How can small firms benefit from open innovation? The case of new drug development in Taiwan

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Abstract: How can small firms manage and benefit from open innovation? We study three Taiwan's biotechnology firms leveraging open innovation in developing new drugs. At the phase of the new drug discovery, two companies acquired technology from external sources. CSRC Synpac Company acquired technology from Professor Yuan-Tsong Chen at Duke University (USA) in 1991. GlycoNex Company acquired technology from Professor Sen-itiroh Hakomori at University of Washington (USA) in 2001. AbGenomics Company developed its own technology at Professor Rong-Hwa Lin's team at National Taiwan University (Taiwan) in 2000. Through technology transfer, CSRC Synpac Company licensed out the new drug Myozyme to Genzyme Corporation (USA) in 2000. AbGenomics Company licensed out the new drug AbGn-168H to Boehringer Ingelheim Pharmaceutical (Germany) in 2005. GlycoNex Company licensed out the new drug GNX-8 to Otsuka Pharmaceutical (Japan) in 2009.

Keywords: open innovation; small firms; external partners; new drug development; Taiwan; biotechnology firms.

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1 Introduction

The concept of open innovation provides an illustration of the benefits of external cooperation beyond the boundaries of firms (Chesbrough, 2003a, 2003b). Research on open innovation has grown gradually and generated great interest. In the era of knowledge-based economy, knowledge has been recognised as a particularly valuable resource for competitive advantage and corporate growth (Miller and Shamsie, 1996; Wasko and Faraj, 2005). External networking allows enterprises to acquire specific knowledge without spending time, effort or money to connect to external partners. External knowledge may help firms manage their own R&D projects more efficiently (Chesbrough, 2003a; Kafouros and Forsans, 2012). The open innovation paradigm brings together literature streams from different sources of external knowledge (van de Vrande et al., 2010).

Most past studies on open innovation focused mainly on the firm level of large corporations. But now, the landscape of innovation has change enormously. Because of labour mobility, abundant venture capitals, and widely-dispersed knowledge across multiple public and private organisations, enterprises can no longer afford to innovate on

their own. With increasing disintegration, outsourcing, modularisation nowadays, the concept of managing open innovation in small companies is becoming more important. Recent research suggests that small and medium enterprises (SMEs) are important players in the open innovation scope and deserve to be studied in more detail. In this study, we are interested in the mechanism of open innovation, particularly in SMEs working on new drug development in Taiwan. More and more companies are inclined to cooperate with other organisations or firms in the industry either with their partners or with their competitors. Due to the concern of intellectual property and different strategies, the degree of openness has become very different over time in different companies. Furthermore, how to analyse open innovation on the project level is another significant issue. This study focuses on project-level analysis. From the perspective of open innovation, most past literature focused on external networks (Chesbrough, 2003a; van de Vrande et al., 2010; Kafouros and Forsans, 2012; Lee et al., 2012a). We fill the gap by discussing not only internal capability but also the alignment of the internal capability and external network. Our research shows that Taiwan's biotechnology companies should have different capabilities in different stages of the new drug development process. Thus, we also emphasise the firms' core capabilities and how can they attract external organisations and companies to cooperate with them.

The purpose of this paper is to fill the gap in the project level of small firms. Since Taiwan's biotechnology firms play an important role in the global value chain of the pharmaceutical industry, we tried to provide empirical evidence that past research has not mentioned. We interviewed three local firms on new drug development in Taiwan. These three cases all have different modes of open innovation. For instance, these firms are involved in their projects in certain stages of new drug development process. Once the task was completed, they licensed out or sold their innovation to other international pharmaceutical companies. What we are interested in is the dynamics of exploration and exploitation during different stages of new drug development. In other words, these Taiwanese firms explore resources from the external alliance networks and also exploit its current internal capabilities.

The biotechnology industry is an emerging industry that has great potential for development. In Taiwan, the biotechnology industry has been seen as one of the twin star industries in the nation that benefits from strong government support for sector activity. Most Taiwanese biotechnology firms are SMEs, and these new drug development SMEs have their specific core capabilities, making them very unique and open. They usually cooperate with other firms or outsource their pre-clinical or clinical trials to other contract research organisations (CROs) or hospitals. In addition, they often license out or sell their clinical results to other international pharmaceutical firms ultimately.

These Taiwanese biotechnology companies take over some jobs in the process of new drug development. In other words, they use open innovation to align with other organisations or firms to implement in some stages of new drug development process. Thus, they intend to cooperate with other companies with rich resources to complete the pre-clinical and clinical trials in the process of new drug development. In that way, these Taiwanese SMEs can leverage their resources and risks in new drug development with other international and domestic firms and organisations.

A key research question remains to be addressed in this study. How can small firms manage and benefit from open innovation? We conduct an in-depth case analysis of three Taiwanese biotechnology companies, namely CSRC Synpac Company, AbGenomics

Company and GlycoNex Company. We aim to contribute to the literature by filling the gap in open innovation by providing a side-by-side comparison of three cases. Drawing from these three cases, we find that the success factors in Taiwanese biotechnology companies include not only their own internal core capabilities, but also external networks. The most important factor is the alignment of internal capability and external networks on the different stages of new drug development. In addition, the dynamics of new drug development process in different stages is discussed in this study.

This paper includes five sections. Section 2 presents the theoretical background. Section 3 demonstrates the research method. Section 4 applies research frameworks to analyse three cases of Taiwanese biotechnology companies in the process of new drug development. Section 5 concludes by discussing research findings, research contributions, research limitations and directions of future research.

