdrawal of certain FDCs. These norms, coupled with few others, point

towards a more stringent drug regulatory environment, which could increase compliance and facility upgradation costs, for the industry, over the medium term.

*2.4.1.11 New drugs (Prices control) order (DPCO), 2013*

Prior to the 2013 regime, the DPCO 1995 included 74 bulk medicines within its ambit and the pricing of the drugs were fixed on the basis of manufacturing costs declared by the drug manufacturers. The new DPCO 2013 empowers the National Pharmaceutical Pricing Authority (NPPA) to regulate prices of 348 essential drugs under the National List of Essential Medicines (NLEM) through market-based pricing. The prices will be fixed at the weighted average price of brands that have more than 1% market share.

*2.4.2 Future direction of growth for the Indian Pharmaceutical Industry*

The domestic market for pharmaceutical products is growing rapidly in India owing to a number of factors such as rising population, increased interest in research and development, increased availability of skilled labor, changing lifestyles of the Indian population and increased disposable income. The industry is classified into several segments. Some of the main segments are generics, retail drugs, nutraceuticals, clinical trials, bulk drugs, and Contract Research and Manufacturing Services (CRAMS). India exports pharmaceutical products to numerous countries around the world, including to the U.S, Germany, France, Russia and United Kingdom. In addition to highly regulated markets in U.S and European nations, Indian players are looking to expand further in the semi regulated markets of Latin America and CIS and strategic options such as overseas acquisitions. Overseas acquisitions may aim to target specific geographies and customer segments as in the case of Taro's acquisition by Sun Pharma because over 90 per cent of Taro's revenues are derived from the U.S. market and it has a strong presence in therapeutic segments where Sun Pharma is not dominant. These strategies will be mainly geared towards expanding product portfolios, brand building and having a well-established distribution network. A competent work force, cost-effective chemical synthesis, legal financial-information technology framework has added to the advantage of the Indian Pharmaceutical Industry. India is significantly ahead in chemistry services such as analog preparation, analytical chemistry, focus library, combinatorial chemistry, structural chemistry, structural drug design, computer aided drug

design, high throughput screening and assay development. However, India 's strength in biology sector is very limited especially in genetically modified animals' biochips and basic molecular biology. Indian biopharmaceutical players who largely export recombinant vaccines to semi-regulated markets and launch biosimilars in the domestic market can also look at cross border acquisitions for overcoming regulations to fully tap their capabilities to supply. The pressures of declining Research and Development output and increasing costs for global pharmaceutical firms has resulted in the globalization of clinical research and emerging markets have begun playing a significant role in the drug development value chain. India too has seen a surge in clinical research activity with an evolution over the last decade to increasingly being viewed as service provider of choice by the global pharmaceutical and biotechnology community in the arena of *Phase I-IV trials and allied services*. Business of *CRAMS (Contract Research and Manufacturing Services)* has come as a boon to the mid-cap pharmaceutical companies in India as they are taking full advantage of the features enjoyed by India as a country of diverse origin and strong manufacturing base in pharmaceutical industry for years. However, key markets like the United States are entering into a number of FTA 's (Free Trade Agreements) with different countries with intent to contain Indian exports. The Department of Pharmaceuticals, Government of India has prepared a "*Pharmaceutical Vision 2020*" for making India one of the leading destinations for end-to-end drug discovery and innovation and for that purpose provides requisite support by way of world class infrastructure, internationally competitive scientific manpower for pharmaceutical research and development (Research and Development), venture fund for research in the public and private domain and such other measures.

*2.4.3 Impact of the implementation of WTO guidelines for patent protection of Pharmaceutical products in India*

In 1970 the Indian Patents Act removed product patent protection from pharmaceutical products and introduced a 7 years process patent protection in India. This legislation was to encourage the emergence of local manufacture of cheap copies of Western drugs. This did not require formal technical assistance from abroad and has been attributed to the well-developed chemical infrastructure and process skills in India. Process R&D (Research and Development) which is actually producing a variant of an existing drug, is far easier and costs

are negligible compared to basic research. The negative balance of trade in drugs in the 1970s was turned into a trade surplus by 1990. The PBIT (profit before Interest and Taxes) or Operating Income has increased steeply over its previous year in the years 1994, 2002, 2007 and 2010. The annual growth rate of the operating income has been positive throughout except in 2005 and 2009.Since it was decided in 1995 that intellectual property legislation would be introduced in India by 2005, generic manufacturers faced the risk that they would eventually be unable to manufacture drugs which were still covered by patents. At the same time, they could expect in the future to be able to invent and develop proprietary drugs, if they could acquire the relevant capabilities. This offered both a threat and an opportunity.

### 2.4.3.1 Regulatory environment in India

The Pharmaceutical Industry is characterized by maintenance of high-quality standards as it concerns the lives of people. Regulatory bodies impose regulations to ensure that drugs meet the safety and quality standards. Regulatory bodies not only ensure that pharmaceutical companies meet the set quality standards, but also ensure that the pharmaceutical companies do not charge unreasonable prices from consumers. The stringency of regulatory procedures varies across countries. On the basis of established regulations and patent laws, the global pharmaceutical industry can be broadly classified into regulated and semi-regulated markets. Regulated markets include the USA, EU and Japan that have established systems of patent laws and sophisticated regulatory systems for controlling drug quality. On the other hand, semi-regulated markets include countries such as China, India and South Africa, which have less stringent systems of patent laws and less sophisticated regulatory systems for drug quality control. However, there is no single harmonized protocol for drug approval across countries. Countries have their own regulatory authorities and drug approval mechanisms.

| Country | Regulatory authority | Abbreviation |
|---------|---------------------|--------------|
| United States | US Food & Drug Administration | USFDA |
| United Kingdom | UK Medicines and Healthcare Products Regulatory Agencies | MHRA |
| South Africa | Medicines Control Council of South Africa | MCC |
| India | Food & Drug Administration | - |
| Brazil | National Health Surveillance Agency | ANVISA |
| Europe | The European Medicines Agency | EMEA |

*Table 5 List of regulatory authorities across key countries*

*Source: "The Indian Pharmaceutical Industry: Changing Dynamics & The Road Ahead" Yes bank report 2015.*

The Pharmaceutical regulatory environment in India comprises of the participants as displayed in the schematic arrangement below.
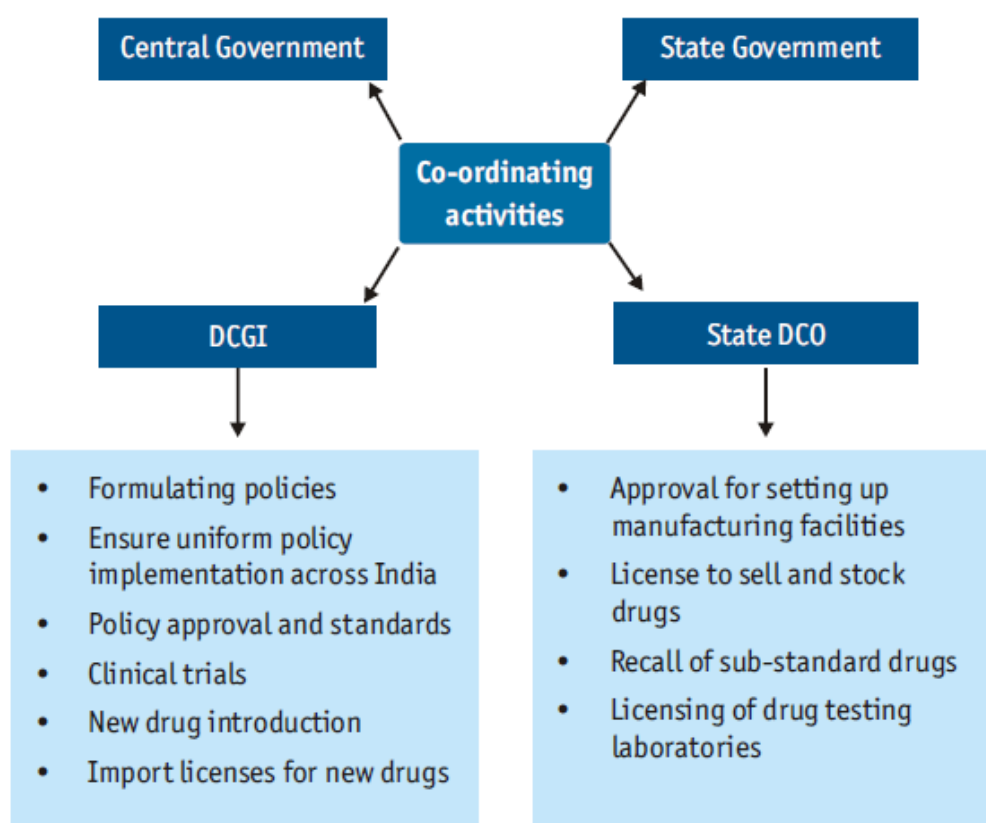


*Figure 25: Regulatory Bodies*

*Source: "The Indian Pharmaceutical Industry: Changing Dynamics & The Road Ahead" Yes bank report 2015.*

The Drugs and Cosmetics Act, 1940 (Drugs Act) and Drugs and Cosmetic Rules, 1945 (Drug rules) regulate the import, manufacture, distribution and sale of drugs in India. Under the provisions of these Acts, the Centre appoints the Drugs Technical Advisory Board (DTAB) to

advise the Central Government and the State Governments on technical matters. The responsibility to enforce the Drugs Act is entrusted with both the Central Government and the respective State Governments. Under the Drugs and Cosmetics Act, State authorities are responsible for regulating the manufacturing, sale and distribution of drugs, whereas the central authorities are responsible for approving new drugs and clinical trials, laying down the standards for drugs, controlling the quality of imported drugs, and coordinating the activities of State drug control organizations. The Drugs Controller General of India (DCGI) is the central body that co-ordinates the activities of state drug control organizations, formulates policies and ensures uniform implementation of the Drugs Act throughout India. It is also responsible for approval of licenses of specified categories of drugs, such as blood and blood products, IV Fluids, Vaccine and Sera. Indian Pharmaceuticals Industry is mainly regulated on the basis of patents, price and quality.

### 2.4.3.1.1 Patents

Before 2005, the regulatory system in India focused only on process patents. Indian pharmaceutical companies thrived during the process patent regime. They would re-engineer products of global innovator companies, which were unavailable in India, and launch them in the country as generics, as India did not recognize the product patents. In this manner, Indian companies gained process chemistry skills, but did not focus on R&D for new drug discovery.

In January 2005, India complied with the World Trade Organization (WTO) to follow the product patent regime sale of re-engineered products (for drugs patented after 1995) is restricted. However, enterprises, which had made significant investments and were producing and marketing the concerned product prior to January 1,2005 and which continue to manufacture the product covered by the patent on the date of grant of the patent, are protected, and the patentee cannot institute infringement suits against them, but would be entitled to reasonable royalty.

### 2.4.3.1.2 Drug prices

The Drug Price Control Order (DPCO) fixes the ceiling price of some APIs and formulations. APIs and formulations falling under the purview of the legislation are called scheduled drugs and scheduled formulations. The National Pharmaceutical Pricing Authority (NPPA) collects

data and studies the pricing structure of APIs and formulations and accordingly makes recommendations to the Ministry of Chemicals and Fertilizers. The new Pharmaceutical Policy, notified in 2012, intends to bring 348 essential drugs in the National List of Essential Medicines (NLEM), under the purview of the DPCO. With this policy, the market size of drugs under price control will increase from 15-20% of the domestic formulations market to 20-30%. The policy also introduces a radical change in the mechanism of control - shifting from the current cost-based control to a market-based price mechanism.Under the policy, the ceiling price for each drug under control would be fixed as the simple average price of brands having more than 1% market share (by value) in the sales (MAT - Moving Annual Turnover) of that particular molecule. Thus, prices of brands which are higher than this ceiling will need to be lowered. The ceiling prices will be allowed an annual increase as per the Wholesale Price Index (WPI). Prices will be recalculated using MAT only once in five years or when the NLEM is updated. Price of drugs that were part of the earlier policy, but do not come under the current policy, would be frozen for a year and, thereafter, allowed a maximum annual increase of 10%. A 10% increase would also be the limit for prices of drugs outside the Government's price control.

2.4.3.1.3 Quality

No drug can be imported, manufactured, stocked, sold or distributed in India unless it meets the quality standards laid down in the Drugs Act. All companies have to comply with Schedule M of the Act, which outlines various requirements for manufacturing drugs and pharmaceuticals by applying cGMP (current Good Manufacturing Practice). cGMP has to be followed for control and management of manufacturing and quality control testing of drugs.

*2.4.4 A brief process of new drug development*

It is important to understand the process of new drug development. The new drug development process helps us in understanding the critical points which can be influenced in the value chain of the pharmaceutical industry at the new drug discovery stage. There have been major linkages in the value chain of the pharmaceutical companies which have individually or together driven merger and acquisitions in many cases. The following steps are

major value adding activities in the pharmaceutical supply chain with reference to new drug development.

