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The interplay between new technology based firms, strategic alliances and open innovation, within a regional systems of innovation context. *The case of the biotechnology cluster in Belgium*

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Abstract

Purpose: New technology based firm (NTBF) survival and growth are connected with strategic partnering alliances and open innovation within technology clusters. Strategic partnerships in the biotechnology industry allow new technology based firms to gain a foothold in this high-cost, high-risk industry.
In this article, we examine the impact of strategic partnerships and open innovation on the success of new biotechnology firms in Belgium by developing multiple case studies of firms in regional biotechnology clusters.
A longitudinal follow up of the Belgian biotech startup ecosystem is presented. We find that, despite their small size and relative immaturity, 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.

Design/methodology/approach: This is a theory-driven paper with suggested theoretical model and case study research design.

Originality/value: Although the literature on strategic partnerships is well developed, the majority of studies focus on large, established firms. There is absence of studies that look at strategic partnerships – and specifically the role of open innovation – in the development of small and innovative biotechnology firms. This article addresses this gap in the literature with a focus on new firms in the biotechnology cluster in Belgium, where there is a growing trend towards technological and market-driven relationships between large and small biotechnology firms.

Practical implications: Our conclusion is that the future of new biotechnology firms in Belgium lies in the effective establishment of strategic partnering alliances. In future research, the impacts of open innovation and novel business models warrant further attention.

Keywords: New technology based firms; New biotech firms; Strategic alliances/partnerships; Open innovation; Regional system(s) of innovation

Background

The application of new discoveries and advances in science towards commercial use and for public purposes depends mainly upon actions by entrepreneurs who create new technology-based firms.

Whether a broad or narrow definition is used, the evidence shows that new technology based firms constitute only a small proportion of the firms established each year in Belgium and in Europe. According to Storey and Tether (1998), NTBFs are thought to embody the technologies of the future which will provide secure employment opportunities for several generations. The quality of jobs provided in NTBFs are also thought to be significantly better than those in traditional activities.

There is also the role of NTBFs in industrial networks and technology clusters, in which they are thought to play an important part in the transfer of technologies and in strengthening the industrial fabric. However, in the life sciences industry (pharma, healthcare, biotechnology, medical devices, diagnostics) the high cost of commercialization make it unlikely that any new, small firm can succeed on its own. To overcome this challenge, many smaller firms enter into strategic partnership alliances with larger firms.

Although the literature on strategic partnerships is well developed, the majority of studies focus on large, established firms. There is absence of studies that look at strategic partnerships – and specifically the role of open innovation – in the development of small and innovative biotechnology firms. This article addresses this gap in the literature with a focus on new firms in the biotechnology cluster in Belgium, where there is a growing trend towards technological and market-driven relationships between large and small biotechnology firms.

For this research, a sample of stock-exchange-listed biotechnology firms in Belgium are screened and monitored. Most of these new biotechnology firms are unlikely to become fully integrated pharmaceutical companies, because they are heavily dependent on their large strategic partners, especially for:

- marketing outlets;
- resource manufacturing when they reach the commercialization stage;
- continuing product development efforts;
- licensing agreements;
- milestone payments.

Product and market characteristics, affecting firms' financing options, are important enablers or inhibitors (Knockaert et al., 2015). While aiming for sustainable growth, most of the new biotechnology firms in Belgium have not yet reached this level of maturity and are acutely aware of the possibility of takeover. The objective of this article is to develop an understanding of how strategic partnerships influence the development of these new and innovative biotechnology firms and the role that open innovation might play in the success of these relationships.

Research methodology

This study is structured as follows. The first section provides an overview – supported by the literature - of biotechnology business models to show how strategic

partnerships and open innovation are commonly leveraged in this industry and in the regional system of innovation policy framework. In the second section, we explore the biotechnology cluster in Belgium and present the longitudinal case based evidence for this cluster.

To investigate the impact of strategic partnering – and specifically the role of open innovation – on the growth and survival of new biotechnology firms, we employed a qualitative case study research design (Yin, 2009).

Our focus is new technology based firms - in particular new biotechnology firms - operating within the regional biotechnology clusters in Belgium. The data and findings are derived from personal interviews, company and public sector reports, IPO prospectuses, financial media coverage, OECD REGPAT databases, OECD and EU Outlooks and other available secondary data.

Methods

Biotechnology cluster in Belgium: the regional framework

Science and technology offer tremendous opportunities to innovate.

Biotechnology is defined as the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services. A number of biotechnological fields that have traditionally been distinguished include health, agriculture, food and beverages processing, natural resources, environment, industrial processing and bioinformatics (OECD 2009a). Next generation biotechnology opens new frontiers in personalized medicine, advances in imaging and the use of powerful bioinformatics.

The emphasis of this study is specifically on the valorization of red biotechnology. Red biotechnology brings together all those biotechnology uses connected to medicine. Red biotechnology includes producing vaccines and antibiotics, developing new drugs, molecular diagnostics techniques, regenerative therapies and the development of genetic engineering to cure diseases through genetic manipulation. Some relevant examples of red biotechnology are cell therapy and regenerative medicine, gene therapy, novel scaffolds, genomics, biomarkers, companion diagnostics and medicines based on biological molecules such as therapeutic antibodies.