2 Theoretical background

2.1 Open innovation

The concept of open innovation broadly includes different dimensions of innovation practices and processes in firms. According to Chesbrough (2003a), open innovation has been defined as "the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and to expand the market for external use of innovation respectively". In opposition to the traditional vertical integration model, the open innovation paradigm assumes that firms shall adopt the external ideas or paths to advance their technology for the market (Chesbrough and Crowther, 2006). The open innovation model argues that valuable ideas may come from inside or outside the firm as well as launched to the market from inner or outer paths of the firm (Chesbrough, 2003a; Su et al., 2009).

Recently, more researchers have started to focus on the management of open innovation. Innovative firms employ a wide range of external actors and sources, such as a range of lead users, suppliers, firms, universities, research laboratories, and institutions in the innovation system, to achieve sustain innovation through the open innovation concept (von Hippel, 1988; Su et al., 2009). In other words, open innovation implies that firms may depend on critical external knowledge assets for the successful realisation of their innovative endeavours. This, combined with the knowledge flows from different external partners in uncertain environments, could improve innovation outcomes.

In recent years, more and more research on open innovation has gradually started to focus in detail on the governance modes. Felin and Zenger (2014) classify open innovation governance modes as markets, partnerships, contests and tournaments, and users or community innovation to provide a framework for managing innovation. Verbano et al. (2015) carried out a survey among Italian manufacturing SMEs, and divided 105 companies into three different open innovation clusters as selective low open, unselective open upstream, and mid-partners integrated open. West et al. (2014) bring up an important idea: that the trend of open innovation research in the next decade may extend in the three themes of better measurement of innovation, understanding the role of appropriateness in open innovation, and integrating the management and economics research to establish theory in literature.

2.2 Open innovation perspective in the small firms

Compared to the traditional vertical innovation system, the concept of open innovation illustrates that companies can accept external resources or capabilities to improve their technology and products. Since the resources and market scale of SMEs may differ from large companies, the open innovation practices are different between large firms and SMEs. Nevertheless, previous studies on open innovation mainly focused on large companies (Chesbrough, 2003a, 2003b; Chesbrough and Crowther, 2006). Recently, research focusing on open innovation in SMEs has emerged gradually. In this knowledge-intensive era, technology changes rapidly and dramatically. Companies have to face emerging problems in the mobility of knowledge personnel, shortened product life cycles, and rise of R&D costs. Innovation in SMEs is usually hampered by lack of financial resources, scant opportunities to recruit specialised workers, and small innovation portfolios, therefore the risk associated with innovation also become higher (van de Vrande et al., 2009).

Because smaller firms do not have sufficient internal capabilities to launch more advantageous products or services on the market, they have to look for partners to bring in assets that they do not own (Narula, 2004; Dahlander and Gann, 2010). However, small firms with strong competences in unique focused specialties may turn into attractive collaboration partners for other firms. Due to lower absorptive capacities or deficiencies of value creation in the whole value chain, small firms usually depend on large firms as their key customers or suppliers. SMEs must not only be able to develop their internal development activities, they also have to be able to strengthen their abilities to collaborate with other companies as well as with customers (Bougrain and Haudeville, 2002; Konsti-Laakso et al., 2012). In technology-intensive environments, SMEs can expand the market for their technologies through sales internationalisation. Internationalisation should provide advantages to SMEs by enlarging the market for their goods and shifting competitive dynamics (Lee et al., 2012a, 2012b).

Moreover, small firms have a greater ability to specialise than larger firms, and this specialisation is more efficient and precise in the global value chain. SMEs can complement their limited internal R&D with knowledge generated by external actors and obtain access to external complementary assets (Colombo et al., 2012). Because most smaller firms lack marketing channels and manufacturing facilities, they usually focus on commercialisation-related open innovation pathways. In contrast, large firms mainly focus on cooperation with external sources for research and development (Nurala, 2004).

The internal R&D capabilities of small firms have a positive effect on their innovation output. In Kim and Park's (2010) empirical study on Korean firms, they find that not all open innovation activities of SMEs have positive effects on innovation output. The study mentions that small companies that invest in R&D and set up internal systems have a higher innovation performance. In general, small firms have limited internal capabilities to launch products with high speed and low cost to the market, and have been forced to look for external partners to bring in assets as they need. Parida et al. (2012) suggest that SMEs have less bureaucracy, increased willingness to take risks, and faster ability to react to changing environments; therefore, they may obtain greater profit than larger firms from open innovation. Results of Spithoven et al.'s (2013) study show that SMEs could introduce new products on the market more effectively by using different open innovation practices.

SMEs have been noted to use external resources to shorten innovation time, reduce risks and costs, and increase the flexibility of their operation, which is a major determinant of innovation success and firm performance (Lee et al., 2010; Lichtenthaler and Muethel, 2012). To improve the innovation output, SMEs are required to seek more external partners, such as research institutions, universities, and intermediary institutions to establish cooperation networks (Zheng et al., 2009). Hossain's (2015) study reviewed current open innovation research in SMEs and found that open innovation improves the overall innovation performance of SMEs.

2.3 New product development in the biotechnology industry

The biotechnology industry is a highly innovative and knowledge-intensive industry. Because of the long period of research and development in technology, biotechnology companies have to invest huge money and time before listing a new product successfully. Generally, a new drug development requires different resources and professionals from multi-disciplinary fields and cross-organisations integration to shorten the period of drug development, and accelerate the launch of new drugs. Only a few major global biotechnology and pharmaceutical companies, such as Amgen, Merck, Pfizer or Novartis have sufficient capacity to complete the process from the development of a new drug to launching the final product in the market. Other smaller biotechnology firms often seek innovative resources and gain competitive advantage through specialisation, strategic alliances or acquisitions (Su and Wu, 2015a, 2015b).

