Towards a Typology of Business Models in the Biotechnology Industry

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Towards a Typology of Business Models in the Biotechnology Industry

Abstract

The purpose of this paper is to identify a selection of key business models - "typology" - applied in the biotechnology industry. The focus is on the differences between traditional/closed or stand-alone business models opposed to open or networked business models.

A number of illustrative case studies and good practices are presented to show that new biotechnology firms are gradually adopting a "best of both worlds" strategy, with both closed business models and open, networked models as a way for gaining access to the market, in close collaboration with large global pharmaceutical companies. The case firms and good practices are taken from a recent country study for Belgium.

Introduction

Biotechnology is developing in several forms such as bioclusters and bioRegions, i.e. regional clusters of life science activities and networks. A bioRegion is defined by the definition of the European Commission (PwC, 2011; Zechendorf, 2008; 2011): "Any geographically meaningful entity which can, but has not necessarily, to be a political or administrative entity for which the promotion of biotech and/or life sciences has been defined as a priority.

The global biotechnology economy is knowledge-based and a major engine for regional economic growth with clusters of biotechnology companies. The pharmaceutical-biotechnology regional and sectoral innovation system is characterized as an international and dynamic network architecture involving numerous players engaged in drug discovery. The biotechnology industry typically develops within an international network involving universities, research institutions, incubators, new biotechnology firms and global pharmaceutical companies.

It is “a complex network of corporate players, dominated by large firms with strong marketing capabilities and start-up firms that focus on research and development” (Pereira, 2006). New biotechnology firms partner with large pharmaceutical companies to advance the potential of their lead product(s) due to lack of infrastructure for late-stage clinical trials and/or marketing resources and the need for external investment.

The biotechnology industry faces a high-cost research and development, limited commercialization and constant technological change. The industry is characterized by a dynamic combination of the following features (Segers, 2017):

- geographical proximity (clustering);
- the translation of innovative (academic) research into potential drugs;
- limited commercialization: firms years away from actually marketing a drug;
- High risk – capital-intensive (declining expected return on R&D);
- a strong science base: a value chain with a long cycle of product development and many technical uncertainties;
- heavy dependence on patents (patent legislation) and intellectual property rights;
- big Pharma constantly in need of drug candidates to replace expired patents and failed projects;
- new biotechnology firms in need of adequate financing for expensive clinical trials and the marketing channels of big pharmaceuticals;
- external partnerships versus in-house efforts to generate innovative medicines and create new value;
- large firms using small firms as a window on leading-edge technological developments, not doing the expensive research themselves;
- trade-off between interfirm cooperation (strategic alliances) and vertical integration (from discovery to manufacturing and marketing/sales);
- clear institutional and regulatory frameworks;
- heavy regulation of drugs by governments and healthcare systems through approval processes and price controls (Rugman, 2005);
- different health systems in different countries;
- ethical clearance mandatory;
- aging population demanding improved healthcare;
- growing attention for open innovation and/or open source.

Typology of business models

As Pisano (2006; 2007) argued, biotechnology needs a variety of business models. Pisano (2006) distinguishes between "types of pharmaceutical innovations which call for vertical integration and which call for alliance-building and R&D outsourcing". According to Fisken and Rutherford (2002), "for a biotechnology company, the business model serves to secure value from the company's proprietary technology and know-how and is currently often heavily reliant on large (bio)pharmaceutical or established biotechnology company customers, collaborators and partners". Sabatier (2010) refers to the "business model portfolio".

The following section outlines a selection of key business models applied in the biotechnology industry - with own research versus outsourced research, depending on the therapeutic fields in which a given new biotechnology firm or large pharmaceutical company is operating. The focus is on the differences between closed or stand-alone business models opposed to open or networked business models.

① Closed business models

The first generation business model – based on blockbuster drugs – was a replicable model of vertical integration from research and development to marketing. It is a closed model of innovation, where all the key activities are performed inside the four walls of the company (Chesbrough, 2011).

The second generation of biotechnology startups focused on early stage research and collaborated – through alliances – with established pharmaceutical companies to develop and market the products. The third generation were biotech firms selling access to technology platforms, rather than specific therapeutic applications (Pisano, 2006; 2007).

Fisken and Rutherford (2002), Friedman (2010) and Phillips (2016) distinguish between the product-based, platform-based and hybrid business models – the traditional business models – based on the value chain structure of the biotechnology industry.

1. Product-based

As a general value creation and capture scheme, the dominant logic of the drug industry is product-based (Sabatier et al., 2012). The product business model originates from the pharmaceutical model where value is added along the activities of the value chain to deliver a final product to market.

The fully integrated pharmaceutical company (FIPCO) is a form of vertical business model focused on developing a pharmaceutical product. The FIPCO might fall under the category of a "producer business model" (Phillips, 2016).

