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Barriers to Outbound Open Innovation in large biopharmaceutical enterprises

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Abstract

Open Innovation (OI) represents a newly emerging business model across a wide range of industries, enabling an 'open' flow of internal and external expertise across company barriers in order to enhance innovation and commercialization success. Two dimensions of OI can be distinguished: inbound OI refers to accessing external expertise in order to advance internal development (e.g. via in-licensing), whereas outbound OI refers to the transfer of internal assets or expertise to an external party (e.g. via out-licensing).

A sector showing strong signs of OI implementation already is represented by the biopharmaceutical industry. Whereas among the larger established pharmaceutical companies inbound OI represents a yet long established tradition, the outbound dimension is still largely neglected. However, outbound OI (OOI) engagement can positively affect firm performance by offering the opportunity to exploit non-core assets and enhancing the probability of success of strategic assets by transferring them to suitable external parties depending on the needs for successful development and commercialization.
It was the goal of this research to identify the associated barriers hindering large established pharmaceutical companies from pursuing OOI practices despite these compelling rationales for outbound OI adoption. To this end, a qualitative multiple case study approach was chosen where twelve representatives of nine (non-biotech) pharmaceutical companies were interviewed regarding their company's position towards OOI.
Major identified barriers consisted in resource competition of inbound vs. outbound activities, a too high effort-return ratio, as well as psychological barriers such as the fear of weakening one's own competitive position, and external players doubting asset quality.
In order to overcome those barriers, managerial measures should encompass systematization of the OOI process in order to decrease the associated effort. Furthermore, overall corporate alignment regarding awareness on OOI benefits has to be established to ensure suitable resource allocation and support minimizing inbound-outbound competition. In addition, the involvement of a third party acting as 'OOI intermediary' organizing the process, finding partners, etc. could represent a suitable approach to mitigate OOI-associated barriers. Psychological barriers will presumably disappear once the community of larger pharmaceutical enterprises has become more familiar with this new approach and more practical examples of successful OOI are available.
Summarizing, OOI engagement among large established pharmaceutical companies is still in its initial phase, its implementation hindered by several barriers. Yet, efforts to systematize the OOI process are already discernable, indicating that in the future OOI might become part of the new business model within the sector of established pharmaceutical companies providing added value complementary to the main product business.

Table of Contents

Problem description

In the current knowledge-based setting of our global economy, leverage of knowledge and creation of new commercializable ideas are crucial processes which have to be managed properly if a company wants to sustain its competitive advantage and thus its survival.

This is particularly the case for traditionally knowledge-intensive sectors like the pharmaceutical industry. In addition to competitive pressure exerted by multiple players wanting to reap the benefits from this lucrative market, this sector faces severe challenges from a multitude of directions, ranging from significant decrease in R&D-productivity (Hughes, 2009), spiralling costs and increasing complexity of drug development (Belsey, 2007) to considerable revenue losses due to patent expiration of many major drugs to be expected in the forthcoming years (Frantz, 2006). Furthermore, payors (government and health insurances) are exerting pressure on the price levels of marketed drugs and on safety regulations, which further reduces the achievable revenues for pharmaceutical companies.

All these challenges currently faced by the pharmaceutical industry indicate that the current business model is far from optimal. This is also apparent when considering that the number of newly approved innovative drugs (new molecular entities (NMEs)) has remained constant during the last 60 years whereas R&D spending has grown 12.3% annually since the 1970s (Munos, 2009). Clearly, there is a need for a new business model delivering higher innovative output. This is also apparent when considering that during the period of 1998-2007 more than half (56%) of all 'scientifically novel' drugs approved by the FDA (US Food and Drug Administration) were originally discovered by biotech companies and academia and not by the larger pharmaceutical companies (Kneller, 2010).
As a reaction, the pharmaceutical industry has already reconsidered its traditional fully integrated model where the entire drug discovery and development value chain was performed by primarily drawing on internal sources of knowledge and innovation. Although already pursued to some extent in the past, especially in the past decade, Big Pharma has increasingly relied on in-sourcing assets and knowledge via in-licensing and M&A activities (Tralau-Stewart *et al.*, 2009). Realizing that doing everything by themselves is risky, connected to significant investments (Gilbert *et al.*, 2003) and does not deliver the required R&D-productivity, Big Pharma is now relying extensively on external sources of innovation (Mullen, 2007; Jones, 2007).

In a cross-industry context addressing this phenomenon of opening up to external sources of innovation, Henry Chesbrough has coined the term 'open innovation' which he defines 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" (Chesbrough, 2003, p.xxiv). Depending on origin of the idea and the chosen path to market, open innovation (OI) can be divided into two dimensions: (i) **inbound OI** (**IOI**) comprising practices leading to the acquisition of external knowledge and expertise which are then developed internally and marketed by the focal firm and (ii) **outbound OI** (**OOI**) which is concerned with the transfer of internal knowledge to external organizations for commercial purposes (Chesbrough & Crowther, 2006; Bianchi *et al.*, 2010). Examples for inbound OI include in-licensing of intellectual property (IP), external networking and

alliances, customer involvement, and outsourcing of R&D (van de Vrande *et al.*, 2009). Outbound OI activities on the other hand include for instance out-licensing of intellectual property, venturing (spin-off, joint ventures), supply of scientific services, and alliances for exploitation (van de Vrande *et al.*, 2009, Bianchi *et al.*, 2010).

Due to the reciprocal nature of the OI process, an inbound activity of one party is simultaneously an outbound activity for the providing counterpart. Consequently, there are always as many inbound as outbound activities ongoing. However, there seems to exist an imbalance regarding the preference to pursue one mode or the other.
Whereas inbound OI represents an already quite established practice in most companies (Lichtenthaler, 2010; Bianchi *et al.*, 2010), outbound OI has been found to be practiced to a much lesser extent (Bianchi *et al.*, 2010). This indicates that a small number of companies specialized on outbound activities are providing a large variety of companies with assets.
In the pharmaceutical sector this observed preference for IOI is particularly true for large pharmaceutical companies ('Big Pharma'), as already alluded to above. They are indisputably the masters of performing inbound OI due to their established tradition of internalizing assets and external knowledge (Jones, 2007). With respect to outbound OI however, figures from the period of 2008/09 show that only 27% of the licensing deals by the top 10 pharmaceutical companies (by sales) were devoted to out-licensing activities (Datamonitor, 2010).
In the past, those outbound activities that larger pharmaceutical companies did engage in were primarily driven by the need for financial support, development capabilities and/or market access in order to successfully market a strategically valuable asset. An example would be the co-promotion deal of Germany-based Boehringer Ingelheim (BI) with Pfizer in 2001 on the bronchodilator Spiriva[1]. BI struck this deal in order to gain access to the US market and profit from the regulatory expertise of its partner. The outbound activity was therefore specifically aimed to enhance the success of a product vital to the corporate strategy.
Recently, new models of outbound OI activities have emerged that also include non-strategic/non-priority assets. Exemplary in this respect is the deal of Roche and Synosia in 2007, where 5 discontinued early development assets targeting the central nervous system were acquired by Synosia for further development[2]. These outbound deal types involving 'non-core' assets however currently are relatively scarce in the pharmaceutical sector.

In both variations involving strategic or non-strategic assets, outbound OI can have a pronounced positive impact on firm performance as exemplified by the pioneer IBM that made $1.2bn in IP-transfer (licensing) and supply of scientific services (custom development income) in 2009, representing 11% of its net income (IBM Annual Report 2009). Also a quantitative study by Lichtenthaler (2009) confirmed a positive effect on firm performance. This can vary from financial benefits such as the addition of significant revenues from licensing fees (as in the case of IBM) or strategic benefits like setting industry standards to increase the market share (e.g. introduction and

Web sources:
[1] http://sis.windhover.com/buy/abstract.php?id=200120360
[2] http://www.synosia.com/userfiles/file/Roche-Synosis_partnership.pdf

licensing of the VHS videotape format by JVC) (Arora *et al.* 2001 cited in Lichtenthaler, 2009; Huizingh, 2011).
These described positive OOI effects are owed to the fact that in Open Innovation "any intermediate product of innovation processes is considered as an economically good that can be exploited internally and/or externally [...] as a replacement of internal commercialization or in addition to it" (Huizingh, 2011, p.3). However, despite these potential upsides of employing outbound OI practices, the majority of companies are still struggling to find a proper implementation of this particular dimension of Open Innovation (Lichtenthaler, 2010; Dahlander & Gann, 2010).

Surprisingly, the associated reasons for failures in adopting OI practices have so far not been researched extensively. Two notable exceptions should be named. On the one hand van de Vrande *et al.* (2009) performed a study on Dutch SMEs in the manufacturing and service industry which aimed at identifying motives and challenges of companies involved in OI. They found that organizational and cultural differences between the interacting partners constituted the main managerial challenges for this type of firms. On the other hand, Lichtenthaler (2010b) explored the risks associated to adopting OI practices in 31 medium-sized and large European industrial firms. With regard to outbound OI the major perceived risk was strengthening existing competitors and/or developing new competitors.

Yet, in general, the current literature on open innovation has primarily focused on the benefits of OI but does not go into detail regarding the potential disadvantages and associated barriers to OI adoption (Dahlander & Gann, 2010). Precisely these insights, however, could prove to be valuable in order to assess the reasons for incomplete adoption of OI and the respective inability of companies to benefit accordingly.

Research question

Therefore, my research aims to address this lack of knowledge regarding barriers to Open Innovation, focusing on its outward dimension as a potentially beneficial strategic approach to further improve company performance which, in contrast to the inbound dimension still displays major deficits regarding its adoption.

To this end, this paper will focus on the biopharmaceutical industry, representing a knowledge-intensive industry where new approaches to innovation are currently in high demand and where thus the identification of barriers and potential solutions could provide considerable added value. Within this industry, the focus will be laid on established larger pharmaceutical companies which display a low degree of outbound OI (Datamonitor, 2010), as opposed to biotech companies that out-license to Big Pharma in a frequent and established fashion.
Furthermore, those outbound activities and associated barriers will be especially considered that entail non-strategic/non-core assets as these have been neglected in outbound activities of pharmaceutical companies in the past.

In order to answer the main research question: **What are the barriers to outbound Open Innovation in large biopharmaceutical enterprises and how can they be overcome?** the following set of sub-questions will be addressed: (i) What are the reasons/objectives of large pharmaceutical companies for pursuing outbound OI? (ii) Which decisions/criteria are driving outbound OI asset selection? (iii) What are the associated barriers of the outbound OI process? (iv) How can the identified barriers be overcome?

Justification

During the last decade, 'open innovation' has attained increasing attention in the field of innovation and managerial studies. Pioneered by the work of Henry Chesbrough (2003), there is now the conception that a shift has occurred from the traditional 'closed' innovation business model where idea generation and commercialization was performed internally, using internal resources only, towards a more flexible 'open' innovation model which is combining internal and external expertise along the innovation process. More precisely, open innovation is defined as "the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively" (Chesbrough *et al.*, 2006, p.1).

