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Heterogeneity in learning processes and the evolution of dynamic capabilities: Evidence from the Indian pharmaceutical industry

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Abstract

This paper examines heterogeneity in the response of Indian firms to the emergence of a new disruptive market segment - biosimilars. Using the novel analytical tool of a technology?market capability matrix we show that path dependency and managerial vision are key drivers of heterogeneity in the reconfiguration processes and strategies employed by incumbent firms to compete in a new disruptive market. Analysis reveals that entry into international markets and accessing external sources of knowledge formed core elements of experimentation with strategy.

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1.0 Introduction

Transitions to new technology, science, a new market sector or changed regulatory regimes are difficult to manage for any organisation, public or private. The emergence of a new market or technology can catch off-guard incumbent firms that are locked into existing markets. This may affect their survival in a new era (Christensen, 1997). In the last two decades the ways firms respond to changes in the external environment has emerged as a major concern of the dynamic capability and industry evolution literature.

In the healthcare sector, the emergence of a new technology or market presents challenges for policy makers and regulators though incumbent firms also need to respond to the challenges posed by the new technology, evolving policy and transitioning regulatory frameworks. In this scenario, firms have to reconfigure existing capabilities and business models as a response to emerging disruptive markets (Teece et al. 1997). To a large extent, the dynamic capability literature has focused on firms in advanced countries. However, for firms in developing countries, the challenge is harder as technological, political and economic complexities make the transformation of capabilities a difficult process (Amann and Cantwell, 2013). This paper fills a gap by investigating how Indian pharmaceutical firms are reconfiguring their existing capabilities in response to the emergence of a market for biosimilars.

Biosimilars are generic versions of biologics - a therapeutic drug category comprising large complex molecules. The market for biosimilars has been created by three drivers; increased demand for affordable therapies, evolving regulatory frameworks and the saturation of small molecule generics markets. The complexity of biological drugs and evolving regulation create new challenges and opportunities for developing country firms (Huzair and Kale, 2011). In this context the Indian pharmaceutical industry provides us with informative case studies to explore the development of dynamic capabilities by resource-constrained firms operating in emerging countries.

Post 2000 the Indian pharmaceutical industry emerged as a cheap global supplier of generic drugs. Indian firms accomplished this by targeting small molecule generic markets in advanced countries, enabling growth and development (Athreye et al., 2009; Gehl-Sampath, 2006; Kale and Wield, 2008). However increasingly competitive generic markets in advanced

countries are witnessing a significant drop in value (Kamath, 2011). For Indian firms reduced opportunity in advanced countries raises important questions for long-term growth and survival. Thus the decline in traditional generic markets along with evolving regulation and technological complexity associated with the emerging biosimilar markets has created significant hurdles for the Indian pharmaceutical industry. This gives rise to the key research question; how are firms reconfiguring their strategies for the development of capabilities in response to the emergence of biosimilar market opportunities? To answer this question we investigate the processes involved in the reconfiguration of capabilities in four Indian pharmaceutical firms.

Using case studies of four Indian firms we demonstrate the heterogeneity in firms' reconfiguration strategies and further explore the origin of heterogeneity when different firms operate in the same environment with the same resource base. We develop a novel analytical tool (a 'technology - market' capabilities matrix) to map and investigate heterogeneity in strategy reconfiguration. Our paper makes three critical contributions to the dynamic capabilities and industry evolution literatures. First, it demonstrates how a change in market re-orientates technological capabilities even in the absence of a radical technological discontinuity. The saturation of existing global generic markets, emergence of a disruptive biosimilar market and the evolution of regulation for biosimilars have significantly altered Indian firms R&D and market priorities. Reduced value of the traditional generic market has created a need for alternative strategies, shaping the evolution of technological capabilities and strategies all along the value chain of biosimilar commercialisation.

Second, the paper shows the kinds of dynamic capabilities that can be developed as a response to the emergence of a new disruptive market. They are of two kinds and are significantly inter-related: diversification of knowledge and technological capabilities through entry into international markets; and partnering with overseas firms related to a new technology (biosimilars). The analysis further shows key subtle differences in strategies employed by each firm to develop dynamic capabilities. It reveals that Indian firms have adopted two distinct types of strategies; first, an organic growth model with R&D technological capabilities at its core and second, an acquisition model with complimentary capabilities like marketing and distribution capabilities forming its main base. We show that this heterogeneity in reconfiguration processes and firm strategies are a function of past firm specific technological trajectories, managerial vision and inter-organisational learning through the observation of other firms' strategies.

Third, this paper shows that unlike the current small molecule generic market business focused on advanced countries, Indian firms are focusing on biosimilar markets in other emerging countries. This is firstly because, the high cost associated with regulatory requirements in advanced countries. Secondly Indian firms de-risking investment by catering to the unmet needs of emerging country markets for affordable biosimilars. We argue that these findings together highlight the clear impact of the external environment on the strategies of emerging country firms in the healthcare sector.

This paper is structured as follows: Section 2 discusses size and growth of the biosimilar market, and subsequent opportunities for emerging suppliers. Section 3 explains the salient features of the Indian pharmaceutical industry and tracks the challenges and opportunities of the biosimilar sector. Section 4 briefly reviews the literature focused on heterogeneity and the dynamic capabilities approach. Section 5 details our data collection methods and the four Indian pharmaceutical firm case studies that are used to illustrate the evolution of firm strategy and biosimilar R&D capability. In section 6 we present our results on the different strategies and the reconfiguration of capabilities of Indian pharmaceutical firms in response to market opportunities. Section 7 concludes.

2.0 The emergence of a disruptive new market: Biosimilars

A biologic or biological drug is a large complex molecule that has been sourced from a living cell, for example, insulin. They are too complex to manufacture in the same way as simple small molecule drugs (e.g. aspirin). The growth in the biosimilar market and the subsequent disruption to the market for small molecule generics and its players is driven by a number of factors such as original biologics coming off patent, pressure on governments all over the world to reduce healthcare costs, development of regulatory guidance in key markets around the world and saturation of markets for small molecule generics.

2.1 Growth in demand for biosimilars

The global market size of biologics was estimated at US\$134 billion in 2009 and with patents for top selling biologics expiring between 2012 and 2019, biosimilars are poised to acquire a significant share of the generics pharmaceutical market (Wechsler, 2011). Table 1 shows key biological products that have already expired or will go off patent in the near future.

(Table 1 here)

The increasing demand for biosimilars is further driven by the universal need for more affordable drugs. Biologicals account for an increasing portion of newly approved therapies for chronic inflammatory diseases, arthritis and cancer treatments. There is significant pressure on governments and pharma companies to make these drugs available at more affordable prices. Biosimilars show a strong potential to deliver therapies at affordable cost as increasing evidence suggests that biosimilars offer reductions of up to 30% compared to an original biologic (Krull and Rathore, 2010).

2.2 Evolving regulation

Governments in different countries and regions are establishing new regulatory guidelines to facilitate the entry of affordable biosimilars. For example, the comprehensive set of guidelines for biosimilars adopted by the EU in 2006 and the WHO in 2009 demonstrates important steps towards harmonisation and consistency (Schiestl, 2011). The passing of the Biologics Price Control and Innovation (BPCI) Act of 2009 in the US is credited with creating a regulatory pathway for biosimilars. Fig 1 charts the evolution of regulatory guidelines against the market potential of different pharmaceutical markets.

(Fig 1 here)

Fig 1 shows that high potential market such as EU, Japan have adopted regulatory framework for biosimilars whereas emerging country markets are slow in development of regulatory framework. As national regulatory agencies in emerging countries now begin to draw their own guidelines for biosimilars, we are observing convergence around regulatory requirements and the emergence of a significant new market opportunity.

2.3 Saturation of the market for 'small' molecule generics in advanced countries

Business models based on generating revenue from small molecule generics markets in advanced countries are now under threat. Kamath (2011) suggests that the value of drugs going off-patent between 2016 and 2020 will fall by 62% from the value in the preceding five-year period (2011-15). In addition, the entry of large pharmaceutical firms into international generic markets has led to increased competition, further eroding the profit margins of Indian manufacturers.

Finally, price erosion is not the only factor. Until 2003, innovative Indian firms tried to create strong profits by aiming first to file status in the US generic market, which provided 180 days market exclusivity to generic manufacturers. In 2003 however, this provision was diluted

allowing more than one generic drug company to enjoy 180-day exclusivity, provided they filed their ANDAs¹ on the same day, denting profit margins significantly. For innovative Indian firms, this created a survival challenge and a need for alternative drivers. Biosimilars represent one such key opportunity for Indian firms. While the production of generic versions of biologics are not an obvious disruptive technology as defined by Bower and Christensen (1995), the challenges facing innovative Indian firms are somewhat akin to those confronting firms facing the innovators dilemma (Christensen, 1997). The emergence of a new market and new process innovations that have accompanied the emergence of biosimilars can catch incumbent firms off guard, since most are locked into existing markets for small molecule generic in advanced countries. As a result, to survive and grow, innovative Indian firms with interests largely in generic markets in advanced countries must consider alternative business models and investment in capability building for biosimilar production.

For resource constrained Indian firms this significant shift in global generics markets will demand a new set of R&D, regulatory and distribution infrastructure and capabilities. In this scenario winners and losers are selected in function of the dynamic firm capabilities most appropriate for the emerging market environment. In this context our investigation focuses on how Indian pharmaceutical firms are reconfiguring strategies and business models in response to emergence of this disruptive new market.

3.0 The Indian pharma-biotech industry

The Indian pharmaceutical industry ranks 12th in the world in terms of value and by volume is the second largest in the world. Taking advantage of weak patent law introduced in the 1970s by the Indian government, local firms used reverse engineering to develop cheap generic drugs, and as a consequence, extensive process R&D capabilities.

The industry grew rapidly in the 1990s, with an average industry growth rate of about 15% for bulk drugs and 20% for formulations (OPPI, 2001). In the 1980s Indian firms consolidated their business in the domestic market and entered other emerging markets to become key suppliers of cheap generic drugs all over the world. In the post TRIPS agreement era, building on their experience in emerging countries, Indian firms targeted small molecule generic markets in advanced countries and built their businesses using their superior process R&D skills, cheap production processes and strong marketing capabilities (Kale, 2010). The shift in global generics markets and the emergence of biosimilar markets has created new opportunities and significant challenges for leading Indian firms.