It is also referred to as the:

- fully integrated biopharmaceutical company (FIBCO);
- fully integrated life science company (FILCO);
- fully integrated pharmaceutical network (FIPNET).

The ultimate goal for many biotech companies is to pursue a traditional FIPCO structure controlling the value chain for their product offering. The traditional model of fully integrated companies covers the whole value-creation cycle from discovery through development and commercialization. A large amount of capital is required. Medicines are developed by the company from the point of discovery up to the end of clinical trials or up to approval by the regulatory authorities.

However, for dedicated new biotechnology firms, the high risk and high cost of developing and commercializing a new product on their own make the platform-based and hybrid business models attractive, through multiple alliances (interfirm partnerships) with large pharmaceutical companies.

2. Technology Platform-based

The platform business model is a form of horizontal model. This business model generally focuses on the early drug development phases (molecule development). It leverages on licensing technologies to downstream firms. The model is based on the development of research tools or platform technology that can provide a service to another organization or can be licensed for further development along the value chain, through co-development partnerships.

With this business model, companies develop a set of tools or integrated technologies and license them out. Revenue can be generated relatively quickly through contract research and services. This business model reduces risk and the need for venture capital.

Alternatively, Thong (2015) refers to the so-called "bioscience platform companies", whose business model includes scientific core competencies that are deployed to enable the generation of a succession of new therapeutic or diagnostic product candidates. Such a company is often centered around a branded proprietary technology. According to Thong (2016), discovery platform technology companies are a natural fit with the partnering-centric approach. Over time, platform companies evolve into hybrid companies.

3. Hybrid business model

This is a hybrid of the product-based and platform-based business models. Technology platforms are combined with services and the generation of a pipeline of products.

The hybrid business model involves identifying internally new potential applications of the technology/discovery platform. New biotechnology firms share their technologies with other companies via partnerships (strategic alliances) and develop their own proprietary projects, to be eventually brought to market in partnership with commercial collaborators. The pipeline of products can be developed organically or through additional in-licensing or purchasing access to another's technology.

The hybrid model is the preferred business model for new and existing biotechnology companies - particularly by platform or tool-based companies - to maintain growth. They enjoy stable revenues from licensing or sales, which allows for attracting investors or using their own income stream to develop products. Investors benefit from reduced risks and the possibility of near-term revenue generation.

Figure I summarizes the traditional business models in the biotechnology industry.

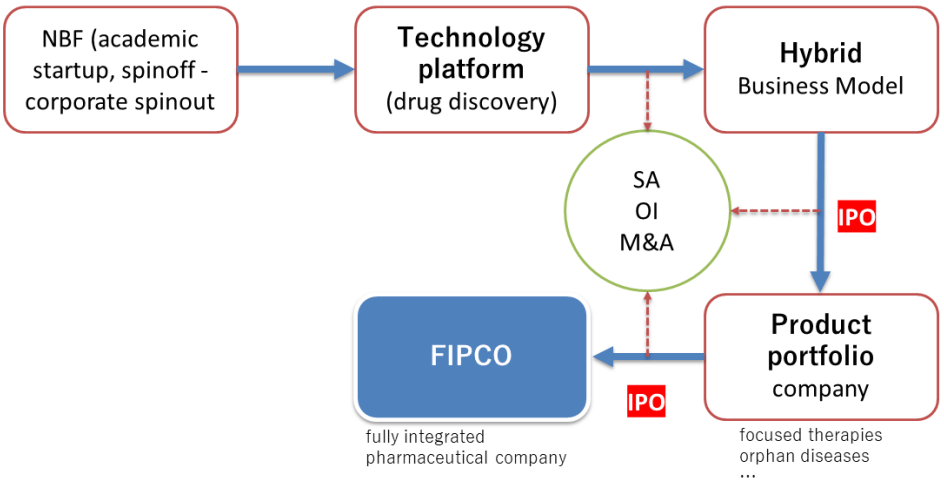

Figure I – Traditional business models (Thong, 2015 – adapted)

4. Royalty Income Pharmaceutical Company model (RIPCO)

With limited financial resources, the vast majority of new biotechnology firms start out as RIPCOs – research intensive or royalty income pharmaceutical companies. The RIPCO model covers platform and tool-based companies seeking to commercialize drug targets, services and technologies that can be sold or licensed to other companies. They focus on the earlier stages in the value chain, such as discovery and preclinical development. They research and develop new drugs, which they eventually license to a big pharmaceutical company in exchange for a royalty on sales. The large company finishes the research, produces the drug and commercializes it.

5. No Research-Development Only model

The no research - development only model is a derivative of the specialty pharmaceutical model. In this model, new biotechnology firms buy or in-license a promising 'discarded' drug from large pharmaceutical companies. They complete the late-stage clinical trials, bring it to market and try to make it profitable.