In line with this definition, OI can further be divided into inbound and outbound dimensions according to Chesbrough and Crowther (2006), depending on the purpose of the collaborations aiming at knowledge generation or commercialization respectively.

According to a literature review performed by Dahlander & Gann (2010), up to now most of the literature has primarily focused on the benefits of open innovation in terms of increased access to

valuable resources and knowledge, not considering associated disadvantages or barriers impeding implementation of OI practices.
One such disadvantage applicable to OI activities in general is the difficulty to capture value. In this context, Chesbrough and Appleyard (2007) proposed different types of value capture models related to OI practices which they identified from the software industry. They include (i) deployment (support, services), (ii) hybridization (proprietary extensions), and (iii) complements (e.g. devices) (Chesbrough & Appleyard, 2007, pp. 65/66). However, since these models were derived from the software industry, their applicability to the pharmaceutical industry is doubtful. This is also supported by a detailed qualitative case study on a large global pharmaceutical player performed by Hughes and Wareham (2010) where no evidence could be found for the presence of such value capture models. Thus, the question remains how the pharmaceutical industry does or could best capture value from engaging in OI activities.

A further lack in the current literature is that outbound OI in particular has not been a major focus of attention among OI researchers (Lichtenthaler, 2010).
From the limited existing studies on this subject in can be deduced that outbound OI practices have a positive impact on a company's performance, supporting the potential of outbound OI to provide added value complementary to a company's product business (Lichtenthaler, 2009). This applies both to core assets and non-core assets as found in a study by Kollmer and Dowling (2004) on biotech companies that achieved profitable revenues from out-licensing in both cases.
Yet, most firms struggle with capturing the value from outbound OI and thus fail benefitting from it (Lichtenthaler, 2009), underlining the need for appropriate value capture models.
According to Lichtenthaler (2005), four main themes can be identified from the present literature that impose challenges to successful external knowledge exploitation, i.e. outbound OI. These include (i) identification of possible applications and potential partners, (ii) commercialization of knowledge which often has a tacit character, (iii) assessment of the value of intellectual assets, and (iv) development of capabilities to adequately manage those mostly long-term relations (Lichtenthaler, 2005, p.235). Furthermore, in the literature it is repeatedly alluded to the reluctance of firms to take part in outward technology transfer due to the fear of losing 'corporate crown jewels' and thereby weakening their own competitive position (Fosfuri, 2006; Lichtenthaler, 2009; Lichtenthaler, 2010b).
While these themes represent some indication as to where these barriers might lie, more specification is needed in terms of ranking of importance and dependence on company- or industry-type. Only this way, useful advice can be given in order to overcome these barriers and to identify best practices regarding the successful management of outbound OI processes.

Aiming to address this lack of knowledge concerning a more detailed view on perceived challenges in context with OI, van de Vrande *et al.* (2009) performed a survey among Dutch SMEs of the manufacturing and service industry. Organizational difficulties and cultural differences of partners involved in OI activities resulted to be the main perceived challenges. Other factors included among others the balancing of innovation and daily tasks, lack of internal commitment and contractual problems.

This study gives a first valuable quantitative view on challenges associated with OI practices, especially since a distinction was made between inbound and outbound OI processes and associated challenges.
However, the focus on SMEs and on the manufacturing and service industry represents a limitation in terms of generalizability of the results and applicability to the pharmaceutical industry. This is also supported by the finding of van de Vrande *et al.* (2009) that OI adoption was practiced to a different extent according to firm size, with larger firms showing a stronger propensity of engaging in OI than smaller firms. Therefore, it cannot be assumed that the findings by van de Vrande *et al.* are easily transferable to the case of 'Big Pharma' which very likely faces different challenges than SMEs or at least in a different order of importance and/or relevance.
Nevertheless, the identified topics in this study represent a suitable starting point for identifying barriers to OI in the pharmaceutical sector as well.

Representing a first step into identifying best practices with regards to OOI management, Bianchi (2009) recently performed a detailed case study on three Italian pharmaceutical companies of different sizes involved in outbound OI activities. Since the "diversity of tasks [...] requiring multidisciplinary skills, i.e. technical, marketing, legal, IP related" (Bianchi, 2009, p.4) was seen as an important challenge with regard to outbound OI, he focused on identifying which types of organizational structures were in place to support such processes. He found that according to firm size- and deal-level-associated factors, the formalization of structures could vary from dedicated organizational units to *ad hoc*-approaches. A decisive point was the degree of strategic relevance attributed to outbound OI within the corporate strategy and the volume of outbound OI transactions.
These findings underline the flexible character of outbound OI activities, indicating that according to the respective specific outbound OI activity, different managerial structures will have to be put in place. This underscores the importance of making distinctions between different outbound OI practices and their respective degrees of implementation as far as future research on this topic is concerned.
While Bianchi's results mainly focus on the organizational/structural aspects related to outbound OI management, the procedural aspects of outbound OI (OOI) are the focus of the quantitative success factor study into external technology exploitation (i.e. OOI) by Lichtenthaler (2008). He divided the outbound OI process into 5 main tasks of planning, intelligence, negotiation, realization and control, and analyzed the effect of systematization and proficiency in carrying out these individual tasks on OOI performance. He found that a systematic process correlated positively with OOI performance, especially in terms of licensing revenues. Furthermore, he found managerial deficits with regard to the planning, intelligence and control stages which were carried out less professionally than negotiation and realization stages.
This combination of structural and procedural aspects serves as the basis for the managerial framework employed in this research, in order to capture the most important managerial dimensions, by analyzing associated structures, processes and people involved in prior OOI activities of the respective interviewed company.

Usefulness

The identification of barriers to outbound open innovation will provide a theoretical contribution to close the existing gap in innovation literature on the disadvantages and barriers associated with OI implementation. Furthermore, as these insights were used to derive managerial advice to foster and/or enable outbound OI at large pharmaceutical enterprises despite of the identified barriers, this research also provides a societal contribution, since the successful implementation of OI practices offers the potential to generate more innovative products/drugs from which patients can benefit. This is especially the case for projects that have been discontinued internally for strategic reasons (non-core assets) that due to the implementation of OOI practices will be made available to external parties for future development.

Scope

Since research on OI and particularly on outbound OI is still quite limited, there are still a range of different areas to assess in addition to the pharmaceutical industry. Yet, since the pharmaceutical companies are in need of new innovative approaches regarding drug development and already display different organizational modes comparable to the OI definition (Hughes & Wareham, 2010), this industry choice still represents a suitable area to focus on to derive insightful conclusions on OI practices. Secondly, outbound OI has been under-represented both in practice by companies involved in OI and in theory by scholars dealing with OI research. Therefore, the outbound OI focus promises new insights to the whole field of OI research. And since every outbound transfer needs a receiving end which manages the respective inbound transfer, findings regarding barriers to outbound OI might also deliver some useful insights regarding inbound transfer, complementing the OI paradigm.

Related/Relevant Innovation Theories

Given that open innovation involves a high degree of interaction between the internal and external firm environment, transaction cost economics (TCE) are often referred to in OI studies to describe the underlying/associated processes related to for instance licensing decisions (Fosfuri, 2006; Lichtenthaler, 2009). TCE is used to make decisions as to whether to produce an asset internally ('make') or to acquire it externally ('buy') by comparing production and transaction costs of a given asset incurred for both options. With regard to technology transfer there are three main sources of transaction costs to be considered: (i) incomplete contracts leading to opportunistic behaviour, (ii) investments leading to lock-in or switching costs, and (iii) knowledge leakage to competitors (Teece, 1988, cited in Fosfuri, 2006). Whereas 'make or buy' decisions reflect the inbound dimension of OI, the same line of thought can be extended to 'keep or sell' decisions to also cover the outbound dimension (Lichtenthaler, 2009), where transaction costs have to be considered as well.

Since especially regarding outbound OI, difficulties of companies to capture value were observed (Lichtenthaler, 2009), the theoretical framework put forward by Teece in his seminal paper on "profiting from innovation" (Teece, 1986) provides a suitable basis. Therein he identified the 'appropriability regime' and 'complementary assets' as critical contingency factors influencing whether an innovator will be able to reap the commercial benefits from his invention or whether imitators or other actors will attain the main market share. The appropriability regime refers to the ease of imitability which depends on legal factors (e.g. degree of IP protection) and on the nature of the knowledge itself (tacit or codified) (Teece, 2006). If the appropriability regime is strong, innovators are more likely to benefit from the commercialization of their product.
In addition to the appropriability issue, complementary assets also play a crucial role for profiting from innovation, as they provide essential functions in order to commercialize an innovation. They include distribution and marketing channels, services, manufacturing, complementary technologies, etc. Depending on the nature of the invention and the asset, the required complementary assets can be generic, co-specialized or specialized.
Assessing the strength of the appropriability regime and the type of required complementary assets delivers handholds for devising strategies as to how these complementary assets should be accessed (via contracting, integration or creating alliances) in order to maximally profit from the invention.
For the scope of this research, identification of the required complementary assets for the commercialization of a certain product is thus hypothesized to represent a critical step for both 'keep or sell' decisions as for finding suitable partners for outbound OI activities. For the former, the presence or absence of complementary assets should define whether a certain product is developed internally or not, whereas for the latter, the complementary assets can serve as guidance for identifying partners which display the most promising characteristics with regards to a successful product commercialization.

A further theoretical stream associated with OI processes revolves around the concept of absorptive capacity, developed by Cohen & Levinthal (1990), which essentially refers to the ability to use and exploit knowledge taken up externally which depends on the internal level of knowledge built in the respective area. Thus, the success of taking up external knowledge critically depends on the expertise

already present in a company. This is primarily important for inbound OI processes which are concerned with the uptake of external ideas and assets.
For outbound OI processes on the other hand, capabilities are required that enable an efficient transfer of the respective in-house knowledge to the external partner to ensure successful knowledge exploitation by the other party. This also relates to the strategic choice of partners for knowledge/technology transfer (Gassmann & Enkel, 2004; Hughes & Wareham, 2010). Companies have thus to be able to identify, codify and share (multiply) the relevant knowledge required for commercialization, which Gassmann and Enkel (2004) refer to as 'multiplicative capabilities'.

Outbound OI (OOI) modes

As already described above, outbound OI is defined as taking ideas originated internally outside to an external player that takes over commercialization. On an operational level, outbound OI can take the shape of spin-offs, joint ventures, out-licensing or strategic alliances including public-private partnerships (van de Vrande *et al.*, 2009, Bianchi *et al.*, 2010). Both strategic and non-strategic assets can be involved in all of these modes depending on the rationale of the respective originating company.