1**. Target identification and validation**: Based on new findings in basic research (genomics, proteomics) new potential —drug targets‖ may be determined. Drug targets are molecular structures (e.g. proteins) which (i) are the cause of, or are involved in, a disease or condition, and (ii) can be accessed using drugs. Target identification and validation are typically a very early stage of drug discovery.

2*. Drug discovery*: Drug discovery describes the process of finding a chemical or biological substance (e.g. an antibody) that alters the action of the drug target in a manner to improve the medical condition. Drug discovery is often a trial-and-error process in which fully automized systems are used to perform screenings of thousands or millions of drug candidates.

3. **Pharmacology**: Lead compounds are then typically tested for their pharmacology (ADMET: absorption, distribution, metabolism, excretion, toxicology) and sometimes chemically modified to improve their tolerability by the human body.

4. **Clinical development**: Once the candidate drug has gone through a set of rigid tests to prove its safety in principal, the developing company may file an Investigational New Drug (IND) application. Once it gets granted permission, it may start the actual development of the drug. Today, the drug development process is not as strictly separated in its phases anymore, as combination of phases (I/II or II/III) are often used to shorten development times, but the concept still is valid. Phase I, the safety of the drug is verified by applying increasing doses of the drug candidate to healthy patients (typically 10-20). If no side effects are measured, the drug is progressed to phase II, in which the efficacy is tested in volunteer patients. Phase III finally applies the drug to a larger group of patients to detect frequent side effects and includes often other (older) drugs as comparator.

5*. Review Process*: The whole documentation is then filed with the regulatory bodies (FDA or Food and Drug Administration in the US, EMEA or European Medicines Agency in Europe) for review through a New Drug Application (NDA). The regulator will review the data provided

formally (protocols used, soundness of data collected, statistical significance of results). Once this product is on the market, the indications are extended to second-line and then first-line treatments, thereby multiplying the addressable patient population.

5. **Proprietary marketing phase**: Drug developers may protect their market exclusivity in three ways: First, by having a patent on the drug they developed. Because patents have to be filed very early in the development process, and development times are so long, patents may run out quite soon after market launch. Hence, most governments in developed countries may provide protection certificates that extend patent protection if the costs and duration of development were excessive. Third, a developer may apply for regulatory exclusivity for the first launch of a drug in a new indication (even if the patent is long expired); if this is granted, no other company can use or refer to the clinical data produced by the originator to launch a new drug; however, other players can repeat the studies to have similar type of products. Whereas the cost for drug development is huge, market launches can cost again the same amounts. A drug that is prescribed by general practitioners require large sales forces and substantial investment in promotion for their launch, at a cost similar to the clinical studies.

6. **Generic marketing phase**: The effect of the loss of marketing exclusivity due to the expiry of patent protection or regulatory exclusivity depends on nature of the drug. For chemical drugs, regulators grant marketing authorization if the manufacturer can prove that its version of the original drug has, within certain boundaries, the same pharmacology as the original drug. Hence, entry barriers for copy-cat generic drugs are small, and competition can be fierce. For biological drugs, the situation is more complex. As the effect of a biological drug can vary from one preparation to another due to subtle changes in the fermentation process, regulators demand clinical safety and side-effect studies in patients very much like phase I and phase III studies in new drug developments, for each new process (hence it is called —biosimilar‖). The cost for these studies easily amounts are higher, and failure rates are significant. Hence, only few players manage to enter the arena of biosimilars for each original. Marketing post-exclusivity is driven by three parameters: price, price and price. Manufacturing costs are an issue. Hence, generic drug providers typically produce or let produce in low-cost countries. Interestingly, we observe that several large pharmaceutical companies have started to build their own generic drug units.

## 2.4.5 The pharmaceutical supply value chain
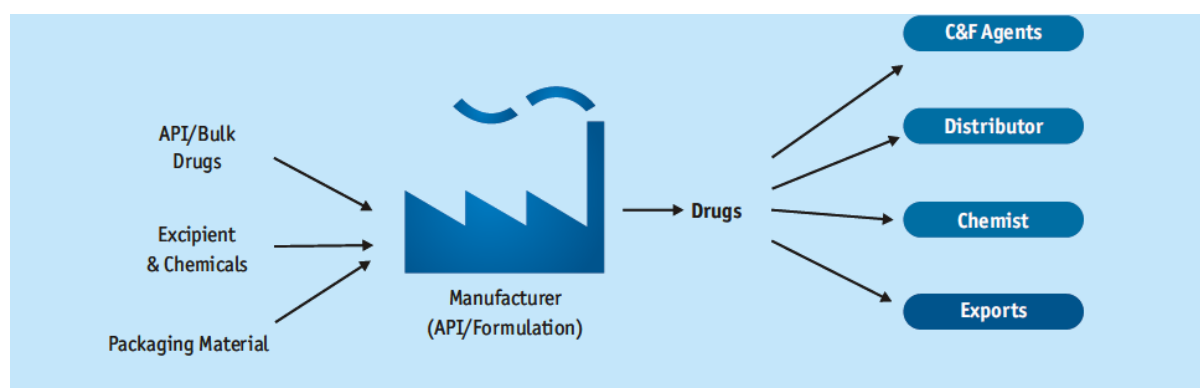


*Figure 26: Pharma Value chain*

*Source: "The Indian Pharmaceutical Industry: Changing Dynamics & The Road Ahead" Yes bank report 2015.*

Bulk drugs or active pharmaceutical ingredients (APIs) are raw materials used to manufacture formulations, which are ready to use forms of bulk drugs (including capsules, tablets, syrups and injections) administered to patients. Bulk drugs are manufactured by combining more than two chemicals or intermediaries. They directly influence the diagnosis, cure, mitigation, treatment or prevention of a disease.

Drug distribution in India has witnessed a paradigm shift. Before 1990, pharmaceutical companies established their own depots and warehouses. Now, they have been replaced by clearing and forwarding agents (CFAs).

- **CFAs**: These organizations are primarily responsible for maintaining, storage (stock) of the company's products and forwarding drugs to the stockist on request. Most companies keep 1–3 CFAs in each Indian state. On an average, a company may work with a total of 25–35 CFAs. The CFAs are paid by the company yearly, once or twice, on the basis of the fixed percentage of total turnover of products

- **Stockist**: is the distributor, who can simultaneously handle more than one company (usually 5–15 depending on the city area) and may go up to even 30–50 different manufacturers. They pay for the products directly in the name of the pharmaceutical company after 30 to 45 days

- **The Retail Pharmacy:** obtains products from the stockist or sub stockist through whom it finally reaches the consumers (patients)

*2.4.6 SWOT analysis of the Indian Pharmaceutical Industry*

In order to have a better understanding of the pharmaceutical industry, the SWOT (Strength, Weakness, Opportunity and Threat) analysis has been presented here. The policy recommendations made by the Department of Pharmaceuticals, Government of India under the twelfth growth plan have highlighted the strengths, weaknesses, opportunities and threats for the Indian Pharmaceutical Industry. They are described as follows:

- Strengths
    - Strong Low-cost manufacturing sector
    - Significant breadth and depth of product expertise
    - Low cost of growing Human resources in the Pharmaceutical sector

- Weaknesses:
    - High emphasis on generics both for domestic and international markets where filing and approval of ANDAs and DMFs have left little room for Research and development on drugs development
    - Inadequate Research and Development Infrastructure
    - Poor Industry-Academia linkage
    - Lack of required high end product development capable human resources
    - Lack of SME (Small and Medium Enterprise) base for high-end manufactures

- Opportunities:
    - Global opportunity for increasing Generics and bio-generics market both in developed and emerging countries due to pressure on budgetary limitations of these countries as well as emergent patent cliff due to off- patenting of major high value drugs
    - Low cost good skill destination for contract research and manufacturing and resultant opportunities in drug discovery as well as clinical trials
    - High growth of domestic market attracting multinationals both for brown field and green field investments in production and capacity building

- Threats:
  - Ever-greening strategy of Multinational Corporations for denying and limiting the patent cliff opportunities with debatable recourse to TRIPs and FTAs (Free Trade Agreements)
  - Increasingly stringent regulatory and non-tariff barriers to generics markets in developed countries
  - Increased competition for generics and bio-generics production in terms of high capacity and production costs
  - High entry barriers to enable market share in development of new drugs

*2.4.7 Structure of Pharma sector in India*

Pharmaceutical market in India is divided into Domestic and Export Markets each with distinct subdivisions (IBEF, 2018),

- The domestic market is driven by Branded Formulation and Active Pharmaceutical Ingredients (APIs), India is the 3rd largest global producer of APIs in 2016, with a 8 % market share in the world. India is the largest exporter of Formulations worldwide in terms of volume, with 14% export market share and 12th position in terms of export value.  The domestic market size is valued at USD11.2 billion with a double-digit growth expected over the next five years
- The export-outsourcing market is driven by:
  - Generics/Biosimilars, Biosimilar's sector is expected to touch USD1.4 billion by 2016 and the sector is expected to grow annually at a rate of 30 % in India to over 40 Billion $ by 2030
  - Contract manufacturing organization (CMO) is a company that supplies products to pharma groups on a contract basis
  - Clinical Research Organization (CRO) is a company that provides support to pharma groups of research and particularly human clinical trials on a contract basis.
  - CRO and CMO together are known as Clinical Research and Manufacturing (CRAMs), **CRAMs** industry is estimated to reach USD18 billion in 2018 and

expected to witness a strong growth at a CAGR of 18-20 % between 2013-2018. It is a fragmented market with more than 1,000 players
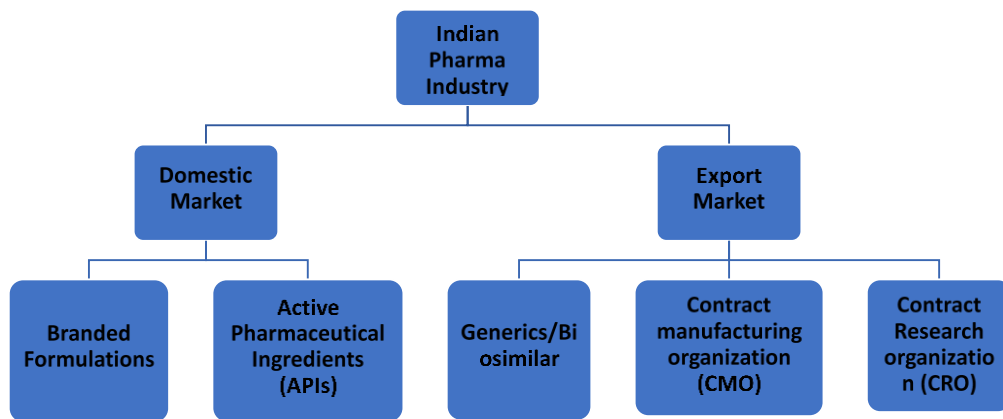


*Figure 27: Structure of Pharmaceutical market in India*

*Source: Compiled from the Data in IBEF reports on Indian Pharma industries*

## 2.5 Relative cost comparison in India

The Indian pharmaceutical industry holds a strong position in terms of production volumes in the global pharma market as the country contributes around 10% of the world production volumes and in terms of value, India holds a share of around 2.4% globally.

The Indian pharmaceutical industry is largely dominated by generics drugs as the industry earns around 70% of its revenues from the same. This can also be implied from the fact that India holds 13th position in terms of production value in spite of holding third position in terms of production volume globally.

IPI registered revenue of around USD 33 billion in 2016. Exports form a major part of the industry's turnover and over 50% of the sales comes from exports. Lower cost of production coupled by efficient scientific and technical skills of human resources are the prime reasons for growth in exports from India. The cost of drugs manufactured in India is one of the lowest in the world (Ratings, 2017).