6. Pure licensing business model

This model leverages on strong intellectual property rights that are licensed to other firms. The licensors retain ownership of their licensed assets. These are often new biotechnology firms, hampered by their lack of financial resources and often unable to develop the final products by themselves. Their business model is to operate in the first phases of the value chain, generating revenues in the form of licensing payments, while licensees choose to rely partially or extensively on these upstream licensors to capture innovation. Part of the value in the pure licensing business model is lost to other firms.

7. Research service companies

These companies specialize in a specific niche in the value chain. They are Contract Research Organizations (CROs) that support pre-clinical and clinical trials or Contract Manufacturing Organizations (CMOs) that specialize in biological products and chemical drugs. The panorama of service companies connected to red biotech is very wide.

Some new biotechnology firms operate a hybrid model via both service/technology provision by strategically selected CROs and co-discovery alliances.

8. The IPO (Initial Public Offering) financing model

Most new biotechnology firms earn no money. They cannot be valued on the basis of earnings. Their value depends almost exclusively on their ongoing R&D projects and on the interpretation of publicly announced results of clinical trials. Deal and licensing information is commercially sensitive (Deloitte, 2016).

Pisano (2006) argues that this publicly held model will work only for companies that have earnings, allowing investors to judge their prospects. The IPO exit strategy is increasingly limited by the lack of product revenues.

Table I illustrates the use of closed business models discussed above by a selection of Belgian new biotechnology firms. These illustrative cases will be explained further on in this contribution.

Closed Business Models	BM1	2	3	4	5	6	7	8
CF1: ThromboGenics (THR)	■			■				■
CF2: Ablynx	■	■	■	■				■
CF3: Argenx		■		■			■	■
CF4: Galàpagos (GLPG)	■		■	■				■
CF5: Celyad		■		■		■		■
GP1: Janssen (J&J)	■							
GP2: Biocartis								
GP3: THR-GLPG	■					■		
GP4: UCB	■							

Table I – Use of Closed Business Models by Belgian firms

② Open business models

According to Chesbrough and Brunswicker (2013), establishing new partnerships, exploring new technological trends and identifying new business opportunities are the leading strategic reasons to engage in open innovation. Chesbrough (2003) defines open innovation as "a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as firms look to advance their technology".

Open innovation is an innovation paradigm shift from a closed to an open model. It is the opposite of the conventional (closed), vertically integrated research and development model, in which companies rely heavily on internal knowledge and resources (Chesbrough et al, 2006; Chesbrough (2003; 2006). To offset the trends of rising development costs and shorter product life cycles, companies must experiment with creative ways to open their business models by using outside ideas and technologies in internal product development and by allowing inside intellectual property to be commercialized externally (Chesbrough, 2007).

According to Chesbrough (2003), there is a continuum from fully open to fully closed enterprises, with the degree of openness depending upon a number of internal and external factors affecting that particular enterprise. This includes the reliance on intellectual property (IP) concepts and the complex highly regulated environment (Carroll et al., 2017).

According to Carroll et al. (2017), the (bio)pharmaceutical industry has been relatively slow to adopt open innovation approaches. In open innovation, companies don't restrict their drug development activities to their own internal compounds. Instead, they actively scan the external environment, from universities and research institutes early on, to startups and specialty pharmaceutical companies later on, for possible drug candidates that fit their business model (Chesbrough, 2011). They focus on the rights for diseases they serve in their markets, and license to others the rights for alternative markets.

Open business models attack the cost side – rising development costs – by leveraging external research and development resources and the revenue side by licensing technologies or products worldwide. These models are more efficient to show shareholders a return on investments in research

and development. The core of the model resides in that firms should leverage innovation outside. Openness is then mostly a strategy that allows rapid access to valued innovation worldwide while reducing operating costs and removing supply chain dependencies.

According to Gay (2014), in the open innovation approach, there is a greater reliance on connection, collaboration and partnerships for innovative success. She argues that open business models must delve into alliance management.

The following open business models are considered. They include different types of extensive collaboration and cooperation, open innovation, open access and data sharing.

9. The open innovation-based R&D model

The increasing need for startups, academic research centers and universities to generate their own funding instead of relying on government grants and public financing sources will likely drive the adoption of open innovation. The open innovation-based R&D model seems to be the way forward for biopharmaceutical companies, as it appears to be a more cost- and time-effective way to bring drugs to market (Deloitte, 2015a). In this context, most pharmaceutical companies have started to concentrate on their core competencies centering around technology platforms and therapy areas. They switched to streamlining and externalization of (part of) their R&D activities (Reepmayer, 2005).