A general observation to be made is that the respective outbound OI modes each require a different degree of involvement by the focal firm which is schematically shown in **Fig.1**. On a single asset basis, out-licensing deals require little to no interaction with the external party once the deal has been signed. If the out-licensing deal includes options to buy the asset back if certain milestones are reached, then interactions with the external player do also take place after the deal has been signed, since the two parties have to exchange the most current data regarding the asset's development. Spinning-off of multiple assets into a new company might involve more commitment from the originator company, as often the originator company keeps a partial equity stake and thus an interest in the fate of the assets in question. Joint ventures are fully owned by the respective originating companies, thus making the degree of involvement in and commitment to the joint venture even bigger than for spin-off activities. However, since a joint venture represents a separate entity taking care of all relevant processes having to do with the development and commercialization of the respective assets, the influence of the originator companies is limited. Last but not least, strategic alliances require the highest level of involvement for the focal firm, considering that there is no additional company established that takes care of managing the interactions between the respective parties as in the case of joint ventures or spin-offs.

An increased degree of involvement consequently means an increase in effort (time and cost) the company has to put into the activity. However, an increase in involvement also goes along with an increased degree of control over the activity. It is thus up to the management to consider and balance how much control they want to retain at the cost of higher effort when choosing which outbound OI activity to engage in. Presumably, this will also be dependent on the strategic value the focal company assigns to the asset to be externalized, since it is conceivable that the more value is associated to an asset the more control over its 'faith' the originating company will want to have.

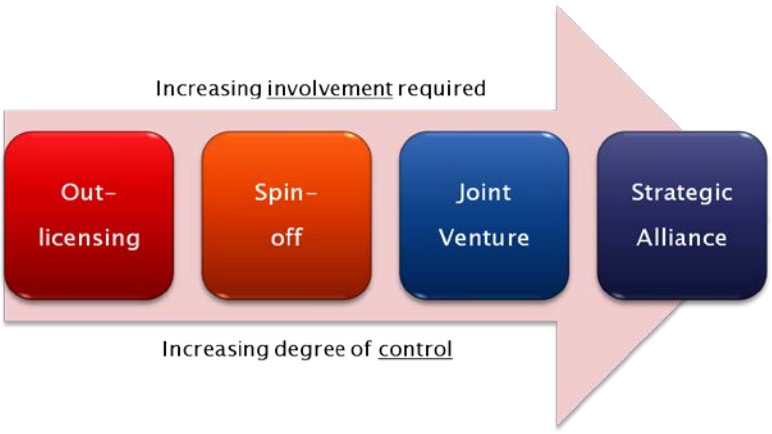

Figure 1: OOI modes. Schematic depiction of the degree of involvement required and resulting extent of control when engaging into different outbound OI practices. Source: Author

OOI – examples within the pharmaceutical industry

In the following, selected examples from the pharmaceutical industry for the above presented modes will be given. This is to serve as an overview of the ways the pharmaceutical industry has implemented outbound OI practices thus far.
The examples include both strategic and non-strategic assets. Notably, assets of higher strategic importance are found more in a joint venture and strategic alliance setting, correlating with the increased degree of control of the originating company over the respective asset as already alluded to in the previous section.

Out-licensing:
In 2006, **GSK and Asklepios Biopharmaceutical** entered into a cross-licensing agreement where GSK licensed its recombinant adeno-associated virus vector serotypes for gene therapy treatments to Asklepios, who in turn licensed its Biological NanoParticle technology to GSK (EvaluatePharma, 2010).

This cross-licensing example shows how companies can benefit from each other by accessing relevant knowledge through sharing internal knowledge not representing their core capabilities.

A further variation of out-licensing deals in the pharmaceutical sector is granting licenses for developments in a specific indication only. An example is the out-licensing deal of **Roche** in 2009 where they licensed IP rights to **NeuroNova** for development and commercialisation of products containing VEGF for **Amyotrophic Lateral Sclerosis** (ALS)-treatment (EvaluatePharma, 2010). As Roche has no intention to enter this market and NeuroNova has more specialized capabilities – being a company specialized in treatment of disorders of the central nervous system – this represents a suitable way for Roche to secure additional revenues through royalties in an indication area which it would not have pursued itself.

A noteworthy example of out-licensing of multiple assets is the deal **Roche** struck with **Synosia** (recently acquired by **Biotie** in February 2011) in 2007. Synosia had acquired five drug candidates (four in phase I) targeting the central nervous system from Roche whose development had been stopped due to reprioritization[2]. Synosia was in charge to pursue clinical development and in some cases also commercialization of these assets. Roche retained opt-in rights for 2 of the 5 programmes on completion of pre-defined milestones.

Next to out-licensing of assets, there are also examples of Big Pharma out-licensing technology as in the case of **Johnson & Johnson** that in 2006 out-licensed their "transdermal patch delivery technology to **CeNeS** for which it will receive royalties" (EvaluatePharma, 2010).
This out-licensing deal exemplifies how Big Pharma can achieve additional revenues by out-licensing their internal assets to complement other companies' product development.

Spin-off:
Convergence Pharmaceuticals is a biotech company specializing in pain therapy and was spun off from GlaxoSmithKline (GSK) in October 2010, with 2 clinical stage assets (phase I and II) and 6 earlier pipeline assets for the indication of pain treatment. The spin-off was due to a decision of GSK to exit the pain therapy indication[3]. GSK holds a minority stake of 18% with eligibility of gaining additional shares upon completion of certain asset-related milestones[4].

Another example is represented by **Novexel**, a specialty pharmaceutical company that was spun off from the anti-infectives unit of sanofi-aventis in 2004 with a pipeline of both development and discovery assets. It was fully acquired by AstraZeneca in March 2010[5], supporting the notion that assets that are of no immediate use for one company (in this case sanofi-aventis) can be of considerable value for another company (AstraZeneca). This example thus nicely underscores the rationale of performing outbound OI.

Joint venture:
ViiV Healthcare is a joint venture created by GSK and Pfizer in 2009 specialized on drug development for HIV treatment. Its HIV portfolio is composed of compounds from both companies, equaling a 19% market share. GSK holds an 85% interest in ViiV Healthcare and Pfizer holds 15%[6].
It currently distributes 11 marketed compounds whose sales will be invested into their current pipeline.
Next to the compounds stemming from GSK and Pfizer already belonging to the ViiV portfolio, the originator companies grant ViiV a right of first negotiation for any new HIV-related compound

Sources taken from the web:
[2] http://www.synosia.com/userfiles/file/Roche-Synosis_partnership.pdf
[3] http://www.fiercebiotech.com/story/gsk-spinout-gets-35m-bankroll-phii-pain-program/2010-10-06
[4] http://www.gsk.com/media/pressreleases/2010/2010_pressrelease_10106.htm
[5]http://www.novexel.com/includes/cms/_contenus/mod_press_releases/09_NXL_06%20AZN_Novexel_Final_EN.pdf
[6] http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10123.htm

developed by them[7]. This is part of a strategic alliance under which ViiV will also invest in R&D-measures for HIV medicines conducted by their parent companies.

The GSK/Pfizer joint venture is exceptional considering that two top 4 players (by sales in 2009) of the pharmaceutical industry – thus actually competitors – joined forces to create a specialty pharmaceutical company for a single indication: AIDS. The underlying rationale was the awareness of both companies that together they could devise "solutions in ways that neither company could do alone"[8]. This idea of making knowledge and expertise available to other parties with different competencies to achieve added value such as successful product development and commercialization mirrors the concept of outbound OI.

Strategic alliances:
A successful example of outbound strategic alliances is the worldwide collaboration between **Bristol-Myers Squibb** (BMS) and **AstraZeneca** (AZ) formed in 2007 for developing and commercializing Diabetes Type II compounds. Two compounds developed by BMS in phase III and phase IIb were part of the agreement for which AZ made an upfront payment to BMS and took over the majority of development costs from 2007-2009. All additional development and commercialization costs were split up equally[9].
Saxagliptin, one of the two drugs part of the agreement, got approval for the US and European market in 2009[10], underlining the success of the collaboration.

A similar alliance has only very recently been announced by **Boehringer Ingelheim** (BI) and **Eli Lilly** in January 2011. BI and Lilly will jointly develop and commercialize four mid- and late-stage compounds for treatment of Diabetes Type II in order to "leverage the collective scientific expertise and business capabilities" of the two companies[11]. BI brings two late stage (phase III) to the alliance and Lilly two mid-stage (phase II) compounds as well as the option for BI for a further phase II anti-diabetes Lilly molecule.

Both of the above described alliances are examples of a company partially giving away rights for their internal strategic assets in order to access financial resources as well as development and commercialization expertise. That way both risk mitigation and improvement of the probability of success is achieved.

Sources taken from the web:
[7] http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10123.htm
[8] http://www.pfizer.com/about/leadership_and_structure/conf_british_industry_112309_jk.jsp
[9] http://www.fiercebiotech.com/node/5197
[10] http://www.astrazeneca.com/Media/Press-releases/Article/20091005--ONGLYZA-saxagliptin-Receives-Marketing-Authorisatio
[11] https://investor.lilly.com/releasedetail2.cfm?ReleaseID=542971

Public Private Partnerships (PPPs) form another type of strategic alliances which involve both public and private institutions.

The RNAi Consortium (TRC) is of public-private nature with participants from several public and academic institutions such as Broad Institute, Harvard Medical School, MIT, Dana-Farber Cancer Institute, Massachusetts General Hospital, as well as industry representatives such as Bristol-Myers Squibb and Sigma-Aldrich.

Its objective is to create a library of RNA inhibitors targeting murine and human genes in order to determine gene functions contributing to the understanding of normal physiology and disease.

To date, a library of 160,000 RNAi constructs has been built which can be accessed worldwide by scientists through Sigma-Aldrich and Open Biosystems.

It is the rationale of this OI mode to jointly invest knowledge and resources into building a common knowledge base (here: about gene function in normal and diseased tissue), from where new discoveries regarding drug development can be made.

Another public-private partnership is represented by the **Pool for Open Innovation on Neglected Tropical Diseases**. This initiative was created by GSK in 2009 and is managed by the non-profit organisation Bio Ventures for Global Health. It has the objective to "facilitate and encourage development, commercialization, and access of therapeutics to treat NTDs [neglected tropical diseases]" which comprise 16 diseases such as Malaria, Cholera, Sleeping Sickness, etc. as defined by the FDA[12].

Parties contribute patents to the pool accessible to other participants. However, contributors retain ownership rights to their intellectual property (IP). Participants include among others industry representatives like GSK (originator) and Alnylam, governmental organisations like Technology Innovation Agency (TIA), Department of Science & Technology, and academic institutions like MIT, Caltech, UC Berkeley, etc.

According to the initiative's website, eligible parties can use the available IP pool and get a "non-exclusive worldwide license to research, develop, manufacture, and export therapeutics for NTDs for sales into LDCs [least developed countries]" under the patents of the contributors, for which no royalties will be charged.