The new biotech(nology) firm (NBF)

Biotechnology firms use biotechnology to produce goods or services and/or to perform biotechnology R&D. Dedicated biotechnology firms are a subgroup of the biotechnology R&D firm. They devote at least 75 % of their production of goods and services - or R&D - to biotechnology.

A dedicated biotechnology firm is defined as a biotechnology active firm whose predominant activity involves the application of biotechnology techniques to produce goods or services and/or the performance of biotechnology R&D.

The central task of most biotech companies is the development of drugs or new diagnostic methods. The large majority of firms working in medically oriented biotechnology are either still in the preclinical stage of therapeutical research or developing technology platforms in modern drug development. In general, biotechnology

companies conduct research in the discovery phase I of a new drug and biopharmaceutical companies take the new drug through phases II-III(IV, post-approval) and market it globally.

According to the OECD key biotechnology indicators (2009b); OECD 2011a; OECD 2013), the number of biotechnology firms is the most widely available indicator but it is not the best measure of a country's activity in biotechnology, owing to large differences in firm size and R&D intensity.

Business enterprise research and development expenditures on biotechnology as a share of total business sector R&D expenditure (BERD) is an indicator of a country's research effort. On average, it accounted for 5.7 % of BERD in 2009 and 5.9 % in 2011. With 19.4 % in 2011, Denmark spent the most on biotechnology R&D as a percentage of BERD, followed by Ireland (17.2 %), Switzerland (12.6 %) and Belgium (12.6 % in 2009).

The revealed technological advantage as defined by OECD is a country's share of patents in a particular technology field divided by the country's share in all patent fields. The index is above 1 when a positive specialisation is observed. In this regard, Denmark has the largest specialisation ratio in biotechnology followed by Singapore and Belgium.

An alternative measure of research focus on biotechnology is biotechnology R&D intensity, defined as biotechnology R&D expenditure as a share of total value added of the industry sector. This ratio was 0.31 % for the USA, followed by Switzerland (0.28 %), Ireland (0.27 %), Belgium (0.26 %) and Sweden (0.24 %).

Next to the United States (>40 %), Denmark, Belgium, Singapore and Canada all have a strong revealed technological advantage in biotechnology with more than 10 % of their patent portfolio dedicated to biotechnology.

With lesser, but bigger New Biotechnology Firms compared to its neighbour-countries, Belgium accounts for about 350 NBF's, i.e. 7 % of European biotech firms and 10 % of R&D expenditures (OECD 2011b; OECD 2014).

Within Europe, Sweden is frontrunner when it comes to public biotech market value. Belgium is in second place. Based on average market value per company, Belgian public biotech companies even rank first.

Suggested model

One of the primary concerns is to design a theoretical model or framework that capture(s) the real world of New Technology Based Firm-creation in Belgium. The validity of the model is supported by empirical observations and cased based evidence for New Biotech Firms.

The collaboration and strategic partnerships between universities and research institutions on the one hand, and the big pharmaceutical companies and biotechnology industry on the other hand opens up opportunities for the translation of innovative (academic) research into potential drugs, new therapies and medical diagnostics.

We screened a sample of stock-exchange listed new biotechnology firms (Table 1), which are representative for the Belgian biotechnology cluster and for the different business models described. These NBFs are representative for the different business models described.

Number of firms active in biotechnology, 2012 or latest available year

	Biotechnology firms	Dedicated biotechnology firms	% dedicated	Year	Type of firm
United States	6,862	2,178	31.7	2011	Biotech R&D firms
Spain	3,070	625	20.4	2012	Biotech firms
France	1,950	1,284	65.8	2012	Biotech R&D firms
Korea	937	370	39.5	2012	Biotech firms/Dedicated biotech R&D firms
Germany	700	570	81.4	2013	Biotech firms
UK	614	#N/A	#N/A	2013	Biotech firms
Japan	552	#N/A	#N/A	2013	Biotech firms
Australia	527	384	72.9	2006	Biotech firms
New Zealand	369	135	36.6	2011	Biotech firms
Belgium	350	127	36.3	2011	Biotech firms/Dedicated biotech R&D firms
Italy	300	166	55.3	2011	Biotech firms/Dedicated biotech R&D firms

OECD (2014), Key Biotechnology Indicators, http://oe.cd/kbi, October (adapted)

We expect to find that:

Proposition ① New biotechnology firms in the Belgian cluster will have to work together with international (bio)pharmaceutical firms to create substantial added value;

Proposition ② The success of future new biotechnology firms in Belgium will depend on setting up strategic partnering alliances and accommodating open innovation;

Proposition ③ Most of the new biotechnology firms in Belgium are unlikely to become fully integrated pharmaceutical companies, i.e. they are unlikely to adopt a product-based business model Fig. 1.

Biotechnology business models

To varying degrees, new biotechnology firms depend on strategic (technology) partnerships with other organizations or large firms. In most of the partnerships, the initial research and innovation developed by the smaller firms is transferred to their larger counterparts. According to Contracter and Lorange (1988; 2002), the term *alliances* covers several governance modalities ranging from relational contracting to licensing, to logistical supply-chain relationships, to equity joint ventures or to the complete merger of two or more organizations.