10. Networked business models

The traditional model of fully integrated companies has evolved towards a networked model. Companies establish collaborations of varying intensities – from service providers to co-development partners – with large companies, in order to seek out synergies depending on their project and stage of development (Biocat, 2009). According to Gay (2014), the recent emphasis on networked business models of big pharmaceutical companies and venture capital firms which interact in open innovation with small biotech companies reflects that single companies cannot possibly master all the significant resources needed in R&D, production, and marketing. By opening their business models through economic transactions, companies can be more

effective in creating as well as capturing value. Firms thus leverage other companies' technologies, products, or organizational capabilities but also let other organizations leverage their assets.

11. Collaborative discovery business model

This model is similar to the networked business model. The partnership and joint R&D aspects of these alliances are significant in business model innovation terms, since they require new approaches to collaboration and property rights ownership where partners, rather than addressing the mass product markets, collaborate with individual patients in designing one-off personalized or group-specific treatments (Sabatier et al., 2012). This involves collaboration with drug and diagnostics companies for discovery of new candidates through customization of in-house platforms to meet specifically defined customer goals. Collaborative models have been predicted to be the business models of the future, although Gay (2014) points out that the question of how profits should be split between partners has not been addressed.

12. IP-oriented business models

Intellectual property (IP) rights are of critical value in a knowledge-based society. Patent policies are particularly important in biotechnology in support of the activity of smaller technology-based firms and university licensing. This aspect is of particular relevance to the pharmaceutical industry since the nature and development of pharmaceutical products make companies highly dependent on proper IP protection and enforcement (European Commission, 2014) and on the value created from IP rights. In the founder-oriented biotech, life sciences and pharma industry, patents are what create the value of an invention. The "final product" of drug discovery is a patent on the potential drug.

Open innovation is not about abolishing patenting (Holgersson et al., 2016). Open IP approaches are emerging through patent portfolios or patent pools. The patents portfolio and other intellectual property rights are in need of an entrepreneurial approach in order to provide sufficient returns to the individual (new) biotechnology firm.

According to Pisano (2006), monetizing IP was seen as the best way to finance long-term product development. This involves financing research and innovation through licensing, partnerships, royalties, etc. (i.e. asset-based income), but not necessarily through product sales (i.e. commodity-based income) (Birch, 2016).

Kerry and Danson (2016) refer to the use of a business model where IP protection actually enables companies to collaborate confidently in the knowledge that they will be able to enjoy some protection from direct imitation by others. The company portfolio of technologies and products is usually sold or licensed out. A suitable network and cooperation strategy is required to ensure the successful commercialization of the intellectual property.

Stevens et al. (2016) outline the differences between an open collaboration intellectual property framework and a partnership focused public-private partnership model. The latter is an investment-friendly model, as preferred access is a major incentive for industrial partners. West and Olk (2016) investigate how firms reconcile the open nature of research and development consortia with their traditional IP-based business models.

According to Holgersson et al. (2016), better patent management could also incentivize the repositioning of old substances to new diseases (abandoned compounds for rare and uncommon diseases) through the application of method of use patents or formulation patents. The method of use patent extends the protection time of the chemical substance for that specific use.

13. The virtual R&D model

This is not a common model. The virtual R&D-model has emerged in the biotechnology industry, where small groups of scientists discover and develop a new drug candidate with the help of external resources (Schuhmacher et al., 2013; PwC, 2010). According to Sabatier et al. (2010), the business logic and source of value of this model are in orchestrating a network to develop drug products. Virtual firms depend entirely on their partner alliances for access to knowledge, equipment and markets.

A virtual biotech company is basically a drug development company with an extensive development pipeline of candidate molecules, but with no employees. All the development is contracted with a contract research organization. The available capital is directly invested in drug discovery and development (Labiotech, 2017).

Dixon (2011) refers to the Virtually Integrated Pharmaceutical Company Organisation (VIPCO). This is a business model, whereby companies may outsource/contract extensively for services at any point(s) in the value chain, providing access to complementary assets outside the firm. This allows a company to maintain control of the product development process and defer the point at which they plug into the value chain.

Shire has implemented elements of an open, virtual and partnership-oriented concept: an open, collaborative and networked R&D model of 'early alliance' whereby pharmaceutical and biotechnology companies collaborate in early R&D. The biotechnology company provides the innovation, whereas the pharmaceutical partner contributes its capacities to discover and develop jointly an early drug candidate with the purpose of having access to the drug project later. Alternatively, it can use the early alliance to familiarize with a new technology or therapeutic area without investing too many resources (Schuhmacher et al., 2013).

According to Thong (2016) virtual biotechs are inevitably acquired quickly by large companies if their projects are successful.