¹ Abbreviated new drug application

3.1 Challenges for biosimilar development

Switching to biosimilars is not an easy, minimum risk strategy, but a decision that requires considerable financial and organisational investment in developing regulatory, technical and scientific capabilities. The technical competencies that are required include pharmacovigilance and verification of similarity or comparability with an innovator product. As biosimilars can compete not just on price, but with improved formulations² and different methods of drug delivery, some innovative capability is also needed (Barei et al., 2012).

3.1.1 The challenge of developing a knowledge base

Over the years Indian pharma firms have developed a knowledge base firmly embedded in organic and synthetic chemistry. In the case of biosimilars, these firms need expertise to reverse-engineer the biologics and develop stable, therapeutically active cell lines. They also need to develop manufacturing processes to meet specifications and to invest in new infrastructures for controlling living cells, purification, and producing biologic products consistently at commercial scale (Lee et al., 2011). The main constraint for Indian firms is the lack of expertise in particular areas of medicinal chemistry and biology pertinent to biosimilars. A senior scientist in Serum Institute of India points out that there is a lack of knowledge among Indian firms regarding issues of quality, safety and efficacy.

“In biosimilar development it is quite hard to spot small differences in production processes. These can lead to significant changes to drug safety and efficacy. But in India there are very few people who have this knowledge”

(author’s interview, 2013)

3.1.2 The challenge of regulatory requirements

Indian firms are also facing severe challenges of evolving regulation in the biosimilar sector (fig.1). In the case of advanced country markets, regulatory frameworks demand stringent clinical trials and extensive clinical data. This creates financial and technological capability challenges for Indian firms. In the case of emerging country markets the delay in confirming regulatory requirements and in some cases, the evolving nature of regulation, is creating investment challenges for Indian R&D firms. The head of Biosimilars at Serum Institutes laboratories phrased this situation as ‘changing goal posts’. He elaborated this with the

²Differentiated biosimilars and biobetters can result in lower dosage, reduced side effects, reduced rate of degradation in the blood stream and reduced risk of immunogenicity (Barei et al, 2012).

example of immunogenicity³. In the case of small molecules, drugs rarely elicit immune responses but large molecules such as biologicals are capable of triggering immune responses of varying consequences. To understand and monitor immunogenicity, firms have to present pharmacovigilance data which involves significant investment and monitoring over a longer period of time including during the post market phase. This is riskier where regulation is uncertain.

Referring to some of these challenges, a senior pharmaceutical scientist based at Utrecht University in the Netherlands argues:

“[US and European] markets will be dominated by ‘Big Pharma’. It takes between 50 and 100 million euros to develop a biosimilar that meets the regulations in Europe, the US and Japan.... that’s in addition to post-marketing costs and pharmacovigilance demands. I do not see how a small company, especially from India and China, even if they have the technical skills and money to develop a high quality biosimilar could be able to compete with Teva, Sandoz or Hospira”

(Jayaraman, 2010)

The above discussion confirms that the saturation of existing global generic markets, the emergence of a growing biosimilar market and the evolution of new regulation are creating a new set of challenges and opportunities for Indian firms. Furthermore, the growth of Indian firms in the biosimilar sector depends on their capacity to identify and develop dynamic capabilities to exploit opportunities.

4.0 Firm strategies and dynamic capabilities

Firm capabilities were explored as early as 1959 in the works of Penrose who suggested that the growth of firms is conditioned by their resources and the desire to fully exploit them. Taking an evolutionary view, Nelson and Winter (1982) posited that each firm’s access to technological and organisational knowledge differs and is conditioned upon past learning. Highlighting the influence of path dependency and mechanisms of knowledge transfer, Cohen and Levinthal (1990) point out that a stock of past capabilities and mechanisms of knowledge transfer provides the base upon which firms develop the capabilities to cope with new technological change. Change then, is possible, but is conditioned by the past.

³ Immunogenicity is defined as an immune reaction to the introduction of a foreign protein and is the most important safety issue in biosimilar development.

Firm capabilities are known to evolve over time as firms encounter endogenous market changes and exogenous shocks (Athreye et al., 2009). In markets where the competitive landscape is continuously shifting, dynamic capabilities become the source of competitive advantage (Teece et al., 1997). Here 'dynamic capabilities' refer to the 'firm's ability to integrate, build and reconfigure internal and external competencies to address rapidly changing environments'. These capabilities are rooted in high performance routines operating inside in the firm, embedded in firm's processes, and are conditioned by its history.

Eisenhardt and Martin (2000) add that dynamic capabilities are a set of identifiable processes including product development, strategic decision-making and alliancing, which are path dependent in their emergence. The dynamic focus of this perspective is based on stressing the importance of continually developing new capabilities as well as exploiting old ones in the context of a shifting environment. This perspective highlights the dynamic dimension of the capability building process and the role of organisational capabilities in that process. This strand of research has put greater emphasis on organisational issues about integrating the complex diversity of technologies and competencies required to innovate at the technological frontier as seen in works of Henderson (1994) and Iansiti and Clark (1994).

Building on this, Athreye et al. (2009) suggest that dynamic capability development involves effort at all levels in which distinct processes of search and experimentation come to the fore. Firms engage in technological and business strategy experimental search processes to reconfigure relevant capabilities and technologies needed to succeed in an emerging environment. This raises issues of understanding 'how' and 'why', associated with increased diversity in innovative activities and business strategies, conditions under which different types of firm become more innovative and role of interactions with other firms in the development of higher-order capabilities. These learning related interactions include not only linkages with other firms (locally and internationally), local universities and public research institutes but also learning between different categories of firms (e.g. learning in large indigenous firms as a basis for learning in emerging firms). However Amann and Cantwell (2013) point out that in the catch-up literature few studies have sought to analyse and explain such variability in latecomer firms' strategies and technological capabilities.

In the catch-up literature, the majority of research has focused on the roles of government policy and societal institutions in the development of technological capabilities (Fagerberg and Godinho, 2005). This research certainly acknowledges the role of firm level capabilities in technological catch-up but tends to focus on the environmental context in which such

capabilities are developed rather than firm itself as the locus of such development (Teece, 2000). However, a few studies have tried to explain the building of firm level innovative technological capabilities in the late industrialising countries, specifically the firms from East Asian countries (Mathews, 2006; Hobday, 2000; Kim and Nelson, 2000). This literature highlights cumulative deepening of technological and related capabilities at the firm level. Few such firms moved from imitation to innovation through routes of reverse engineering to incremental improvements to creating innovations close to technological frontiers (Ernst, 2000). In this context, Bell and Figueiredo (2013) argue that the study of the dynamic capability development in latecomer firms has been limited and under researched with the exception of Amsden and Tschang (2003), Dutrenit (2000) and Athreye et al. (2009). In the case of Indian firms' response to regulatory change, Athreye et al. (2009) found that Indian firms have developed three kinds of dynamic capability: diversification of knowledge and technological capabilities; internationalisation of production and distribution units; and integration in the innovation process of Western country firms through providing services related to innovative R&D. Amsden and Tschang's (2003) research highlights that in transition to a new era, difficulties may involve issues specifically associated with the technological dimension of dynamic capabilities. This paper builds-on and adds to the research focused on the evolution of dynamic capabilities in emerging country firms by focusing on Indian firms' responses to the emergence of a biosimilar sector.

This paper goes beyond establishing a descriptive portrait of firm level processes involved in the development of dynamic capabilities and associated innovative patterns to engage with the question of why particular patterns have established themselves. It investigates how, if at all, these paths of learning within firms have influenced, or been influenced by, the development of dynamic capabilities in other firms. An attempt is also made to determine what relationship exists between the external research environment and firms' ability to progress along the hierarchy of innovative effort.

5.0 Strategy and dynamic capabilities: Case studies of four firms

The Indian biosimilar market is worth around \$200 million and there are 7-9 companies with capabilities in the manufacture of recombinant products (Ariyanchitra, 2010). Some Indian firms have evolved capabilities for the development of biosimilars and introduced biosimilar products to the Indian domestic market and other emerging countries (see table 2) (Frost and Sullivan, 2011).

(Table 2 here)

To explore Indian firms' strategies, we will present case studies of four Indian pharmaceutical firms involved in development, production and marketing of biosimilars (Table 3).

(Table 3 here)

Primary data for the case studies was collected through interviews with R&D presidents, senior scientists and heads of biotech R&D in the four firms. In parallel we conducted interviews with a key member of the Indian pharmaceuticals industry association and with a senior sector specialist journalist. This data was triangulated by using information in annual reports, analysts' presentations and articles in the business press. Comparative data for the four firms are given in table 3.

A semi-structured questionnaire was used with questions focused on the response of Indian firms to the emergence of biosimilar market opportunities and evolving regulations. Interviews focused on firm strategy, challenges and organisational learning activities involved in the acquisition of new knowledge required for biosimilar capability development. It also covered questions regarding the relevance of existing pharmaceutical R&D and manufacturing in the development of biosimilar capabilities.

Our reasons for focussing on these firms are threefold. One, the firms selected for study are in different stages of developing biosimilar product portfolios and thus provide ideal cases to study the reconfiguration of firm level capabilities (Table 3). Firms such as Biocon and DRL are early entrants while firms such as Cipla and Lupin are late entrants. Second, these cases provide a mix of different types of Indian firms with biosimilar capabilities; pharma firms, biotechnology dedicated firms and pharma-biotech firms. For example, Biocon is a dedicated biotech firm while Lupin and Cipla represent pharmaceutical firms moving into the biosimilar area. DRL represents a biopharmaceutical firm, which has presence in both pharmaceutical and biotechnology markets. This allows us to examine the significance of path dependency, differences in strategies and the role of established routines in the reconfiguration of capabilities. Third, there is a very strong correlation between size and R&D intensity in the Indian pharmaceutical sector (Pradhan, 2007). Therefore, any investment in the biosimilar market is likely to emerge only from the top 30 firms. All the case study firms are among the top 30 Indian pharmaceutical firms.