According to Porter (1985), "the business model outlines how a company generates revenues with reference to the structure of its value chain and its interaction with the industry value system". In the biotechnology industry, the business model for a new, small company is necessarily dependent on collaboration with other organizations. As Fisken and Rutherford (2002) explain: "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".

Biotechnology companies have traditionally used a variety of business models to enter the life sciences, pharmaceutical, or healthcare markets. Fisken and Rutherford (2002) and Pareras (Pareras 2008a) distinguish between three key business models based on the value chain structure of the biotechnology industry:

Table 1 Belgian New Biotechnology Firms (red biotech) & Strategic Partnership Alliances

Firm Name	Technology Platform	Product/Portfolio	Strategic Partnerships/Alliances	Acquisitions/Takeovers	Location Region
ThromboGenics[a]	Ophthalmic medicines	Jetrea	Alcon (Novartis)Novartis		Flanders (Leuven)
↓	Oncology		Bioinvent Int. AB		
Oncurious					
Ablynx[a]	Nanobodies	Alpha-pharmaceuticals Caplacizumab Ozoralizumab	Merck & Co.; AbbVie; Eddingpharm; Novartis; Merck Serono; Shire; Eli Lilly; Algeta Genzyme; Taiso		Flanders (Gent)
Argen-X[a]	Nanobodies		Lonza (GS Xceed)LEO Pharma		Flanders (Gent)
Galàpagos[a]	Rheumatoid arthritis	Filgotinib	AbbVieGlaxoSmithKlineEli LillyJanssen Pharmaceuticals (J&J) Servier Roche Ono Pharmaceuticals	01/2013: acquisition of Cangenix (drug discovery) Biofocus + Argenta: drug discovery divisions (sold)	Flanders (Mechelen)
Tigenix[a]	Stem cellsCell therapy	ChondroCelec Cx601	Cellerix/Grifols Lonza	Cellerix (acquisition)	Flanders (Leuven)
Movetis	Gastroenterology	Resolor	Shire-Movetis	2010: public takeover by Shire	Flanders (Turnhout)
Genticel[a]	Therapeutic vaccines	ProCervix (HPV)			Paris and Toulouse (France)
Bone Therapeutics[a]	Stem cellsCell therapy	PreobAllob			Wallonia (Gosselies)
Promethera Biosciences	Stem cellsCell therapy		ShireBoehringer Ingelheim		Wallonia (Louvain-L-N)
Celyad[a] (Cardio3 BioSciences)	Stem cellsCell therapy	C-Cure		Oncyte (Celdara Medica, USA)	Wallonia (Mont-Saint-Guibert)
Mithra[a] Pharmaceuticals	Intrauterine platform	Estelle (Estetrol)	GlaxoSmithKline		Wallonia (Liège)
Uteron Pharma	Intrauterine platform			2013: Actavis (USA) <> 2015: buy back	Wallonia (Liège)
MastherCell	Stem cellsCell therapy			Orgenesis (USA)	Wallonia (Gosselies)
MDxHealth[a]	Molecular diagnostics	ConfirmMDx	Exact SciencesOncgnostics		Wallonia (Liège)
Biocartis[a]	Molecular diagnostics	Idylla	Johnson & Johnson Abbott Fast-Track Diagnostics		Flanders (Mechelen)

Table 1 Belgian New Biotechnology Firms (red biotech) & Strategic Partnership Alliances *(Continued)*

UCB[a]	Neurology/immunology	Zyrtec, Keppra	AstraZeneca Pfizer Amgen Bayer Neuropore Therapies	Brussels
		Cimzia, Vimpat, Neupro		
		Brivaracetam, Epratuzumab, Romosozumab	Oncodesign	