According to Biedenbach and Muller (2012), the characteristics of biotechnology industry are complex and lengthy R&D development processes which last up to 15 years (Cuatrecasas, 2006; Ingelgård et al., 2002). During the long period of R&D, the interactions between regulatory authorities and international health care institutions (Coombs and Metcalfe, 2002; De Carolis, 2003), and cross-functional collaboration within other organisations may turn an idea into a commercial product (Khilji et al., 2006).

Over the last several decades, new product development (NPD) processes, best practices, and management methodologies have been emphasised by intense research (Marion et al., 2012). NPD processes have usually been considered as the most important dynamic capability within a firm (Marion et al., 2012). Biedenbach and Muller (2012) emphasise that selecting the right projects and efficient resources are important for portfolio management. Project and portfolio management are core elements for the operation of pharmaceutical and biotechnology organisations, where the R&D process is crucial for successful innovative product development (Biedenbach and Muller, 2012). To execute appropriate projects, organisations shall absorb external resources for project effectiveness and adapt their portfolio to new market opportunities (Biedenbach and Muller, 2012). Through establishing the global NPD team, companies may exploit knowledge resource from inside and outside (Ahuja et al., 2003; von Hippel and von Krogh, 2003; Muethel et al., 2012). Innovations rely highly on the application of knowledge. The open source of biotechnology may be the key knowledge for innovation in new drug development and the solution to increasing population problem in developing countries.

Along with the different stages, timing and differentiation of management tools are important for the success of innovation activities. Vanhaverbeke (2006) argued that companies have to manage over different time periods to represent their commitment to

new technology in a credible way for their potential partners. As the product matures and the market expands, firms can possess the flexibility to work with different actors in the innovation system (Pavitt, 1998; Laursen and Salter, 2006). The position of firms in the innovation system and the stage of the technology may be considered as indicators of the scope and limitations of innovation strategies for different firms (Christensen et al., 2005). In other words, the successful factors of open innovation are determined by the specific timing and framing of innovation strategy, the level of openness, and the choice of complementary partners.

Open innovation has been increasingly adopted in SMEs. While smaller firms began to set the innovative agenda in the early stages, large incumbents have tended to play an increasingly dominant role in organising and maturing the technology (Christensen et al., 2005). Christensen et al. (2005) suggested that open innovation mechanisms can be analysed within different time periods. In the emerging phase, different technologies compete with each other. To some extent, technology-based startups have pioneered the embryonic stage of the technology cycle. In the transition stage of the technology cycle, small technology suppliers are likely to suffer, if they do not engage in more intricate partnerships. As the technology matures, entry opportunities for small firms become fewer. The focus shifts towards incremental improvements and some leading players establish themselves during the growth phase when the dominant design of the technology emerges. In brief, open innovation plays a crucial role in the competitive dynamics of industry development.

2.4 Theoretical gap in open innovation

The concept of open innovation suggests that a firm may adapt a range of external sources to meet its requirements for innovation (Chesbrough, 2003a, 2003b; Chesbrough and Crowther, 2006; von Hippel, 2005; Laursen and Salter, 2006). Open innovation implies that firms depend on critical external knowledge assets for the successful realisation of their innovative endeavours (Christensen et al., 2005). Through the implication of open innovation, companies may reduce the cost and risk of innovation and improve the integration and efficiency of innovation.

The companies which neglect to develop strong technological competences internally may depend highly on external partners (Vanhaverbeke et al., 2002). Most previous studies on open innovation have investigated the practices in large companies at the initial stage of open innovation research (Chesbrough, 2003a, 2003b; Chesbrough and Crowther, 2006). However, the relevant literature also notes that companies have to consider the coordination of their resources and capabilities to implement open innovation effectively. Besides different strengths and weaknesses, SMEs and large enterprises have differing demands and strategy for innovation. Large companies usually focus on collaboration with external sources for research and development (R&D), and small companies mostly apply open innovation practices on the commercialisation of technology with limited marketing channels and manufacturing facilities (Narula, 2004).

Although major open innovation practices focus on large firms, a number of researchers suggest that SMEs play important role in global market and innovation systems (Bianchi et al., 2011). Recently, numerous studies have begun to consider open innovation implementation in smaller firms (e.g., Laursen and Salter, 2006; van de Vrande et al., 2009; Lee et al., 2010). Some research have recognised the

importance of open innovation of SEMs; nevertheless the theories and management model of open innovation in SMEs are not well-established in the literature. In addition, the relation between external network and diversification of open innovation in SMEs has been neglected all the while.

Newcomers in biotechnology usually undertake open innovation as solutions to exploit the complementary resources to enter the pharmaceutical industry. Small and young companies may complete the discovery and preclinical trials first, then proceed with clinical trials and marketing through collaborative arrangements (Gupta et al., 2007). Because of the long value chain and the complicated R&D process in the pharmaceutical industry, the firms have increasing demand for professional services supported from external organisations [e.g., CROs, contract manufacture organisations (CMOs)]. The governance of open innovation shall consider more factors such as time of R&D process, management of external networks and various demands in different stages. However, very few studies have been conducted on the operation of open innovation in the bio-pharmaceutical industry (Michelino et al., 2015). Here, we have further investigated the open innovation mechanisms of Taiwan's SMEs in the process of new drug development.

3 Research framework and research method

Given the nature of this research on the theme of open innovation, and the corresponding need for deep insights into the external partners of different phases in developing new drug, this paper is based on a case study research (Yin, 2003). The case study can answer 'how' and 'why' questions within real-world contexts, and is especially unique at dealing with a variety of evidences, e.g., documents, artefacts, interviews, and observations (Yin, 2003; Campbell and Ahrens, 1998; Gargeya, 2005; Andersen and Drejer, 2009). The case study is thus recommended when the issues studied are complex and evolving. When the concepts studied are abstract and the boundaries between phenomenon and context are not clearly evident, the case study approach will be used (Yin, 2003).

