Open innovation in new drug research: the Indian perspective

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Abstract

This article sketches open innovation strategies pursued by eight Indian pharmaceutical firms and provides an account of strategic flexibility charted by firms in the wake of changes in the legislative environment. The findings examined through the lens of open innovation and dynamic capabilities identifies 'technological competencies' and 'funding' as two very important reasons, which push the traditionally closed R&D firms to pursue open innovation. Within the dynamic capabilities framework, the findings suggest that resources and competencies play a vital role in enabling open innovation in the complex new drug research setting.

Keywords: open innovation strategies, dynamic capabilities, new drug research

Introduction

The national environment in India for the pharmaceutical sector underwent changes post 2005 following the implementation of Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement, which resulted in a change in the legislative environment. India extended the product patent recognition in the area of pharmaceuticals, marking a significant transition point for the pharmaceutical industry, heavily dependent on generic business. The change in patent regime aimed to mark a shift from incremental innovation towards more substantial innovation. The purpose of this article is to a) examine the open innovation strategies pursued by Indian pharmaceutical firms to undertake new drug innovation b) to understand what factors influence their strategic choices. This paper views open innovation strategies pursued by firms in the context of firm's current resources and competencies through a dynamic capabilities lens.

Theoretical Background

Adaptive Open Innovation Strategies

The theoretical background is reviewed covering literature on innovation, open innovation and dynamic capabilities. The open innovation approach (Chesbrough, 2003b) rests on the underlying argument, that the traditional in-house R&D structure is losing ground in the wake of revolutionary factors like globalization of technology, resources, knowledge, and funds defining new ways in, which innovation is taking place (Chesbrough, 2003b, Chesbrough and Crowther, 2006). Firms differ in how they pursue open innovation (MacKinven et al., 2014), the inbound open strategy allows firms to exploit discoveries of others in their own R&D labs while the outbound open innovation strategy allows firm to opt for external pathways to exploit their innovation (Chesbrough and Crowther, 2006, Chesbrough, 2003a). This classification was extended to include the 'coupled process', which integrates outside-in and inside-out processes by aligning with complementary partners (Gassmann and Enkel, 2004, Enkel et al., 2009). The table below summarizes the open innovation strategies used in pharmaceutical sector by various authors.

Table 1: Open Innovation strategies in pharmaceutical sector

Open Innovation Strategies		Industry/Sector	Study
In-licensing	Internationalization of R&D	Pharmaceuticals /Biotechnology	(Enkel et al., 2009, Gassmann, 2006, Arora et al., 2009, Getz, 2011, Cockburn and Henderson, 1996, Chesbrough, 2003b)
Collaborative Innovation	Firm-centric network with offshore outposts	Across range of R&D companies	(Jelinek et al., 2012)
	Bidirectional Information exchange Transfer of basic knowledge from public funded institutions to firms	Pharmaceutical firms	(Cockburn and Henderson, 1996)

	Industry wide, targeted, collaborative innovation efforts	Across range of R&D companies	(Jelinek et al., 2012)
	Public private partnerships for neglected diseases	Neglected diseases	(London School of Economics and Political Science, 2005)
	Modular approach to R&D		
	Virtual, ad hoc networks of resources.	Drug R&D	(Jelinek et al., 2012)
	Open Source Model in drug discovery	New drugs	(Årdal and Røttingen, 2012)
Out-licensing	External commercialization of intellectual property	Pharmaceuticals /Biotechnology	(Chesbrough, 2006, Rothaermel and Deeds, 2004, Grootendorst, 2009, Lichtenthaler, 2007)

Dynamic Capabilities Perspective

The resource-based view as key approach to strategy formulation and a way to attain competitive advantage found various endorsers in the strategic management literature (Regnér and Zander, 2011, Barney, 2001, Hansen and Nohria, 2004, Peteraf, 1993, Wernerfelt, 1984, Wright, 1994). Dynamic capabilities framework defines a firm's 'position' as 'current specific endowments of technology, intellectual property, complementary assets, customer base and its external relations with suppliers and complementors'(Teece et al., 1997, p 518). Two important pillars of the dynamic capabilities framework are: a) the firm's resource 'position' in shaping boundary decisions b) the firm's ability to change in a changing environment context (Teece et al., 1997). As innovation represents a high degree of change and uncertainty, dynamic capabilities is an essential component of the innovation process (Lee and Kelley, 2008).