[a]*BEL-Brussels and/or FRA-Paris (double) EURONEXT stock exchange listing*

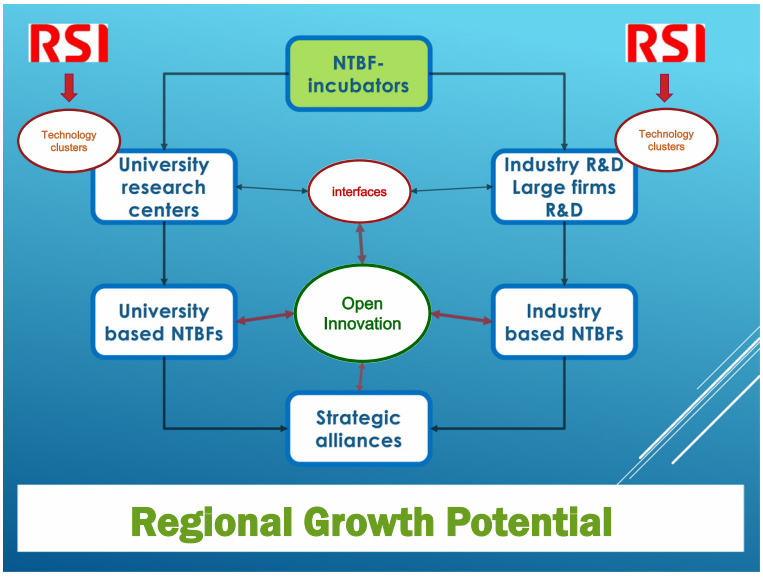

Fig. 1 theoretical model. RSI: regional system of innovation

1. Product-based: this vertical business model has its origins in the "fully integrated pharmaceutical company", where medicines are developed by the company from the point of discovery up to the end of clinical trials or up to approval. According to Fisken and Rutherford (2002) this business model "aims to generate value in progressing products along the drug development process and either licensing them out to pharmaceutical and top tier biotechnology companies or taking them straight through to commercialization."
2. Platform-based: 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. Thus, this business model reduce risk and the need for venture capital. Parares (Pareras 2008b) calls companies following this model "royalty income pharmaceutical companies". These small companies research and develop a new drug, which they eventually license to a large pharmaceutical company in exchange for a royalty on sales.
3. Hybrid: this is the dominant business model in the biotechnology industry. It is a hybrid of the product-based and platform-based business models and focuses on generating a pipeline of products. Investors benefit from reduced risks and the possibility of near-term revenue generation. In the hybrid business model, technology platforms are combined with services and the creation of products.

The choice of business model may depend on the type of innovation; indeed, Pisano (2006) distinguishes between "types of pharmaceutical innovations which call for vertical integration and which call for alliance-building and R&D outsourcing". However, for new, small technology companies 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.

Roth & Cuatrecasas (2010) defined a new paradigm for efficiently advancing new therapeutic products in the value creation chain. In their distributed partnering model for drug discovery and development, product definition companies (PDC) focus solely on advancing a portfolio of discoveries through the initial definition research phase. PDCs would acquire early stage discoveries from research institutions and invest in defining product applications with a goal of selling the successful ones to pharmaceutical companies for further development and delivery. The PDC business model focuses on identifying and licensing promising discoveries from research institutes (and biotech/pharma).

Open innovation

Companies are increasingly forced to join forces in complex regional innovation networks or startup/ spinoff ecosystems where they organize open innovation activities.

Open innovation and open business models are two concepts that have been launched by Henry Chesbrough (2003; 2006). It is a popular approach within innovation practice, in contrast to the traditional closed innovation strategies.

Oakey (2013) criticizes Chesbrough for exaggerating the applicability of open innovation systems because R&D is often long-term, expensive and always risky and requires necessary protection of outcomes. He argues that closed innovation is still an effective way for R&D investment (Hossain, 2015).

"Open Innovation is a new paradigm that assumes that firms can and should use external ideas as well as internal ideas and internal and external paths to market, as the firms look to advance their technology". Open innovation is defined as "the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and extend the markets for external use of innovation, respectively" (Chesbrough et al., 2006). It implies collaborating with researchers, customers, suppliers – even competitors – as well as research institutions and universities.

The central idea behind open innovation is that, in our knowledge society, companies cannot afford to rely entirely on their own research, but should instead buy or license processes or inventions (e.g. patents) from other companies. In addition, internal inventions not being used in a firm's business should be taken outside the company (e.g., through licensing, joint ventures, spin-offs).

Various network forms of cooperation thus come into play to support the value creation process, such as strategic alliances, consortia, ecosystems and business/technology platforms.

At the heart of the open innovation model is the recognition that today, competitive advantage often comes from inbound as well as from outbound connections. Leveraging inbound connections means leveraging the discoveries of others: companies should not rely exclusively on their own R&D. Leveraging outbound open innovation means that, rather than relying entirely on internal paths to market, companies can look for external organizations with business models that are better suited to commercialize a given technology (Chesbrough, 2002).

The adoption of open innovation may be sequential, starting with customer involvement, followed by employee involvement and external networking, and ending with more "advanced" practices such as IP licensing, R&D outsourcing, venturing, and external participations (Van de Vrande et al., 2009).

A lot of research has been devoted to strategic alliances and innovation partnerships, such as the motives for, and the impacts of, collaboration (Contractor & Lorange, 1988; Segers, 1993). According to Solesvik & Westhead (2010), selection of the right partner is probably the most crucial aspect of open innovation success.

In most traditional partnerships, smaller firms perform research and development for the larger firms or transfer innovations to them. However, open innovation is changing the way these firms interact. In the early stages of R&D, open innovation offers a neutral platform for companies to jointly investigate new and emerging technologies and applications, while sharing risks and costs.

The open-innovation approach is providing new ways for firms of all sizes to collaborate, and it is creating opportunities for smaller companies. According to Weverbergh (2013), "cross pollination between the corporate and the startup world – whether through corporate accelerators, venturing or open innovation – is fast becoming the trend".

Open innovation and biotech clustering

The work of Su and Hung (2009) defines five critical success factors in the evolutionary process of a biotech cluster: (1) a strong science and industry base; (2) finance supporting mechanisms; (3) entrepreneurship; (4) social capital; (5) networking; with the later three factors being intertwined.

Davies et al. (2015) examine models of life sciences startups through presenting a science base in its role to facilitate new enterprise, alongside networking efforts to strengthen the region.