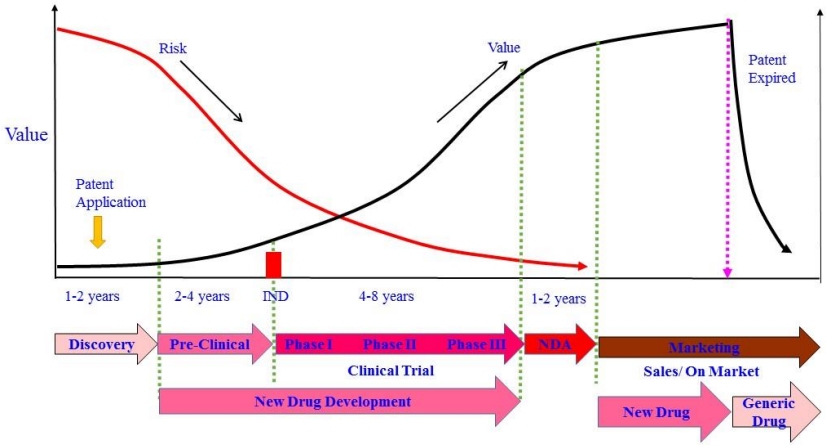
The case study has two major designs. The first design is a single case study, where a single subject is examined in-depth. The second design is a multiple case study, where several cases or events are studied. Compared to the single case design, the multiple case study design has all the advantages in capturing real-world contexts (Galloway and Sheridan, 1994; Campbell and Ahrens, 1998). Yin (2003) describes how multiple case studies can be used to either, "(a) predict similar results (a literal replication) or (b) predict contrasting results but for predictable reasons (a theoretical replication)" [Yin, (2003), p.47]. By using a multiple case study, one can test how the framework operates, and seek variation from the results (Sainio and Puumalainen, 2007). To explore the biotechnology industry in depth, a multiple case study design will be better than a single case study for sampling the whole industry (Eisenhardt, 1989; Yin, 2003; Ireland and Hine, 2007).

In this study, we employed a multiple cases study to examine three cases of new drug development projects in Taiwan, namely CSRC Synpac Company, AbGenomics Company, and GlycoNex Company. We conducted in-depth interviews with project leaders, researchers and department managers who are involved in the process of the new drug development. We discussed the important external partners of Taiwanese biotechnology firms in the process of new drug development. We then analysed the

similarities and differences of open innovation modes among these three projects of new drug development.

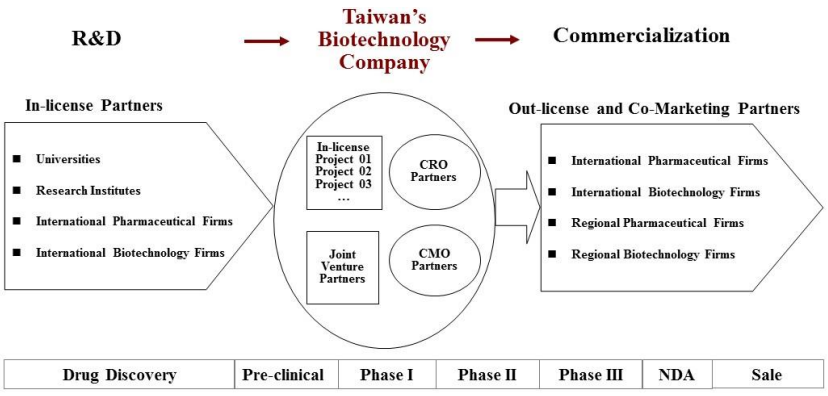
In this study, the process of new drug development is summarised in Figure 1. Following up on Su and Wu (2015a, 2015b), we summarise our research framework of open innovation model of new drug development in Taiwan's biotechnology company in Figure 2. And we summarise the overview of three cases of new drug development of Taiwan's biotechnology companies in Figure 3.

Figure 1 The value curve and stages of new drug development (see online version for colours)



Notes: Investigational new drug (IND) application; new drug application (NDA).
The average cost to develop and gain marketing approval for a new drug is pegged at US$2.558 billion, which is based on estimated average out-of-pocket costs of US$1.395 billion and time costs (expected returns that investors forego while a drug is in development) of US$1.163 billion (Tufts Center for the Study of Drug Development, 2016).

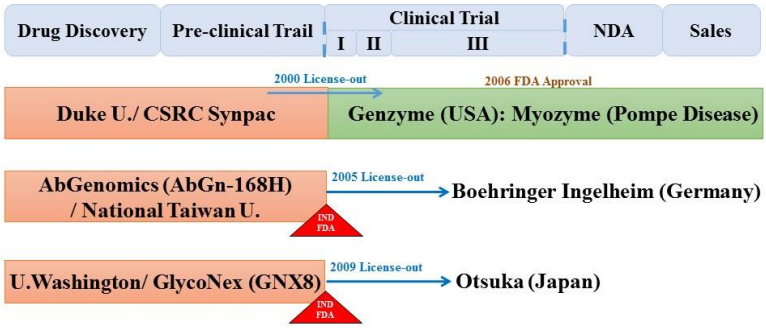
Figure 2 Open innovation model of new drug development in Taiwan's biotechnology company (see online version for colours)



Notes: Contract research organisation (CRO); contract manufacturing organisation (CMO); new drug approval (NDA)

Source: Adapted form Su and Wu (2015a, 2015b)

Figure 3 Three cases of new drug development in three Taiwan's biotechnology companies (see online version for colours)



Note: Investigational new drug (IND) application; new drug application (NDA); Food and Drug Administration (FDA) in the USA.