5.1 Case study firms

5.1.1 Biocon: Dedicated biotech firm

Biocon, established in 1978, is a fully integrated biotechnology company focused on biopharmaceuticals, custom and clinical research. Biocon was the first Indian company to manufacture and export enzymes to the US and Europe in 1979. In the 1990s, Biocon decided to focus on biopharmaceuticals rather than enzymes and set up an in-house biotech research programme. Early R&D efforts were focused on manufacturing 'statins', a class of drugs that lowers cholesterol. In 2001, Biocon became the first Indian company to be approved by FDA for the manufacture and distribution of Lovastatin, one of the earliest cholesterol blockers, in the US. The main milestones in the company's biosimilar capability development are summarised in fig 2.

(Fig 2 here)

Biocon understood that biotech R&D is risky and that it is necessary to formulate and implement a strategy for risk management. As a result Biocon established Syngene, a contract research company, in 1994 and Cyngene, a Clinical Research Organisation, in 2000. These ventures helped Biocon to develop complimentary capabilities in clinical R&D, generate a steady stream of revenue and establish collaborative linkages with overseas pharma companies.

The big breakthrough for the company came with the development of human insulin in 2003. Biocon became the first company in the world to manufacture insulin on a Ptichia expression system. Biocon launched human insulin in the Indian domestic market causing an almost 40% drop in price of insulin and a 20% increase in usage. In 2005, Biocon started supplying human insulin to other emerging countries in Africa and the Middle East.

In 2006, Biocon initiated its Biosimilar strategy by establishing India's largest multi-product Biologicals R&D facility at Biocon Park in Bangalore and primarily focused on products for diabetes and oncology as areas of growth. Biocon concentrated on filling knowledge gaps through collaborative R&D partnerships and by building a strong, well-focused research team. In 2006 Biocon entered a joint venture with the Cuban Institute of Monoclonal Antibodies (CIMAB) to develop antibodies and cancer therapies and followed that with a joint venture with Abraxis Bioscience to develop a biosimilar version of Filgrastim in 2007. In the same year, Biocon hired Dr Barve from a US biotech firm to lead its clinical research organisation and two years later promoted him to head of biotech R&D.

Under the leadership of Dr Barve, Biocon adopted an aggressive strategy of targeting emerging as well as advanced country markets and to achieve that, entered into a range of collaborations and joint ventures (Fig 2). In 2008, for €30 million, Biocon acquired a majority stake in the German pharmaceutical company AxiCorp GmbH (70%) to market and distribute its biosimilar insulin and analogues in the German market but dissolved this partnership in 2011 whilst retaining rights to market products in Germany. In 2009 Biocon formed a strategic joint venture with Mylan, an MNC generics firm, to co-develop four biosimilars and enter the global biosimilar market. In 2013, the Biocon – Mylan partnership achieved its first success with regulatory approval for Trastuzumab.

In 2010, a big moment for Biocon came with its collaboration with Pfizer. Biocon entered a landmark \$350mn deal with Pfizer to globally commercialise several of Biocon's insulin products - Recombinant Human Insulin, Glargine, and Lispro. It was expected that this deal would pave the entry of Pfizer into advanced country markets and gain Biocon an international reputation for biosimilar capability. This deal signalled the coming together of Pfizer's strong marketing and commercialization capabilities, especially in the highly regulated developed markets of the world, and Biocon's expertise in biotech R&D. The insulin products started to roll out in emerging markets in 2011, followed by Europe in 2012 with the US planned for 2015. Shortly after completing its highly profitable US \$350 million deal with Pfizer, Biocon started setting up a manufacturing plant in Malaysia to supply products to advanced markets. The high risk in Biocon's strategy is reflected in the eventual breakdown of the deal with Pfizer. Pfizer changed its strategy and pulled out of the deal in 2012 leaving Biocon struggling with its expansion plans (Banerjee, 2012).

Biocon's successful growth into a fully integrated biotech company with a strong biosimilar portfolio and an extensive presence in international markets was founded on a targeted programme of organic growth and investments in biotech R&D. It showed good foresight in grasping the significance of the emerging biosimilar market long before other firms. In expanding its R&D capability the firm paid attention to human resource recruitment as a means to fill knowledge gaps and initiate collaborations to enter international markets. The breakdown of the Pfizer and AxiCorp GmbH deals along with high R&D investments indicates a major challenge for Biocon is to de-risk its biosimilar strategy.

5.1.2 Cipla (Chemical, Industrial and Pharmaceutical Laboratories Ltd): Pharmaceutical firm

Cipla was established in 1935 by Dr A K Hamied with the aim of making India self sufficient in healthcare needs. Cipla emerged as a technology leader in Indian pharma in the 1970s with its ability to reverse engineer many patented molecules and successfully launch low priced generic versions in the Indian domestic market. Over the last five decades Cipla has developed extensive capabilities in process R&D and emerged as a supplier of cheap generic drugs around the world. Cipla's international generics strategy received a big boost in 2001 with the launch of antiretroviral drugs (ARVs) in emerging country markets at extremely low prices compared with other products. Cipla led the way in supplying ARVs to some of the world's poorest regions at affordable rates. By 2012 Cipla was credited with transforming the global HIV-AIDS treatment landscape and also emerged as one of most successful Indian firms with an average annual growth rate of more than 20%..

According to Capron and Mitchell (2012), Cipla's success in international generics markets lies in matching its business model to markets it wants to grow in, building a broad portfolio of products to achieve economies of scale in production and creating a network of alliances and licensing agreements with a wide range of other organisations with complementary skills and resources. Cipla also differed from other Indian firms in its approach to international markets. Over the years Cipla focused on emerging as a main supplier of APIs to other MNCs and selling cheap generic version of drugs. However, the transformation of the Indian domestic market due to the strengthening of Indian patent act in 2005 and increased competition from global generic manufacturers has created new challenges for Cipla's existing business model. In 2000, these challenges forced Cipla to embrace biosimilars as a key area of future growth. But to achieve any success in the biosimilar market, Cipla faced major hurdles in the form of R&D and manufacturing capabilities. Cipla had no previous experience of biotech R&D or innovative drug discovery R&D and lacked a manufacturing presence outside of India. As a family owned business Cipla further lacked the professional management required to manage international expansion and succeed in the emerging biosimilar market. To overcome these knowledge gaps Cipla embarked on a two-pronged strategy (see fig 3). First, acquisitions of biotech firms and entering inward co-licensing deals. Second, to create top management teams experienced in international expansion by hiring senior management professionals from competitor MNC firms.

(Fig 3 here)

To accelerate biosimilar development in 2004 Cipla created Avesta Biologicals Ltd, a new biotech company in partnership with Avesthagen, an Indian biotech company. Avesthagen

was responsible for biosimilar R&D while Cipla's role was to scale-up, market and distribute in domestic and international markets. In 2007, Avesta Biological acquired Siegfried Biologicals, a biotech company based in Germany, to access biological R&D expertise. Siegfried was a contract-manufacturing company with extensive experience in the development of biologicals including cell line generation, upstream process development and scale-up of manufacturing processes that comply with Good Manufacturing Practices (GMP). However this did not lead to the expected progress on biosimilar R&D and in 2009 Cipla decided to dissolve Avesta Biologicals and Therapeutics due to lack of progress on the development of biosimilar from Avesthagen.

To overcome this failure in 2010 Cipla acquired a 25% stake in MabPharm, an India based biotech firm. In 2011, Cipla helped MabPharma set up a state of the art biotechnology manufacturing facility in India and, in 2014, Cipla gained full ownership of the manufacturing plant by acquiring the remaining 75% share. In parallel to the MabPharm acquisition, Cipla invested \$65 million to acquire a 40% stake in Bio Mabs, a Shanghai based biotech aimed at developing ten monoclonal antibody (mAb) drugs and fusion proteins against rheumatoid arthritis, cancers and asthma for marketing in India and China.

To complement these acquisitions, Cipla decided to build a biosimilar product portfolio through in-licencing. In 2013, Cipla launched its first biosimilar product, Etanercept, through in-licensing from China-based Shanghai CP Guojian Pharmaceutical Co, remarkably at a 30% reduced price than any other competitor brands. In 2014, Cipla in-licensed a second biosimilar, 'Darbepoetin alfa', by entering a co-marketing deal with Hetero Drugs, an Indian biotech company. On completion of this deal Dr Jaideep Gogtay, Chief Medical Officer, Cipla explained,

“We look forward to partner with companies in India and around the world to bring wider access of biosimilar products to patients in need. We have been recognised as the partner of choice because of our expertise in specialist therapies and efficient supply and distribution. Therefore, we anticipate more number of deals across therapy areas in near future”

(Express Pharma, 2014)

Over the years, Cipla has created partnerships in manufacturing, sales and marketing with firms all over the world. In 2012, a new management team initiated a strategy to convert these partnerships into subsidiaries and joint ventures to bolster complimentary capabilities. In 2012, Cipla acquired a distribution partner in South Africa, Cipla Medpro South Africa, for \$512 million and followed that by increasing its stake in a Uganda-based joint venture,

Quality Chemical Industries Ltd (QCIL) from 14.5% to 51.05% for \$15 million. In 2013, Cipla acquired a 100% stake in Celeris, its Croatian distributor, a 51% stake in its UAE distributor and a 60% stake in a pharmaceutical company based in Sri Lanka for \$14 million. Cipla aims to start selling both of these biosimilar products in the international markets using these newly acquired marketing and distribution entities.

In the biosimilar market Cipla is reducing its risk by creating a product portfolio through in-licensing and investing in expanding its international presence by converting its existing partnerships into company owned subsidiaries. This indicates that the company is using its strong complimentary capabilities in the form of sales and distribution infrastructure while depending on partnerships and acquisitions for creating a biosimilar portfolio.

5.1.3 Dr Reddy's Laboratories (DRL): Pharmaceutical firm

DRL was founded in 1984 by Dr Anji Reddy with the aim of creating an innovative Indian pharmaceutical company. In 1989, DRL's major success came with launch of Omezaprozole at a price 50% lower than competitors based on its superior process R&D capabilities. In 2001, DRL became the first Indian company to launch Fluoxetine with 180-day market exclusivity (para IV applications) in the United States. This R&D success was followed by the launch of Ibuprofen tablets in the United States under its own brand name. This represented a key step in the emergence of DRL as a global generics player with innovative process capabilities and strong marketing network in the USA and other advanced countries. In parallel, DRL also invested significantly in developing capabilities for new drug discovery research by setting up R&D labs in India and the USA and creating dedicated R&D teams. However, in 2004, DRL's risky and expensive generic strategy of Para IV applications received a severe setback when it lost the patent challenge in the case of Pfizer's drug Norvasc. Further lack of success in drug discovery R&D led DRL to change its business model and biosimilars were identified as the main area of future growth.