Basically, biotech firms have worked with the open innovation concept for many years now, using knowledge existing inside and outside the organisation. The new approach is that of clustering and intensive partnering. A number of recent examples underline this:

- Johnson & Johnson's pharmaceutical division, *Janssen* (Belgium), opened "Janssen Labs" (J&J, 2015) (i.e. concept labs and open collaboration spaces) in San Diego, Boston and Beerse (Belgium). This shared laboratory – and its open-plan office space –provides life-science entrepreneurs with an affordable environment for early-stage research and encourages interaction between startups. It enhances sourcing external innovation.
- Roche (Pharmaphorum (2015)) announced a new open innovation research alliance in biotechnology, nanotechnology and engineering to develop new and faster diagnostic tests. Roche is working together with Biomed X, a new open innovation lab. It hopes to produce speedier diagnosis and synergies with its drug treatments.
- Open source biotechnology in big pharma with open access to data, i.e. sharing of clinical trial data or data on newly approved medicines to researchers. This is already the case for Pfizer, Novartis, Sanofi, GSK, Johnson & Johnson.
- The Innovative Medicines Initiative (2010) http://www.imi.europa.eu/ is the largest public-private partnership aiming to boost pharmaceutical innovation in Europe and to speed up the development of better and safer medicines for patients. IMI is a joint undertaking between the European Union and the pharmaceutical industry association EFPIA. Large biopharmaceutical companies and small- and medium-sized enterprises are working together with patients' organisations, research organisations, hospitals, regulatory agencies and other industrial partners.

Strategic partnerships

The number of strategic partnerships between large, established firms and NTBFs has multiplied over the past decades, due to a growing trend towards technological and marketing relationships between large and small firms. The issue of the clustering of NTBFs relates to agglomeration economies, especially with regard to access to knowledge and information. Proximity is generally thought to enhance both formal and informal knowledge and information flows, between NTBFs and both universities/research institutes and other firms, especially the NTBFs customers which tend to be large firms. This in turn relates to the issue of networking, and the dynamic complementarities (Rothwell, 1983) between small and large firms in innovation. It is therefore the concept of strategic alliances, between small and large firms, with mutual benefits for both, which is stressed here.

(O'Doherty 1990a; 1990b) argues that "strategic partnerships and alliances perhaps represent the greatest need but also the greatest challenge for small firms and small countries". The challenges include both determining the strategic direction of the firm but also finding "suitable and willing" partners to collaborate with. In the biotechnology industry, open innovation might have a role play in meeting these challenges and in the success of the strategic partnerships, both from the perspective of new, small companies and established, large companies. As Nigel Sheail (Bayer Healthcare, 2012) says: "Partnering and even open innovation is becoming increasingly important for our industry in a world where health systems are undergoing profound transformations." According to the Holst Centre (2013), an independent open-innovation R&D centre, "due to the increased complexity of physics, life-sciences, materials, electronics, software, etc., the cost of R&D is growing faster than company revenues. The goal of partnering is to share ideas and efforts, cost and risk of R&D and to reduce the time to market of new product generations".

In most traditional partnerships in the biotechnology industry, smaller firms perform research and development for the larger firms or transfer innovations to them. However, open innovation is changing the way these firms interact. In the early stages of R&D, open innovation offers "a neutral platform for companies to jointly investigate new and emerging technologies and applications, while sharing risks and costs" (Holst 2013).

Regional systems of innovation - innovation ecosystems

Widespread research emphasizes the role of regional systems of innovation (RSI) in augmenting the competitiveness and performance of regions and companies. RSI can be defined as the ".. wider setting of organisations and institutions affecting and supporting learning and innovation in a region" (Asheim, 2009). The regional production structure or knowledge exploitation subsystem often displays clustering tendencies (Asheim & Gertler, 2006). Cooke (1992) in particular has pioneered the concept of the RSI.

Cooke et al. (2006) described the emergence of the Welsh Regional Science Policy which placed life Sciences and health as a challenge area to be tackled though the EU approach of Smart Specialisation, and the associated concentration of investment into excellence. The mix of industry and cluster policy development objectives was discussed by Cooke (2004) and more recently by Ketels (2013). Cooke and Leydesdorff (2006) point to the creation of infrastructure of excellence to provide basic and applied research capabilities, and in turn construction of regional competitive advantage.

Klepper (2011) points at the valuable agglomeration economies and the Marshall (1920) theory that suggests that firms cluster geographically because it is beneficial in

terms of better access to skilled labor (labor market pooling), specialized suppliers (shared inputs), and knowledge spillover from competing firms. Clustering facilitates learning from other firms, lowers transaction costs for firms and suppliers and enhances productivity.

According to Klepper, the following patterns are expected in industries subject to clustering:

- clusters begin with a successful diversifier;
- clusters experience a high rate of spinoffs;
- the leading firms in clusters are predominantly spinoffs of other leading firms in the cluster;
- spinoffs in clusters are more competent on average than spinoffs elsewhere and/or new firms/startups.

According to Edquist (2005), the system of innovation approach focuses on the fact that firms do not innovate in isolation but rather in collaboration and interdependence with other organizations such as other enterprises, universities and government research institutes.

The Innovation Ireland Report (2010) sums up the following elements that make up an innovation ecosystem:

- entrepreneurs and enterprises;
- investment in R&D
- education system, in particular higher education institutions;
- risk capital;
- tax and regulatory environment;
- public policy and institutions;
- international networks.

A successful innovation policy requires all elements of the ecosystem to co-operate and collaborate together. This is in line with the "triple helix"-model by Etzkowitz & Leydesdorff (1997; 2000) which creates constructive and mutually reinforcing activities between academia, government, and industry.