Source: This study

4 Cases analysis of three new drug projects in Taiwan's firms

We study three cases of new drug development in Taiwan's biotechnology firms. Three cases are Project Myozyme in CSRC Synpac Company, Project AbGn-168H in AbGenomics Company, Project GNX-8 in GlycoNex Company.

4.1 Case 1: Project Myozyme in CSRC Synpac Company

4.1.1 CSRC Synpac Company and Duke University (USA)

Inaugurated in 1973, China Synthetic Rubber Corporation (CSRC) acquired Continental Carbon Company in 1995, and is one of the top four carbon companies in the world specialising in the production and sales of carbon black (CB), gelatine, steam and electricity. The top four carbon black companies worldwide are Cabot (USA), Degussa Chemical (Germany), Columbia (USA) and CSRC (Taiwan).

Synpac Pharmaceuticals Ltd. is a subsidiary of CSRC established in 1991 after CSRC acquired a penicillin pharmaceutical in the UK. CSRC Synpac Company is primarily responsible for the production and sales of penicillin G. In the early '90s, Founder and Chairman of CSRC Mr. Koo Chen-Fu shifted from focusing on CB production to diversifying the development of biotechnology in an effort to disperse business risks. This task was subsequently handed over to his son, Mr. Leslie Koo.

Mr. Koo Chen-Fu collaborated with Dr. Andrew T. Huang, CEO of the Koo Foundation Sun Yat-Sen Cancer Center, in establishing the CSRC Synpac Company. CSRC Synpac Company plays a critical role in the development of Myozyme, a drug for the treatment of Pompe disease. Myozyme was developed by Professor Yuan-Tsong Chen at Duke University. Professor Yuan-Tsong Chen started working at Duke University Hospital after completing his post-doctoral career in human genetics, specialising in the treatment of rare disease.

With the help of Mr. Leslie Koo and Dr. Andrew T. Huang, Duke Professor Yuan-Tsong Chen was able to successfully develop Myozyme after 15 years of

concentrated effort. Because the cost of developing new drugs is high, Professor Yuan-Tsong Chen conveyed his funding problem to Dr. Andrew T. Huang, who then mentioned it to CSRC director, Mr. Leslie Koo who at the time had expressed an interest in the biotechnology industry. Subsequently, Mr. Leslie Koo invested almost a million USD in Professor Yuan-Tsong Chen's laboratory at Duke University. In 1998, the Myozyme animal experiment was successfully completed.

4.1.2 Out-license partner: Genzyme Corporation (USA)

Genzyme Corporation is an American biotechnology company. Founded in 1981 in Boston, Massachusetts, Genzyme Corporation evolved from a tiny start-up with just a handful of employees to one of the world's leading biotechnology companies. In its first year of establishment, the Genzyme Corporation acquired Whatman Company, a UK biomaterial company.

Genzyme Corporation is committed to discovering and delivering transformative therapies for patients with rare and special unmet medical needs. Genzyme Corporation has pioneered the development and delivery of transformative therapies for over 30 years. Acquired by Sanofi in 2011, Genzyme Corporation has been a fully owned subsidiary of Sanofi. Genzyme Corporation now benefits from the reach and resources of one of the world's largest pharmaceutical companies.

Genzyme Corporation embraces a diversified management approach by dividing its operating departments into five major divisions:

1 renal division, with its operating revenue accounting for 20% of the total revenue

2 treatment division, with its operating revenue accounting for 55% of the total revenue

3 transplant drugs division, with its operating revenue accounting for 5% of the total revenue

4 biosurgical product division, with its operating revenue accounting for 12% of the total revenue

5 genetic disease division, with its operating revenue accounting for 8% of the total revenue.

4.1.3 CSRC Synpac Company Project Myozyme successfully licensed to Genzyme Corporation

Myozyme, a drug for the treatment of Pompe disease, was developed by Professor Yuan-Tsong Chen at Duke University in the USA. Child patients with Pompe disease typically have deficiency in enzymes that break down glycogen, which eventually build-up in muscles and the heart, causing heart enlargement and muscle weakness. Patients slowly die from the inability to breath or from heart failure.

Myozyme is known as the 'orphan drug' because users of this drug are up to 25,000 worldwide. After entering human trial, Myozyme required a considerable amount of investment. However, major manufacturers typically have no interest in investing in this type of research project.

In 2000, CSRC Synpac Company earned US$18 million to authorise Genzyme Corporation to conduct Myozyme subsequent new drug development. CSRC Synpac Company can then acquire royalties from Genzyme Corporation depending on the progress.

The royalty agreement was achieved in 2006; specifically, between 1 October 2006 and 29 March 2023, sales regions where Genzyme Corporation has acquired patent rights, will pay CSRC Synpac Company royalties equalling 13.5% of the revenue, and from April 2013 to 2023, the royalty will be increased to 15% of the revenue. For regions where patent rights are not obtained, Genzyme Corporation will pay CSRC Synpac Company a royalty totalling 6.75% of the revenue. If Genzyme Corporation obtains the right to sell Myozyme in Japan, and if Japan approves the patent, CSRC Synpac Company will gain a further US$5 million.

In 2006, Myozyme's application for sales on the market of the United States and European Union countries was approved. According to the agreement entered between Genzyme Corporation and CSRC Synpac Company, if the sales made through the Orphan Drug Myozyme exceed US$400 million, CSRC Synpac Company will recognise the royalty according to the ratio and obtain an additional income US$20 million in Milestone payment. If the sale achieves a specific level, CSRC Synpac Company will receive an additional payment up to US$30 million.