Conceptual Framework

The conceptual framework is a congruence of two bodies of literature, dynamic capabilities approach and open innovation. The focus of the study is to understand the influence of firm position (resources and competencies) in pushing firms to follow open innovation strategies (in-licensing, out-licensing and collaborative R&D) in changing contextual conditions. The scope of the study is new drug innovation in the Indian pharmaceutical industry.

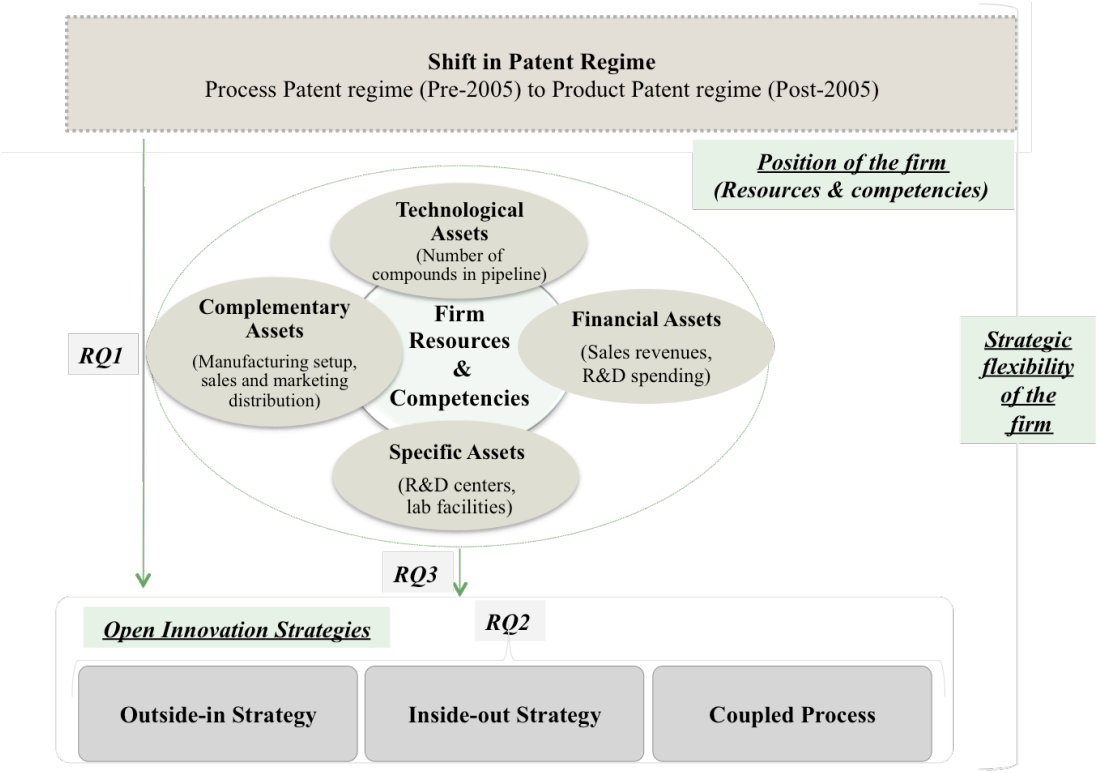

Figure 1- Conceptual framework, synthesized from (Chesbrough et al., 2006, Chesbrough, 2003b, Enkel et al., 2009, Gassmann, 2006, Teece et al., 1997, Teece, 2009)

The main research questions are:

a) How has the product patent regime influenced the adoption of open innovation strategies in pharmaceutical companies?
b) Which strategies do firms adopt for new drug research?
c) How do firm resources and competencies influence the adoption of open innovation strategies?

Research approach

The Indian pharmaceutical industry dealing with contemporary issues entails posing of 'what' and 'how' or 'why' questions, and this provides a rationale to pursue case study research design (Gummesson, 2007). The research framework leads to qualitative case study-based research design and the primary data collection mode was semi-structured interviews. The secondary data for the case study companies was collected through company websites, annual reports and cross checked with two key online pharma news magazines – 'Express Pharma' and 'Pharma Biz' and own research. The information on collaborations used for analysis excludes marketing or technology agreements related to generics business. It only includes new drug discovery and development collaborations.