According to Leten et al. (2013), innovation ecosystems generate value for partners by reducing development costs and risks and by combining complementary knowledge, enabling partners to address problems with high complexity. Ecosystem partners can subsequently use the knowledge created within ecosystems to support their own businesses.

Country-specific institutional features support or impede the accumulation and diffusion of knowledge between the scientific and industrial communities.

Clusters, taken as concentrations of "interconnected companies and institutions in a particular field" (Porter, 1998) continue to be of interest to policymakers.

Biotechnology clustering in Belgium is the result of a longitudinal"regional systems of innovation" approach in the Flanders, Brussels and Walloon regions (Segers, 1996). The region-specific technology policy in Belgium (Segers, 1992) has been organized around two focal points:

- the existence of state-of-the-art research potential in the country's universities and

- emerging technology centres, charged with supporting new technology based firms (Segers, 1993).

Over the years, a wide range of incentives have been created for assisting new technology-based firms. The main categories are:

- financial and fiscal incentives (e.g., the Belgian patent income deduction regime)
- employment incentives
- access to seed, venture, and growth capital
- government-supported laboratories and industry-specific collective research centres
- technology clusters and infrastructural incentives
- establishment of incubators in the proximity of universities for stimulating and assisting university spin-offs

The critical success factors are:

- access to key scientific personnel and mobility of researchers
- access to seed and venture capital
- the number of initial public offerings (IPOs)
- operating losses in the early stages of development
- regulatory approval from the Food and Drug Administration (FDA; http://www.fda.gov/) in the United States and from the European Medicines Agency (EMA; http://www.ema.europa.eu/ema/) in the European Union
- patents and intellectual property rights
- dependence on the strategic large partner(s)
- expected revenues derived from the strategic large partner(s) (e.g., milestone payments)
- manufacturing, clinical trial and regulatory compliance capabilities

The life sciences and biotechnology industry have become important regional clusters of new economic development in Belgium, and many new biotechnology firms in Belgium are university spin-offs. Due to strong collaboration between research institutes, universities, venture capitalists, high-risk finance providers, and existing large companies (big pharma), strong biotechnology clusters have developed in the regions of Flanders (e.g. Ghent and Leuven) and Wallonia (e.g. Liège and Louvain-La-Neuve).

The Belgian biotechnology industry is now firmly positioned as a key player in Europe, with a market capitalization of about 30 % in the eurozone.

Results and discussion

Case study results

Within Belgium's strong regional biotechnology clusters, we found a large number of strategic technology partnerships between large, international, and established chemical or (bio)pharmaceutical firms and new biotechnology firms (Segers, 2013).

Table 1 lists a sample of biotechnology firms, along with details on their strategic partnership alliances.

We observed strong collaboration between research institutions, universities, venture capitalists, high-risk finance providers, existing large companies, and new biotechnology firms. The basic innovative activity occurs mainly in university-based new biotechnology firms,(i.e., new, small firms that are spin-offs from university research centres performing state-of-the-art research).

On the other hand, large and international chemical or (bio)pharmaceutical firms participate in or establish joint ventures with university research centres and small, university-based new biotechnology firms. Of the new biotechnology firms in Belgium that were included in this study, most are unlikely to become fully integrated pharmaceutical companies, because they are heavily dependent on their strategic large partners, especially for marketing outlets, for manufacturing resources when they reach the commercialization stage, and for continuing product development efforts. They have to rely heavily on licensing agreements and milestone payments.

While aiming for sustainable growth, most new biotechnology firms in Belgium have not yet reached an independent stage of maturity and are predominantly driven by the takeover alternative, as was the case in recent years for Movetis (takeover by Shire) and Devgen (takeover by Syngenta). Up to this point, only ThromboGenics, Galapagos, and UCB have succeeded in becoming mature, self-sustaining biotechnology/biopharma firms.

ThromboGenics is a biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of eye diseases. The company was established in the 1980s as a spin-off of the University of Leuven. ThromboGenics developed over the years from a university spin-off to a fully integrated specialty pharmaceutical company. Its lead product, Jetrea (ocriplasmin), was approved by the FDA and the EMA in 2013. The company signed an important strategic partnership with Alcon (Novartis) to commercialize Jetrea outside the United States. Since that time, ThromboGenics experienced difficulties in selling Jetrea and revenues and share value dropped extensively.

Conclusions

Over the past decade, both academics and practitioners have increasingly recognized the need for collaboration and knowledge exchange for successful business development. The challenges are especially large in resource intensive industries, where huge investments are needed to develop new products. The way to overcome these costs and to stay competitive is through embracing open innovation strategies.

Companies are increasingly forced to join forces in complex regional innovation networks or startup/ spinoff ecosystems where they organize open innovation activities. Both emerging companies (startups) and high-growth (technology) firms will have to embrace open innovation to stay relevant. The open innovation approach provides small and large firms and regions new ways and insights to collaborate in order to create regional growth potential and mutual long term benefits. The development of innovation ecosystems is a prerequisite for future sustainable regional growth.