4.2 Case 2: Project AbGn-168H in AbGenomics Company

4.2.1 AbGenomics Company and National Taiwan University (Taiwan)

AbGenomics Company was established in June 2000 by Prof. Rong-Hwa Lin, a professor at the Institute of Immunology of National Taiwan University (NTU) College of Medicine. AbGenomics Company's management teams comprise mainly of individuals from the NTU College of Medicine who are chiefly involved in the research and development of antigens.

Its outstanding technologies have attracted investments from major shareholders, including Bank of Communications and Liantai Venture Capital. Its shareholding structure also includes Taiwan Mobile Company, Chang Yih Technology Company, China Steel Corporation, and Yuen Foong Yu Corporation.

Currently, the R&D Center of AbGenomics Company is located in Taipei. Headquartered in the San Francisco Bay Area, AbGenomics Company is a clinical-stage biopharmaceutical company focused on developing novel best-in-class therapeutics for inflammatory and autoimmune diseases and cancers.

AbGenomics Company' persistence in learning-based organisation and management has attracted investment from Gains Investment Corporation and German pharmaceuticals. The management approach is based on both strategic cooperation and independent research and development. In the short term, AbGenomics Company actively establishes strategic alliance and collaboration with international manufacturers to create short-term revenue, and in the long-run, the company will endeavour to focus on the entire R&D process of new antigen drugs and become a biotech pharmaceuticals that offer a comprehensive range of services.

4.2.2 Out-license partner: Boehringer Ingelheim Group (Germany)

The Boehringer Ingelheim Group is one of the world's 20 leading pharmaceutical companies. Founded in 1885, the focus of the family-owned company is researching, developing, manufacturing and marketing new medications of high therapeutic value for human and veterinary medicine. Boehringer Ingelheim Group, headquartered in Ingelheim, Germany, operates globally with 146 affiliates and a total of more than 47,700 employees.

In 2015, Boehringer Ingelheim Group achieved net sales of about 14.8 billion euros. It invests a considerable amount in research and development each year, a portion of which is greater than a fifth of the net operating revenue earned by its largest sales department involving prescribed drugs. In 2015, R&D expenditure corresponds to 20.3% of its net sales.

4.2.3 AbGenomics Company Project AbGn-168H successfully licensed to Boehringer Ingelheim Group

In January 2002, AbGenomics Company successfully developed with its own technology its first antigen, AbGn-168H (also called Neihulizumab), for treating immune diseases. AbGn-168H preferentially induces apoptosis of late-stage activated T cells. This novel activated-T cell apoptosis-inducing antibody effectively eliminates chronic pathogenic T cells while fully maintaining host defence. Its substantial clinical benefits are a long lasting drug-free remission and less concern of increasing risks of infection and cancer.

AbGn-168H showed efficacy in phase 2 clinical trials for psoriasis and psoriatic arthritis. Current biologics are poor at treating diseases like psoriatic arthritis, graft-versus-host disease (GvHD), transplantation, inflammatory bowel disease, multiple sclerosis, type I diabetes and allergic diseases. AbGn-168H will have a great potential to provide meaningful clinical benefits to those patients with unmet medical needs.

Boehringer Ingelheim Group believes that this new drug features a unique mechanism of action, which makes it a new drug with the potential for treating autoimmune disease. The use of Boehringer Ingelheim Group's professional technology accelerated the new drug development, marketing, and commercialisation processes.

In June 2005, AbGenomics Company and Boehringer Ingelheim Group entered into an agreement for the manufacturing of this product, with a worldwide scope of authorisation. Boehringer Ingelheim Group achieved exclusive rights over the development, manufacturing, and commercialisation of AbGn-168H, whereas AbGenomics Company gained co-marketing rights to specific Asian countries.

After signing the agreement, AbGenomics Company obtained approximately US$130 million signing bonus and achieved its first R&D milestone payment. In the future, once the product is launched into the market, AbGenomics Company will receive a proportional royalty. Before phase 1 clinical trials, the transaction ranged between NT$2.8 and NT$4.2 billion. Thus, a break-even point was achieved through the royalty obtained after signing the agreement.

This project AbGn-168H is the first case in which a Taiwanese company authorises an international pharmaceutical company to develop, manufacture, and commercialise its self-developed new drug.

4.3 Case 3: Project GNX-8 in GlycoNex Company

4.3.1 GlycoNex Company and University of Washington (USA)

GlycoNex Company was founded in 2001 by Chairman Dr. Tong-Hsuan Chang who received his doctoral degree of pharmacy in University of Tokyo in Japan, and did his post-doctorate research in the USA, which included Johns Hopkins University, University of Maryland, and University of Pennsylvania. In 2001, GlycoNex Company was founded through the technology collaboration with Prof. Sen-itiroh Hakomori and The Biomembrane Institute (TBI) at University of Washington in Seattle in the USA. The Project GNX-8 is regarded as the key internationalisation indicator of Taiwan's biotechnology industry.

Prof. Sen-itiroh Hakomori has been dedicating his research and career on the structure and function of glycosphingolipid and cancer correlation. Prof. Sen-itiroh Hakomori has been appointed as Professor of Pathobiology in University of Washington since 1971, and the director for the Biomembrane Institute (TBI) at University of Washington since 1987. Prof. Sen-Itiroh Hakomori's research shows that the extended type 1 chain carbohydrate antigen mainly exists on cancer cells and scarcely exists on normal cells. This discovery is monumental on cancer cell detection, and has been licensed to GlycoNex Company along with its patents.