DRL set up biotechnology R&D in 1999 as a separate business unit and within two years launched its first biosimilar product, Filgrastim. In 2003, this effort received a boost with the hiring of Dr Cartikeya Reddy from Genentech Corporation as head of the Biological division. With extensive experience and knowledge in biotechnology R&D, Dr Cartikeya Reddy helped DRL to accelerate the development of its biosimilar business and in a period of 10 years succeeded in launching three more biosimilars; Darbepoetin, Alfa Pegfilgrastim and Rituximab,. In 2007, DRL had breakthrough in biosimilars when it became the first company

anywhere in the world to launch its own version Rituximab, a biosimilar referencing Roche's original \$6 billion cancer drug (see fig 4).

(Fig 4 here)

Gradually, DRL increased R&D investments for its biological division and by 2014, it reached 35% of all total R&D expenses. By 2010, DRL was operating with three biological dedicated manufacturing facilities and a team of more than 300 scientists and engineers. At this stage, DRL adopted a strategy of commercialising its biosimilars in emerging markets as a step towards gaining approval in the US and Europe. This strategy allowed DRL two advantages. First, it helped the company to gather crucial real world experience and clinical data on the performance of its products and, second, it provided DRL an opportunity to generate revenue that could be utilised for developing assets for approval in advanced country markets. Following on from that strategy, in 2010, DRL began selling its generic version of Rituximab in emerging markets at a 30-50% discount compared to the innovator brand.

In 2012, DRL started planning to enter the regulated advanced markets of US and Europe. As part of that strategy, DRL entered into an alliance with Merck Serono, a division of Merck KGaA, Darmstadt, Germany, in June 2012. Merck KGaA is a global pharmaceutical company with proven expertise in developing, manufacturing, and commercialising biopharmaceuticals and chemical compounds. The partnership is to co-develop and globally commercialise a portfolio of biosimilar compounds in oncology, primarily focused on monoclonal antibodies (mAbs). Such an alliance allows DRL to mitigate the risks involved in developing a biosimilar — the cost is pegged at \$100-200 million, with 70% going towards clinical development. By 2013 DRL started applying for approvals from regulators from advanced countries. In 2013, the company filed a US investigational new drug (IND) application for its proposed Rituximab biosimilar and peg-filgrastim and received permission to proceed with the Phase-I trials in 2014. At present, DRL is involved in planning, designing and executing studies under these INDs.

5.1.4 Lupin Laboratories limited: Pharmaceutical firm

Dr. D B Gupta started Lupin in 1968 and made it a private limited company in 1972. Over the years Lupin gained international recognition by becoming one of the world's largest manufacturers and major supplier of cheap anti-tuberculosis drugs including cephalosporin. To succeed in international generic markets Lupin adopted a strategy of focusing on a few

select products and built significant operational efficiencies to emerge as a global leader in those therapeutic segments.

In 2008, Lupin entered the biosimilar sector by setting up the Lupin Biotechnology Research Group as a separate division (see fig 5). In 2010, Lupin established a dedicated biotech R&D unit in Pune and hired Dr Cyrus Karkaria from a US based biotech firm as president of Biological R&D to lead its efforts in biosimilars. Dr Karkaria had extensive experience of biotech R&D which helped Lupin to bridge a key knowledge gap of biosimilar development. Following on this investment in 2010, Lupin set up Lupin Bioresearch Center (LBC), a clinical research organisation, to conduct in-house and outsourced clinical and bioequivalence studies. This facility allows Lupin to develop in-house clinical R&D expertise, generates crucial short-term revenue and establishes links with overseas firms. Gradually Lupin created a pool of 150 biotech scientists dedicated to biosimilars development at its R&D lab in Pune.

To accelerate biosimilar development, in 2012 Lupin in-licensed cell-line technology from NeuClone, an Australian biotech company, to be used in processing of biosimilars for oncology.. This effort by Lupin resulted in the successful launch of two biosimilars in the Indian market by 2013.

(Fig 5 here)

In 2014, Lupin took a major step towards internationalising its biosimilar operations by forming YL Biologics (YLB), a new biotech company, in a joint venture with Japan based Yoshindo Inc.. This new company will in-license monoclonal antibodies (mAbs) from Lupin and also partner with other companies for the Japanese market. YLB will be responsible for conducting the clinical development of certain biosimilars and obtaining marketing authorisations in Japan. Lupin's Etanercept biosimilar, developed by its Biotechnology Research Group, will be the first product to be licensed for clinical development to YLB. Lupin will be entitled to milestone based licensing income in addition to commercial supplies of the drug substance. Both Lupin & Yoshindo will then market the product under their own brand names by leveraging their respective sales networks. This joint venture marks Lupin's first step towards entering biosimilar markets in advanced countries. In 2014, Lupin entered a strategic distribution agreement with LG Life Science, a South Korean company to sell Insulin Glargine, a novel insulin analogue in India. This agreement is aimed at improving Lupin's biosimilar portfolio in the diabetic segment and judging response in the crowded Indian market.

The evolution of Lupin's path towards development of biosimilar capabilities shows significant influence of strategies adopted by Cipla, Biocon and DRL.

5.2 Analytical framework

To analyse our firm level cases of reconfiguration strategy we developed a novel technology-market capability matrix (Fig 7). This matrix provides an analytical tool to map and investigate firm level heterogeneity in business models and its linkage with capabilities. In this matrix we classify technological capabilities on the basis of three component capabilities comprising R&D capabilities, manufacturing, and regulatory handling capabilities while market capabilities are classified on the basis of diversity of a company's markets, management of the product portfolio in each therapeutic segments and presence of distribution and sales network infrastructure.

R&D capabilities include capacities for clinical trials, PK/PD studies, preclinical research, biological characterisation, physiochemical characterisation and development of processes to improve manufacturing efficiency. Manufacturing capabilities are linked with ability to scale up R&D processes to commercial level, capability to handle several stages of cell culture and purification processes, and management of cost associated with building bio-manufacturing units, Regulatory handling capabilities are concerned with preparation of clinical trial data, specifically efficacy studies and pharmacodynamics data in a format required by regulatory authorities. It further involves demonstrating their manufacturing methods are satisfying prescribed guidelines.

Market capabilities will be required for to ensure successful introduction of product into the market and are concerned with a global distribution channels, network of sales representatives and create key partnerships. These capabilities are closely linked with regulatory and technical capabilities in that advanced country markets have more stringent regulatory requirements relative to emerging and developing countries. Therefore firms operating in advanced country markets or a significant number of other emerging markets show superior marketing as well as technological capabilities. Market capabilities will involve also making decisions such as setting up own sales and distribution infrastructure or creating local partnerships to facilitate entry into diverse markets. The risk and investment associated with these decisions guides technology strategies of the firm in biosimilar markets.

6.0 Analysis and discussion

The case studies of Indian firms clearly demonstrate that the emergence of a biosimilar market has significantly altered Indian firms R&D and market priorities and led to the reconfiguration of existing strategies. This suggests that the evolution of the Indian pharmaceutical industry depends on firms' capacity to identify and develop dynamic capabilities to exploit biosimilar opportunities in the domestic and international markets. It is observed that all these firms are employing two reconfiguration strategies viz. the acquisition of skills for the development of biosimilar capabilities and entry into international markets. Table 4-7 indicates the extent to which each mode was employed by the case study firms, pointing out learning through the observation of other companies and revealing subtle differences in firm strategy.

These findings also present evidence of the heterogeneity in firm strategies in terms of learning processes, technology and market. Finally it shows clear linkage between path dependencies and managerial vision in shaping the heterogeneity and technological trajectories of the Indian pharmaceutical firms.

6.1 Heterogeneity in reconfiguration strategies: Technological capabilities

The case study evidence summarised in Table 4, lists the main indicators of rising technological ability in the biosimilar area and the strategies employed to gain these capabilities.

(Table 4 here)

It shows that all firms have invested in the development of biosimilar capabilities by setting up dedicated biosimilar R&D, manufacturing and regulatory facilities. This has created a basic knowledge base for acquiring relatively inaccessible knowledge from external sources and provided a basis for understanding what to search for in external sources of knowledge.

Acquisition of tacit 'inaccessible' knowledge

Firms in our study lack some R&D resources in-house to carry out certain functions and activities such as bioprocess development and cell-line development. These firms have adopted a combination of three strategies to fill these financial and technological gaps: i) increasing R&D investments and setting up in-house clinical research organisations (CRO), ii) establish collaborations with overseas firms and research institutes and iii) hire scientists with extensive experience of biotech R&D.

R&D investments and setting up of in-house CRO

Strategies to develop biosimilar capability involved increasing the level of biotech R&D investments. DRL and Lupin have established biotech as a separate business division and have invested in building separate R&D facilities. In terms of R&D employment, Biocon and DRL have larger proportions of their employees in biotech R&D compared to Cipla and Lupin. Biocon and Lupin have set up in-house CROs as a way to develop their absorptive capacity in the areas of biosimilar commercialisation where they perceive the significance of their own capabilities and sense cost advantages—e.g. clinical trials. Biocon exploited their process development skills to undertake contract research (in clinical research trials and process development) for multinational firms. DRL has preferred to out license clinical trials rather than invest in in-house building of these complimentary capabilities.

Tapping into external sources of knowledge

The Indian firms in this study choose to collaborate and interact with overseas research institutes and firms in advanced countries to fill knowledge gaps and reduce development costs. Table 5 below, illustrates some of these key R&D collaborations.

(Table 5 here)

A typical strategy involves Indian firms handling early product development and early stage clinical trials, while overseas firms produce the compound and handle late-stage clinical trials. An R&D head at a leading firm commented,

Now we are focusing on more global development efforts so we are investing in technologies, investing in partnerships that can give us some late stage capabilities and that can help us access markets like the US and Europe.

(author interview, 2013)

Some early starters such as DRL and Biocon developed collaborations with international research institutes and companies in order to develop basic capabilities in biological R&D. For example, in 2009 Biocon and Amylin Pharmaceuticals entered into a collaborative development agreement for a potential treatment of diabetes.