However, these licenses are only granted if the contributor does not develop (or actively considers development) or already commercializes the therapeutic for the NTD themself. Also, the contributor can request royalties to be paid, if the compound is sold outside LDCs which is decided on a case-by-case basis. LDCs as defined by the United Nations comprise 49 countries (33 in Africa, 15 Asia/Pacific, 1 South America).

This patent pool stands out as an exceptional example for performing Open Innovation in the Biopharmaceutical Industry. Knowledge is shared openly between the participants who are free to exploit it and use it for drug development and commercialization. The only limitation however consists in that they are restricted to certain disease types and countries and in that they have to make sure that they are not pursuing the same path a patent originator is already pursuing.

Sources taken from the web:

[12] http://ntdpool.org/

But still this initiative exemplifies how commercialization goals not of interest to the knowledge-originating party can be made available for other parties, endowing them with a better chance of achieving economic and societal benefit regarding development of successful treatments against neglected tropical diseases.
However, it remains to be seen how big the impact or output in terms of innovative drugs derived from this initiative will be in the end. Considering that this patent pool only started in 2009, it might still take 10-15 years until the results become apparent.

The above given examples support the compelling rationales of pursuing outbound OI activities for both strategic and non-strategic assets. Furthermore, they provide the actual proof that these are feasible not only in a theoretic but also in an actual setting.
Nevertheless, the absolute number of outbound deals by Big Pharma is far lower compared to inbound deals (see **Fig.2**). In the past 5 years, the ratio of in-licensing versus out-licensing and joint venture deals performed by the top 20 pharmaceutical companies (by sales in 2009) as recorded by the EvaluatePharma database ranged between 6:1 to up to 27:1 (EvaluatePharma, 2011).
What is also apparent from **Fig.2** is that the number of products involved in outbound deals is fluctuating as is the number of inbound deals. Therefore it is next to impossible to discern a trend as to whether outbound practices are increasing or decreasing. According to a study performed by Elsevier's Strategic Transactions (InVivo Magazine[13]), out of 725 alliances of their 2007-10 dataset, 20% were out-licensing deals that declined further to 10% for current alliances of 2010.
What does discourage the Big Pharmas from engaging more into outbound activities? Are the potential benefits achieved by outbound OI perceived as less impacting than benefits from inbound activities? Is it regarded as too tedious to find external partners willing to take over an internal asset? These are the questions this research aimed to tackle by getting first-hand insights of industry representatives involved in asset valuation, research strategy, licensing and business development decisions.

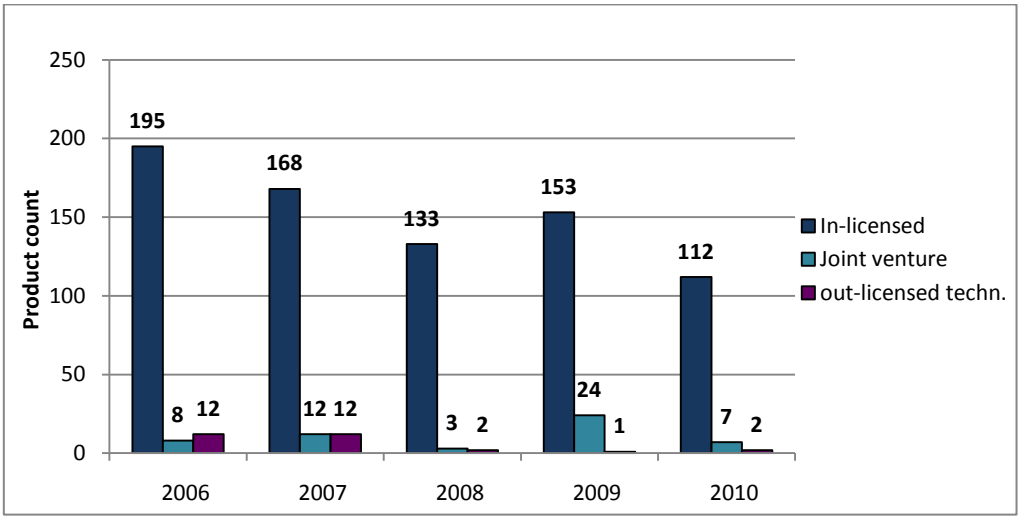

Figure 2: Count of products involved in in-licensing, joint venture and out-licensing deals of the top 20 pharmaceutical companies (by sales in 2009) between January 2006 and December 2010 (EvaluatePharma, 2011).

[13] Online article no. (A#2010800157) of the October 2010 edition if InVivo Magazine

Conceptual framework and hypotheses

For the purpose of this research and to highlight associated potential barriers, the focus was laid on the main stages of the OOI process. According to the insights generated by Lichtenthaler (2008) and others (van de Vrande, 2009; Hagedoorn, 2002), the division of the OOI process into four main steps was seen as the most suitable for the purpose of this research to map the associated barriers, consisting in (i) setting the deal objective, (ii) asset selection, (iii) deal making and (iv) deal implementation (see **Fig.3**). The step of 'monitoring and control' in Lichtenthaler's framework (Lichtenthaler, 2008) was not explicitly considered, as it is only a supporting activity underlying all main process steps.

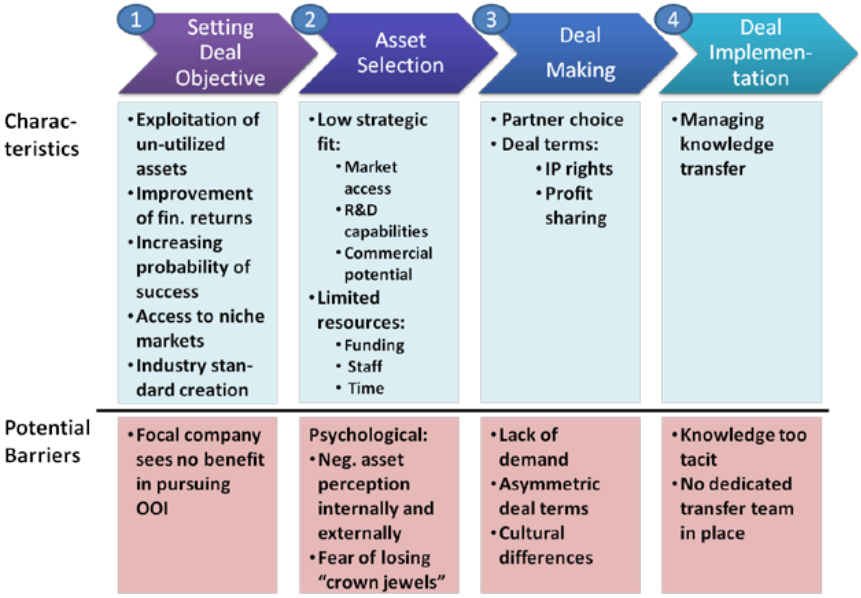

Figure 3: Outbound Open Innovation (OOI) process. Characteristics and potential barriers. Source: Author

Step 1 is concerned with establishing the deal objective or rationale for pursuing OOI activities instead of continuing asset development internally in the first place. As they are part of inter-firm R&D partnerships, these can range from strategic to financial (cost-economic) motivations as reviewed by Hagedoorn (2002). Or put differently, objectives can follow offensive motives (related to growth stimulation) or defensive motives (reduction of costs and/or risks) (Huizingh, 2011, p.4). One potential barrier in this step could be that the respective company does not perceive OOI activities as beneficial or relevant for their business as they regard it as too risky (Lichtenthaler, 2009; Lichtenthaler, 2010b).

H.1.:	*A negative attitude with respect to outcomes of OOI activities lets companies refrain from pursuing OOI.*

Once the decision has been made to engage in OOI, step 2 consists in selecting the relevant assets to be developed externally which depends upon the respective deal objective laid down in step 1. The company has to evaluate which of their assets can be developed internally and which assets have a

higher chance of success if developed externally. According to Ford & Ryan (1981) as cited in Kollmer & Dowling (2004), reasons to out-license are:

(i) **Strategic misfit** in terms of market access, R&D-capabilities of the focal company, return on investment, probability of success and

(ii) **Lack of resource availability** in terms of funding, staffing and time

Any mismatch in these strategic- or resource-related characteristics will either lead to a decrease in strategic priority of the asset ('non-core asset') or to a decreased probability of success for a 'strategic asset' if development is continued alone without the involvement of other parties. Consequently, other options have to be sought such as engaging in OOI.

In terms of putative associated barriers during this step, valuation of intellectual assets in general can represent a major challenge according to Lichtenthaler (2005). An additional high potential barrier is expected to be a negative perception connected to the asset to be given outside. On the one hand, internally, in-house and in-licensed assets will be considered as more important since they better match the internal strategy. The asset to be out-licensed was de-prioritized and thus is considered to be worth less than active internal projects. This lack of internal commitment was also found to hinder the OI processes in the study performed by van de Vrande (2009).
On the other hand, external players could also have a negative perception of the asset, doubting the quality of the asset as it was de-prioritized by the focal company.
A further psychological barrier is expected to exist with respect to the fear of giving away assets that could give a potential competitive advantage to an external player as mentioned by Fosfuri (2006), Lichtenthaler (2009) and Lichtenthaler (2010b).

H.2.	*In terms of asset selection, psychological barriers are expected to be the main drivers to block OOI activities.*
H.2.1.	*Assets to be out-licensed are neglected and not characterized sufficiently from an internal perspective, compared to active in-house and in-licensed projects.*
H.2.2.	*The quality of assets available for out-licensing is externally suspected to be of low quality.*
H.2.3.	*Adequate asset selection is difficult, as companies fear to weaken their own competitive position when giving out an asset that could provide competitive advantage to an external player.*

In step 3, after asset selection has taken place, the deal has to be struck which includes finding a suitable partner and negotiating the deal terms. Potential barriers that especially apply to OOI activities are firstly the lack of demand, meaning that no partner is available or can be adequately identified (Lichtenthaler, 2005) that has the capabilities (scientific as well as financial) and willingness to develop the asset. Secondly, asymmetric views regarding the deal terms involving IP rights, profit sharing or other contractual problems could prevent a deal from being formed (van de Vrande, 2009). Furthermore, organizational and cultural differences could impose a challenge to a successful deal making process as observed by van de Vrande (2009) in SMEs of the Dutch manufacturing sector.

H.3.	*Main barriers associated to the deal making step of OOI activities are connected to:*
	H.3.1. *partner identification*
	H.3.2. *negotiation of deal terms*
	H.3.3. *cultural/organizational differences*

In the final stage (step 4) of deal implementation, the knowledge transfer has to be coordinated. Since this involves a "diversity of tasks", the absence of adequate structures supporting the OOI process represents a main impediment, as outlined by Bianchi (2009). Moreover, barriers could occur if the knowledge to be transferred is too tacit to achieve successful implementation (Teece, 2006; Lichtenthaler, 2005).

H.4.	*Main barriers associated with deal implementation are connected to*
	H.4.1. type of knowledge to be transferred
	H.4.2. presence of structures supporting the transfer process

Figure 4 summarizes the above described hypotheses into a conceptual framework which served as the basis for the operationalization of variables as discussed in the methodology section.