GlycoNex Company is the pioneer that specialises in combining glycosphingolipid antigen and human monoclonal antibody technologies to develop cancer drugs. Nowadays, both glycosphingolipid antigen and therapeutically monoclonal antibody are the major focuses of cancer drug development. As a result, the related research projects have been strongly supported by national long-term plans. For example, a subsidy worth NT$57.87 million for a three-year science and technology project was obtained from the Taiwan's Ministry of Economic Affairs in 2003, and in 2008, Project GNX-8 was subsidised in accordance with the Act for the Development of Biotechnology and New Drug Industry by Taiwan's Government.

4.3.2 Out-license partner: Otsuka Pharmaceutical (Japan)

Otsuka Pharmaceutical is headquartered in Tokyo. Otsuka Pharmaceutical is one of the top 20 pharmaceutical companies in the world and the largest pharmaceutical in Japan. Its antidepressant, Abilify, is the best-selling product in the antidepressant market worldwide, bringing in annual sales revenue of US$6 billion. Since its establishment in 1921, the company has been involved in the manufacturing and sales of chemical raw materials. In 1946, Otsuka Pharmaceutical started investing in supplemental nutrition drinks and subsequently began targeting new drug development and the pharmaceutical market. The vision of Otsuka Pharmaceutical is to become an all-rounded healthcare group. Otsuka Pharmaceutical participates in the merger and acquisition of health-related industries or products to facilitate its expansion into the healthcare market.

4.3.3 GlycoNex Company Project GNX-8 successfully licensed to Otsuka Pharmaceutical

GNX-8 is a new drug developed specifically for treating colorectal cancer and metastatic colon cancer. GNX-8 is a human monoclonal antibody that exhibits therapeutic effects on colorectal cancer at 50% or more efficacy, and on metastatic colon cancer at 57% or more

efficacy. This antibody demonstrates better performance compared with other types of targeting antibodies in the market. GNX-8 has already acquired patent approval in 13 countries, including the USA, European Union countries, and Japan.

The growth of the monoclonal antibody market increased from US$27 billion in 2007 to US$33 billion in 2008. For cancer treatment, antibody has become promising target therapy tool with its superior specificity. That is because traditional chemotherapy will cause cancer patients severe side-effects. Antibody can attack cancer cells exclusively and not harm normal cells, significantly improving the life quality of cancer patients.

GlycoNex Company has possessed advanced and complete technology platform: glycosphingolipid antigen production and identification, monoclonal antibody production, cancer drug screening, stable cell line production for monoclonal antibody. GlycoNex Company can develop monoclonal antibodies to fight cancer by utilising the carbohydrate antigens, since the relationship between abnormal glycosylation on cell and human cancer has been proved.

GlycoNex Company signed a collaborative agreement with Otsuka Pharmaceutical since April 2008. In September 2009, both companies officially signed an authorisation agreement, with the preliminary royalty set at US$200 million. After a year of joint development, both companies initiated the first phase of human clinical trials. Otsuka Pharmaceutical paid a US$2 million signing bonus to GlycoNex Company. The royalty for this agreement is paid annually in stages.

After completing the clinical trial on GNX-8 in Japan in the future, GlycoNex Company and Otsuka Pharmaceutical will sign an agreement for the products production and sales on the market. Based on an estimated annual sales amount of US$300 million for similar colon cancer drugs in the market, GlycoNex Company is expected to achieve a royalty equalling 5% to 20% of the total sales at least more than NT$1 billion. GlycoNex Company estimates that once the drug is successfully listed on the market, this product will contribute an annual income of approximately US$500 million to GlycoNex Company.

5 Discussions

5.1 Research findings

We summarise our research findings of three new drug development projects in three Taiwanese biotechnology companies in Table 1. Several research findings arise from these three cases of new drug development in different stages.

First, different internal capabilities of the firm are required in every phase of the new drug development. We analyse the internal capability according to different time periods in the new drug developments: drug discovery phase, pre-clinical trial phase, clinical trial phase, and technology transfer phase (or technology licensing out phase).

Table 1 Three cases of new drug development in three Taiwan's biotechnology companies

Company	*CSRC Synpac Company*	*AbGenomics Company*	*GlycoNex Company*
Founding year	1991	2000	2001
Founder	Mr. Koo Chen-Fu	Prof. Rong-Hwa Lin	Dr. Tong-Hsuan Chang
Background of founder	Founder and Chairman of China Synthetic Rubber Corporation (CSRC) (Taiwan)	Professor at Institute of Immunology at National Taiwan University (Taiwan)	Doctoral degree in University of Tokyo (Japan) Post-doctorate research in Johns Hopkins University, University of Maryland, and University of Pennsylvania (USA)
Startup/subsidiary	Subsidiary of CSRC	Startup	Startup
Project name/drug name	Myozyme	AbGn-168H (Neihulizumab)	GNX-8
Project focus	A new drug for Pompe disease.	A new drug for T-cell mediated diseases, such as psoriasis, psoriatic arthritis.	A new drug for colorectal cancer and metastatic colon cancer.
Key person of in-license partner	Prof. Yuan-Tsong Chen at Duke University	Prof. Rong-Hwa Lin at National Taiwan University	Prof. Sen-itiroh Hakomori at University of Washington
In-license partner/co-development partner	Duke University Duke University Hospital (USA)	Institute of Immunology National Taiwan University (Taiwan)	The Biomembrane Institute (TBI) University of Washington (USA)
In-license (year)/co-development (year)	1991	2000	2001
Out-license partner	Genzyme Corporation (USA)	Boehringer Ingelheim Group (Germany)	Otsuka Pharmaceutical (Japan)
Out-license (year)	2000	2005	2009
Parent firm/joint venture partner	Parent firm is China Synthetic Rubber Corporation (CSRC) (Taiwan)	A startup spun off from Institute of Immunology at College of Medicine at National Taiwan University (Taiwan).	A startup co-invested by Taiwan Advance Bio-pharmaceutical Company (Taiwan) and The Biomembrane Institute (TBI) at University of Washington (USA) and Prof. Sen-itiroh Hakomori.
Current stage of new drug project	Sales (since 2006)	Phase 2 clinical trial	Phase 1 clinical trial