Life sciences and especially the biotechnology industry have become important regional clusters of new and sustainable economic development in Belgium. The implications for the national and regional systems of innovation are numerous. Our case-based analysis of the biotechnology cluster in Belgium shows that strategic technology partnerships

between new biotechnology firms and established, large, and international (bio)pharmaceutical companies have a significant impact on the survival and growth of these new biotechnology firms.

In order to achieve sustainable development, it is advisable that the clusters have good access to scientists, that they employ the new collaborative model or open campus model where open innovation leads to creativity. It implies mobility of researchers between companies or from universities to companies. On the firm level, it is important that firms have multiple projects and product portfolios, high ability to adapt, and solid technology platforms.

Our evidence supports the assertion by Fisken and Rutherford (2002): "while a small number of companies with access to a large supply of capital may be able to complete downstream integration and revert to the [fully integrated pharmaceutical company] model, the majority of biotechnology companies will instead need to further develop sophisticated relationship management skills in order to extract greater value from relationships with customers, collaborators and strategic partners".

The interplay between biotech firms, investors, universities, large and raditional pharmaceutical companies, government regulators may lead to new business models, organisational structures, and financing arrangements that place greater emphasis on integration and open innovation (e.g. cross-industry collaboration, the sharing of knowledge and resources) instead of monetisation of intellectual property.

Our conclusion is that the future of new biotechnology firms in Belgium lies in the effective establishment of strategic partnering alliances. In future studies, the impacts of open innovation and novel business models warrant further attention.

Competing interests
The author declares that he has no competing interests.

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References
Asheim, B. (2009). Guest Editorial: Introduction to the Creative Class in European City Regions. *Economic Geography, Clark University, 85*(4), 355–362.
Asheim, B, & Gertler, MS. (2006). The geography of innovation. Regional innovation systems. In J Fagerberg, D Mowery, & R Nelson (Eds.), *The Oxford Handbook of Innovation*. Oxford: Oxford University Press.
Chesbrough, H. (2002). Graceful Exits and Missed Opportunities: Xerox's management of its Technology Spin-off Organizations. *Bus Hist Rev, 76*, 803–837.
Chesbrough, H. (2003). *Open Innovation: The New Imperative for Creating and Profiting from Technology*. Boston: Harvard Business School Press.
Chesbrough, H. (2006). *Open business models: How to thrive in the new innovation landscape*. Boston: Harvard Business School Press.
Chesbrough, H, Vanhaverbeke, W, & West, J (Eds.). (2006). *Open innovation: Researching a new paradigm*. Oxford: Oxford University Press.
Contractor, F, & Lorange, P (Eds.). (1988). *Cooperative strategies in international business: Joint ventures and technology partnerships between firms*. Boston: Lexington Books.
Contractor, F, & Lorange, P. (2002). The growth of alliances in the knowledge-based economy. *Int Bus Rev, 11*(4), 485–502.
Cooke, P. (1992). Regional innovation systems: competitive regulation in the new Europe. *Geoforum, 23*(3), 365–382.