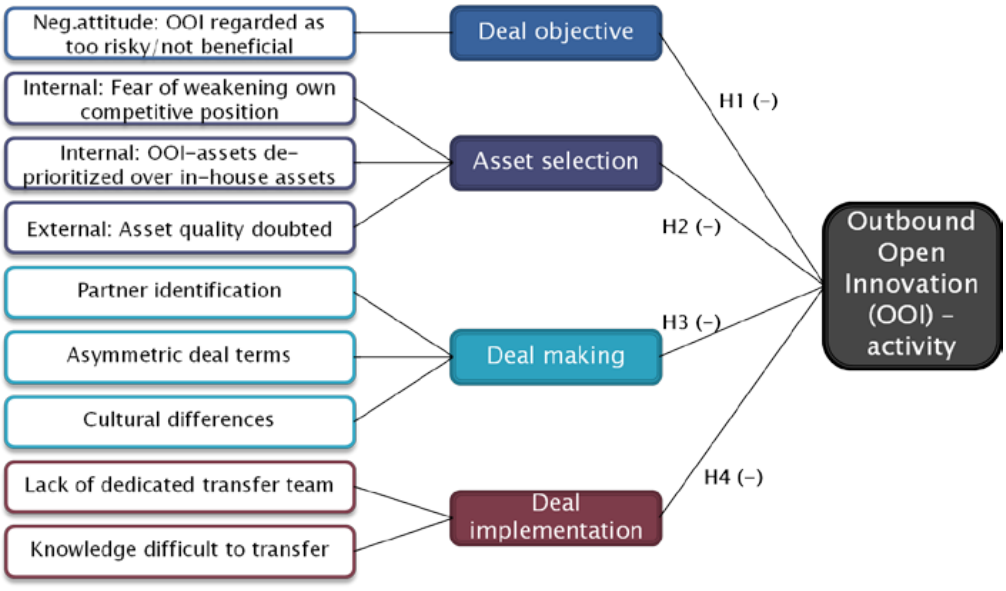

Figure 4: **Conceptual framework**

Managerial framework

In order to organize and manage the OOI process adequately, different managerial tasks and decisions, as well as choices regarding the most suitable organizational structure have to be made (Bianchi, 2009; Lichtenthaler, 2008).

According to the framework of Bianchi (2009) and Lichtenthaler (2008) the managerial process of OOI activities is characterized by several main tasks which are supported by underlying functions. The main tasks involve:

(i) **Planning**: in terms of target setting, resource allocation, partner selection (Bianchi, 2009, p.7)

(ii) **Intelligence/Evaluation**: opportunity identification, scanning and monitoring of environment, information search, evaluation and communication (Lichtenthaler, 2008, p.6)

(iii) **Negotiation**: setting up contractual agreements (Bianchi, 2009, p.7)

(iv) **Realization**: conducting and supporting technology transfer (Lichtenthaler, 2008, p.6)

(v) **Monitoring & control**: evaluating and controlling OOI involving "identification of information needs, information generation, information evaluation and information communication" (Lichtenthaler, 2008, p.8)

Supporting tasks are required throughout the whole OOI process to different extents and include legal, administrative, IP-related, financial, coaching and supply of additional technical and market information (Bianchi, 2009, p.8).
It is important to note that these tasks do not necessarily have to proceed in this order, but take place in iterative feedback loops (Lichtenthaler, 2008, p.5).
This framework was however adapted for the purpose of this paper, as the 'monitoring & control' function was not considered as a main task but as a supportive function since it is required throughout the whole OOI process, relying on the main steps to take place.

During the process depicted above, different kinds of managerial decisions have to be taken which can be of a strategic or operative nature. Strategic decisions include keep-or-sell decisions regarding the selection of a technology considered for out-licensing and the final go/no-go decisions about whether a technology transfer will actually take place (Bianchi, 2009).
Operative managerial decisions are of lower level and deal with the individual OOI process steps, ensuring that they are carried out appropriately to move the whole OOI process forward (Bianchi, 2009). This interplay of main and supporting tasks as well as managerial decision types are depicted in **Fig.5A** below.

The OOI management process is embedded in organizational structures which can either be built on a temporary basis in an *ad hoc* approach or can be formalized in the form of a dedicated function.
A dedicated function according to Bianchi (2009) is defined as a "separate dedicated organizational entity that is charged with the responsibility for making OOI happen […] on a continuous basis" (p.9).

It can either be positioned on a corporate level, having access to company-wide resources and intelligence, or on business unit (BU) level which is more localized (Bianchi, 2009, p.10).
When an *ad hoc* approach is chosen, the responsible teams are usually set up in one of two ways. Either cross-functional project teams are built which are "temporary built hybrid structures […] within the established organization but outside the existing management hierarchy" (Bianchi, 2009, p.9), or an in-line/functional design involving several divisions is chosen, which is "completely integrated into the regular organizational and management structure" (Bianchi, 2009, p.9/10). Also in these temporary structures the power to make decisions can either lie concentrated with upper management or be delegated down to lower management hierarchies (see **Fig.5B**).

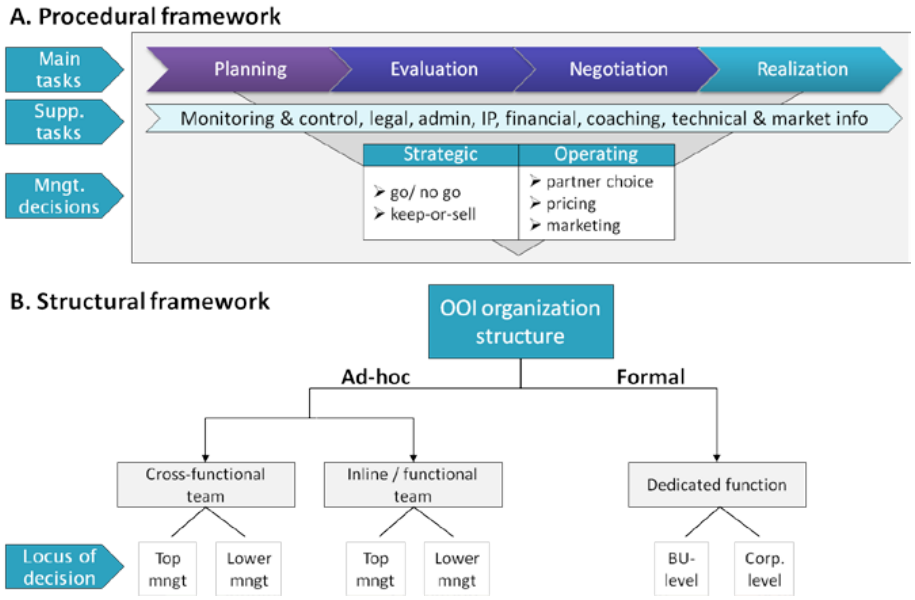

Figure 5: Managerial framework depicting OOI process & task types (A) and organizational structure (B) required for the management of Outbound Open Innovation. Adapted from Bianchi (2009)

The above presented framework will serve as a guideline to identify managerial processes and structures supporting the OOI activities in the interviewed companies and to assess how far the different practices have been implemented.

Methodology

Research design

The proposed research question has a two folded functionality. Firstly, it is descriptive regarding the identification of barriers to outbound OI of large biopharmaceutical enterprises. The second part of the question has an evaluative functionality as it tries to assess possible solutions as to how to overcome the barriers identified in the first part of the research.

The biopharmaceutical industry was chosen as intended domain, as it exhibits a wide range of OI related activities (Hughes & Wareham, 2010), making this industry a suitable subject for further studies on OI. The surprisingly few available studies on OI focusing on this sector (Bianchi 2009, Bianchi *et al.*, 2010; Hughes & Wareham, 2010) further underscores the suitability of this sector choice due to its high potential of newsworthiness.

For the empirical analysis, representatives of the following nine global biopharmaceutical companies were interviewed which together represent the achieved domain:

Large Pharma: AstraZeneca, GlaxoSmithKline, Roche
Medium Pharma: Bayer Healthcare, Merck KGaA, Merck Serono
Small Pharma: Boehringer Ingelheim, Ferring, Lundbeck

For reasons of confidentiality, company names were anonymized.

The sample includes biopharmaceutical companies of different sizes (€1bn - €30bn annual revenues) (see **Table 1**) in order to verify whether the observed trend of a reluctance to engage in OOI is only true for very large pharmaceutical companies like the top 10 pharma (Datamonitor, 2010), or is exemplary for the overall biopharmaceutical sector of non-biotech companies.

Table 1: Overview of companies/industry experts interviewed

Category	Anonymized Companies	Annual revenues 2010 [€bn]	# of interview partners	Field of interviewee expertise
Large Pharma	A	> 30	2	Portfolio Management; Business dev.
	B		2	Research Strategy; Pharma Partnering
	C		1	Business development
Medium Pharma	D	5-20	2	Business development
	E		1	Innovation
	F		1	Business development
Small Pharma	G	1-2	1	R&D
	H		1	R&D Strategic Operations
	I		1	Business development
Pharma Industry Expert		n.a.	1	Bernard Munos: Expert in Open Innovation matters in the pharmaceutical industry field

The methodological approach is of qualitative nature and will consist in identifying potential barriers to outbound OI from previous scientific literature on OI and theoretical considerations stemming from relevant streams of the innovation studies field. The list of potential barriers will then be compared with the statements of interviewees responsible for Business Development & Licensing decisions (or other areas associated with outbound OI decisions such as R&D strategy) of the ten pharmaceutical companies interviewed.

Data gathering

Information gathering was done by conducting interviews with 12 current or prior managers from the 'Business Development' or 'Research Strategy' business units of the companies listed in Table 1. In addition to the company-related insights, an industry expert on the overall biopharmaceutical sector was interviewed (Bernard Munos[14]), who has already published various articles on the subject of Open Innovation in the biopharmaceutical industry. His extensive experience in this field and his comprehensive view on the overall biopharmaceutical sector represents an external source for validating the obtained results, thus enhancing construct validity (Yin, 2003).

Interviews usually took 45min-1 hour and were performed in a semi-structured fashion to ensure replicability among the different interviews, but still allowing enough freedom and flexibility during the interview to account for new insights that had not been thought of when preparing the interview questions (Yin, 2003). The interviewees were asked about the outbound OI activities of their company and on the issues that they perceive as challenging in pursuing these activities both from an internal and external perspective (see **Appendix**). For this purpose, challenges identified in previous scientific studies (e.g. van de Vrande *et al.* (2009); Lichtenthaler, 2005; Bianchi, 2009; Fosfuri, 2006) served as a basis to assess which of these issues are perceived as the most challenging ones.

The interviews were recorded with the permission of the interviewee and transcribed to ensure accurate data collection and an easier comparison of statements of the respective interviewees.