Table 1 Three cases of new drug development in three Taiwan's biotechnology companies (continued)

Company	*CSRC Synpac Company*	*AbGenomics Company*	*GlycoNex Company*
Benefit for Taiwan's biotechnology firm	• Signing bonus in 2000: US$18 million. • Royalty in 2006–2023: 13.5%~15% (sale region with patent right) and 13.5% (sale region without patent right). • Milestone payment: US$20 million (if sale exceed US$400 million). • An additional payment up to US$30 million (if sale achieves a specific level).	• Signing bonus approximately US$130 million. • First R&D milestone payment. • Proportional royalty (once the product is launched into the market). • The transaction ranged between NT$2.8 and NT$4.2 billion (before phase 1 clinical trial). • Co-marketing rights to specific Asian countries.	• Preliminary royalty: US$200 million. • Signing bonus: US$2 million. • Royalty: paid annually in stages. • Estimated royalty: 5% to 20% of total sale. • Estimated annual income of approximately US$500 million (if launching on the market).
Benefit for international pharmaceutical firm	• Exclusive rights over the development, manufacturing and commercialisation of Myozyme.	• Exclusive rights over the development, manufacturing, and commercialisation of AbGn-168H.	• Exclusive rights over the development, manufacturing, and commercialisation of GNX-8.

Second, the three companies rely on external resources and networks to implement the new drug process. Two kinds of technology acquisitions are identified in this study. The first is by developing technology on its own. For example, AbGenomics is a spin-off firm founded by Dr. Rong-Hwa Lin's team at Graduate Institute of Immunology at National Taiwan University. The second is acquiring technologies through the individual's connection. For example, CSRC Synpac Company acquired technology from Dr. Yuan-Tsong Chen at Duke University in the USA. Another example is GlycoNex Company, whose chairman Dr. Tong-Hsuan Chang received his PhD degree from University of Tokyo in Japan, and acquired technology from Dr. Senitiroh Hakomori at the Biomembrane Institute (TBI) at University of Washington in the USA. The three companies all have key members of professional knowledge and are well-experienced in the particular field, which has helped these companies to successfully collaborate with different external partners. There are different collaboration modes and partners in all three companies due to different internal capabilities in each company.

Third, the degrees of openness of the three companies are changing over time based on their internal capabilities. At the phase of the new drug discovery, two companies acquired technology from external sources. CSRC Synpac Company acquired technology from Professor Yuan-Tsong Chen at Duke University (USA) in 1991. And GlycoNex Company acquired technology from Professor Sen-itiroh Hakomori at University of Washington (USA) in 2001. And one company AbGenomics developed its own technology at Professor Rong-Hwa Lin's team at National Taiwan University (Taiwan) in 2000. In the following phases, every firm would assess its own abilities in every phase and decide the degree of openness.

Finally, as the result of limited resources in Taiwanese biotechnology firms, the three companies exploit their internal capabilities and explore external resources and networks effectively and successfully over time. They know their own advantages and chose appropriate external partners to implement the process of new drug development in different stages. In the stage of technology transfer, Taiwanese biotechnology firms license out their drug candidates to international pharmaceutical companies successfully and profitably. For example, CSRC Synpac Company licensed out the new drug Myozyme to Genzyme Corporation (USA) in 2000. AbGenomics Company licensed out the new drug AbGn-168H to Boehringer Ingelheim Pharmaceutical (Germany) in 2005, and GlycoNex Company licensed out the new drug GNX-8 to Otsuka Pharmaceutical (Japan) in 2009.

5.2 Research contributions

This study offers three contributions. First, we have found that the perspective of open innovation is fully adopted by Taiwanese biotechnology firms in developing new drugs. The three cases represent typical Taiwanese SMEs in the industry of new drug development. Recently, numerous studies have begun to consider open innovation implementation in smaller firms (e.g. Laursen and Salter, 2006; Lee et al., 2010). Second, we analysed three cases of new drug development at the project level. Selecting the right projects and project management are core elements for the operation of pharmaceutical and biotechnology organizations (Biedenbach and Muller, 2012). Finally, we discussed the dynamics of the new drug development process of three Taiwan's projects in different stages. We contribute to very few studies that have been conducted on the operation of open innovation in the bio-pharmaceutical industry (e.g. Michelino et al., 2015).

5.3 Research limitations

There are three limitations in this study. First, we cannot gain a comprehensive perspective of new drug development in Taiwanese biotechnology industry with only a few cases, as this study was a multiple case study. Second, the information and data used in this study are limited to the interviews, the industrial reports, and the governmental reports. Third, validity data collected from all biotechnology firms in the field of new drug development in Taiwan were incomplete. We did not have the resources to interview all relevant project team members. It is possible that these absent perspectives could have influenced the data analysis of different open innovation models of new drug development. It is possible that a different interpretation of open innovation modes may emerge with more interviews from different projects on new drug development.

5.4 Directions of future research

Several future research directions arise from the study. First, interviews can be combined with surveys to gain more in-depth and comprehensive perspectives and findings in the discussion of open innovation modes in Taiwan's new drug development projects. Second, issues of open innovation in SMEs remain undeveloped, such as governance modes, the alignment of internal and external capabilities, exploitation and exploration, the dynamics and evolution of open innovation in different stages, etc. Other related issues that may be interesting to explore in future research include: can the open innovation of Taiwan's biotechnology SMEs be applied to other industries? Can the open innovation of Taiwan's biotechnology SMEs be applied to other countries such as Singapore or South Korea?

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