Relative costs of Indian Pharma are particularly significant in:

- Production costs, where India has roughly 50% of Developed Countries costs

- R&D costs are even lower with India at 12,5% of Developed Countries

- Similarly, Clinical Trial costs are at 10%
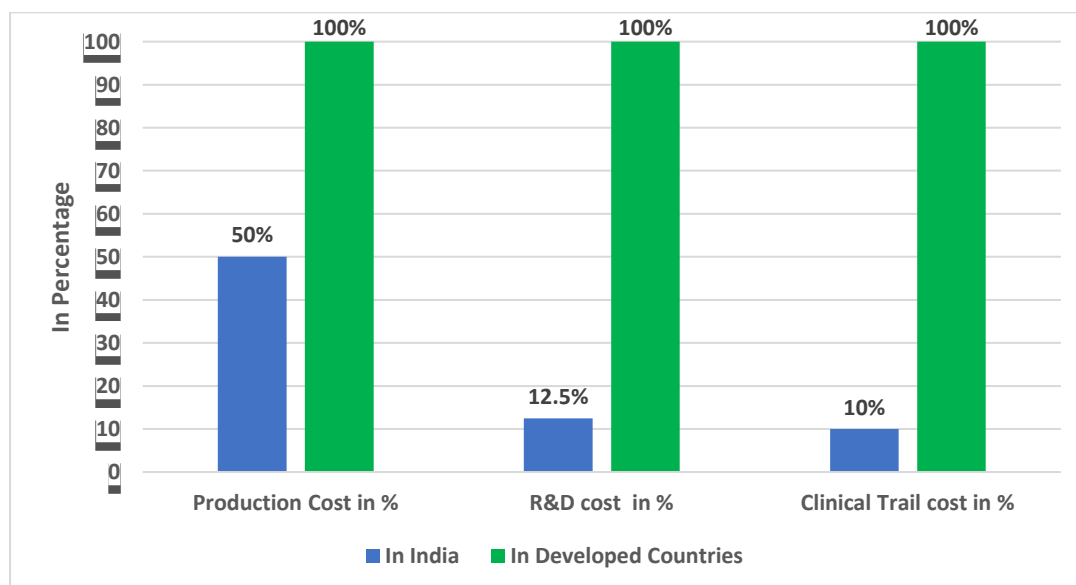


*Figure 28: Relative cost comparison: India v/s Developed countries 2016*

*Source: Compiled from the Data in IBEF reports on Indian Pharma industries and Care rating report July 2017*

### 2.5.1 India advantages in the life sciences Industry

India has emerged as a pharmaceutical supplier in the international markets. This is not only because of a low-cost manufacturing, operations and research base but also a combination of additional factors such as process improvements in manufacturing API, faster recruitment for conducting clinical trials, availability of skilled manpower and developed regulatory skills. In Contract Research Business, India is also an ideal location due to availability of skilled manpower and a large patient population which results in faster recruitment of patients. With low costs, highly competitive market and only process patents till recently, Indian companies have developed expertise in process innovation. The above factors have resulted in India producing low-cost high-quality products, which have spurred exports of Indian products to international markets, especially to the higher regulated markets like USA and Western

Europe. Of the main export varieties, formulation and API sales are the major portion. However, Contract Research has also grown into a significant contributor to total exports from the pharmaceutical market over the past few years. Given the technical expertise of human resources in India, pharmaceutical exports have grown at a CAGR of 27% from 2007-14.

## 2.5.2 Key success factors in the generics market

Indian companies have done well in the generics market internationally. This can be said to be because of competitiveness in some key areas which spell success in the generics space (Life Sciences & IT Knowledge Banking (LSIT), 2015).
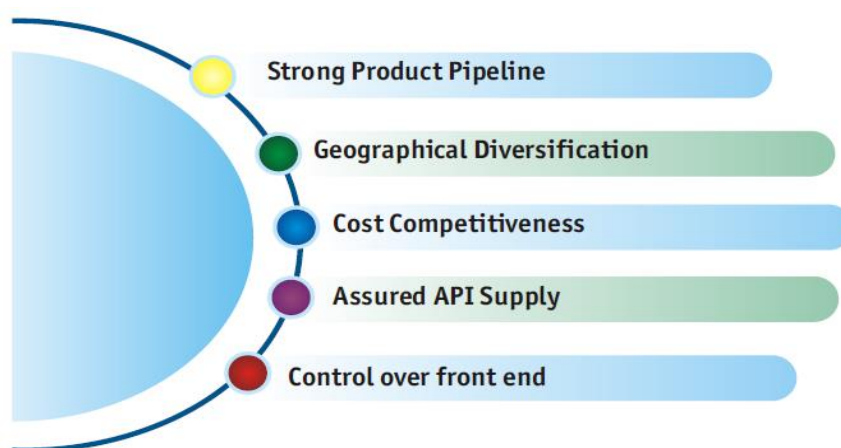


*Figure 29:Key areas influencing the factors of success*

*Source: "The Indian Pharmaceutical Industry: Changing Dynamics & The Road Ahead" Yes bank report 2015.*

## 2.5.3 Product pipeline

Most Indian pharma companies have significant competitive advantages in R&D to build a generic product pipeline. Indian advantages include high technical skill levels in the development of non-infringing processes, bio-equivalent formulations, and development of regulatory submissions, at lower cost.

## 2.5.4 Geographical Breadth

Indian companies in the recent past have ventured beyond partly regulated markets. Apart from servicing the markets of Africa, Eastern Asian countries, Russia and other CIS countries,

Indian companies have made significant foray into highly regulated markets of Europe and North America as well as lesser accredited markets of Australia and South Africa. In recent years companies have also started setting up subsidiaries and registering products in Japan. The wide reach of companies ensures that using the same basket of products, a company can attain greater sales in markets with varying competitiveness and pricing pressures.

### 2.5.5 Low Cost

Labor costs in India are about 1/7th the levels in developed countries and offer an obvious cost advantage. Also, Indian companies are able to reduce the upfront capital cost of setting up a project by as much as 25-50% due to access to locally fabricated equipment and high-quality local technology and engineering skills.

### 2.5.6 API Supply

Most Indian companies entering the regulated markets have internal API manufacturing and development capabilities. Clearly, either strategically managed internal API development and manufacturing or strategic sourcing partnerships are essential to generics company success. American or European generics companies without API capabilities almost always have to source from India or China.

### 2.5.7 Growth of revenues of Indian Pharma market

Pharmaceutical Industry is a highly knowledge-based industry, which has remained on a strong growth trajectory, over the past few years. Indian Pharma industry is ranked 3rd globally in volume and 13 in value, supplying 10 % of global production. The increasing attractiveness of Indian Pharma Market is supported by relatively lower costs and increasing revenues.
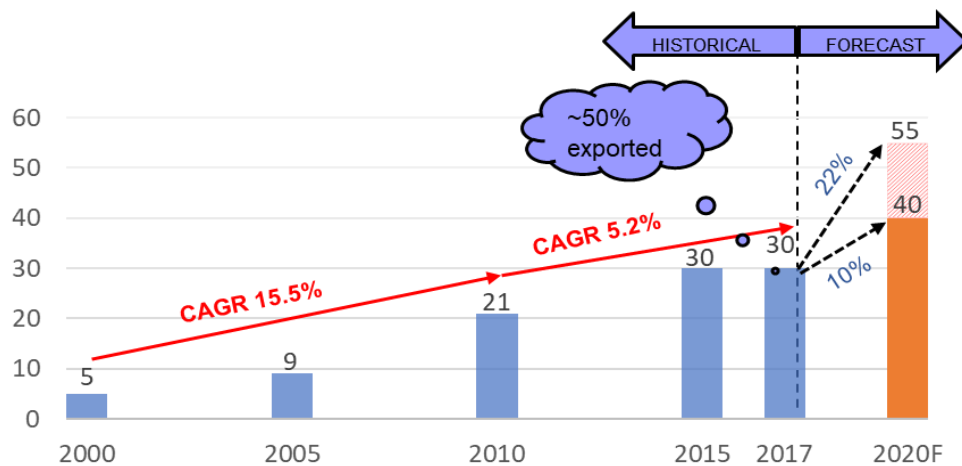
*Figure 30: Revenues of Indian Pharma (Bn $)*

*Source: Compiled from the Data in IBEF reports on Indian Pharma industries and Indiogene analysis*

From Figure 30, we can see that there are 3 distinct periods,

- The first period goes from year 2000 to year 2010 with a sustained CAGR of 15,5% in the growth of Indian Pharma Revenues

- After the beginning of the 2008-09 crisis there has been a definite slowdown in growth from year 2010 to year 2015 and a near standstill to 2017. Thus the 2010 to 2017 average CAGR has been of only 5.2%

- Exports in the period have been around 50% of total with significant difference in the years

- Forecasts given by the official source IBEF seems rather optimistic:
  - This source expects the market to grow from 30 Bn $ in 2017 to 55 in 2020 with a high CAGR at 22%
  - At Indiogene we believed it seems more cautious to expect a growth to 40 Bn $ in 2020 with a CAGR at 10%

- The reasons for these more optimistic forecasts come from the cost conditions shown above and growth-based drivers

*2.5.8 Indian pharma market comparison Therapeutic area segmentation with the WW pharma market Therapeutic area segmentation*
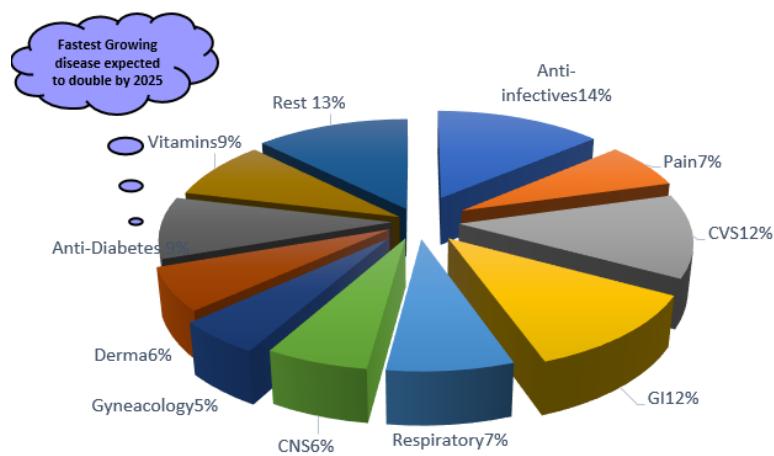


*Figure 31: Indian pharma market segments by value 2018 in percentage*

*Source: Compiled from the Data in IBEF reports on Indian Pharma industries*

The Indian market is dominated by Anti-infectives, CVS and GI with Anti-diabetic growing fastest. Comparison with the WW pharma market Therapeutic Area segmentation.

With 70 per cent of market share (in terms of revenues), generic drugs form the largest segment of the Indian pharmaceutical sector. Over the Counter (OTC) medicines and patented drugs constitute 21 per cent and 9 per cent, respectively.
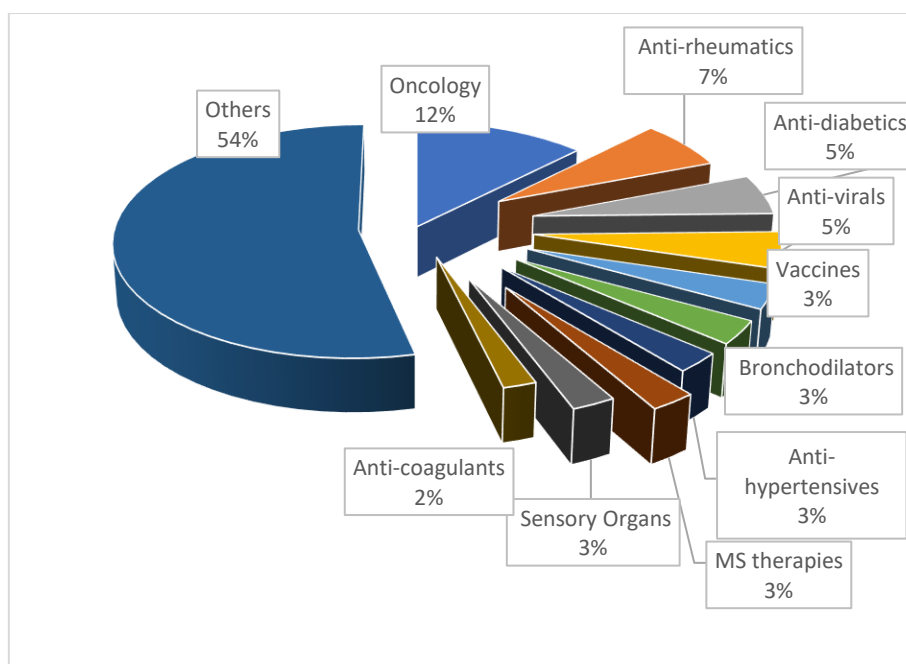
*Figure 32: Worldwide pharma market segments by value 2017 (percentage)*

*Source: Compiled from the Data in IBEF reports on Indian Pharma industries 2017*

In 2018 TA (Therapeutic Area) was valued at 17.9 Bn $, most of the market has been captured by:

- Anti- infective (An agent that is capable of acting against infection) with a share of 14% followed by
- CVS (Cardio Vascular system) and GI (Gastro-intestinal) at 12% each and likely to grow
- Anti-diabetic at 9% shows the highest growth rate from 7% in 2015 to 9% in 2018.
- Respiratory at 7%

Comparison of the worldwide pharma TA segment with the Indian TA segment:

- In WW market Oncology occupies 12% of the total market share whereas in Indian market it is not reflected even in the top 10 TAs
- Anti-rheumatics is in the second place with a 7% market share whereas CVS occupies the second place in India
- The worldwide market share of diabetes is 5% vs 9% in India, India is also known as the diabetes capital of the world. Since more than 62 million people in India suffer from diabetes