[14] "Bernard Munos is the founder and Chief Apostle of InnoThink, a partnership dedicated to bringing evidence-based innovation models to the pharmaceutical industry and its stakeholders. Before that, he was Advisor in corporate strategy at Eli Lilly and Company where he focused on disruptive innovation and the radical redesign of the industry R&D model. His research, which has been published in Nature and Science, has helped stimulate a broad rethinking of the pharmaceutical business model by companies, investors, policy-makers, regulators, and patient advocates." Source: http://www.biovision.org/bv2011/speaker-info.html/346-bernard-munos (accessed on March 2011)

Data analysis

For the purpose of data analysis, the variables defined in the conceptual framework were operationalized as depicted in **Fig.6** and **Table 2**. Since barriers might be different depending on the respective OOI type, OOI characterization is necessary. This was accounted for by assessing OOI type, frequency, stage and associated OOI partners.

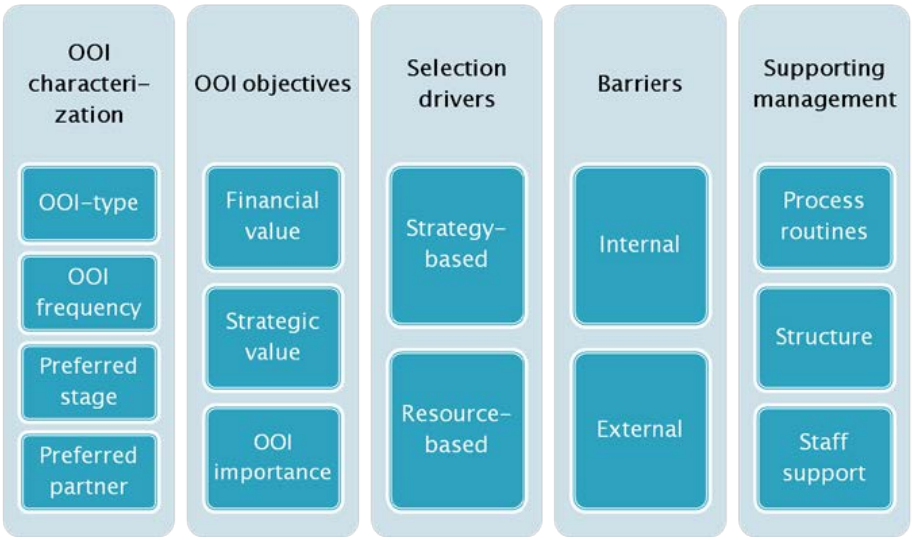

Figure 6: **Operationalization of dimensions and variables under consideration for the research process**

Based on this structure, the gathered interview data was compared among the different respondents and with the list of potential barriers identified from the literature following a cross-case synthesis approach to identify common patterns (Yin, 2003).

For the second part of the research, the adapted management framework put forward by Lichtenthaler (2008) and Bianchi (2009) was taken as a basis to analyze OOI supporting management processes and identify potential shortcomings by focusing on dimensions such as structure, processes (routines) and staff support. Also here a cross-case synthesis approach was followed in order to identify common patterns reflecting managerial challenges as well as common practices in the context of OOI management.

By the means described above, a consolidated view on issues connected to OOI implementation in the pharmaceutical sector could be obtained.

Table 2: **Operationalization of variables**

Variable	Dimension	Characteristics (Indicator)	Measurement
OOI activity characterization	OOI type	- Out-licensing - Joint-venture - Spin-off - Collaboration	Nominal
	Frequency of engaging in OOI activities	- Never - Rarely - Repeatedly - Regularly	Ordinal [never, 1-2 times in the past 10 years, (≥ 3x in the past 10 years, ≥ once/year]
	Preferred stage of OOI engagement	- Research - Preclinical - Clinical - Marketed	Nominal
	Preferred partner type	- Big Pharma - Small/Mid-sized Pharma - Biotech - Academia	Nominal
OOI Objectives	Strategic	- Access to niche markets - Disposal of assets of low strategic importance	Nominal
	Financial	- Improvement of financial returns - Cutting costs	Nominal
	Strategic importance	- High, medium, low	Ordinal
Selection drivers	Strategy-based	Limited presence of: - R&D-capabilities - Market access - Probability of success - Commercial potential	Nominal
	Resource-based	Shortages in: - Funding - Time - Staff	Nominal
Barriers	Internal	- Asset selection - Identification of suitable partners - Fear of weakening own competitive position - In-licensing higher priority than OOI activities - Reluctance to give asset away that is owned by the company	Nominal

		- Misalignment regarding OOI objectives at the executive level	
	External	- No demand - External player doubting asset quality - Contractual/Negotiation problems - Cultural/Organizational differences	Nominal
Supporting management	Process routines	- General process done formal or opportunistic? - Existence of formal selection criteria - Existence of formal criteria for performing partner choice	Nominal
	Structure	- Existence of dedicated OOI functions/teams	Nominal
	Staff support	- Is staff informed about benefits and risks of OOI activities - Are employees trained for engaging in OOI activities - Existence of incentive systems to foster/reward OOI activities	Nominal

Research quality

The chosen methodological approach of using theoretical insights as an input for structuring the interviews allowed for a high level of triangulation since multiple scientific findings and subjective insights were combined, triangulated and thus cross-validated.

Moreover, in the case of three analyzed companies, a stronger validation was possible as two representatives were available for interviews, enabling a more diverse view on the company at hand.

Furthermore, since representatives of differently sized pharmaceutical companies were interviewed, a more objective and consolidated picture of the overall sector was attained regarding the empirical data. This also ensured a higher external validity in terms of applicability to the whole pharmaceutical industry.

Via the employment of semi-structured interview guides and by undertaking a cross-case analysis of multiple companies, reliability of this research was enhanced (Yin, 2003).

Yet, certain limitations are associated to the chosen approach which will be discussed in detail in the limitations section of this report.

Results

Before going into detail regarding the individual results of the dimensions considered in the operationalization, first a summary on OOI examples will be given that the interviewed companies had engaged in in the past. This is to illustrate the different approaches and corresponding experiences the individual companies have had with regards to OOI activities.

Selected OOI examples from interviewed companies

Company A – Big Pharma
After the strategic exit of a therapeutic area, company A strongly pursued generating spin-offs and additionally engaged in the divestment of assets not part of the spin-off deals.

Company B – Big Pharma
In June 2010, company B initiated a programme where scientific questions that company B cannot answer are collected and sent to an American ivy-league university. University professors subsequently write proposals on how to tackle the respective scientific question. After proposal evaluation, the 'winner' receives contributions in terms of money and expertise. Similar projects of that kind have been done that covered developmental stages between research and phase IIa.

Company C – Big Pharma
Company C and another pharmaceutical company pooled compounds and expertise in two independent indication areas to improve probability of success in the drug discovery stage. Further development is done by each company separately in their particular therapeutic area. The other party will get royalties if a compound from this joint effort makes it to the market.

Company D – Medium pharma
Company D preferably engages in externalization deals where the company keeps an interest in their assets by retaining rights or options to buy assets back for a pre-defined sum if certain pre-defined milestones are met. It has also built a dedicated function responsible for carrying out this type of deals.

Company E – Medium pharma
Company E set up a programme where deals are struck in such a way that company E brings in the IP and the partner finances or co-finances the development. There are no upfront payments involved, but company E will be entitled to royalties or equity stake in the case of the partner being a biotech company. However, no public announcements concerning this programme have been made since 2005, making the success of this endeavour difficult to assess.

Company G – Small pharma
Since 3-4 years, company G offers internal research projects to academic institutions where no direct drug application could be found by the internal scientists. Together with the project information, company G also provides the associated tools, compounds, cell lines, transgene animal models, etc. This whole transfer of information and assets is carried out very unbureaucratically with "no strings

attached". The only requisite is that labs are asked to give annual updates on their findings to track whether some developments could in turn be used for drug discovery purposes.

Result overview

In the following results obtained from the qualitative interviews will be presented according to the respective dimensions used for the operationalization. Firstly, a graphic overview on the overall results will be given, followed by a detailed description of the individual findings.
The following graph (**Fig.7**) depicts which of the proposed hypotheses can be sustained by the empirical findings made after interview analysis.

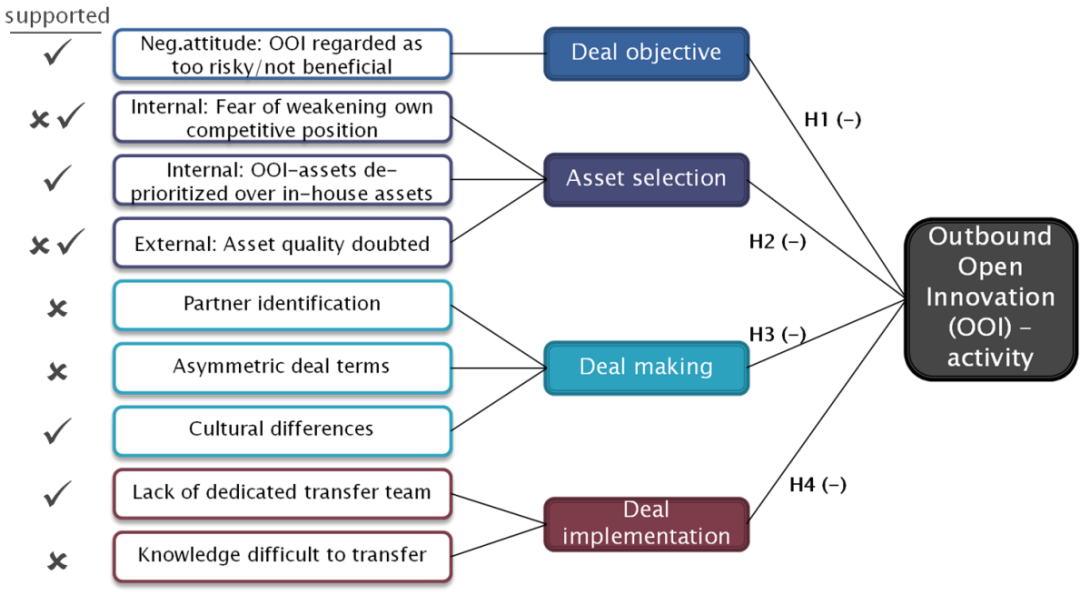

Figure 7: Overview on which hypotheses could be supported (✓), partially supported (✗✓) or not supported (✗) according to the empirical data

In the first step of the OOI process – setting the deal objective – interviewees unanimously stated that they did not perceive OOI practices as financially beneficial, resulting in a negative attitude towards OOI thus supporting hypothesis 1.
For the barriers associated to step 2 – asset selection – consensus among interviewees existed regarding the internal barrier of neglect of OOI assets over in-house and in-licensed assets (H.2.2). With regards towards the other two proposed hypotheses, only partial support could be found after interview analysis. Whereas some did not perceive the fear of weakening one's own competitive position (H.2.1) as a real barrier, others did. Similarly the barrier of external players doubting asset quality (H.2.3) was only perceived as hindering by a part of the interviewees. In both cases the opponents of these items being a barrier referred to due diligence processes which allow to adequately evaluate the quality of an asset or the danger of giving away 'crown jewels'.