This finding suggests that firm level dynamic capability development cannot happen in isolation and external linkages with other firms formed a key part of Indian firms dynamic capability development strategies, even though the nature and motive of their relationships differed in each firm's.

Hiring of scientists with biotech R&D experience

Indian firms are trying to acquire specific knowledge (in biosimilar production, development and regulation) by hiring Indian scientists working with MNCs and biotech firms in the advanced countries. All case study firms show evidence of development of biosimilar R&D capability through hiring of scientists (Table 6).

(Table 6 here)

Indian firms attract these scientists by offering leadership positions and providing scope to develop their biological business. But analysis suggests clear differences in motives of hiring in Cipla compared to other case study firms. Cipla's hiring is focused on filling top management positions in marketing, regional and strategy while hiring in other firms is targeted towards improving biotechnology R&D knowledge. This corresponds to Cipla's strategy of building a biosimilar business model around strengths in marketing and distribution capabilities rather than R&D capabilities.

6.2 Heterogeneity in reconfiguration strategies: Market capabilities

The case study evidence summarised in Table 7, lists the main indicators of rising market capability in the biosimilar area and the strategies employed to gain these capabilities.

(Table 7 here)

Entry into international markets

In the case of small molecule generic markets, Indian firms have extensive presence in advanced country markets whether measured through their exporting activity or through their foreign investment activity (Table 7). Indian firms achieved entry into the global small molecule generics market through exporting activity and then setting up of manufacturing facilities in particular countries. Cipla, DRL and Lupin have already established strong marketing and distribution networks in advanced countries due to their presence in small molecule generic markets. This has created significant complimentary capabilities (Teece, 1986) and in-depth understanding of overseas market facilitating entry of Indian firms into international biosimilar markets.

The marketing capabilities and strategies used for entering international small molecule generics market have provided these Indian firms a vital springboard to enter international biosimilar markets. Evidence points to Indian firms reverting to strategies prevalent amongst

pharma firms in the pre -1990 era; targeting the rest of the world (excluding advanced country markets) and domestic markets for growth. Similar to entry into the small molecule generic market, in the case of biosimilars, Indian firms started with a focus on the Indian domestic and other emerging country markets. The Head of Strategy of a leading Indian firm points out:

Taking the emerging country market route helps us do two things: one, stay close to our purpose of accelerating access to affordable biosimilars in emerging countries and second, to access short term revenue that de-risks our business journey and makes business more sustainable.

(author interview, 2013)

This strategy is based on the need for short-term revenue to balance R&D investments, unmet needs for affordable biosimilars in emerging countries and cost associated with regulatory systems in advanced countries. The evolving nature of regulatory systems in advanced country markets and demands of an extensive data creates challenges of cost and time for Indian firms. The strategy of targeting emerging markets offers Indian firms opportunities to collect necessary clinical data and generate revenues to balance R&D investments. This also suggests that external research environments in the form of evolving and diverse states of regulation in advanced markets are influencing Indian firms' strategies in the biosimilar market.

Modes of entry

Table 7 reveals some key subtle differences in terms of modes of entry used by each firm to internationalise their bisomilar business. It suggests that Indian firms used three different routes for setting up of manufacturing facilities in overseas countries: greenfield investments, acquisitions and joint ventures. Biocon is using green field investment and the partnership route while Cipla is adopting the acquisition route to expand in overseas markets.

Biocon has set up a manufacturing plant in Malaysia and established a partnership with Mylan and other firms to serve advanced country and other emerging country markets. In contrast Cipla is acquiring a stake in other biotech firms and converting many of its existing overseas partnerships in manufacturing, sales and distribution into its own subsidiaries through equity deals and joint ventures.

Internationalisation through partnerships with overseas firms

Biocon, DRL and Lupin are collaborating with overseas firms based in emerging and advanced country markets to access overseas markets. Table 7 lists key market focused partnerships of Indian firms. For example, in 2013, Biocon entered into a partnership with

CCM healthcare, which has a strong marketing and distribution presence in emerging markets, particularly Malaysia, Brunei and some others. A head of biologicals from an Indian firm suggests,

We basically have a business-to-business model in biosimilar markets; we access various regions of the world through commercial partners. For example, to pick up the Latin American region we work with the local pharma company to get access to that market. We still haven't built up the strength ourselves in understanding nuances of the domestic biosimilar market; how the regulators work, how the prescriber players behave, setting up the distribution network, these kind of nuances. Instead of investing in those ourselves it is easier for us to find a like-minded partner to take us to market quickly and bring us those capabilities right away.

(author interview, 2013)

Some of these partnerships involve co-development agreements, which help Indian firms to share the cost of development with overseas firms along with the main purpose of accessing international markets.

6.2 Heterogeneity in capabilities, markets and business models

This analysis highlights differences in competencies and the heterogeneity in business models adopted by the Indian firms in the biosimilar product market (table 4-7) It shows that Biocon and DRL have developed superior R&D competencies, compared to late entrants such as Lupin and Cipla. The technological capability and market matrix (fig 7) helps to map differences in capabilities, market and business models of firms in the study.

(Fig 7 here)

High technology capabilities - Advanced markets (first mover)

In this category we use the example of Biocon to illustrate the organic growth model based on building strong R&D capabilities. Biocon was the first company to identify the opportunity offered by the emerging biosimilar market. The company was a biotechnology company from the beginning and set up a clinical research organisation, factors that created path dependency and complementary competencies. Biocon entered advanced country markets using partnership models but the high risk associated with the Biocon model is evidenced in the break-up of its partnerships with Pfizer and AxiCorp.

High technology capabilities - Emerging markets (early entrants)

In this category, we draw upon the example of DRL to illustrate a follower model of high investment, low risk and moderate profit strategy. DRL has shown strong technological capabilities in biotechnology R&D evidenced by its product portfolio and being the first company in India to develop Rituximab. DRL is yet to develop a comprehensive portfolio of biosimilar products and has focused on emerging country markets. This helps DRL to de-risk R&D investments and generate revenue to sustain their biosimilar investments.

Low technological capabilities – Emerging markets (Late entrants)

This category exemplifies Cipla and Lupin as firms that utilise a low investment, low risk and low profit margin pathway. Currently biosimilars are not a priority area of focus but these firms are building R&D infrastructure and creating path dependency for future expansion. Both of these firms have in-licensed biosimilars from overseas firms and are strengthening marketing and distribution networks in emerging and advanced countries.

Low technological capabilities – Advanced market

Currently there are no firms that represent this quadrant but its clear that firms such as Cipla and Lupin are moving to occupy this quadrant. These firms lack experience of reverse engineering large and complex molecules but are driven by strong cash flow, ambitious leadership and well-established marketing networks in advanced countries. These firms are compensating for a lack of R&D capabilities by in-licencing technology and products from overseas firms. These companies aim to use complimentary assets and a partnership or acquisition model to build their biosimilar business. For example, Lupin entered into collaboration with Yoshindo Inc. to access the Japanese biosimilar market while Cipla has acquired the business of its Croatian distributor.

This analysis reveals that in transitioning to biosimilars, these firms choose different paths – Biocon adopting an organic route of investing in R&D and collaborating with overseas firms, DRL through building strong human resources and Cipla along with Lupin through an in-licensing, acquisition and joint venture route. These differences in strategy both give rise to, and result from, capabilities acquired through different means clearly highlighting the influence of path dependency on capability development. However, the success of Biocon and DRL in biosimilar markets points towards the emergence of Biocon's model based on R&D capabilities as the dominating model for growth in the biosimilar market.

6.3 Strategy, disruptive market and dynamic capabilities

The preceding section shows that there are clear relationships between existing capabilities and the changed capabilities built in response to new opportunities. There are capabilities targeted by firms, that is, which are identified as being likely to capture competitive advantages in biosimilars. While existing technological competence played an important role as did the firms' historical trajectories, two other factors also have important roles to play in defining the strategy mixes adopted by Indian biosimilar producers: namely, 'firm specific managerial vision', and 'inter-organisational learning' through the observation of compatriot leader firms.

In transitioning to a biosimilar era, we find that firms choose different paths and business models to create a market- technological capabilities mix. Yet the strategies firms have used to achieve these transitions have also been borrowed from each other. Biocon, an early entrant in the biosimilar segment for example, has built complementary capabilities in clinical R&D. Late entrants such as Lupin are following Biocon's example and have invested in the development of complimentary capabilities by setting up clinical research organisations (CRO's). De-risking biosimilar investment through targeting emerging country markets was initiated by Biocon but is now followed by other Indian firms. It suggests that 'inter-organisational learning through observation of other firms' successful strategies has significantly influenced the strategies pursued by firms and may be as important as own firm learning. In this sense the heterogeneity in business models and inter-organisational learning initiated by firms constitute a search and experiment exercise for the whole industry.

It is also quite evident that firm specific managerial visions are driving reconfiguration strategies and shaping firm level technological learning in Indian firms. The vision of Yosuf Hamied that Cipla could be a significant global player in biosimilars led to change in the management team and drove the company's ambitious acquisition strategy. In a similar vein, Biocon is guided by the ambition of Kiran Muzumdar Shaw to draw global recognition for Indian firms in the biotechnology sector. Her unique vision has guided Biocon's transition from an industrial enzymes company to an integrated biopharmaceutical company on the cusp of entering biosimilar markets in advanced countries.

7.0 Conclusion

This paper highlighted the heterogeneity in the reconfiguration of capabilities and transformation by Indian pharmaceutical firms in order to compete in the biosimilars market. It demonstrated that dynamic capabilities can co-evolve with firm strategies as a response to the emergence of a disruptive market through three main findings.

First, saturation and reduction of value in small molecule generic markets in advanced countries has forced Indian firms to look at complex biosimilars and alternative strategies. Indian firms are targeting biosimilar markets in India and other emerging countries to avoid the high cost of regulatory requirements in advanced countries and de-risk their investments. This clearly indicates the impact of regulation in influencing firm level strategies in the healthcare sector.