14. Patient-centricity

Patient-centricity is an evolving and increasingly important element of the pharmaceutical business model, as governments and healthcare providers move toward a healthcare system that focuses on outcomes rather than on products and services. Reimbursement and pricing reflect the trend towards cost efficiency of healthcare systems. This puts increased pressure on the future returns of new biotechnology firms and large pharmaceutical companies (PhRMA, 2014; Deloitte, 2015b).

Aging populations, consumerism, increases in chronic and orphan diseases, new medical technologies and treatments (Cotter, 2006) are

putting new strains on healthcare systems. Patients are more aware of available treatment options and are demanding choice. The technology-driven ability to leverage health data is enabling providers to make better and faster diagnoses – e.g. through bioinformatics and open data – as well as more informed treatment decisions.

The old business model based on blockbuster drugs, incremental innovation and physician preferences is under pressure by innovative patient-centered models (Heidrick and Struggles, 2014; Saias and Kapadia, 2016), making the company's drug development processes more patient-centric. It involves a shift from a product-driven approach towards a connected patient-centered healthcare ecosystem. The involvement of the patient can be applied at every stage of a pharmaceutical company's efforts, from drug discovery to winning regulatory approval to post-market disease management.

Allarakhia (2015) distinguishes a newly devised continuum of patient engagement across several models of open innovation: crowd research, research partnerships, co-design programs, patient communities and focus groups. It is about engaging patients in open innovation drug discovery research, getting patients to rate their treatment needs and to translate those needs into drug research properties, which may help new biotechnology firms and pharmaceutical companies to find new molecules.

Table II illustrates the use of open business models discussed above by Belgian new biotechnology firms and Belgian large pharmaceuticals.

Open Business Models	BM9	10	11	12	13	14
CF1: ThromboGenics (THR)	■	■				
CF2: Ablynx		■				
CF3: Argenx		■				
CF4: Galàpagos (GLPG)	■	■				
CF5: Celyad		■		■		
GP1: Janssen (J&J)	■	■	■			■
GP2: Biocartis	■	■	■			
GP3: THR-GLPG	■	■	■			
GP4: UCB	■	■	■	■		■

Table II – Use of Open Business Models by Belgian firms

Illustrative case analysis and good practices

Segers (2017) provided a longitudinal follow up (i.e. 1987-2017) of 30 Belgian new biotechnology firms in the bioRegions of Flanders and Wallonia in his country study for the biotechnology industry in Belgium. A number of illustrative case studies and good practices are taken from that study to support the hypotheses that new biotechnology firms in Belgium apply a mix of the closed and open business models as presented in the "typology" section above.

The focus is on red biotechnology, i.e. pharmaceutical and healthcare applications. New biotechnology firms are both beneficiaries and targets of strategic partnering alliances with large and global (bio)pharmaceutical companies. A number of the Belgian new biotechnology firms hold a nodal position as "most preferred partner" with multiple alliances in dynamic R&D networks. Segers (2015; 2016; 2017) found a large number of strategic alliances and networks involving interfirm partnering activities between large and global (bio)pharmaceutical companies like Johnson & Johnson, Pfizer, Novartis, Roche, Merck & Co., Sanofi-Aventis, GlaxoSmithKline, AstraZeneca, Eli Lilly and AbbVie amongst others and Belgian new biotechnology firms.

The Belgian new biotechnology firms are either still in the preclinical stage of therapeutic research, developing targets and compounds in their early stages of existence or developing technology platforms in leading edge drug development. Most of them conduct research in the discovery phases I and/or II. They are involved in interactive collaborations (strategic alliances) with big pharmaceuticals, often with a co-creation goal: therapeutic targets, finding new molecules with a blockbuster potential, transforming the new molecule into a commercial drug.

Belgian new biotechnology firms apply a business model portfolio strategy to capture value from the proprietary technology and know-how, given the high risk and high cost of developing and commercializing a new product on their own. They have a high degree of dependence on milestone and success payments in the early stages of development. The business models most used are the technology platform model, the hybrid model, the royalty income model, the pure licensing model, the IPO financing model and the research services model.

The following illustrative cases and good practices are taken from the Segers (2017) country study on the biotechnology industry in Belgium. All case firms **(CF)** are either listed Euronext Stock Exchange (Brussels – Paris – Amsterdam) and have launched an initial public offering (IPO). Argenx, Galàpagos and Celyad are also listed on Nasdaq in New York.

CF1: ThromboGenics

ThromboGenics (THR, founded in 1998) is (was) the "star" amongst the biotechnology firms in Belgium. The company was established as a spin-off of the University of Leuven (KU Leuven), working on biopharmaceutical drug development between academia and industry. The company developed over the years from a university spin-off to a fully integrated specialty pharmaceutical company, with a promising biotechnology-based pipeline. Its primary goals are to develop and commercialize innovative therapies in ophthalmology (visual disorders, with a special focus on diabetes, i.e. diabetic retinopathy), cardiovascular diseases and oncology (cancer). Over the years, ThromboGenics partnered in a large number of strategic alliances with major players in global biotechnology. These strategic partnerships include research collaborations, co-development and co-commercialization as well as in-licensing agreements.