Primarily, in the Indian new drug research landscape there are 10-12 established firms involved in new drug research business (Chowdhary, 2010). The product patent regime had attracted not only incumbent firms but also startup companies into the new drug research business. There is no published data on the number of startups however extensive secondary research and interviews revealed an estimate of six to eight startup companies involved in the research of small molecules in India. In this study, eight pharmaceutical companies engaged in new drug research of small molecules are chosen

to understand their unique contexts and experiences. The case selection focused on two categories of firms, established and startups.

1) Case Companies - Established firms
- Dr. Reddy's Laboratories Ltd.
- Lupin Limited
- Piramal Life Sciences (previously Nicholas Piramal)
- Ranbaxy Laboratories (now Sun Pharma)

2) Case Companies - Startups
- Advinus Therapeutics Limited
- Curadev Pharma Private Limited
- Invictus Oncology Pvt. Limited
- Lifecare Innovations

The selection of startup companies allowed maximum variation in cases and allowed to gain an understanding on the differences between cases (Flyvbjerg, 2006). Startups are companies formed in 2005 or after and have sales revenues less than $50 mn. Empirical evidence is drawn from 50 semi-structured interviews with senior management executives of pharmaceutical companies, academics, public research scientists and pharmaceutical experts.

Table 2: Resource profile of case study firms

Sample Type	Year of start of new drug research operations	Technological Assets (Compounds in pipeline)	Financial Assets	Complementary Assets	Specific Assets
Established firms	Pre-2005	Upto 20 in different stages of drug research	$1780 million - $2123 million	Manufacturing locations abroad Well entrenched sales and distribution channels in India	R&D centers in India and abroad Equipped with sophisticated facilities
Startups	2005 and later	(1- 15) mostly in early stages of new drug research	$24 million to unreported	Limited/ No manufacturing/marketing capabilities	R&D centers in India. Limited instruments and lab facilities

Findings

The Indian pharmaceutical sector backed by generic drug business is estimated to be USD 16.7 bn in 2014 and accounts for almost 10% of global drug production by volume. The Indian pharmaceutical sector is characterized by three features a) domination of generic business (accounts for 76% of total medicine sales) b) diversified market with 10 large firms dominating 40% of the market c) low R&D expenditure for companies in new drug research (less than 9% of net sales; significantly lower than the global average 17% of sales turnover) (Tripp, 2012, Business Monitor International, 2012, Srinivas, 2004). During the process patent regime (1970 – 2005), Indian firms primarily relied on their in-house expertise and followed a traditional closed R&D model. The interactions with public research labs and universities were limited to testing and validating of research results and funding of academic projects. Collaborations with multinational companies were either for in-licensing of technology or marketing agreements to gain access in different countries.

With the advent of new drug research in India, companies soon realized that new drug is complex, difficult and risky (Interview data) and technical considerations like safety, effectiveness and potential side effects play a deciding role in the progress of the drug compound (Arora et al., 2009). Globally, pharmaceutical research and development is commonly characterized by ten years or more research and development work (Drucker, 1985) and has prominent two stages - drug discovery and drug development. Despite new process strategies to make the new drug development effective, the cost of new drug development is more than one billion dollar (Tufts, 2010, Tripp, 2012). Though the cost of new drug development is relatively low in India, regulatory hindrances in conducting animal research and clinical trials delay the process and increase the costs (Interview data). The limited resources and capabilities of Indian companies coupled with the risky nature of business pose a big challenge to conduct new drug research.

Preliminary findings have revealed that the two primary reasons why companies pursue open innovation strategies are to get a) technical competencies and b) funding. This is further illustrated with examples from our cases, which outlines the idiosyncratic pathways adopted by firms for new drug research.