Second, it is quite evident that Indian firms are reconfiguring existing strategies by targeting emerging country markets to de-risk their investments and entering into collaborations and partnerships with overseas firms and research institutes to augment their own capabilities. However, evidence also reveals some key subtle differences in strategies employed by each firm to develop dynamic capabilities. Furthermore, these firms are learning through observation of other firms' strategies as evident in the examples of our four case study firms.

Third, two distinctive kinds of reconfiguration strategy variations have been identified. These include, first, an organic growth model with R&D technological capabilities at its core and, second, an acquisition model with complimentary capabilities like marketing and distribution capabilities forming its main base. These diverse business models emerged from technological path dependencies and firm specific managerial visions. Most probably the winning combination will include certain elements of the different models and will prove to be a robust way in which to overcome the key challenges of talent unavailability and resource constraints. However evidence from this research does point towards the emergence of the organic growth model as the dominant model followed by other Indian firms.

Analysis of heterogeneity in strategies to exploit biosimilar opportunities points towards an evolution of Indian firms' capabilities throughout the production process, starting from upstream expansion of the knowledge base and re-orientation of R&D to downstream enhancement of partnership and marketing capabilities in emerging markets. It is quite clear that Indian firms still remain uncertain about the payoffs due to evolving regulations, high financial cost associated with biosimilar development and a restricted talent pool. These firms are currently testing the water by experimenting with strategy.

References

ABLE-PWC (2010) The Vision 2020 BioPharma Strategy – Leadership in affordable therapeutic products, A ABLE-PWC report for government of India

- Amann, E and Cantwell, J (2013) Innovative firms in emerging market countries: An introduction, in Amann E and Cantwell J (eds) Innovative firms in emerging country market countries, Oxford University Press, Oxford: UK
- Amsden, A and Tschang, F (2003) A new approach to assessing the technological complexity of different categories of R&D (with examples from Singapore), *Research Policy*, 32, 553-72
- Athreye S., Kale, D. and Ramani, S (2009) Experimentation with strategy and the evolution of dynamic capability in the Indian pharmaceutical sector. *Industrial & Corporate Change*, 18 (4), 729-860
- Ariyanchira, S (2010) The opportunity for India in the global biosimilars market. *Pharmaphorum*. <http://www.pharmaphorum.com/2010/06/21/the-opportunity-for-india-in-the-global-biosimilars-market/> (access on 10th January, 2014)
- Banerjee, N (2012) A deal undone: Pfizer and Biocon go back on alliance, <http://www.biospectrumasia.com/biospectrum/analysis/1101/a-deal-undone-biocon-pfizer-alliance#.UmLOLfnWSAU>
- Barei, F., Le Pen, C. and Simoens, S (2012) From generic to biosimilar drugs: why take an innovative pace? *Farmeconomia. Health economics and therapeutic pathways* 2012; 13 (3), 21-27.
- Bell, M. and Figueiredo, P (2013) Building innovative capabilities in late comer emerging market firms: Some key issues, in Amann E and Cantwell J (eds) Innovative firms in emerging country market countries, Oxford University Press, Oxford: UK
- Bower, J.L. and Christensen, C.M. (1995) Disruptive Technologies: Catching the Wave. *Harvard Business Review*, January-February
- Cohen, W.M. and Levinthal, D (1990) Absorptive capacity: a new perspective on learning and innovation'. *Administrative Science Quarterly*, 35, 128-152
- Christensen, C (1997) *The Innovators dilemma*. New York: Harper business
- Dutrenit, G (2000) *Learning and knowledge management in the firm: From knowledge accumulation to strategic capabilities*, Cheltenham, UK: Edward Elgar
- Eisenhardt, K. M. and Martin J (2000) Dynamic capabilities: What are they? *Strategic Management Journal*, 21, 1105-1121
- Ernst, D (2000) Global production networks and the changing geography of innovation systems: Implications for developing countries, *Economics of Innovation and New Technology*, 11 (6), 497-523
- Express pharma (2014) Cipla collaborates with Hetero to launch its second biosimilar drug 'Darbepoetin alfa' <http://pharma.financialexpress.com/latest-updates/3975-cipla-collaborates-with-hetero-to-launch-its-second-biosimilar-drug-darbepoetin-alfa>

- Frost and Sullivan (2011) Strategic Analysis of Indian Biosimilar Market. *Research and Markets*. Available at:
http://www.researchandmarkets.com/reportinfo.asp?report_id=1877543&tracker=related
 (last accessed on 10th Jan, 2014)
- Gehl Sampath, P (2006) India's Product Patent Regime: Less or More of "Pills for the Poor?" *Journal of World Intellectual Property*, 9 (6), 694-726
- Henderson, R (1994) The evolution of integrative capability: Innovation in Cardio-vascular drug discovery, *Industrial and Corporate Change*, 3 (3), 607-30
- Hobday, M (2000) East versus South East Asian innovation systems: Comparing OEM and TNC led growth in electronics, in L. Kim and R. Nelson (eds) *Technology, Learning and Innovative experience of newly industrialising economies*, Cambridge and New York, Cambridge University Press
- Iansiti, M., and Clark, K (1994) Integration and dynamic capability: Evidence from product development in automobiles and mainframe computers, *Industrial and Corporate Change*, 33, 557-605
- Jayaraman, K (2010) India's Cipla sets sights on Avastin, Herceptin and Enbrel. *Nature Biotechnology*, 28, Pages: 883–884,
http://www.nature.com/nbt/journal/v28/n9/fig_tab/nbt0910-883a_T1.html
 (last accessed on 10th Jan, 2014)
- Kale, D (2010) The distinctive patterns of dynamic Learning and Inter-firm differences in the Indian Pharmaceutical Industry. *British journal of management*, 21, 223-238
- Kale, D & Wield, David (2008). Exploitative and Explorative Learning as a Response to the TRIPS Agreement in Indian Pharmaceutical Firms. *Industry and Innovation*, 15(1), 93–114
- Kamath, G (2011) Four growth drivers beyond patent for pharma companies like Sun Pharma, Sanofi, *The Economic Times*,
http://articles.economictimes.indiatimes.com/2011-10-13/news/30275357_1_generic-biologics-patent-protection-infringement (last accessed on 10th Jan, 2014)
- Kim, L and Nelson, R (2000) *Technology, learning and innovation: Experiences of newly industrialising economies*, Cambridge and New York: Cambridge University Press
- Lee, A., Saran, D. and Mynhier, M (2011) Manufacturing Strategies for Biosimilars. *Pharmaceutical Technology*, 35 (5), p36-36
- Mathews, J (2006) Catch-up strategies and the latecomer effect in industrial development, *New Political Economy*, 11 (3): 314-35
- Nelson, R. and Winter, S (1982), *An evolutionary theory of economic change*. Harvard University Press. Cambridge, Massachusetts

- OPPI (2001) 'OPPI Pharmaceutical Compendium,' Mumbai: Organisation of Pharmaceutical Producers of India, Volume 2001
- Penrose, E. T. (1959), *The theory of the growth of the firm*. John Wiley: New York.
- Pradhan, J (2007) 'New policy regime and small pharmaceutical firms in India', Working Paper 2007/02. Institute for Studies in Industrial Development: New Delhi
- Suresh, N (2008) Dr Reddys aims to be biosimilar leader,
<http://www.biospectrumindia.com/biospecindia/news/157551/dr-reddys-aims-biosimilar-leader>
- Teece, D (1986) Profiting from technological innovation: Implications for integration, collaboration, licensing and public policy, *Research Policy* 15 (6): 285-305.
- Teece, D., Pisano, G. P., & Shuen, A (1997) Dynamic capabilities and strategic Management, *Strategic Management Journal*, 18(7), 509-530
- Wechsler, J (2011) Biosimilars Development Raises Research Questions. *Applied Clinical Trials*, Vol. 20 Issue 7, p20-22

Table and figures

Table 1 Emerging biosimilar market– by patent expiry date (ABLE-PWC, 2010)

Generic name	Company	Therapeutic sub category	2009 (US\$ sales bn)	Patent expiry
Eptacog alfa	Novo Nordisk	Anti-fibrinolytics	1.32	2010
Nonacog alfa	Pfizer	Anti-fibrinolytics	0.98	2011
Etanercept	Amgen	anti-rheumatics	3.49	2012
Filgrastim	Amgen	Immunostimulants	1.28	2013
Insulin Lispro	Eli Lilly	Anti-Diabetics	1.95	2013
Interferon beta-1a	Biogen Idec	MS Therapies	2.32	2013
Epoetin alfa	Amgen	Anti-anaemics	2.66	2013
Imiglucerase	Genzyme	Other therapeutic products	0.79	2013
Insulin Insulin aspart	Novo Nordisk	Anti-diabetics	1.21	2014
Rituximan	Roche	Anti-neoplastic Mabs	5.62	2014
Octocog alfa	Bayer	Anti-fibrinolytics	1.23	2014
Pneumococcal vaccine	Pfizer	Vaccines	0.287	2015
Insulin glargine	Sanofi-Aventis	Anti-diabetics	4.29	2015
Tocilizumab	Roche	Anti-rheumatics	0.44	2015
Follitropin alfa	Merck KGaA	Fertility agents	0.67	2015
Pegfilgrastim	Amgen	Immunosimulants	3.35	2015
Nimotuzumab	YM Biosciences	Anti-neoplastic Mabs		2015
Somatropin	Novo Nordisk	Growth hormones	0.82	2015
Adalimumab	Abott	anti-rheumatics	5.48	2016
Herpes Zoster vaccine	Merck	Vaccines	0.27	2016
Natalizumab	Elan	MS Therapies	0.59	2017
Sipuleucel-T	Biogen Idec	MS Therapies		2017
Liraglutide	Novo Nordisk	Anti-diabetics	0.13	2017

Human papillomavirus vaccine	GSK	Vaccines	2.93	2017
Bevacizumab	Roche	Anti-neoplastic Mabs	5.74	2018
Insulin glulisine	Sanofi-Aventis	Anti-diabetics	0.19	2018
Infliximab	Johnson & Johnson	anti-rheumatics	3.08	2018
Rotavirus vaccine	Merck & co	Vaccines	0.52	2019
Cetuximab	Merck	Anti-neoplastic Mabs	1.6	2019
Insulin detemir	Novo Nordisk	Anti-diabetic	1.1	2019
Trastuzumab	Roche	Anti-neoplastic Mabs	4.86	2019
Peginterferon alfa 2a	Merck	Interferons	1.52	2019
Ranibizumab	Novartis	Eye – preparations	2.32	2020