ThromboGenics lead product JETREA (ocriplasmin-platform; back of the eye disease) was approved by the Food and Drug Administration (FDA) in October 2012 for symptomatic vitreomacular adhesion (VMA) in the eyes and subsequently launched in January 2013. In March 2012, ThromboGenics signed a strategic partnership with Alcon (Novartis). Novartis' ophthalmic unit Alcon acquired the non-US rights to ocriplasmin, giving ThromboGenics access to significant milestone payments and royalties. ThromboGenics experienced problems with its commercial organization supporting JETREA and hence a downturn of its US-sales, which amounted to a lower than expected market demand of its lead product.

From 2013 onwards, ThromboGenics explored new "strategic options" and made a turnaround towards the development and commercialization of next generation therapies for the treatment of severe diabetic eye disorders. ThromboGenics evolved from a university spin-off to a fully integrated biopharmaceutical company and is now a clinical stage biotechnology company, taking its future prospects beyond its lead product JETREA®.

In April 2015, the company's research and development activities in oncology were spun out into a separate entity. Oncurious is a joint venture with the Flanders Institute of Biotechnology, a regional government funded institution that focuses on translating basic scientific results into pharmaceutical, agricultural and industrial applications. Oncurious is leveraging the joint expertise to develop innovative medicines (orphan drugs) for the treatment of pediatric cancer (brain tumors).

In March 2016, ThromboGenics signed a global in-licensing agreement (inbound open innovation) with Galapagos with respect to certain compounds to develop and commercialize THR-687 for the treatment of diabetic eye disease (diabetic retinopathy). ThromboGenics will pay a technology transfer fee to Galapagos. Galapagos will also be entitled to development and commercial milestone payments plus royalties on net sales of products.

In september 2017, ThromboGenics regained full global rights to JETREA® from Alcon, a Novartis company.

CF2 & CF3: Ablynx and Argenx

Ghent (Belgium)-based Ablynx and Argenx both develop llama-inspired molecules (i.e. the llama immune system). This technology has led to collaborations with multiple pharmaceutical companies including AbbVie, Boehringer Ingelheim, Merck & Co., Merck KGaA, Novartis, Novo Nordisk, Shire, Bayer and Sanofi.

They adopt a "best of both worlds" strategy (Thong, 2015) that involves spinning off single asset entities for commercialization and marketing, while retaining the platform core in the original mother company.

Argenx is a clinical-stage biotechnology company developing a pipeline of antibody-based therapies for the treatment of severe autoimmune diseases and cancer (immuno-oncology). The Argenx-case (**Figure II**) is a good example of a business model portfolio maximizing shareholder value. Argenx captures value at different stages through:

- platform deals with Shire and Bayer in the discovery stage via the SIMPLE antibody platform;

- product deals and thriving strategic alliances with Bird Rock Bio, LEO Pharma and AbbVie;
- wholly owned antibodies in early & late clinical development;
- research collaborations through Argenx's Innovative Access Program.

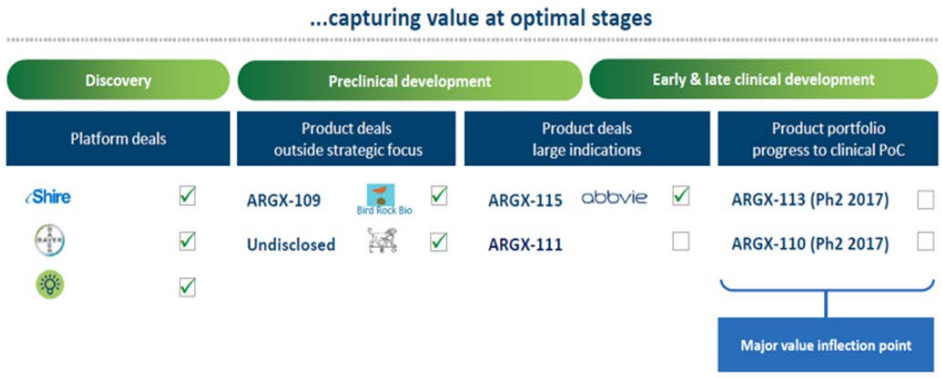

Figure II – Argenx (De Tijd - Finance Avenue, 2016) - adapted

Ablynx is a biopharmaceutical company which is developing single domain antibodies derived from llamas for various diseases. Ablynx is developing several proprietary programs in various therapeutic areas including inflammation, haematology, immuno-oncology, oncology and respiratory disease. Its lead - wholly-owned - candidate Caplacizumab, has been submitted for a marketing authorisation to the European Medicines Agency for approval in the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

CF4: Galàpagos

Galàpagos on the other hand is capturing value in a very competitive landscape from a mix of top-level partnerships with a number of big pharmaceuticals for clinical trials on multiple indications of its lead products, as **Figure III** shows.