During the deal making step, hypotheses on barriers regarding partner identification (H.3.1) and asymmetrical deal terms (H.3.2) could not be sustained as barriers specific to OOI practices. Only cultural differences (H.3.3) were acknowledged to represent some barrier, yet did not represent to be a major issue (see below). Last but not least, the lack of a dedicated function or any other supporting structure (H.4.1) was perceived as main barrier during the deal implementation step, whereas the type of knowledge (H.4.2) did not represent to be a barrier for asset transfer as long as specific scientific personnel familiar with the project to be transferred was available to support the process.

Table 3 below will provide an overview on the collected interview answers according to dimensions and variables defined during operationalization which will be discussed in detail in the following sections.

Table 3: **Overview on interview results**

	Anonymized companies		A		B		C		D		E		F		G		H		I	
	Revenue [€bn] (rounded)		> 20						5 - 20						1 - 2					
OOI type and frequency	Out-licensing	Frequency	x	rare	x	rare	x	rare	x	regularly	x	regularly	x	regularly	n.a.		x	very rare		never
	R&D collaboration		n.a.		x	regularly	x	rare	x	regularly	x	regularly	n.a.		x	regularly	n.a.		x	regularly
	Spin-off		x	rare	x	rare	x	very rare	x	rare			x	rare			x	rare		
	Joint Venture		x	very rare																
Preferred partners	Big Pharma				x		x		x		x		x				x		n.a.	
	Biotech		x		x				x		x				x				n.a.	
	SM Pharma		x										x						n.a.	
	Academia				x		x								x				n.a.	
Preferred phases	pre-clin		never		never		x		x		x				x		x		n.a.	
	phI		x		x														n.a.	
	phII				x				x		x		x				x		n.a.	
	phIII						x						x				x		n.a.	
Benefit - strategic	Direct		- risk + dev. cost abolished - image-benefit		- Access to better capabilities - risk sharing - development of more products possible		- IP - Improving services		exploiting un-used assets		exploiting un-used assets								regaining some remote value from written-off assets	
	Indirect		networking and learning curve				learning how VC community works		n.a.				freeing resources for other projects		network establishment				none	
Benefit - financial	Short-term		none		none		none				none		yes		none				none	
	Long-term		uncertain		uncertain		still to be seen		uncertain		n.a.		expected		expected		uncertain		none	
Asset selection strategic	Low probability of success		x		x		x		x								x			
	Exit of whole therapeutic area		x				x				x		x							
	Low commercial potential		x				n.a.		x				x						x	
	No R&D capabilities		x		x		n.a.		x		x				x					
Asset selection resource	Time		-				n.a.				x									
	Funding		x		x		n.a.		x		x		x				x			
	Staff		-				n.a.		x		x									

Note: n.a.: not applicable: issue not addressed during interview

Table 3 continued: Overview on interview results

	Anonymized companies	A	B	C	D	E	F	G	H	I
Internal barriers	Staff motivation		x	x	x			x	x	n.a.
	Fear of losing 'crown jewels'	no	yes/no	x	yes/no	no	yes	no	no	no
	Partner identification	no	no	n.a.	no	yes[1)]		no	no	n.a.
	IOI more important than OOI	n.a.		yes	no		no		x	yes
	Competition IOI vs OOI	x		yes					x	n.a.
	Asset transfer	yes	yes/no	yes	no	yes	yes			n.a.
External barriers	Quality doubted	yes	yes/no	yes	yes/no	yes	yes		no	yes
	Negotiation difficulties	n.a.	no	yes	yes/no	no	no	no		n.a.
	Lack of demand	yes	n.a.	n.a.	sometimes	no	yes			n.a.
	Organizational differences	yes	n.a.	yes	n.a.	no	yes			n.a.
Manage-ment	Dedicated function	x			x	IOI + OOI				IOI +OOI
	Incentive system	n.a.			x[2)]	x	x[2)]	x		n.a.
	Ad hoc/formal	ad-hoc	ad-hoc	ad-hoc	mixed		formal	ad-hoc	ad-hoc	ad-hoc
	OOI importance	low	very low	very low	low		low	high	low	very low
	Training/education	n.a.				x		n.a.		n.a.

Notes: [1)] Partner identification difficult for early stage projects; [2)] Bonuses provided in an irregular fashion; n.a.: not applicable: issue not addressed during interview

OOI activity characterization

Preferred OOI type and frequency

In terms of types of OOI activities, R&D-collaborations, out-licensing, and spin-offs (in descending order of frequency) were primarily pursued by the interviewed companies, a joint venture representing a very rare event.

With regard to out-licensing, two different types have to be distinguished: divestments where the originator company receives upfront payments from the licensee and in case of success also milestone payments and royalties.
If on the other hand, an externalization deal was struck, the originator company has the option to buy the asset back for a pre-determined rate if certain development milestones have been met by the licensee company.
The latter option is very much preferred by pharmaceutical companies, as it enables them to retain control over the externalized asset and to profit more from the development capabilities of an external party.

Spin-offs are done more rarely, since it not only involves the divestment of one or more assets but also of associated personnel, which implies more complex coordination. Yet, such activities are seen as having more success potential than pure out-licensing, since knowledge and experience are transferred together with the asset in question. As stated by a research strategy specialist of a Big Pharma company "*a compound on its own is not worth much*".
Engagement into spin-off-activities was usually reported by the interviewees after the decision to exit a whole indication area had taken place.

Preferred phases

On the topic of preferred phases, no unanimous picture can be drawn. Some companies preferably engage in OOI in the early pre-clinical stages to gain from the broader scientific knowledge of outside parties. Others in turn, would never consider OOI in this specific stage as it is still too unclear for them to assess whether the respective assets will provide value to the company or not.
Others like to out-license assets in the clinical stage before proof-of-concept, normally phase II. This is especially the case for companies engaging in externalization-deals which have a buy-back option. In these cases, assets are out-licensed to an external and mostly smaller party who has better capabilities to bring an asset to proof-of-concept. Afterwards, the originator company takes over again to develop the asset further in phase III for which it has a better financial basis (phase III is the most expensive stage as it involves a high number of patients) and better access to clinicians and regulatory personnel than smaller players.
On the other hand, the further along an asset is in the development chain, the higher the value that can be gained from OOI activities as uncertainty regarding success decreases. Therefore, some companies prefer the later development stages for OOI activities.

Preferred partners

Similar to the phase preference, no unanimous pattern for the partner preference can be discerned among the respective interviewed companies. Most companies indicated that they usually have two preferred partners ranging from Big Pharma and biotech, biotech and Academia, biotech and small and medium-sized (SM) Pharma, Big Pharma and Academia, etc.

In general, a certain correlation with the preferred phases could be observed. In earlier phases, academia and biotech companies are preferred partners, whereas in later stages, small/medium-Pharma and Big Pharma are favoured due to their larger financial resources.

OOI objective

The objective for engaging in OOI activities can, theoretically speaking, be of either financial or strategic nature.

In terms of **financial benefit**, the interviewees unanimously stated that especially the **short-term** financial returns were too little compared to the effort of engaging in OOI activities. This is especially true for early stage projects (discovery – phase II) for which due to their high level of uncertainty regarding their efficacy in the clinic only low upfront payments are made. A benchmark for upfront payments stated by interviewees lies in the area of double digit millions. Below this amount, deals are not considered worth pursuing considering the effort in organization and enabling the OOI process or stated in the words of a business development-representative of a Big Pharma company *"from a day-to-day bookkeeping point of view it doesn't make any sense*".

Considering the potential monetary benefit of OOI activities in the **long term** (through royalties, equity stakes, etc.), the interviewees could not yet make a definite statement. Due to the long development time required for pharmaceutical products it was in all cases too early to assess whether OOI activities would deliver substantial long-term revenue or as a one interviewee put it: *"the industry still has to see the benefits of [engaging in OOI]"*.

Whereas no indication could be found that substantial financial returns are part of the objective to engage in OOI activities according to the current state of knowledge/experience, a variety of direct and indirect strategic effects could be identified in the interviews.

Among the **direct strategic benefits** referred to in the interviews were the exploitation of otherwise un-used assets, image improvement in the community by engaging in new innovative business models, access to better (R&D) capabilities, and abolishment/diminishing of risk + development costs. All these reasons represent a way to directly profit from engaging in OOI activities.

Next to these direct effects, some of the interviewees also experienced **indirect or synergistic effects** such as the establishment of networks through searching for OOI partners which could then also be used for performing IOI activities. This was seen as especially beneficial as the outside party already knew through the previous OOI interaction on which aspect the originating company focused on and were already familiar with the working style of the company.

Furthermore, the prevention of R&D-resource drain was named as a beneficial indirect effect. By externalizing an asset which was previously part of the development pipeline, resources in terms of money, staff and time are freed up and can be devoted to other projects which better suit the

corporate strategy. A further positive effect of engaging in OOI activities was that the experience gained in conducting OOI activities could also be used to improve and optimize the inbound process, as companies could better relate to the perspective of the externalizing party and the associated issues that arise during the externalization process. Thus gaining experience during the OOI process has synergistic effects for the IOI process as well.

Summarizing, hypothesis 1 regarding the negative attitude towards outcomes of OOI activities letting companies refrain from pursuing OOI applies especially to the financial outcomes expected from engaging in OOI. Most interviewed industry representatives did not expect substantial returns from OOI activities neither in the short- nor long-term.

Importance of OOI within corporate strategy

When asked about the degree of priority OOI activities have on corporate strategy level, most interviewees state that it has little (*"part of strategy but certainly not the focus"*) to no importance for corporate strategy as it is the main focus of pharmaceutical companies to develop and commercialize products by themselves: *"we are not here to create value for anyone else"*. On a business unit level though, usually business development, OOI is sometimes part of the strategy. Yet in those cases, the interviewees complain that since OOI is not seen as important for the overall strategy, their level of empowerment is not sufficient or phrased much shorter by a business development-representative: *"[OOI is] relevant but not significant enough"*.
This again has to do with the position of corporate management that their main focus is on building and extending their own internal pipeline and bring assets to market.

Inbound vs. outbound

From this line of reasoning also the preference of pharmaceutical companies for inbound over outbound practices can be derived. This is mainly due to the perception that IOI addresses the primary need of the pharmaceutical industry to improve portfolio quality more directly than OOI. Furthermore, there are more incentives NOT to engage in OOI than to pursue it (cost vs. return not optimal, assets considered for OOI are perceived as "damaged", fear of image loss, etc.).
Last but not least, IOI is perceived as having a bigger profitability motive. Companies are convinced that their in-house capabilities will further increase the value of an in-licensed asset. The success of an externalized asset, however, depends primarily on the expertise of the other party which is not or only partly in control of the originator company depending on the choice of the OOI mode. This might be one of the reasons why pharmaceutical companies are reluctant to perform OOI activities.
The above is exemplified by the following quotes:

"In-licensing has more a sense of opportunity [than OOI practices]"
"Out-licensing will always be second to developing in-house"
"[OOI:] a lot of work but no appreciation"
"We didn't accept that someone else could develop a compound better than we could".