## 2.6 Position mapping of global pharma Industry
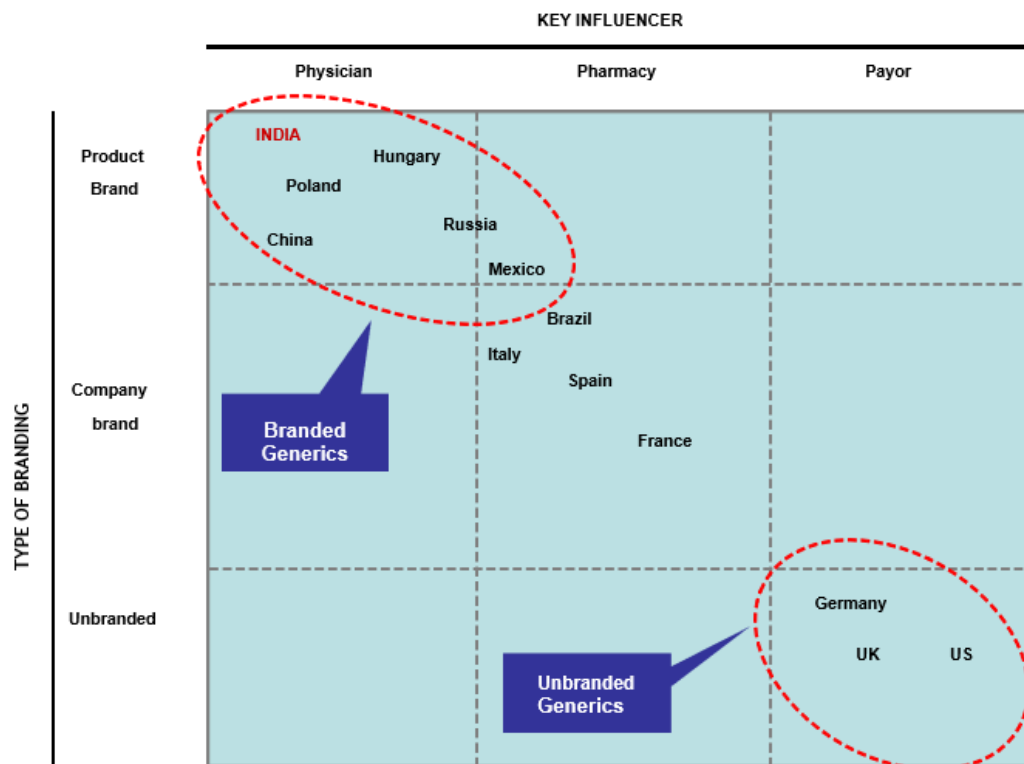


*Figure 33: Position mapping of global pharma Industry*

*Source: Compiled from IDFC Capital," Pharma: Industry Report" 2011*

Products brands and physicians play a significant role in India unlike in US/UK. In Italy the company brand and the pharmacist opinion have the central role.

- Unbranded generics are only used in Government hospitals/ public health clinics. Unbranded generics are virtually absent in private markets
- Patients need the "assurance provided by brands since there is no official FDA/ Govt. Endorsement available for unbranded generics
- Dominance of branded generics, as in other out of pocket markets like China, CIS, CEE and Latin America
- Efforts made by pharmacists to substitute doctor prescribed brands would be generally be rejected by patients or met with suspicion

- In Italy patients mainly look for Company brand and recognize an important role of counsellor to pharmacists

## 2.6.1 Increasing share in ANDA fillings

Dossier Filing to the US FDA is one of the best criteria to determine the focus of a company to enter the US generics market. Over the years, the product pipeline (ANDA filings) of key Indian pharmaceutical players has grown, to become comparable to that of key global generic players. Product pipelines of Indian players such as Ranbaxy, Dr. Reddy's, Aurobindo, and Sun Pharma are comparable with that of global generics giant.
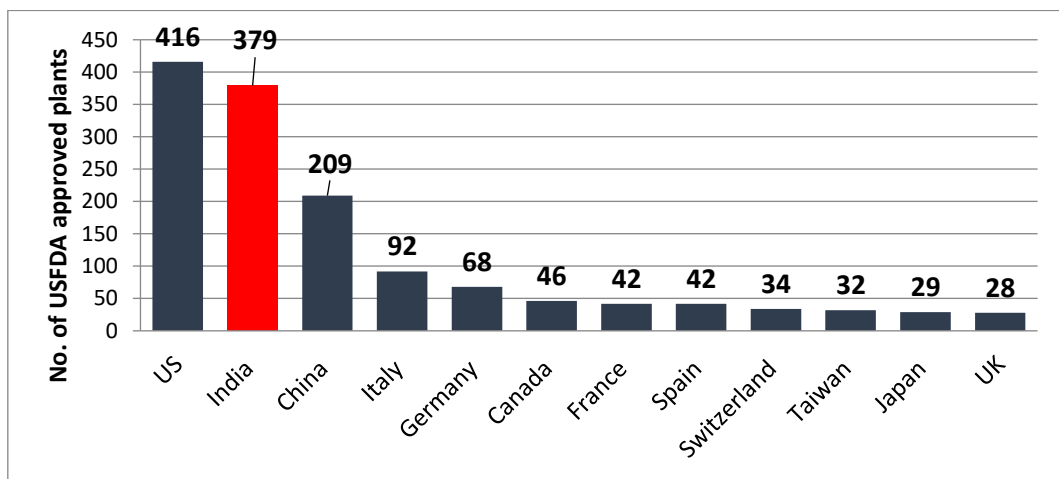


*Figure 34: Number of USFDA approved plants*

*Source: Compiled from data of Bank of America Merrill Lynch report (2015), IBEF 2018, Care Ratings 2017*
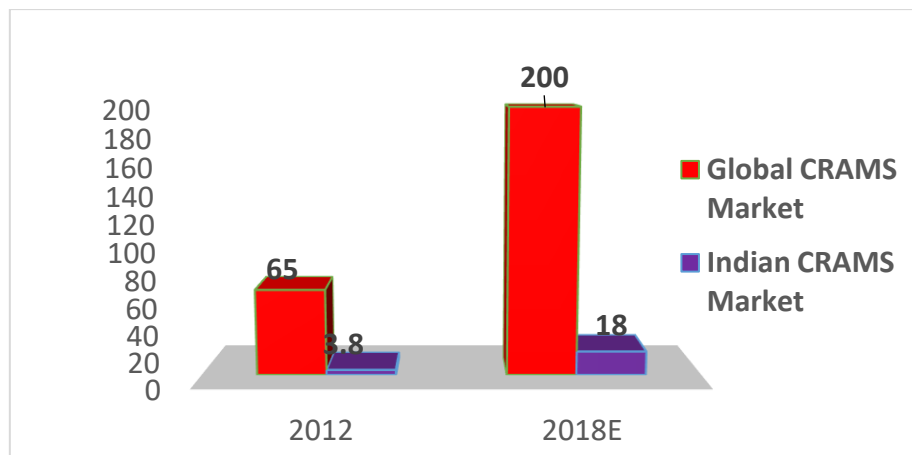


*Figure 35: CRAMS market 2012-2018E (Bn $)*

*Source: Compiled from data of Bank of America Merrill Lynch report (2015), IBEF 2018, Care Ratings 2017*

India remains a location of significant importance to the FDA given the highest number of US FDA-approved plants outside the US and is also the second largest pharmaceutical supplier to the US market in terms of volume of generic drugs.

With 379 plants, India is the first country, outside the US, with USFDA approved facilities followed by:

- China, the closest country, with 209 plants
- And Italy, with 92 plants

Similarly, Indian firms are getting approval to European standards given by EDQM i.e. European Directorate for Quality of Medicine and Healthcare.

- This have given rise to a strong activity in CRAMs, passing from 3,8 Bn$ in 2012 to 18 Bn$ in 2018E with a CAGR of 30%
- Indian CRAMs market in 2012, with its 3,8Bn$ was over 6% of Global CRAMs market, while in 2018E was around 9%

According to Care Ratings, the Indian CRAMs industry is expected to increase approximately to 18Bn$ in 2018. The growth will most be led by increase in strategic alliances and expanding footprints to major geographies through strategic partnerships.

The industry is now looking at mergers and acquisitions, to bring down costs and get drugs to markets.

- Jubilant, Biocon, Shasun, Strides Arcolab, Cadila, Dishman Pharma and Divis Labs have profited by establishing global deals
- Major players like AstraZeneca, Roche, Pfizer and Schering have undertaken outsourcing their manufacturing to enhance profitability but focus internally on core competencies

*2.6.2 India's share of Total ANDA approvals*

Indian companies have had a significant share of ANDA (Abbreviated New Drug Application) approvals from USFDA:

- In general, Indian companies are second only to US-based companies in ANDA approvals

- The share of total approvals has fluctuated in the past 6 years (2012-17) from 30% to a maximum of 39%

- In 2017, USFDA approved a maximum of 847 ANDAs of which Indian companies received 314, the maximum value in recent years
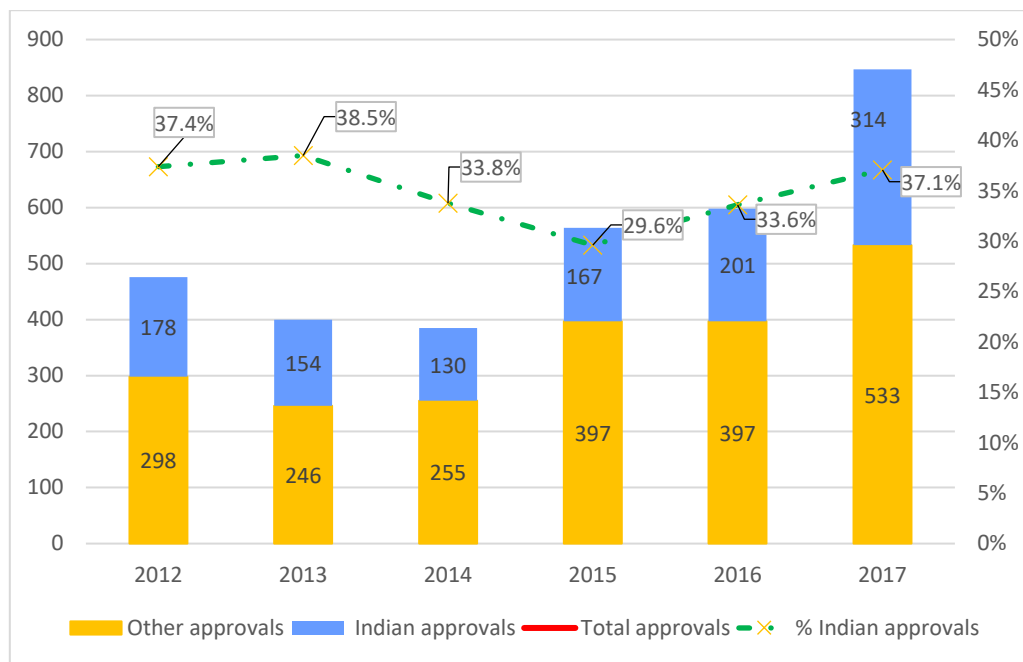


*Figure 36: Approval of abbreviated new drug application (ANDA) by USFDA*

*Source: Compiled from data of Bank of America Merrill Lynch report (2015), IBEF 2018 , Care Ratings 2017*

## 2.6.3 India's share of total ANDA approvals by companies

Approvals in 2017 by Indian company

- Zydus group received most ANDA approvals with 77

- Followed by Aurobindo Pharma with 51 ANDA approvals

- Sun Pharma with 22 approvals

- Other Indian players range from 10 to 18 approvals each

This high approval rate shows that Indian companies are strongly present in a highly regulated market like US. Similar presence is effective in Europe and also in emerging markets.
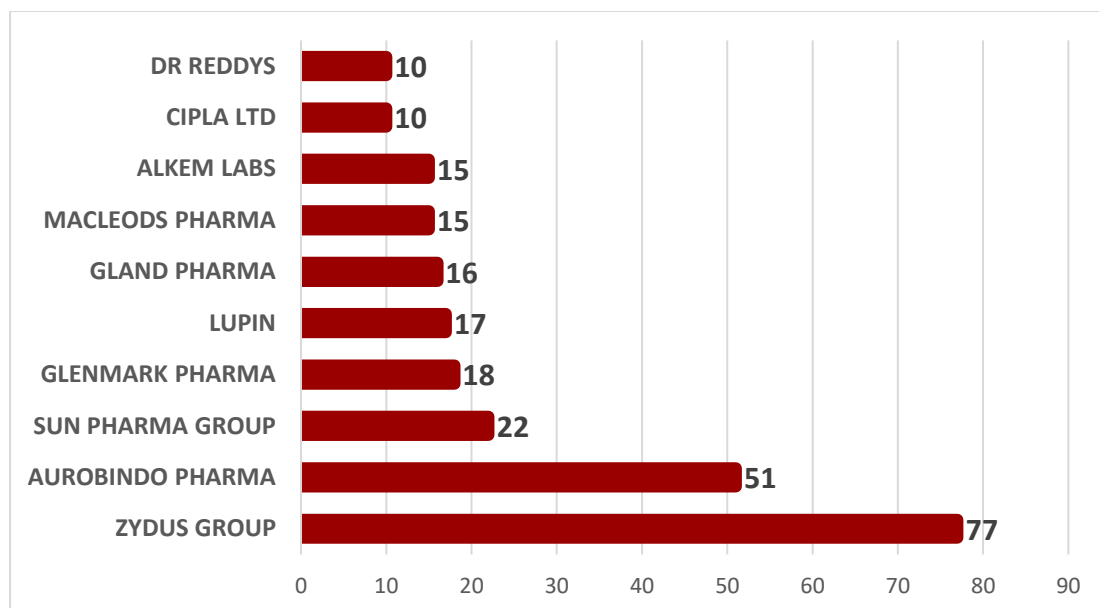
*Figure 37: Number of final ANDA approvals 2017 by top Indian companies*

*Source: Compiled from data of Bank of America Merrill Lynch report (2015), IBEF 2018, Care Ratings 2017*

### 2.6.4 Market share of Top 10 Indian pharma companies

In 2015 the top 10 companies have 43% of the domestic consumption market; only 3 are not Indian companies. The Indian Pharma Market is experiencing a strong contention between over 24 thousand company, many very small.