Galàpagos discovered and developed filgotinib for the treatment of rheumatoid arthritis. The Belgian new biotechnology firm entered into a

strategic alliance with Gilead Sciences, following an earlier surprise decision by AbbVie not to opt into filgotinib's development.

With respect to the strategic alliances portfolio and the product pipeline, Galàpagos is currently the most likely to make it to the fully integrated pharmaceutical company (FIPCO) model stage (Segers, 2017).

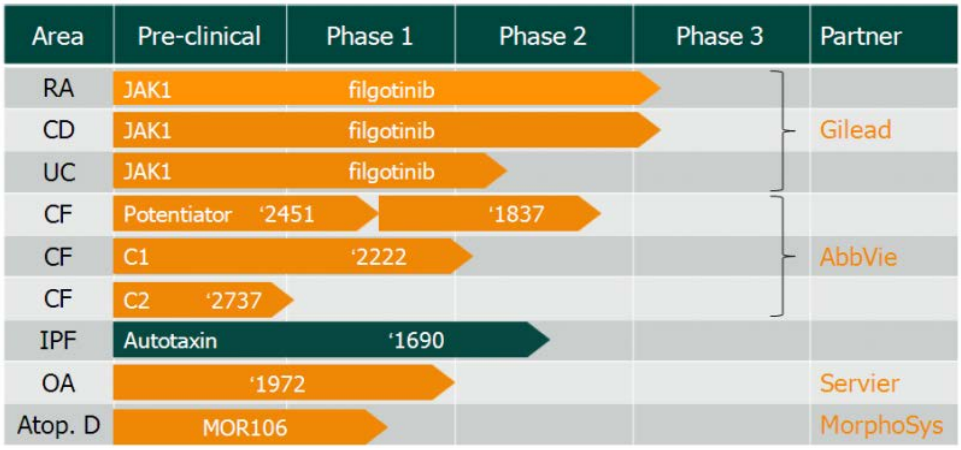

Figure III – Galàpagos' pipeline (labiotech.eu, 2016)

CF5: Celyad

Celyad is a clinical-stage biopharmaceutical company, specialized in cell therapy. It is looking for a pharmaceutical partner to further develop and commercialize its lead cardiology candidate, C-Cure. In addition, Celyad is focusing on its CAR-T pipeline, including its allogeneic NKR-2 T-cell immunotherapy.

The company announced a non-exclusive license agreement with Novartis for Celyad's US patents for the production of allogeneic CAR-T cells. This license agreement is related to two targets currently under development by Novartis.

A lot of attention in recent literature is directed towards the analysis of good practices on open innovation approaches. These approaches are developed with an emphasis on the emerging collaborative models that have shown a certain level of success. Segers (2017) found that Belgian new biotechnology firms are able to adopt innovative business models by providing R&D and services to larger firms and openly cooperating with them through open innovation.

The open business models most used are:

- the open innovation-based research and development model;
- the networked model;
- collaborative discovery.

Four illustrative good practices **(GP)** are presented below.

GP1: Janssen (J&J)

Janssen Pharmaceuticals (part of Johnson & Johnson) set up a regionally embedded innovation ecosystem (Robaczewska et al, 2016). This is an example of a collaborative model where Johnson & Johnson created regional clusters of life sciences start-ups and innovation hubs.

Johnson & Johnson (2015) launched its Janssen Labs (JLABS) network of biotechnology/life sciences incubators in San Diego, San Francisco, Boston, Toronto, Shanghai and London. The innovation hubs provide life science entrepreneurs and scientists with an open collaboration space (Weverbergh, 2013) for early-stage research in developing medical device and diagnostic technologies, consumer health care products and pharmaceuticals.

This approach enhances sourcing external innovation. It goes beyond the traditional focus of open innovation as Johnson & Johnson/Janssen try to leverage external talent and expertise, share public infrastructure, raise funding and influence public policies. The incubated life science start-ups are granted access to J&J's compound library and to its regulatory and commercial experts. Researchers working within the J&J-facilities do not work for Johnson & Johnson. Nor do their discoveries belong to J&J. Some of them even receive funding from J&J's competitors, such as Novartis, Pfizer and Bristol Myers Squibb (Fortune, 2016). Johnson &

Johnson/Janssen Pharmaceuticals gain access to some valuable technology, scientific talents and entrepreneurs in the life sciences space in backing these startups and set up development collaborations that help accelerate their growth.