Table 2: Indian companies marketing biosimilars in India (Jayaraman, 2010; CDSCO, 2013)

Company	Active substance	Therapeutic area	Year of launch
Dr Reddy's Laboratories	Filgrastim (G-CSF)	Neutropenia, cancer	2001
	rituximab	Lymphoma, Leukaemia, rheumatoid arthritis	2007
	darbepoetin alpha	Anaemia, cancer, chronic kidney failure	2010
	Pegfilgrastim	Cancer, Neutropenia	2011
Biocon	erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2006
	nimotuzumab		2006
	Filgrastim (G-CSF)	Neutropenia, cancer	2007
	streptokinase	Acute myocardial infarction	
	Itolizumab	Psoriasis	2012
	Human insulin	Diabetes	2003
	Insulin Glargine	Diabetes	2013
	Transtuzumab	Breast cancer	2013
Reliance Life sciences	erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2008
	Filgrastim, (G-CSF)	Neutropenia, cancer	2008
	interferon alpha-2b	Chronic hepatitis B, Chronic hepatitis C, cancer	2008
	Epoetin alpha	Anaemia,	2008
	Tissue plasminogen activator	Myocardial infarction	2009
	Follitropin alfa	Female infertility	2010
	Chorionic gonadotrophin hormone r-hcg	Fertile infertility	2011
	Interferon beta -1a	Multiple sclerosis	2011
	Abciximab	Angina Cardiac ischemia	2013

Intas	Filgrastim (G-CSF)	Neutropenia, cancer	2004
	Pegfilgrastim (G-CSF)	Neutropenia, cancer	2007
	interferon alpha-2b	Chronic hepatitis B, Chronic hepatitis C, Cancer	2007
	Erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2005
	Epoetin alpha	Anaemia, cancer, Chronic kidney failure	2005
	Follitropin alpha	Female infertility	2013
	Rituximab	Lymphoma	2013
Wockhardt	Erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2001
	Epoetin alpha	Anaemia, cancer, Chronic kidney failure	2001
	human insulin	Diabetes	2003
	Insulin glargine	Diabetes	2009
Cipla	Etanercept	rheumatoid arthritis, psoriatic arthritis	2013
Shantha Biotech	interferon alpha-2b	Chronic hepatitis B, Chronic hepatitis C, Cancer	2002
	streptokinase	Acute myocardial infarction	2004
	erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2005
Serum	erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2011
Ranbaxy	Epoetin alpha	Anaemia, cancer, Chronic kidney failure	2001
	erythropoietin (EPO)	Anaemia, cancer, Chronic kidney failure	2013

Cadila	erythropoietin (EPO)	Anaemia, Chronic kidney failure	2010
	interferon alpha-2b	Chronic hepatitis B, Chronic hepatitis C Cancer	2011
	Filgrastim (G-CSF)	Neutropenia, cancer	2013
Lupin	Peg filgrastim (G-CSF)	Neutropenia, cancer	2013
	Filgrastim (G-CSF)	Neutropenia, cancer	2013

Table 3 Firms studied in the present research (Annual Reports, 2013)

Firms	Nature of firm	No of employed	Turnover 2012-13 US \$ million	R&D intensity (2013)	Biosimilar Products	Supply of Biosimilar in overseas market
Biocon (Group 1)	Biotech	7100 (4% doctorates & post doctorates)	364.16	10% ((US \$ 36.4 million)	Human insulin, Insulin Glargine, Erythropoietin, Filgrastim, Streptokinase, Itolizumab, Transtuzumab	27 countries
Cipla (Group 2)	Pharma	20000 (5% scientists)	1545.00	4.9% (US \$ 79.5 million)	Etanercept	India
Lupin (Group 2)	Pharma	13000 (10.7% scientists)	1309.63	7.5% (US \$ 132.8 million)	Peg Filgrastim, Filgrastim	India
DRL (Group 3)	Pharma	16500	1560.00	6.6% (US \$ 143.6 million)	Filigrastim, Rituximab, pegfilgrastim, darbepoetin alpha	12 countries

Table 4 Biosimilar technological capabilities (R&D, manufacturing and regulatory) (Annual Reports, 2013; Analysts presentation, company reports)

	Biocon	Cipla	Lupin	DRL
Year of starting biotechnology R&D	1999	2010	2009	1999
Dedicated Biological R&D facilities	Bangalore, India	setting up a new R&D facility in Goa, India	Pune, India	Hyderabad, India
Biosimilar manufacturing capabilities	Two integrated manufacturing facilities at Bangalore, India and Johor, Malaysia		One integrated facility at Pune, India.	One integrated facility at Hyderabad containing E Coli and mammalian cell platforms
Key R&D acquisitions	Acquisition of Cuban company CIMAB's 49% stake in their joint venture, Biocon Biopharmaceuticals Pvt Ltd (BBPL) in 2010	Acquisition of Mabpharm, an Indian biotech company Acquisition of 25% stake in BioMab, a Shanghai based biotech company.		
In-licensing of biosimilars		2 biosimilars from	1 biosimilar from LG Life Sciences	

Clinical trials/ Clinical Research organisation	Clinigene, in-house CRO established in 2000.		Lupin Bioresearch Centre, in-house division	Partnership with CRO Argenta (UK)
Biosimilars in Preclinical	1		5	3
Biosimilar in Phase I	5			
Biosimilar in Phase II				
Biosmilar in Phase III	1		1	2

Table 5 Key R&D collaborations (Annual reports, company website)

Year	Indian firm	MNC	Nature of alliance	Territory
2004	Biocon	Vaccinex (USA)	discover and co-develop at least four therapeutic antibody products	
2006	Biocon	Cuban Institute of Molecular Immunology (CUBA)	Development of antibody for treating cancer of neck and head	
2007	Biocon	Abraxis (USA)	Filgrastim GCSF(product development and marketing)	Abraxis: USA + EU Bicon: ROW
2009	Biocon	Amylin	Co-development of novel peptide hybride for treatment of diabetes.	
2009	Biocon	Mylan (USA)	Co-development of five MAbs	Mylan: USA + EU Biocon: ROW
2012	DRL	Merck Serono (Switzerland)	MAbs (joint development)	DRL: ROW + USA
2014	Biocon	Advaxis Inc (USA)	Co-development of its lead drug candidate, ADXSHPV	India, emerging markets

Table 6 Acquisition of tacit biotech R&D knowledge (Annual Reports, 2013)

Company	Year	Current role	Overseas connection
Bicon	2010	Dr Abhijit Barve, R&D President	Working with Astellas, a US biotech company as a Global Development Project Leader
DRL	1999	Dr Cartikeya Reddy, Head Biologicals division	Working with Genetech Inc., as a Group Leader in the area of Cell Culture Process Development
Lupin	2010	Dr Cyrus Karkaria President, Biotech Division	Leading a biotech company in the US
Intas	2011	Dr Himanshu Gadgil, Sr Vice President, Biologicals	Principal scientist, Amgen
Cipla	2012	Subhanu Saxena, CEO	Head, Global Product Strategy, Novartis Pharma AG

Table 6 Market capabilities: Entry into international markets, partnerships and (Annual Reports, 2013, 2012)

	Biocon	Cipla	Lupin	DRL
Exports percentage of sales) (2013)	38%	55%	73%	83%
Geographic distribution small molecule generic markets (2012)	UC	North America: 18% Europe: 8% ROW: 29%	North America: 40% Europe: 2% ROW: 31%	North America: 39% Europe: 18% ROW: 26%
International investments (small molecule generic markets)	Greenfield: 3 JV/Equity share: 2 Acquisition: 2	Greenfield: 2 JV/Equity share: 2 Acquisitions: 1	Greenfield: 1 JV/equity share: 4 Acquisitions: 3	Greenfield: 3 JV/Equity share: 3 Acquisitions: 5
Marketing in advanced country markets under own brand	UC		USA, Japan	USA, Europe
No of biosimilars marketed in India	7 (recombinant insulin, Glaringe insulin, EPO, filgrastim, Herceptin)	1 (Etanercept)	2 (Filgrastim, peg filgrastim)	4 (Rituximab, filgrastim, darbepoetin alpha, peg-filgrastim)
No of biosimilars sold	Insulin in 40 countries and			Presence in small 13

overseas in other emerging country markets	Glaringe insulin in 5 countries			emerging markets such as Myanmar and Vietnam with local partners
No of biosimilars marketed in advanced countries	Completed Phase III trials in EU for Glaringe insulin			Phase I clinical trials in USA for Rituximab and Peg Filgrastin in partnership with Merck
Market sharing agreements with overseas firms for Biosimilars market	Partnership with Pfizer (2009-2012) Partnership with Mylan (2010) Partnership with CCM pharma to enter Malaysian and Brunei markets (2013)		Collaboration with Yoshindo Inc for Japan markets (2014)	Collaboration with Merck Serono to enter Europe market by 2017

Figures

Fig. 1 Evolution of the biosimilars regulatory guidelines (IMS, 2010, author's own analysis)