- The top 10 companies in recent years have held:
  - 42-43% of the domestic market
  - Only 3 of them are Big Pharma
- In particular:
  - **The leader Sun Pharma**: was successful in turning around Ranbaxy and other distressed assets and flawless execution in domestic/US business
  - **The second player Abbot** was capable of absorbing an important asset as Piramal (4th. In 2007)
  - **Cipla:** Strong brands portfolio, front-end strategy and a new credible management team kept the company to the third position, which benefitted from the strong growth in anti-infective, respiratory and gastro portfolio

56

| | 2007 | | | 2015 | | | 2017 | |
|---|---|---|---|---|---|---|---|---|
| **Rank** | **Company** | **%** | **Rank** | **Company** | **%** | **Rank** | **Company** | **%** |
| 1 | Glaxo SmithKline | 5.10% | 1 | Sun Pharma + Ranbaxy | 8.80% | 1 | Sun Pharma + Ranbaxy | 8.60% |
| 2 | Ranbaxy | 5.10% | 2 | Abbott + Piramal + Solvay | 6.20% | 2 | Abbott + Piramal | 6.20% |
| 3 | Cipla | 5.10% | 3 | Cipla | 5.00% | 3 | Cipla | 4.60% |
| 4 | Nicholas Piramal | 4.30% | 4 | Zydus Cadila + Biochem | 4.20% | 4 | Zydus Cadila | 4.20% |
| 5 | Zydus Cadila | 3.50% | 5 | Mankind Pharma | 3.70% | 5 | Mankind Pharma | 3.60% |
| 6 | Sun Pharma | 3.20% | 6 | Alkem | 3.50% | 6 | Lupin | 3.30% |
| 7 | Alkem | 3.00% | 7 | Glaxo Pharma | 3.30% | 7 | Alkem | 3.10% |
| 8 | Pfizer | 2.60% | 8 | Lupin | 3.50% | 8 | Glaxo Pharma | 3.00% |
| 9 | Lupin | 2.40% | 9 | Sanofi India + Universal | 2.50% | 9 | Macleods | 2.80% |
| 10 | Dr Reddy's Labs | 2.40% | 10 | Glenmark Pharma | 2.40% | 10 | Intas | 2.80% |
| | Others | 63.30% | | Others | 56.90% | | Others | 57.80% |
| | TOTAL TOP 10 | 36.70% | | TOTAL TOP 10 | 43.10% | | TOTAL TOP 10 | 42.20% |
| | No of Indian firms in TOP 10 | 8 | | No of Indian firms in TOP 10 | 7 | | No of Indian firms in TOP 10 | 7 |

*Table 6: Market share of Indian Pharma Companies*

*Source: Compiled from data "Motilal Oswal reports"*

*2.6.5 Indian Pharmaceutical players sharpen focus on regulated markets*

Over the past few years, Indian pharmaceutical players have been increasingly tapping opportunities in global generics markets, especially the US and Europe. Meanwhile, mid-sized and small-sized players have targeted semi-regulated markets of Africa, Asia and Latin America to enhance their distribution network before exporting to regulated markets.

Buoyed by the above trends, Indian formulation exports recorded close to 17% CAGR between 2009-10 and 2013-14 (In dollar terms). The increase in growth was led by exports to both regulated markets, which grew by 22%, and also aided by exports to semi-regulated markets, which grew by 13% (CAGR) over the same period. For bulk drugs manufacturers, a burgeoning generic market, and cost reduction measures by global pharmaceutical companies present a huge opportunity in regulated markets. Backed by cost-competitiveness, well-developed process chemistry skills and the largest number of drug master filings globally, India is well placed to tap export opportunities in regulated markets.

*2.6.6 Large players enjoy better profitability and undertake higher capital investments*

Typically, large players (in both formulations and bulk drugs segments) have more profitable business models due to their wide base in regulated markets, which fetch higher realizations. Presence of strong brands in the domestic market further aids large formulation players. However, significant exposure to international markets also exposes these players to risks, such as volatility in currency rates, overall market performance and outsourcing plans of key players in the target destinations, regulatory risk amongst others. In terms of capital expenditure too, large players score over smaller formulation and bulk drugs firms, as the latter have a fewer number of US FDA-approved plants, which significantly reduces their capex requirements.

*2.6.7 Rising M&A activities in the Indian Pharma Industry*

The Indian Pharmaceutical Industry is witnessing increased M&A activities from domestic and international players which will help to boost R&D expenditure to achieve economies of scale and to strengthen the marketing network. As per the Department of Industrial Policy and Promotion (DIPP), the pharmaceutical sector attracted Foreign Direct Investments of USD

11.58 billion during April 2000 to February 2014. Since 2013, there have been 46 M&A deals (including announced and closed deals) in the pharma sector in India.

Some of the key M&A deals were:

- Sun Pharma announced to acquire Ranbaxy in April, 2014 for USD 4 billion, which will make it the 5th largest pharma company in the world
- Aurobindo Pharma acquired 100% stake in Andhra-Pradesh based Hyacinths Pharma and 25% stake in Silicon Life Sciences in September 2013
- Competition Commission of India (CCI) has approved Japanese firm Mitsui's proposed takeover of 26.71 % stake in Arch Pharmalabs Ltd. in January 2013
- Panacea Biotec Ltd. has entered into a strategic alliance with US-based Osmotica Pharmaceutical Corp to develop and market niche generic medicines for several markets including the US in September 2012.
- Nicholas Piramal Healthcare sold its domestic formulations business to US-based multi-national drug major Abbott Laboratories for USD 3.72 billion in November 2011

The outlook for the Indian Pharmaceutical industry remains positive on the back of patent expiries through which the country is expected to gain a larger foothold in the world's generic market. However, as witnessed in the past, there has been an increase in the number of import alerts issued by the USFDA which has hampered the image of Indian Pharma companies and the supplies from such company's units were banned. If this continues in the long term, it may hurt the profitability of Indian generic drug producers. Thus, the need of the hour is that Indian firms should make sure the quality standards are adequately met.

# CHAPTER 3 Brief Introduction of the current situation of the Italian pharma market

## 3.1 An overview of the Italy's Economy, Its challenges, Opportunities and Impact

Italy is the world's ninth biggest economy. The country's economic structure relies mainly on services and manufacturing. The services sector has accounted for about three quarters of total GDP and employs around 65% of the country's total employed people. In the service sector, the most important contributors are the wholesale, retail sales and transportation sectors. Italy's industry accounts for a quarter of total production and employs around 30% of the total workforce. Manufacturing is the one of the most important sub-sectors in the industry sector. Italy's manufacturing is specialized in high-quality goods and is mainly run by small and medium-sized enterprises. Majority of them are family-owned enterprises. Agriculture accounts for the remaining share of total GDP and it employs around 4% of the total workforce.

Majorly the country is often divided into a highly-industrialized and developed northern half where approximately 75% of the nation's wealth is produced; and a less-developed, more agriculture-depended southern part. Because of this, unemployment in the north is lower and per capita income in higher compared to the south.

Italy suffers from political instability, economic stagnation and lack of structural reforms. Prior to the 2008 financial crisis, the country was already idling in low gear. In fact, Italy grew an average of 1.2% between 2001 and 2007. The global crisis had a deteriorating effect on the already fragile Italian economy. In 2009, the economy suffered a hefty 5.5% contraction—the strongest GDP drop in decades. Since then, Italy has shown no clear trend of recovery. In fact, in 2012 and 2013 the economy recorded contractions of 2.4% and 1.8% respectively.

Going forward, the Italian economy faces several important challenges, one of which is unemployment. The unemployment rate has increased constantly in the last seven years. In 2013, it reached 12.5%, which is the highest level on record. The stubbornly high unemployment rate highlights the weaknesses of the Italian labor market and growing global competition. Another challenge is presented by the difficult status of the country's public

finances. In 2013, Italy was the second biggest debtor in the Eurozone and the fifth largest worldwide (ECONOMICS, 2019).

### 3.1.1 Economic History

After World War II, Italy experienced a shift in its economic structure. It transformed itself from an agricultural country to one of the most industrialized economies in the world. The force behind the post-war economic miracle was the development of small- and medium-sized companies in export-related industries. In the following decades, the economy has had both ups and downs.

Being a country with very few natural resources, Italy is strongly dependent on oil imports. The economy was hit hard by the two oil crises during the 1970s. As a result, it experienced a stage of stagflation—weak economic growth combined with high unemployment and a high inflation rate. The economy began to recover in the early 1980s due to the implementation of a recovery plan. Restrictive monetary policies brought inflation down, while fiscal- and growth-oriented policies reduced public spending and tightened the budget deficit.

Before the 1980s, most of the Italian state-owned companies were a key driver of growth. However, in the mid-1980s, the state sector started to create distortion in the economy. The mismanagement of public spending led to a deterioration of public finances and triggered excessive corruption. A round of privatization was carried out at the end of the 1980s and beginning of the 1990s. The diminishing role of the state in the economy created more space for private investment. In 1999, Italy qualified to adopt the euro and entered the European Monetary Union (EMU). The Euro was officially introduced into the economy on 1 January 2002.

Italy was hit by the financial crisis in 2007. Since then, the economy has underperformed. In a bid to face the recession, the government has passed two major austerity packages. The first one, under the administration of Silvio Berlusconi, was implemented on May 2010 and totalled EUR 24 billion. Later, in December 2011, the government led by Mario Monti introduced a EUR 30 billion austerity package. While the former package was focused on a reduction of government spending in order to reduce the nation's budget deficit and public debt, the latter introduced, among other measures, a series of tax increases.

### 3.1.2 Italy's trade structure

Against the backdrop of a weak domestic demand, the external sector's performance is crucial for the Italian economy. One of the most important pillars of the economy is the production of high-quality products such as in the machinery, textiles, industrial designs, alimentary and furniture sectors. These products contribute substantially to the country's exports. However, as a country poor in national resources, its energy and manufacturing sectors are highly dependent on imports. This makes Italy's external position vulnerable to changes in import prices such as fuel. The county recorded trade deficits from 2004 until 2011. However, in the last two years, falling imports have helped to turn the balance into positive figures.

Italy's trade volumes increased significantly after the country joined the Eurozone. Despite growing global competition, in 2013 Italy ranked as the world's 10th largest exporter and 11th largest importer. Italy's main trading partners are inside the Euro area, in particular Germany, which is the country's main exports destination and accounts for around 12.6% of Italy's total exports and France, accounting for 11.1% of total exports. Other important export destinations are the United States, with a share of 6.9% of total exports, and Switzerland with 5.2%. Germany and France are Italy's top imports partners, accounting for 12.4% and 10.8% share of total imports respectively.

### 3.1.3 Exports from Italy

Since the country's manufacturing sector is specialized in high-quality goods, Italy plays an important role in the global market of luxury goods. The country's main exports are mechanical machinery and equipment, which account for around 24% of total exports, as well as motor vehicles and luxury vehicles (7.2%). Home to some of world's most famous fashion brands, Italy occupies a special niche in the global market of fashion and clothing. In fact, exports of clothing and footwear account for around 11.0% of the country's total exports. Other important exports include electronic equipment (5.6%) and pharmaceutical products (4.6%).

Since 2008, the country has experienced anaemic growth in merchandise exports of 1.6% annually. In nominal terms, merchandise exports have gradually outsized imports, which caused the last two years (2012 and 2013) to close with a trade balance surplus.

*3.1.4 Imports to Italy*

Italy's main imports are fuels, which account for around 17% of total imports. This is due to the country's lack of natural resources, which makes it highly dependent on energy imports. Other imports include machinery (14.2%), raw materials (10.0%) and food (7.0%)— Italy is a net food importer because the landscape is not suitable for developing agriculture.

Since the financial crisis, merchandise imports have expended at a slower rate on average than merchandise exports. In fact, in the last six years merchandise imports have grown a meagre 0.4%.