Technical (competencies) collaborations

In the Indian pharmaceutical milieu, most of the technical collaborations take place at the pre-discovery stage or drug discovery stage to gain wider access to scientific talent and opinion. Project complexities, goals, stage of the project, internal expertise, project feasibility and strength of the external party, have emerged to be the key factors, which govern technical collaborations. *"My belief is that if something positive comes up here, I need to work with a world leader, and if it excites him then my chance of success is much higher. In other models, the collaborations are done depending if we require certain technologies or certain targets to be validated, we would directly link up either with a contract research firm or with a firm in a collaborative manner"* (Interview data, Established firm).

i. In-licensing strategy

   Established companies with enough financial resources engage in, in-licensing strategy to fill their pipelines with drug compounds. Ranbaxy Laboratories (now Sun Pharma) was the first company in India to develop and launch a new chemical entity (NCE) drug 'Synriam' for malaria. The new chemical entity 'arterolane maleate' in the drug was discovered by a collaborative drug discovery project funded by the Medicines for Malaria Venture (MMV), involving researchers from the US, UK, Switzerland and Australia. Ranbaxy in-licensed this compound from MMV at drug development stage with a worldwide, royalty-free licence for this compound.

Startup companies limited by their finances use various other strategic options to in-license exciting research work. *"We are open to in-licensing if there are any interesting molecules but being a startup company we cannot pay millions of dollars that large pharma can pay"* (Interview data - Startup firm). Invictus Oncology, a startup company, has been novel in its approach of partnering with the scientific community. It has partnered with India Innovation Research Center (IIRC), a not for profit virtual research institute, which has researchers and scientists from all over the globe. The company hopes to take forward any research output, which comes out of this partnership.

ii. Collaborative R&D Strategy

Both established and startup companies seek collaboration at the drug discovery stage though the modes of interaction may vary. Piramal Life Sciences had effectively used different types of collaborative R&D to gain technical competencies at different stages of the project. The company entered into a research consortium with nine public research institutes to screen molecules from a repository of 14,000 cultures to identify chemical entities. The company then took up three new chemical entities for further development and entered into many research pacts with various organizations such as Anna University, Indian Institute of Science and a German company Pierre Fabre, to screen and identify potential molecules while retaining the rights to commercialize any products coming out the collaboration. Curadev, a startup company has entered into a knowledge based collaboration with University of Greenwich to create novel process improvements for select pharmaceuticals.

Firms engage in open innovation either to in-license a molecule or technology or to engage in interactions with the scientific community. In the in-licensing mode, the company engages in, in-house R&D once it has the IP rights of the molecule. In the collaborative mode, most of the agreements are formalized in such a way to enable the firm to retain ownership of the IP however, there are some joint collaboration deals wherein the IP is jointly owned and agreed with the partners. *"It varies, sometimes we have an agreement where we are testing the downstream assays of say a given compound and then the IP is shared. Supposing we are taking the help of a chemist in designing the compound, then whatever is being synthesized the IP belongs to the company…. the third model is that if IP is generated, we will have a separate agreement where both the parties will come together and form the clauses of that agreement."* (Interview data - Startup firm)

Financial Collaborations

Unlike technical collaborations there is a stark difference in the strategies adopted by established firms and startup companies. Established firms seek financial collaborations primarily during the drug development stage. The risk for late stage failures and the development cost of the drug is too exorbitant to be funded solely by a firm. Startups engage in collaboration to seek financial help at all stages of drug research.

i. Collaborative R&D through public-private partnership

Lupin partnered with four public research institutions to discover a new chemical entity LL3858 named Sudoterb for the treatment of tuberculosis. The clinical trials for this molecule is being supported by the Indian government under a public initiative scheme New Millennium Indian Technology Leadership Initiative (NMITLI). The company has also sought financial support in the clinical development of two more NCEs in the area of migraine and psoriasis. In yet another public initiative, the Department of Science and Technology supported the clinical development of the new chemical entity Synriam, which was launched by Ranbaxy Laboratories in 2013. Startup companies avail of R&D grants and soft loan schemes more frequently to get support in different stages of drug discovery and development.

ii. Collaborative R&D with multinational companies (MNC)

Indian firms also collaborate with MNCs for drug development and to leverage the complementary marketing and distribution assets overseas for product launch

in case the drug candidate moves successfully across different stages. Advinus Therapeutics, a startup firm has a multi-year collaborative deal with Merck to discover and develop the drugs till preclinical stage. Merck would make upfront and milestone based payments while retaining the rights to undertake the clinical development and marketing of the drug. A startup company, Curadev entered into a licensing deal with US pharmaceutical company to discover drugs till the candidate selection stage and then transfer it to the firm at the clinical development stage in exchange for milestones and royalties.