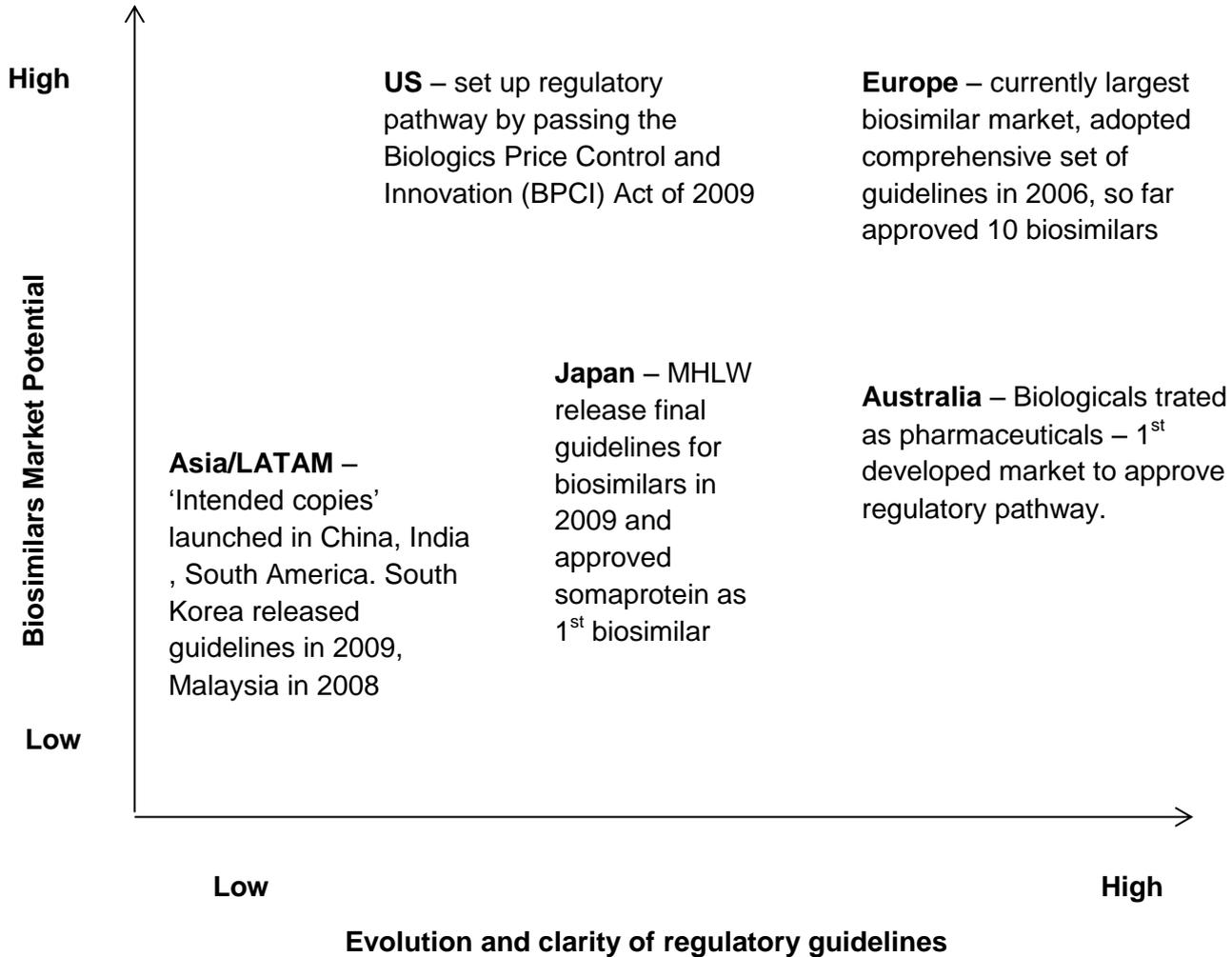


Fig 2 Biocon Laboratories

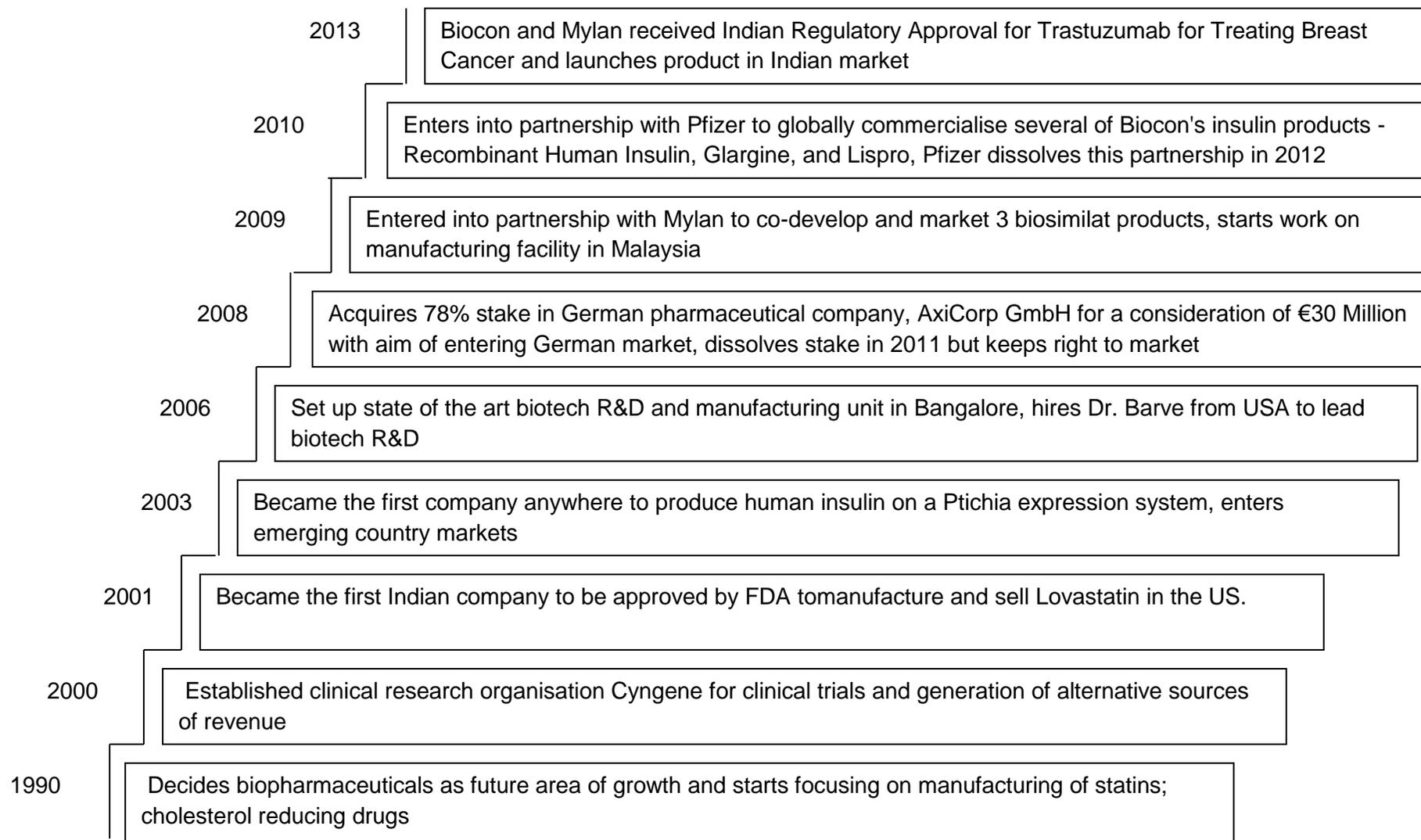


Fig 3 Cipla Laboratories Ltd



Fig 4 Dr Reddys Laboratories Ltd



Fig 5 Lupin Laboratories Ltd

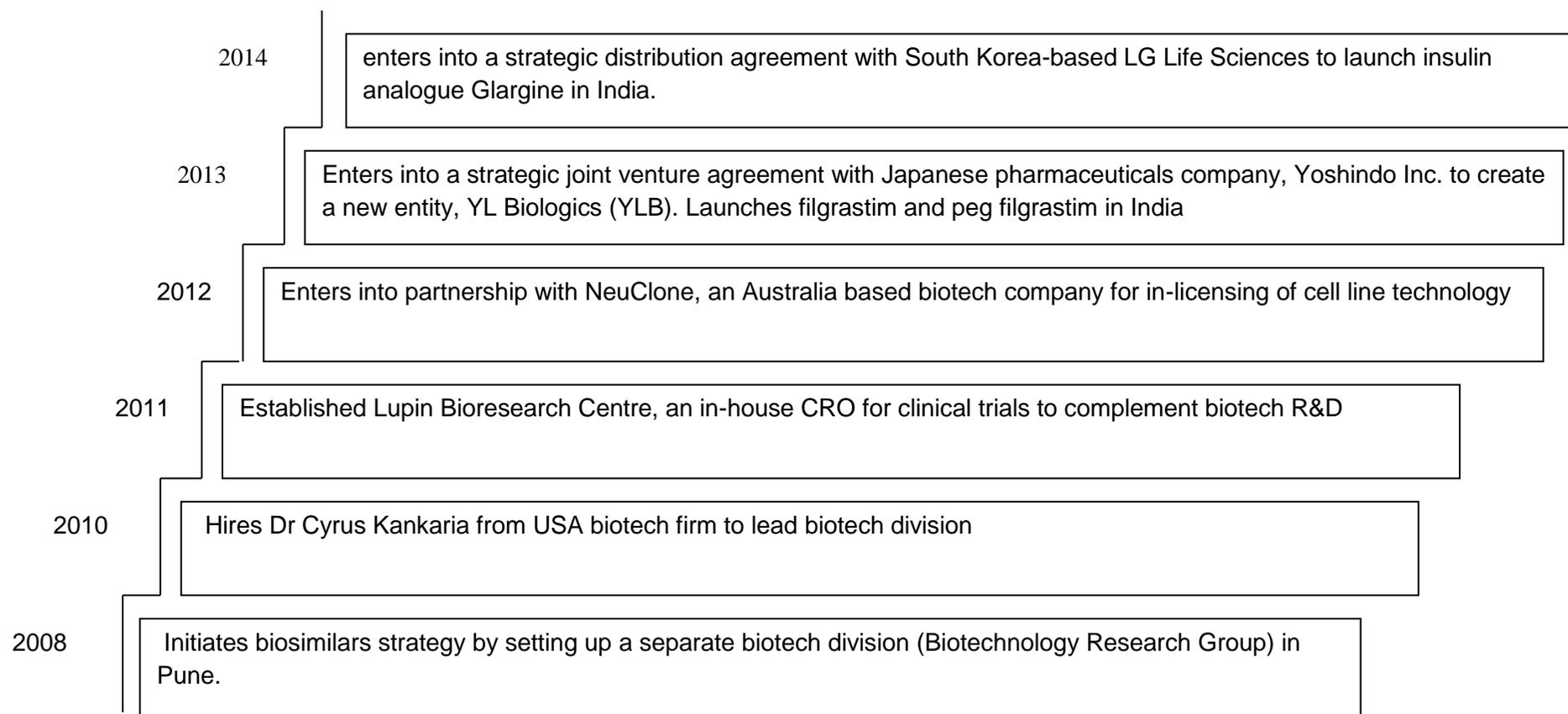


Fig 7 Technology capabilities – market matrix