*3.1.5 Italy's monetary policy*

At the beginning of the 1980s, the Central Bank of Italy raised its interest rate to a record high of 19.0% in order to fight the high rate of inflation. After this policy adjustment, which is seen as a "milestone" in the evolution of monetary policy in the country, the inflation rate decreased constantly. More decisive monetary policies that were conducted in the 1990s brought the inflation rate down further. In 1998, the rate fell to 1.8%. The Central Bank of Italy is completely separated from the influences of the government and has to comply with the rules dictated by the ECB, which are the same for all the member countries of the union. The main aim of these rules is to protect the common currency. The Bank of Italy, as part of the Euro system, helps to draft the monetary policy for the Euro area. The primary objective of the Euro system is price stability. To achieve price stability, the European Central Bank controls short-term interest rates. Changes in interest rates accommodate the financial needs of the banking system. Lately, in June 2014, the ECB reduced the official interest rate and introduced a negative deposit rate. The impact of these monetary-policy decisions in the Italian economy is expected to be observed in the short term.

## 3.2 A brief Introduction about Demography of Italy

Italy's 2019 population is estimated at 59.22 million according to the latest UN projections. The official Census figures are more optimistic, estimating the population at 61,838,227 in 2016. Italy, officially the Italian Republic, is located in Southern Europe and bordered by France, Slovenia, Austria and Switzerland along the Alps. This famously boot-shaped

country is the 4th most populous country in Europe (after France, the United Kingdom, and Germany) and the 23th most populous in the world.

### 3.2.1 Italy's surface area and Population density

Italy's population density is very uneven and the Po Valley is the most densely populated with almost half of the country's population. Other densely packed areas include the metropolitan areas of Naples and Rome. The Basilicata plateaus, the Alps and Apennines highlands, and the island of Sardinia have a very sparse population. The total surface area comes to 301,340 square kilometers within the boundaries, including 7,600 kilometers of coastline. In combination with the total population, the density comes to approximately 197 people per square kilometer overall.

### 3.2.2 Italy Population growth

Italy's population is expected to decline throughout the 21st century with a death rate now greatly exceeding the birth rate, Latest indicators show 1,673 deaths per day, compared to just 1,353 births per day. Despite a positive net migration of 289 per day, the overall trend is now negative. Currently, Italy's foreign residents are outpacing the country's population growth with a foreign population that grew 7.4% in 2012, compared to a population growth of just 0.5%. Italy is a rapidly aging country, and in 2014 a full 22% of its population was 65 or older, with just 13.5% under the age of 15.

### 3.2.3 Italians and their health

Italians' health has certainly changed for the better over these 40 years. This is illustrated by one basic statistic: a girl born in 1978 could hope to live to 77 and a boy to about 70. A girl born today has a life expectancy of 85, and a boy of 81. In these 40 years Italians have gained almost 10 extra years of life: an impressive figure. The gain of ten years, as well as a much better and more satisfactory quality of life, is the result of the spread of the culture of prevention, attention to styles of living, and progress in medical science, especially as concerns pharmaceuticals. Thanks to such progress, Italy - according to the Organization for Economic Cooperation and Development - ranks fourth for longevity after Japan, Spain and Switzerland (Farmindustria).
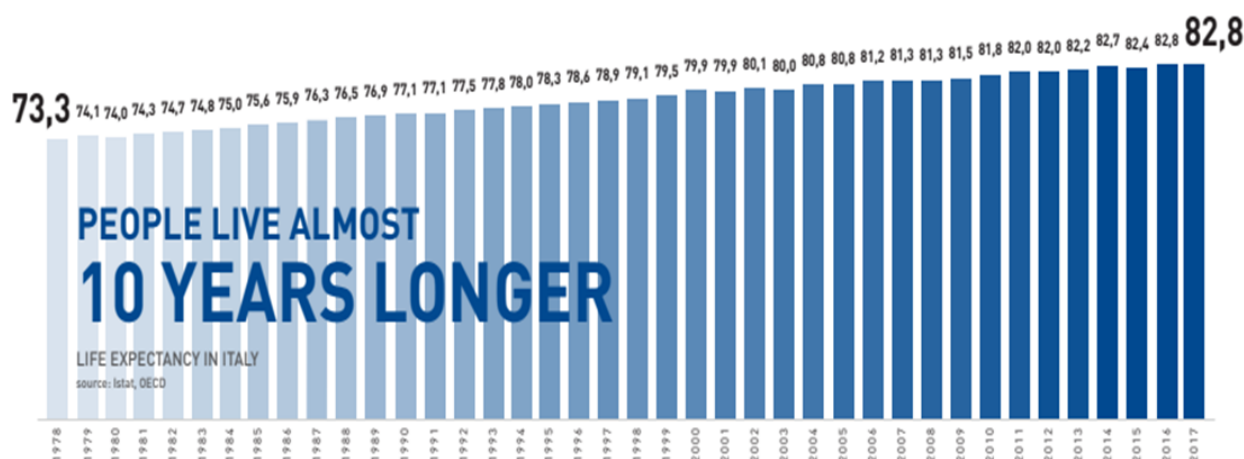
*Figure 38: Life expectancy of Italians from 1978 to 2017 (in years)*

*Source: "ITALY AND ITS PHARMA COMPANIES A SHARED PATH" Farmindustria 2018*

## 3.3 An introduction to Italian Pharmaceutical Industry

The only Italian manufacturing sector currently above the pre-crisis levels is the pharmaceutical industry. Growth in this industry is supported by the strong increase of foreign sales(exports), is widespread across all company class sizes. The Italian Pharma's turnover consistently ranks second in Europe, behind Germany, and ahead of France, UK, and Spain. Pharmaceutical companies are part and parcel of Italy's industrial system. They constitute a national asset based upon research, innovation, development, skills and professionalism. In terms of production, they rank first in the EU and are held to be among the first in the world, thanks to an export performance that surpasses that of their EU competitors. With rising job numbers, these companies represent an important stimulus for Italian economy, its territories and communities that goes far beyond the specific confines of their own industry. The economic performance of the entire production chain generates benefits for patients, as well as providing satisfying and professionalizing employment, new investments, technological innovation, new ties to the country's economy system and greater appreciation of human capital.

Italy is the leading producer of medicinal products in the European Union. At 31.2 billion the value of production exceeds that of Germany and the other major EU countries. This result is entirely due to an increase in exports: in the last 10 years, Italy has registered the largest growth (a cumulative +107%) of all the big EU nations (average growth +74%). European

leadership ensures that Italian pharmaceutical companies will continue to play a growing role in the national, manufacturing system. Currently, pharmaceuticals account for 6% of total exports. These results are reflected in the investments made in Italy, attesting to the pharmaceutical companies' enduring confidence in the country. In 2017, they invested 2.8 billion: 1.5 in R&D and 1.3 in production facilities. This value is up 3% from 2016 and up 20% from 2013 (Farmindustria).
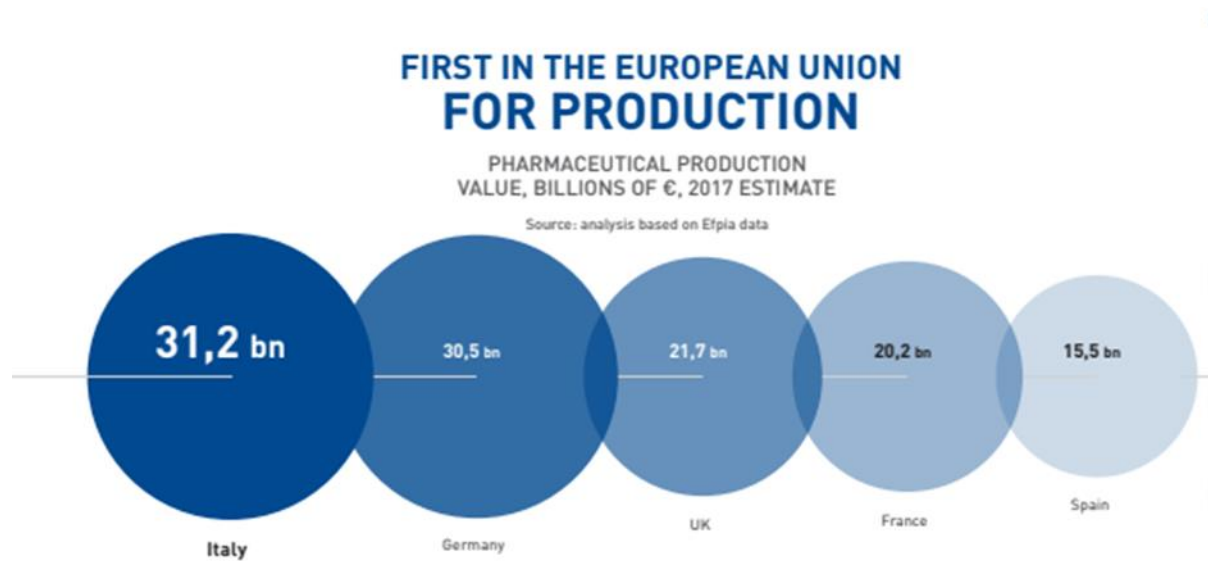


*Figure 39: Pharmaceutical production value in Europe*

*Source: "ITALY AND ITS PHARMA COMPANIES A SHARED PATH" Farmindustria 2018*

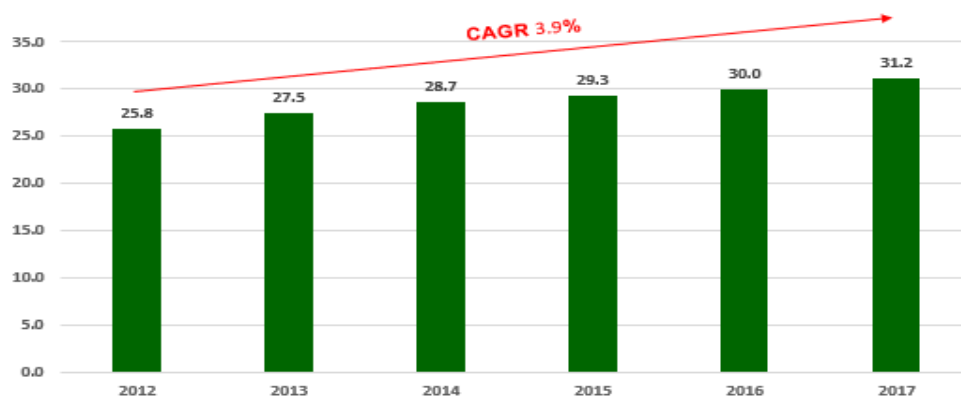### 3.3.1 Growth of the Pharma sector in Italy



*Figure 40: Pharmaceutical production in Italy from 2012 to 2017 in Billion Euro*

*Source: Compiled from data of EFPIA and Farmindustria Iulio 2018*

The above fig shows the growth story of the pharmaceutical production market in Italy, the pharmaceutical industry remains a major development driver for the Italian economy. It represents, in fact, the leading market for growth rates. Over the years it has exceeded the average percentage of Italian manufacturing sectors and in 2016 it has increased its competitive advantage in relation to other productive sectors the Italian Pharma's turnover consistently ranks second in Europe. The Pharmaceutical Production in Italy was of around 25.8 Bn € in 2012, In 2017 it is around 31 Bn € with a CAGR of around 4%.

### 3.3.2 Growth in exports from Italy
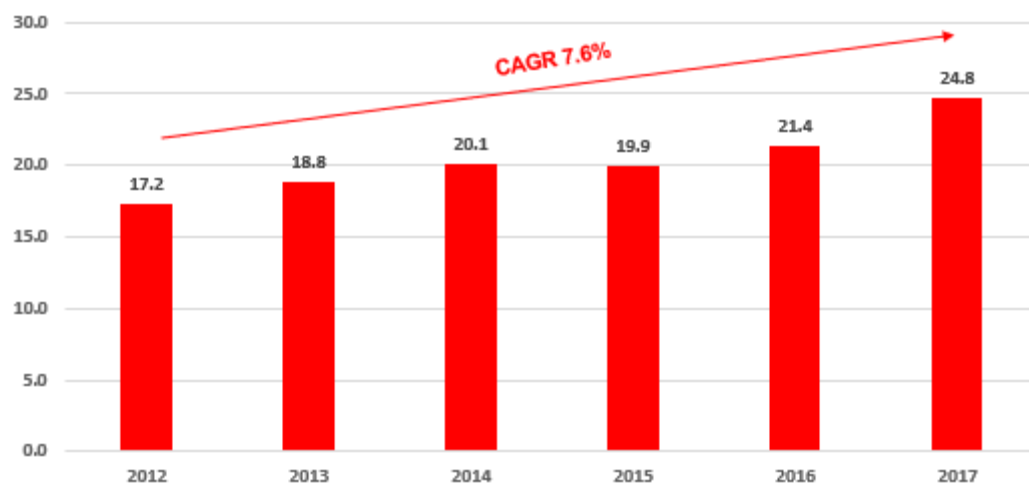


*Figure 41: Pharmaceutical exports from Italy from 2012 to 2017 in Billion Euro*

*Source: Compiled from data of EFPIA and Farmindustria lulio 2018*

From 2012 to 2017 pharma export in Italy has grown more than all big Eu countries and more than big European countries' average. The performance of export is the result of an increased quality of medicines and vaccines exported all over the world.