Cooke, P. (2004). The regional innovation system in Wales, in Regional Innovation Systems. The Role of Governances in a Globalized World. Routledge, London.
Cooke, P, & Leydesdorff, L. (2006). Regional development in the knowledge-based economy: the construction of advantage. *J Technol Transf, 31*(1), 5–15.
Cooke, P, et al. (2006). The biosciences knowledge value chain and comparative incubation models. *J Technol Transf, 31*(1), 115–129.
Davies, GH, Huxtable-Thomas, L, Roderick, S, & Clement, RM. (2015). *Models of life sciences start-ups: don't throw the incubator out with the bathwater*. Berlin: Paper presented at UIIN Conference.
Edquist, C. (2005). Systems of Innovation: Perspectives and Challenges. In J Fagerberg, D Mowery, & R Nelson (Eds.), *The Oxford Handbook of Innovation*. Oxford: Oxford University Press.
Etzkowitz, H, & Leydesdorff, L (Eds.). (1997). *Universities and the Global Knowledge Economy: A Triple Helix of University–Industry–Government Relations*. London: Cassell Academic.
Etzkowitz, H, & Leydesdorff, L. (2000). The Dynamics of Innovation: From National Systems and 'Mode 2' to a Triple Helix of University-Industry-Government Relations. *Res Policy, 29*(2), 109–123.
Fisken, J. & Rutherford, J. (2002). Business models and investment trends in the biotechnology industry in Europe. Journal of Commercial Biotechnology, 8 (3), 191–199. http://commercialbiotechnology.com/article/view/431
Holst Centre (2013). Executive Report. http://www.holstcentre.com
Hossain, M. (2015). A review of literature on open innovation in small and medium-sized enterprises. *Journal of Global Entrepreneurship Research, 5*, 6.
Innovation Ireland (2010), Report of the Innovation Taskforce, March.
Innovative Medicines Initiative (2010). http://www.imi.europa.eu
Johnson &Johnson (2015). https://www.jnj.com/news/all/johnson-johnson-innovation-announces-opening-of-the-california-innovation-center
Ketels, C. (2013). "Recent research on competitiveness and clusters: what are the implications for regional policy?" Cambridge Journal of Regions. *Econ Soc, 6*(2), 269–284.
Klepper, S. (2011). Nano-economics, spinoffs, and the wealth of regions. *Small Bus Econ, 37*, 141–154.
Knockaert, M, et al. (2015). A perspective on the economic valorization of gene manipulated biotechnology: Past and future. *Elsevier: Biotechnology Reports, 6*, 56–60.
Leten, B, Vanhaverbeke, W, Roijakkers, N, Clerix, A, & Van Helleputte, J. (2013). IP Models to Orchestrate Innovation Ecosystems: IMEC, a public research institute in nano-electronics. *Calif Manage Rev, 55*(4), 51–64.
Marshall, A. (1920). *Principles of economics*. London: Macmillan.
O'Doherty, D. (1990a). Strategic alliances - an SME and small economy perspective. *Sci Public Policy, 17*(5), 303–310.
O'Doherty, D (Ed.). (1990b). *The cooperation phenomenon - prospects for small firms and the small economies*. London: Graham and Trotman Ltd.
Oakey, RP. (2013). Open innovation and its relevance to industrial research and development: The case of hightechnology small firms. *International Small Business Journal, 31*(3), 319–336.
OECD (2009). Science, technology and industry scoreboard. http://www.oecd-ilibrary.org/science-and-technology/oecd-science-technology-and-industry-scoreboard-2009_sti_scoreboard-2009-en
OECD (2009). Patent Database. Biotechnology statistics.
OECD (2011). Key Biotechnology Indicators. http://www.oecd.org/science/inno/49303992.pdf
OECD (2011). Science, technology and industry scoreboard., 132–133.
OECD (2013). Science, technology and industry scoreboard., 158–159.
OECD (2013). Key Biotechnology & Nanotechnology indicators: a comparison. http://www.oecd-ilibrary.org/science-and-technology/oecd-science-technology-and-industry-scoreboard-2013_sti_scoreboard-2013-en
OECD (2014). Key Biotechnology Indicators. http://oe.cd/kbi
Pareras, L. (2008). *Innovation and entrepreneurship in the healthcare sector: from idea to funding to launch*. Phoenix Maryland: Greenbranch Publishing.
Pharmaphorum (2015). Roche to use open innovation to develop nanotechnology diagnostics. http://www.pharmaphorum.com/news/roche-to-use-open-innovation-to-develop-nanotechnology-diagnostics
Pisano, G.P. (2006). Science Business: The Promise, the Reality and the Future of Biotech. Boston: Harvard Business School Press.
Porter, M. (1985). *Competitive Advantage: Creating and Sustaining Superior Performance*. New York: Free Press.
Porter, ME. (1998). *Clusters and the new economics of competition*. Boston: Harvard Business Review Boston.
Roth. D., Cuatrecasas, P. (2010). The distributed partnering model for drug discovery and development. Ewing Marion Kauffman Foundation. http://www.kauffman.org/~/media/kauffman_org/research%20reports%20and%20covers/2010/01/distributedpartnershipmodel_12510.pdf
Rothwell, R. (1983). Firm Size and Innovation: A Case of Dynamic Complementarity. Journal of General Management, *8*(3).
Segers, JP. (1992). Region-specific technology policy in Belgium: the significance of new technology based start-ups. *Small Bus Econ, 4*, 133–139.
Segers, JP. (1993). Strategic partnering between new technology based firms and large established firms in the biotechnology and micro-electronics industries in Belgium. *Small Bus Econ, 5*, 271–281.
Segers, JP. (1996). Technology policy: the role of regions and new technology based firms in Belgium. In B Balkin, J De Castro, & G Dale Meyer (Eds.), *Advances in global high-technology management, 6* (pp. 3–25). Greenwich/London: JAI Press.
Segers, J.P. (2013). Strategic Partnerships and Open Innovation in the Biotechnology Industry in Belgium. Technology Innovation Management Review. *3*(4), 23–28.
Sheail, N. (2012). Partnering for innovative healthcare solutions. European Biotechnology Magazine. http://www.european-biotechnology-news.com/people/editorial/2012/nigel-sheail.html
Sheail, N. (2012). http://healthtechevent.com/partnering-and-open-innovation-are-becoming-increasingly-important-according-to-nigel-sheail-bayer-healthcare/. Partnering for innovative healthcare solutions. European Biotechnology Magazine. http://www.european-biotechnology-news.com/people/editorial/2012/nigel-sheail.html

Solesvik, M, & Westhead, P. (2010). Partner selection for strategic alliances: case study insights from the maritime industry. *Industrial Management & Data Systems, 110*(6), 841–860.
Storey, DJ, & Tether, B. (1998). New technology based firms in the European Union: an introduction. *Res Policy, 26*(9), 933–946.
Su, Y-S, & Hung, L-C. (2009). "Spontaneous vs. policy-driven: The origin and evolution of the biotechnology cluster". *Technol Forecast Soc Chang, 76*(5), 608–619.
Van de Vrande, V, de Jong, J, Van Haverbeke, W, & de Rochemont, M. (2009). Open innovation in SMEs: trends, motives and management Challenges. *Technovation, 29*(6–7), 423–437.
Weverbergh, R. (2013). Janssen Labs adds more "coworking lab space" for life sciences startups. Whiteboardmag.com.
Yin, R.K. (2009). Case study research: Design and methods (4th ed.). London: Sage.