Building on this growing JLABS network, Johnson & Johnson (2016) opened JLINX at its Janssen Pharmaceuticals Campus in Beerse (Belgium). JLINX will focus on innovation in pharma and cross-disciplinary healthcare solutions (FierceBiotech, 2016). Janssen Healthcare Innovation (Davies, 2016) is investing heavily in patient support programs. Patients are increasingly provided with the opportunity to participate in decisions relating to their healthcare.

Janssen (2017) also established the Integrated Smart Trial & Engagement Platform (iSTEP), a patient engagement mobile platform that can track medication adherence: "The open innovation philosophy at Janssen led us to develop iSTEP in a way that allows the technology to be available to other pharmaceutical companies. We believe that having a consistent approach across the industry can accelerate the process of bringing medicines to patients".

GP2: Biocartis Idylla platform

The Belgian new biotechnology firm Biocartis (Mechelen, Flanders bioRegion) is active in molecular diagnostics, rapid cancer and virus tests. Biocartis is opening up its Idylla-platform for external developers and is working together with Janssen Diagnostics (Johnson & Johnson) and Abbott Molecular. The Evalution open architecture platform of MyCartis – a spinout/division of Biocartis – enables MyCartis to engage in a strong industrial partnership with almost any company active in the field of bio-assay development.

GP3: ThromboGenics/Galàpagos alliance

In March 2016, ThromboGenics signed a global in-licensing agreement (inbound open innovation) with Galapagos with respect to certain compounds to develop and commercialize THR-687 for the treatment of diabetic eye disease (diabetic retinopathy). ThromboGenics will pay a technology transfer fee to Galapagos. Galapagos will also be entitled to

development and commercial milestone payments plus royalties on net sales of products.

GP4: UCB Pharma

UCB is a Belgian (Brussels) multinational global (bio)pharmaceutical company. Over the years, it transformed from an original chemical group into a pure biopharma company, partnering in a large number of strategic alliances. Its main focus is on neurology and immunology conditions. UCB has a number of blockbuster products in its old (Zyrtec, Keppra) and new product pipeline (Cimzia, Vimpat, Neupro, Briviact, Evenity).

According to Pop et al. (2017), UCB Pharma's transition from product centricity to patient centricity and a patient-centric service ecosystem was triggered by the increased competition and a new internal sense of purpose. Pop et al. (2017) point a the "patient value strategy" that was installed from 2015 onwards. Value is created both for the patient as for the organization. UCB is committed to setting up patient communities.

UCB Pharma gradually transformed from a closed company to more open and collaborative one. It builts its IP through own R&D or by buying other companies, the latter by acquiring Celltech (UK) and Schwarz Pharma (Germany).

According to Pop et al. (2017), UCB is slowly embracing open innovation to find new and improved medicines and treatments for millions of patients worldwide. The Technology Platform Access Program allows partners to access UCB's state-of-the-art technology and to collaborate with the R&D department to discover new drugs.

Discussion and Conclusions

Several business models exist in the biotechnology industry. New and disruptive models have emerged. They do not necessarily replace the older traditional ones. The typology of biotechnology business models in this contribution shows that new biotechnology firms and large global pharmaceutical companies both develop new open business models that compete against or work in symbiosis with traditional closed business models.

The illustrative case studies and good practices for Belgium show that new biotechnology firms in Belgium are gradually adopting a "best of both worlds" strategy, with both closed business models and open, networked models as a way for gaining access to the market, in close collaboration with the large global pharmaceutical companies.

Table III summarizes the business models most used by the Belgian firms.

Case Firms / Good Practices	BM1	2	3	4	5	6	7	8	9	10	11	12	13	14
CF1: ThromboGenics (THR)	■			■				■	■	■				
CF2: Ablynx	■	■	■	■				■		■				
CF3: Argenx		■		■			■	■		■				
CF4: Galàpagos (GLPG)	■		■	■				■	■	■				
CF5: Celyad		■		■		■		■		■		■		
GP1: Janssen (J&J)	■								■	■	■			■
GP2: Biocartis									■	■	■			
GP3: THR-GLPG	■					■			■	■	■			
GP4: UCB	■								■	■	■	■		■

Table III – Applicable Business Models

The biotechnology industry is clearly looking for new business models that can accommodate the shift from a product-driven approach towards a connected patient-centered healthcare ecosystem where open business models predominate, thus making the company's drug development processes more patient-centric.

The novel approaches adopted by both Janssen (GP1) and UCB (GP4) are "a far cry from the traditional paradigm of pharmaceutical companies working in isolation, fiercely protective of their ideas" (Osborne, 2017).

It is therefore fair to conclude that the closed business models based on vertical integration, blockbuster drugs and physician preferences are under pressure by innovative patient-centered models.

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