According to data, the value has gradually increased from 2012 to 2014, going from approximately 17 billion euros to roughly 25 billion euros. In 2015, there was a slight decline. However, in 2017 the value of export peaked reaching approximately 25 billion euros. It has grown in the 2012-2017 period, with a CAGR of 7.6%. During 2014-2015 there was a slight decrease in the exports from 20.1 Bn€ in 2014 to 19.9 Bn€ in 2015.

### 3.3.3 Regulatory Environment in Italy

The regulatory framework governing the manufacturing and marketing of pharmaceutical products in Italy is set out by:

- Legislative Decree No. 219/2006 (the Code of Pharmaceuticals), implementing directive 2001/83/EC of the EU Parliament on the Community Code relating to Medicinal Products for Human Use (and amendments).

- Italian Intellectual Property Code Decree No. 30/2005.

- Consumer Code (Legislative Decree 206/2005) for product liability claims

The Code of Pharmaceuticals governs, inter alia, the national, decentralised and mutual recognition procedures for the issuance of marketing authorisation (while the centralised procedure is directly governed by Regulation (EC) No. 726/2004); the procedure and conditions for the issuance of manufacturing authorisation; and the conditions for advertising of pharmaceuticals, pharmacovigilance requirements, etc.

Matters on pricing and reimbursement of pharmaceuticals fall entirely under the competence of member states, which set out their own rules autonomously from EU institutions or bodies.

In Italy, once a drug is authorised for marketing, it must be classified by the Italian Medicines Agency (AIFA), which is the national regulatory authority, under a specific category for purposes of reimbursement by the National Health Service (NHS): drugs in Classes A and H are reimbursed by the NHS; whilst Class C drugs are not. Further, for a drug to be reimbursed by the NHS, its price will have to be set through mandatory negotiations between the marketing authorisation's holder (MAH) and AIFA, as provided for by Law No. 326/2003 and according to the economic criteria set out in CIPE's Resolution of 1 February 2001 (CIPE Resolution). It is AIFA's exclusive responsibility whether to include a drug under a refundable class and, in that case, what its price should be. For generic pharmaceuticals to be classified under the same class of their corresponding originators, their price must be set at least 20 per cent lower than the originators' price. Notably, MAHs of drugs reimbursed by the NHS may

have to 'pay-back' significant amounts to the NHS if certain budget thresholds both public and related to each MAH – established yearly – are exceeded.

If a drug is not reimbursable by the NHS (ie, it is Class C), the MAH is free to set the price at its own discretion (though certain statutory limitations on price increases still apply).

More recently, Law Decree No. 158/2012 has introduced a new class named Class C-not negotiated, where new drugs are automatically included as soon as they are authorised. In this way, they can be placed on the market as non-reimbursed drugs pending the AIFA's decision on reimbursement and prices. A fast-track procedure is available for certain innovative and orphan drugs. Pursuant to Law No. 648/1996, a drug that is not authorised in Italy may, nonetheless, be provided to patients, and be fully reimbursed by the NHS, if: there is no valid, authorised therapeutic alternative; or (if a valid, authorised therapeutic alternative does exist) the drug is intended to be used 'off-label' (i.e., for a therapeutic indication other than that it was authorised for), on the condition that the off-label therapeutic indication is known and consistent with national and international medical research, and that the off-label marketing of the drug is 'appropriate' and economically viable.

The AIFA assesses whether such conditions are satisfied and, if its opinion is favourable, the drug is included in a specific list and can thereafter be supplied to patients.

It is AIFA's responsibility to enforce the rules described above. This includes, inter alia: granting authorisations to manufacture and trade pharmaceuticals and to conduct clinical trials; monitoring pharmacovigilance activities; supervising the advertising of pharmaceuticals; and ensuring compliance with the restrictions applicable to the public expenditure for pharmaceuticals, etc. AIFA's decisions can be challenged, in the first instance, before the Regional Administrative Court of Lazio and, on appeal, before the Council of State (stefanini, n.d.).

A brief on regulation of Generics in Italy:

- **1991** : Generic formulations are officially introduced into Italy. Before that date these formulations were considered official galenicals. With the law decree 178/91 the

products are denominated according to their API name as pre-packaged formulations fabricated industrially. This is the beginning of the of Generics vs branded products.

- **1991 – 1993** : Introduction in Italy of the Certificate of Complementary Protection (CPC) with the 349 law of 1991. The CPC allowed for a patent extension in Italy for another 18 years, bringing the normal patent coverage to a total of 38 years (20 + 18). Between 1991 and 1993 i the main formulations in Italy obtained this patent extension, increasing the Italian expiring date much after the rest of Europe.

- **1996** : Generic drugs are more precisely identified. The '96 financial law ratified for the first time the international definition of generic drugs.The final law  fixed that the generic drug be offered at least at 20% lower than the corresponding originator formulation.The introduction of the key element of a minimum price difference vs the patented cost of the drug.

- **1999-2000**: The Generic market is inaugurated with the introduction of 5 principal firms: Dorom (Poli-Searle), GNR (Basf), EG (Gruppo Stada), Hexan (Hexal-Angelini), DOC (Zambon-Chiesi-Apoteke).The main molecules proposed were Nimesulide, la Ticlopidine, l'Amoxicilline, l'Aciclovir, il Diclofenac, il Piroxicam and il Lorazepam.The new Generics market begins

- **2001**: In November 2001 a new expenditure saving law n. 405/01 (Decreto Legge 347/01) concerning Generics was introduced. The article 7 of the law introduced important changes

    - The doctor decides whether the pharmacist can change part of his prescription The National Health Service reimburse only the lowest price of the formulation

    - The pharmacist must inform the patient of the lowest cost drug available

    - When the doctor indicates that his prescription cannot be changed, the price difference is paid by the patient.This is a great impulse to the switch possibility of Generics vs branded products

- **2002**: The law n. 112 of June 2002 indicates:

- The duration of the extended patent protection in Italy: CPC (Certificate of Complementary Protection) is halved

- The procedure for the authorization of a generic product can begin one year before the patent elapses

- From January 2003, the Generics packaging has to have an indication of the API contained in the product.A greater opportunity for Generics with shorter patent lives

- **2004**: A new agency AIFA – Agenzia Italiana del Farmaco  or Italian Agency for drugs– is born and becomes the main organ of the Ministry of Health in the Pharma sector
  Its main responsibilities are:

  - Homogeneous drugs

  - The monitoring of the health care expenses

  - The evaluation of new drugs following the cost/benefit rule

  - The evaluation of packaging types,Drug prices were reduced by 4.12%, a new regulatory agency is born.

- **2005**: A new law introduces two key changes:
  - Even class C drugs can be proposed by the pharmacist to the patient in case of lower prices

  - The 20% discount is applied to SOP and OTC products

  - AIFA imposed a beginning 50% price erosion on two patents off patent in that year: Enapren and Rocefin, New changes further liberalise the market

- **2006**:
  - January: Price reduction on all drugs of – 4.4% on the December 2004 prices

  - April: A new text harmonizes the Italian regulations to the EU ones.

  - June: The Central State and the regions decides the information guidelines

  - July: Another price cut of 0.6%.

- August: A new government decree allows traditional distribution as Supermarkets and Hypermarkets (other than pharmacies) to sell unprescribed drugs

- October: Another price cut of 0.5%.

- **2007**: The 2007 financial law allows the Italian Regions to better discipline and programme their health care expenses with a further cut in the Pharma expense budget.

- **2010**: In order to control the public expenditure un pharmaceuticals, the Government introduces more restrictive regulation concerning reimbursement of generics (with lower max value reimbursed for each drugs).At the same time the use of generics is incentivized by Government. The economic crisis will positively impact on the use of generics.

### 3.3.4 Structure of pharma sector in Italy

According to the Italian classification of the economic sectors, known as "ATECO 2007", the pharmaceutical industry is part of the manufacturing sector and can be divided into the following three main activities: 1) Manufacture of basic pharmaceutical products (Fabbricazione di prodotti farmaceutici di base, code 21.10.00); 2) Manufacture of in vivo radioactive diagnostic substances (Fabbricazione di sostanze diagnostiche radioattive in vivo, code 21.20.01); 3) Manufacture of medicines and other pharmaceutical preparations (Fabbricazione di medicinali ed altri preparati farmaceutici, code 21.20.09).

Particularly, the first activity consists of:

- Manufacture of active medicinal substances to be used, for their therapeutic properties, in the manufacture of pharmaceutical products: antibiotics, vitamins, salicylic and acetylsalicylic acids

- Manufacture of blood derivatives for pharmaceutical use

- Manufacture of chemically pure sugars

- Processing of glands and production of extracts of glands

The third activity deals with:

- Manufacture of medicines: immune sera and other blood constituents, vaccines, various medicines, including homeopathic preparations

- Manufacture of contraceptive chemical preparations for external use and hormonal contraceptive medicines

- Manufacture of diagnostic medical preparations, including pregnancy tests

- Manufacture of biotechnological pharmaceutical products

- Manufacture of wadding, gauze, bandages, patches, impregnated or covered with pharmaceutical substances

- Preparation of botanical products (grinding, selection, mincing) for pharmaceutical use
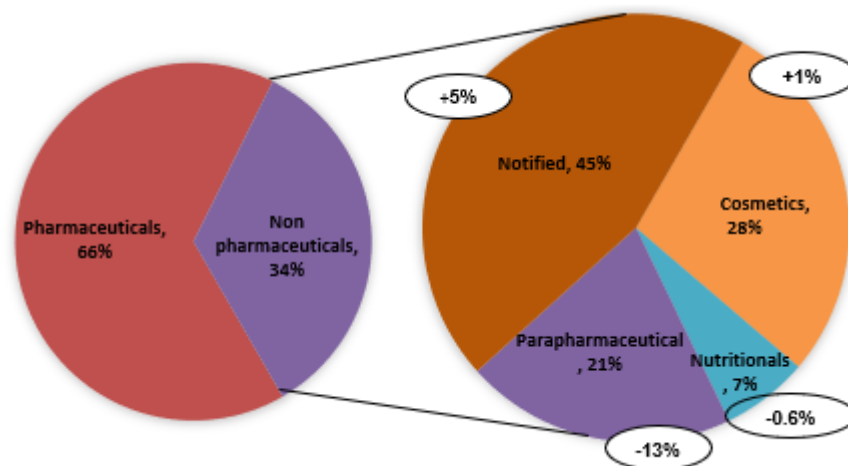
### 3.3.5 Healthcare market of Italy



Figure 42: healthcare market in Italy, 2017 (total value 26 Bn, 2017 (total value 26 Bn €, sell out price)

Source: ANIFA, Report "Il mercato farmaceutico in Italia", 2017- IMS Health data

The Healthcare market in Italy was around 26.9 Bn € in 2011 (-0.37% vs. 2010) and it decreased to around 26.01 Bn € in 2017 (-1.5% vs 2016)

- The Healthcare market includes Pharmaceuticals and Non-Pharmaceuticals
  - **Pharmaceuticals**, accounting for 66 % of total market in 2017vs. 71% in 2011. The reduction is due to the economic crisis but especially to Government decision to reduce drug prices
  - **Non- pharmaceuticals** accounting for the remaining 34% in 2017 vs. 29% in 2011
- In turn Non-pharmaceuticals market includes:

- **Notified products** (vitamin and supplements for example), that cover 45% of non- pharmaceuticals market in 2017, consistently grown vs. 2011 (33%) thanks to new innovative products launched and the transition to this category of many brands. It has grown 5% since 2016

- **Cosmetics** market share was 28% in 2017 which was 31% in 2011. It has grown 1% since 2016

- **Para-pharmaceuticals** market share was 21 % in 2017 which was 29% in 2011. It has declined 13% since 2016

- **Nutritionals** market share was 7% in 2017 which was 8% in 2011.It has declined 0.6% since 2016
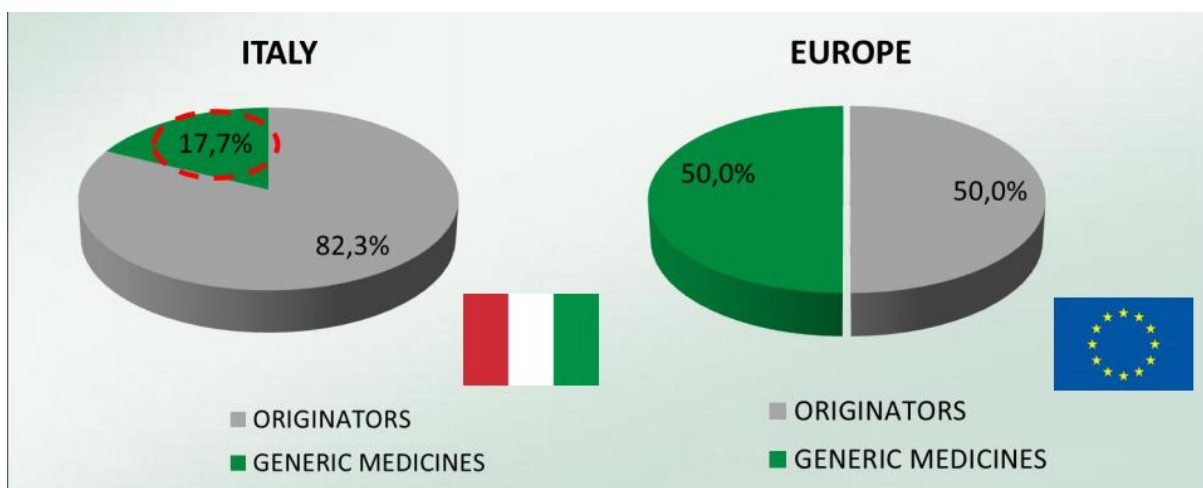
*3.3.6 Generic Penetration in Italy*



*Figure 43:Italian Branded and generics market*

*Source: EGA European Generic Medicines Association*

Generic penetrarion in Italy is lower than in other main EU Countries. Generic medicines are proven to be chemically and therapeutically equivalent to originator brands but are in principle significantly cheaper because they are allowed to enter the market after the patent expiry of the originator brand. In this way, generic manufacturers do not incur R&D costs and are able to offer a significant price advantage to the originator brand. As a result, health insurance is keen to promote generic use among patients as well as encourage generic competition by using a variety of policies with a view to maximizing savings on the drugs bill.