iii. Out-licensing Strategy: Though out-licensing of a drug compound can be done at any stage however, Indian firms prefer to out-license the molecule at the clinical development stage. When Dr. Reddy's out-licensed its two diabetes molecules in 1997 to NovoNordisk, it created history as this was the first time an Indian company had developed a new chemical entity in-house and made it ready for out-licensing. The molecules failed during the clinical trials nonetheless it opened the doors to pursue out-licensing as a viable strategy.

"We have several molecules in the clinical trials now as you can see in our website and the annual report…. we will be engaged in out-licensing of our molecules (means basically IP) to big pharma for a price, so they take it up forward for filing and approvals and commercialization" (Interview data, Established firm).

"Earlier our goal was to discover a molecule, develop it into a drug within India, but over the period of years we have changed this pattern. In the last two years, we started trying to package molecules, at different levels for out-licensing…I think the company realized that the financial implications of developing a molecule although 40% lower in India as per global estimate, it is still very huge for an Indian pharma to sustain for a long time" (Interview data, Established firm).

Startup companies which have drug compounds in early stages of new drug resarch have emphasised that this is an important strategy, which they would consider in the next phases. Startup companies also engage with universities and public research to avail of instrumentation and testing facilities and enter into collaborations for venture funding.

Conclusion

The strategic pathways adopted by firms are idiosyncratic however, common patterns can be observed within the two case company groups, i.e. one among the established firms and other one among startups. The established companies engage in technical collaborations either at pre-discovery stage to in-license molecules or during the drug discovery stage to seek answers to specific questions. Their primary strategy is to rely on their own internal drug discovery programs and engage in collaborative risk sharing model or out-licensing deals only during the drug development phase. On the other hand, startups engage in different collaborative deals throughout the drug research process. In open innovation parlance, this suggests that firms use open innovation perspective as a means to achieve their goals. Within the dynamic capabilities framework, the findings suggest that firms are driven by their internal competencies, financial resources, and other assets to adopt various open innovation strategies. A plausible explanation lies in the concept of dynamic firm capabilities, which evaluates the role of firm resource profile in charting the course of firm behavior (Nelson, 1991, Insead and Eisenhardt, 2001, Teece et al., 1997).

The discussion about the Indian pharmaceutical industry contributes to our understanding of how the companies have adapted strategies to suit their resources and competencies. The new drug research business has been tumultuous in the Indian

pharmaceutical milieu. Two established companies in the cases - Ranbaxy Laboratories and Piramal Life Sciences have exited from the new drug research business. Dr. Reddy's Laboratories has scaled down its new drug research operations after some initial setbacks. The reasons for downscaling of drug research activities are manifold but by drawing on these cases, this paper makes an argument for the dynamic interaction between strategic action and resource profile in constraining extraneous factors. In providing directions for strategic research (Priem et al., 2013) emphasised the need for future research studies linking the resource side and environment contexts of the firm. In this way, the study hopes to make a contribution to the dynamic capabilities literature.

With regards to open innovation, the cases deepen our understanding of inter-firm heterogeneity in charting open innovation strategies. Regarding strategic management research, this study highlights the firm level constraints for technological innovation in a developing country. In this way, this article is also of particular interest from a business process perspective to practitioners and researchers. Lastly in the Indian context, this study aims to extend the prior research work on Indian pharmaceutical industry. (Sampath, 2008) has detailed the emergent strategies in the Indian pharmaceutical landscape in response to the product patent regime. In yet another study, (Athreye et al., 2009) has demonstrated the dynamic capabilities of four large Indian pharmaceutical firms to adapt itself to different environmental changes by adapting its resource and strategies. However, studies comparing open innovation strategies adopted by firms for new drug research mediated by resource position of a firm has not been studied before and in this way the paper hopes to make an original contribution.

The innovative environment in the Indian pharmaceutical sector is rapidly changing with new firms evolving and old firms disappearing from the innovation space. The level of openness and the strategic flexibility suggest that those firms will successfully innovate that cope with these critical challenges.

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