Given the emphasis on health care cost containment and the pursuit of efficiency in resource allocation generic policies and their perceived and actual effectiveness have been at the center of attention for many years in the majority of OECD countries. Branded medicines dominate the Italian market and the generics market is poorly developed. On average, for every Italian citizen, the expense for drugs during 2008 was approximately Euros 410 with a period of treatment of 537 days, showing that there is room for savings at the patient level with generics substitution. While on the other hand India is a market leader in the generics market.
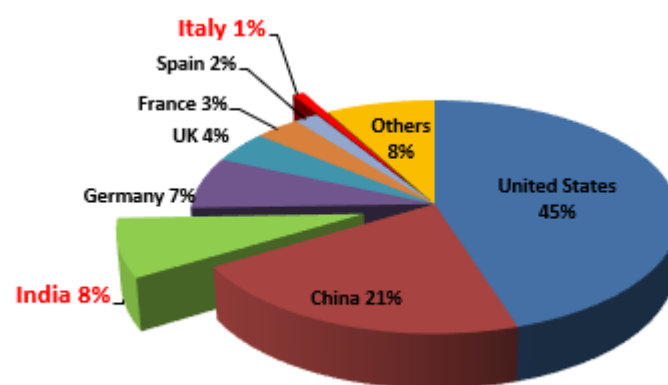


*Figure 44: Worldwide pure generics global market, 2011 124 Bn $*

*Source: Frost and Sullivan*

Global pure generics market was 124 Bn $ in 2011 This market it is expected to grow 8-11% per year up to 2020 according to a study conducted by IMS. This growth is driven by:

- The drugs going off-patent over the next years
- Government encouragement in using generics in order to control public healthcare expenditure, particularly in countries with low generic penetration like France, Spain, Italy and Japan
- Italy accounts for around 1% (roughly 1Bn $) of the Global pure generics market, far from USA with 45% and China (21%)
- India represents 8% of the global pure generics market

### 3.3.7 Market share of Top Italian Pharma companies

Italy has over 200 companies specialize in the production of medicines and vaccines. At Indiogene we calculated the data shown in above shown figures with the help of the data collected from the balance sheets of the individual companies and we were able to shortlist the top 8 companies by sales in 2017.According to the estimates Menarini holds the top position with 3,396 Mn € in sales annually with the domestic sales accounting for just 27% and the sales from the rest of the world accounting for the remaining 73%. Chiesi holds the second position with 1685 Mn € in sales annually with the domestic sales accounting for just 17% and the sales from the rest of the world accounting for the remaining 83%. followed by Recordati and Alfasigma. Top 8 Italian players cover  51.4% of the total pharmaceutical market in Italy .Most of the Italian Pharma companies are Privately held.

| No. | Company | Sales 2017 | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| | | Total Pharma | Italy | | RW(Rest of World) | |
| | | Mn € | Mn € | % | Mn € | % |
| 1 | MENARINI | 3,396 | 903 | 27% | 2,493 | 73% |
| 2 | CHIESI | 1,685 | 294 | 17% | 1,391 | 83% |
| 3 | RECORDATI | 1,288 | 259 | 20% | 1029 | 80% |
| 4 | ALFASIGMA | 1058 | 456 | 43% | 602 | 57% |
| 5 | BRACCO | 928 | 371 | 40% | 557 | 60% |
| 6 | ANGELINI | 845 | 592 | 70% | 253 | 30% |
| 7 | ITALFARMACO | 681 | 238 | 35% | 443 | 65% |
| 8 | ZAMBON | 664 | 178 | 27% | 486 | 73% |
| | TOTAL | 10,545 | 2,915 | | 5,957 | |

Table 7: Market share of top Italian pharma companies

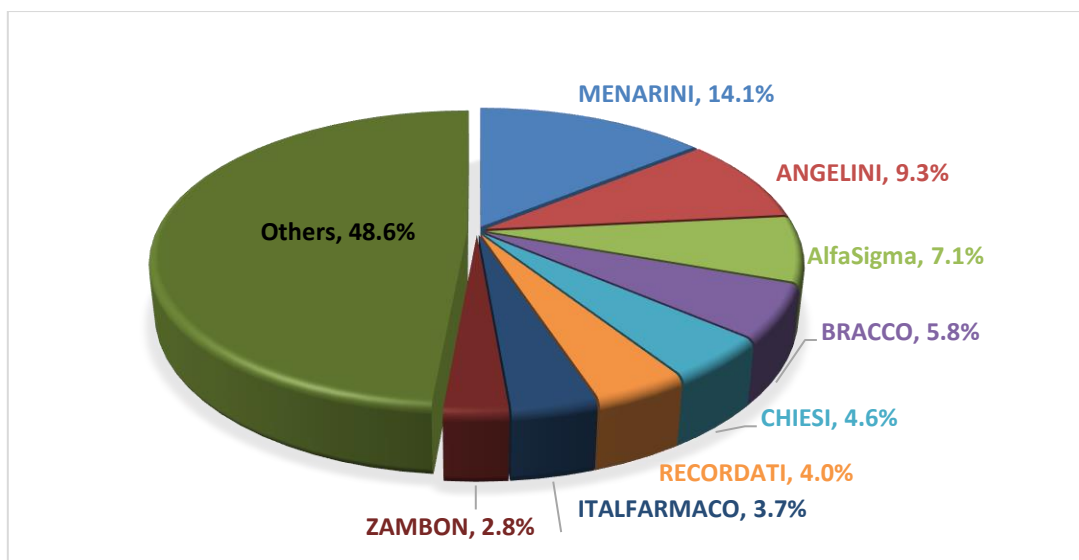Source: Annual reports and balance sheets, Indiogene Analysis

*Figure 45: Market share in Healthcare market in Italy, 2017(total value 31.2 Bn €, Total production price)*

*Source: Annual reports and balance sheets, Indiogene Analysis*

## 3.4 Evidence that even Italian companies have grown through Mergers and Acquisitions
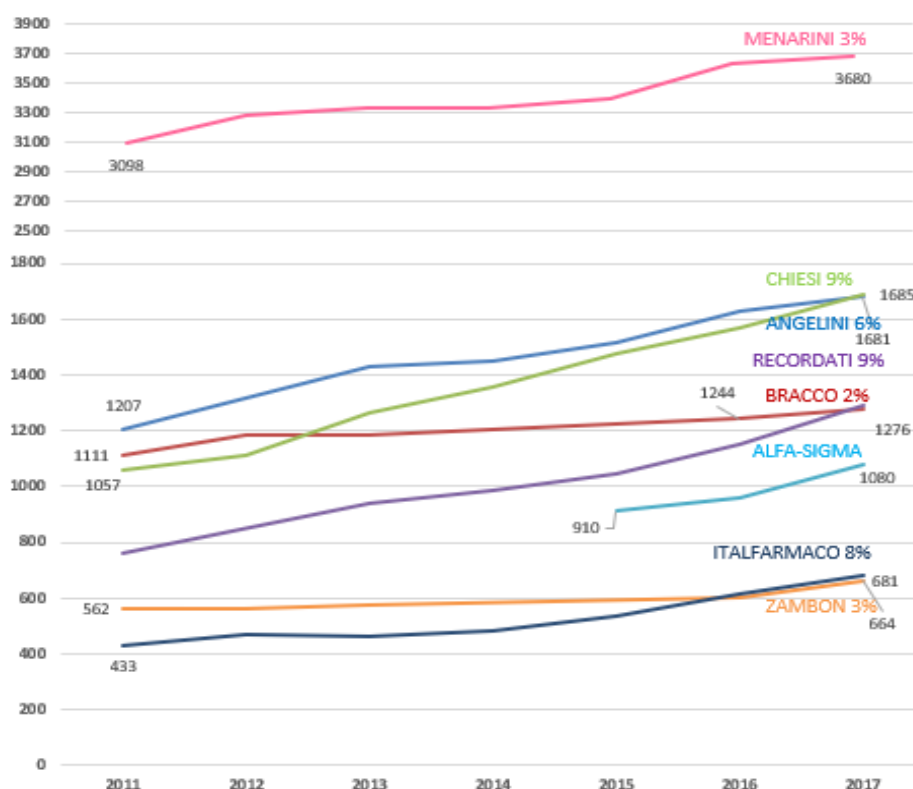


*Figure 46: Top 8 Italian total sales (1) trend, 2011-2017 (Name followed by 2011-17 CAGR)*

*Source: Annual reports and balance sheets, Indiogene Analysis*

The aim of this dissertation is to give clues to the reader about the M&A market in Italy, the characteristics of this instrument and the implications that it has on the economy, considering the Pharmaceutical sector. Thus, here I am going to present a rapid overview of the M&A market in Italy, with the major trends of the sector.

Recordati and Chiesi lead the group with the highest 2011-2017 CAGR, 9%. Chiesi, with CAGR of 9%, has acquired the US Cornerstone in 2009, that has increased the company's sale for around 65Mn €, that has been added to a good level of organic growth too.

Italfarmaco follows with the CAGR of 8%. Alfa-Sigma has also shown a significant growth the birth of Alfasigma dates back to 2015, a group created by the aggregation of two historic Italian companies: Alfa Wassermann and Sigma-Tau.

## 3.5 Conclusions

This study was made to provide the possible opportunities and investments in the pharmaceutical sector in India and Italy by means of mergers and acquisitions. M&A activities have become one of the main ways for Indian companies to stand on the world economic platform. India will be a favourable destination for the Italian investors since the cost of production is very low and has the largest number of skilled resources in almost every field. India's ability to offer end to end services in clinical research covering trials, data management, biostatistics and central laboratory services makes it a preferred destination for trials and research. Also, Italian pharma companies can benefit by catering the growing demand of domestic market in India. Currently there are none of the top Italian companies that are significantly present in the Indian market. The Indian generics business model will Continue yielding good returns for the next 3-4 for at best 3-4 Indian players who have a good pipeline of "first-to-file" molecules, global footprint and low-cost manufacturing. This especially because of many patents expiring that open the market to concurrence. The majority of the remaining companies do not have the muscle (financial/technological) to innovate nor the capability/ time to build global size and scale in generics. These can partner with Global generics players as low-cost options for product development and manufacturing. Also, Innovators looking to create low cost locations for New Molecular Entity (NME) innovation, development and manufacturing. These

strategic partnerships may well take the shape of a majority stake-holding by the global players, as the 2008 Daiichi Sankyo- Ranbaxy deal confirms. At the same time is important to consider that today EBITDA multiples in India are higher than in Europe, requiring buyers to recognize good value to targets.

- Most of the large Italian pharma companies have a difficult situation to handle

  - They feel strong competition from the environment and the impact of Generics

  - Some have major molecules in their product line coming to the end of their patented life

  - Most have already slashed sales forces to meet competition. In the total Pharma market, the estimate is that sales forces have been cut by 20-30%. These costs accounted often for over 1/3 of the total costs

- Integration between one of the big 10 Italian companies and a large Indian group could be highly synergic:

  - **Size**: The combined size would bring the group to be competitive in certain World markets and in selected TA

  - **Geographic distribution**: Italian companies are normally very strong in Italy and have got interesting positions in specific TAs in other European countries, North Africa, Western Asia and in Latin America, some are even strong in North America. This is a complimentary position to most Indian players, strong in India, rest of Asia and often North America

  - **T.A.**: The Italian companies have strengths in the T.A.s of the Developed World and are normally highly complementary to the Indian players

  - **Manufacturing**: Complementarity and cost savings could occur due to lower Indian costs and the "market vicinity" of European plants

  - **R&D:** N.M.E.s development could certainly be enhanced by focusing on target T.A. using lower cost Indian development capabilities.

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