These observations support hypothesis 2.1. that OOI projects tend to be neglected as in-house or in-licensed projects are perceived as being more important. However, this has not only influence on the asset selection step as originally hypothesized, but also on the decision to engage in OOI in general, as will be discussed in detail in the following 'discussion' section.

Asset selection

In terms of asset selection, assets are considered for externalization if they are deemed to have a low probability of success, meaning that the R&D-risks are too high. This could be due to development risks pertaining to the individual compound or to the whole indication area the compound belongs to. If the latter is the case, then companies might decide to exit the indication area as whole, stopping all pipeline development of compounds belonging to this indication. At this point, several assets at different developmental stages become available for potential OOI activities.
Associated development risks are connected with a potential lack of specific R&D-capabilities which might limit the company to develop the compound accordingly.
Further selection criteria are the level of commercial potential and the degree of competitive advantage. If they are considered as being too low, then those assets will get de-prioritized and might be available for OOI activities.
An additional criterion is represented by temporary bottlenecks in terms of funding, staff and/or number of assets in the pipeline. As one interviewee (portfolio manager) pointed out, decisions as to which assets to externalize will depend on the current shape of the pipeline which defines the risk willingness of the respective company to pursue the development of certain assets on their own or to look for other alternatives.

Yet, despite all of these considerations the position prevails that pharmaceutical companies will always try to keep on developing the most promising drug candidates on their own or put differently: *"We are going to take the cream for ourselves"*.

Internal barriers

This brings us to the internal barriers impeding OOI.
In the first place, they are connected to the **attitude and motivation** of management and staff.
On the one hand, most of them see the primary mission for pharmaceutical companies to develop compounds on their own and not to do OOI. It is perceived as being simply against their core business model to spend resources on activities that are not considered part of the core strategy.
On the other hand, **image and reputation-related issues** seem to play a major role when contemplating the statement already mentioned above of a member of the research strategy department of a Big Pharma company: *"We didn't accept that someone else could develop a compound better than we could"*. This exemplifies the conviction that the own company is the best entity to develop a compound and shows the fear that an image loss could occur if an externalized compound would indeed be successfully marketed by an external party. Externalization of assets seems to be associated with the admission of incompetence: *"It's hard to admit that pharma can't do something"*, which lets companies refrain from engaging in OOI activities, even though they do not have the capabilities to develop it themselves.

Another major issue in terms of internal barriers to OOI is the **fear of weakening one's own competitive position** by selling 'corporate crown jewels'. The interview answers regarding this issue were however quite controversial. Interviewees on the one hand were arguing quite rationally that this fear could be mitigated by choosing adequate deal terms (e.g. buy-back options, etc.) or by refraining from out-licensing to a direct competitor. They trusted in their compound assessment and forecasting data that the asset in question was indeed not a priority for the company and thus would not pose a threat to them by making it available for OOI activities.
On the other hand, some interviewees stated that even though they acknowledged that there were rational criteria with which the risk of delivering competitive advantage to an external party could be mitigated, the irrational fear of weakening one's own competitive position overweighed rational criteria, preventing OOI deals from happening.
These observations partly support hypothesis 2.3. that psychological barriers in terms of fear of delivering competitive advantage to an external company let companies refrain from engaging in OOI.

While assessing the barriers of the deal making step, both adequate **partner identification** and **negotiation of deal terms** were not found to represent major impediments to the OOI process.
With regard to the partner identification, the already present knowledge of the pharmaceutical sector and relevant players present in the business development teams was described by the interviewees as sufficient to find suitable OOI partners.
Similarly, the negotiation of deal terms is considered as a time-consuming process, yet not an impediment specific to OOI as usually the same people in charge of negotiating IOI deals are also in charge of the OOI deals. Due to the high frequency of IOI in non-biotech pharmaceutical companies, the staff is sufficiently educated and experienced to carry out such negotiations and deal with the associated complexities accordingly.
Hence, hypotheses 3.1. and 3.2. cannot be sustained which regarded partner identification and negotiation of deal terms as major barriers to the deal making step.

An often referred-to issue was the high **effort** required to carry out an OOI deal (including finding the right partners, setting up the deal, compiling all the necessary documentation for transferring the asset, delivering additional experimental data, etc.). Many stated that the effort was too high compared to the return in royalties, milestones or upfront payments.
In a similar vein, the **asset transfer** *per se* was seen as an impediment by several interviewees due to high efforts involved. This was primarily due to the difficulties of collecting all the necessary documentation required by the external party interested in in-licensing the asset. Upon de-prioritization of internal projects, scientists originally working with the project usually get re-assigned immediately to a different project. For the person in charge to gather all the relevant documents it is therefore very difficult to access the required scientific expertise as the scientists might have no capacity left to support the transfer process or might have left the company.
Other than getting access to the relevant project information, the transfer process was described by most interviewees as a routine process with experienced personnel involved, thus presenting a time-consuming task but not a serious barrier.
Consequently, hypothesis 4 regarding barriers associated with deal implementation can only partly be supported. Absence of supporting structures (H.4.1) seems to be a major issue impeding success OOI, whereas the type of knowledge to be transferred (H.4.2) seems not to play a major role.

External barriers

A major external barrier referred to by the majority of companies interviewed was that **external players** would **doubt the asset quality**. It seems to be the received opinion that unless assets available for OOI deals stem from a strategic decision to exit a whole indication area, they are 'damaged' in some way and will not offer any development potential. Apparently it makes people suspicious if an established pharmaceutical company does not want to develop a potentially promising asset by itself but rather decides to externalize it. This decreases the incentive or motivation of pursuing OOI in the first place and might also affect the external valuation of the asset as being inferior to the perceived value of the originator company.
However, a minority of interviewees did not see this issue as a major barrier, since the quality of an asset can be assessed by due diligence procedures of the external party following rational criteria from which the true potential of the asset can be determined.
Interestingly, these contradicting views were found at interviewees of the same company, which might indicate that this view is not necessarily influenced by company culture but more by personal/individual factors.
Summarizing, hypothesis 2.2 on the psychological barrier of external parties doubting asset quality is only partially supported as representing a major barrier for OOI.

Regarding a potential **lack of demand**, e.g. not finding parties interested in the asset in question, different aspects were named by the interviewees.

On the one hand, some stated that misjudgments could happen regarding the attractiveness of an internal asset to an external party. Certain assets selected for external attractiveness can turn out to be of no interest to the external party.
On the other hand, especially for early stage projects (usually before proof of concept) which still have a high degree of uncertainty, it apparently is difficult to find an external party willing to pay enough to balance the costs connected to the asset transfer process.

Organizational/cultural differences can represent an issue as stated by some interviewees. Misalignments can occur regarding the objectives or manner of executing tasks. This is especially the case when the external party is a smaller player (i.e. biotech company) with potentially differing development and evaluation standards than larger pharmaceutical companies.
Consequently, hypothesis 3.3. regarding cultural differences presenting a barrier to the deal making step is supported. Yet, as not all of the interviewees commented on this issue it could be speculated that it does not represent a major barrier.

Supporting management

Process routines
With regard to the formalization of **process routines**, asset selection and deal making processes were found to proceed in a systematic, formalized fashion in all companies interviewed. **Portfolio evaluation** at different development stages is a frequent task for pharmaceutical companies in order to prioritize their pipeline assets and to allocate sufficient resources. This is done regardless of whether a company intends to pursue OOI activities or not.
Due to the high frequency of inbound deals, also the **deal making** process with all its legal requirements represents a highly established process which can be employed for OOI activities as well.
Partner search on the other hand seems to proceed mostly in an opportunistic fashion by tapping into the existing company network or individual network of the person in charge.
Next to this pro-active approach, some interviewees also described situations where they got approached by an external party, thus representing passive partner identification.

For the actual **transfer of the asset** formal criteria exist regarding which kind of documentation is required, etc. as these requirements mirror the situation of an in-licensing activity. Yet, in practice no clear routines seem to have been put in place to support this process appropriately, as many companies complained about major difficulties is accomplishing asset transfer.

Last but not least, the actual **decision to perform OOI activities** is primarily opportunistic. In line with the core strategy of pharmaceutical companies to develop and commercialize drugs on their own, there is no drug development taking place with the *a priori* assumption that these assets will get out-licensed.

If however, during the development process at some point an asset does not match the pipeline fit criteria anymore, other options such as OOI are considered.
Yet, only some companies stated that they have a formalized process that automatically lets de-prioritized assets get considered regarding their attractiveness for OOI activities. In most other companies the decision to pursue OOI seems to be influenced by a champion who sees a benefit in performing OOI and is willing to support the process ("*it only happened when I myself tried to push it through"*).

Overall, two different approaches towards OOI could be distinguished.
On the one hand, the majority of interviewed companies approach OOI opportunistically but state that there are efforts present to establish a more systematic approach. On the other hand, some companies already have the required infrastructure in place (in form of a dedicated function), but consider OOI not in a systematic fashion but only when the opportunity arises.
This latter approach goes hand in hand with the observation that OOI activity is fluctuating over time, whereas IOI activity is more or less constantly ongoing.
This of course has influence on the respective structure choice needed to support OOI.

Structure
Only two of the interviewed companies stated that they have an explicit **dedicated function** responsible for OOI activities. The other companies mostly chose the *ad hoc*-approach with an **inline functional design** according to Bianchi's OOI structure nomenclature (Bianchi, 2009), using the same team composition as for IOI activities, only changing scientific experts according to the project to be externalized.
Considering the similarities between IOI- and OOI activity processes, most stated that for OOI the business development and licensing (BD&L), legal and commercial functions could remain the same as those used for IOI and only the technical function would have to change according to the respective project. From this one can speculate that the team composition depends rather on the scientific/technical expertise required for a given project than on whether it represents an IOI or OOI activity.
In the opinion of one industry representative of a small specialty pharmaceutical company, the building of a dedicated internal OOI function is not sensible as too high costs are incurred compared to what could be recuperated by OOI activities.

Staff support

Training staff for activities related to OOI activities was only rarely stated by the interviewees and mostly connected to the negotiation phase. It seems like 'training on the job' is the prevalent way for employees to acquire expertise on OOI. Furthermore, no indication could be found that a great importance is attached to informing employees about OOI and its potential benefits for the company.

This observation is in line with the lack of **incentive systems** seen in most interviewed companies. Again only two companies stated that they had explicit incentive systems in place to reward OOI activities in the form of a bonus paid if OOI deals were struck or passed a certain threshold in upfront payments. Yet, for most other companies it was considered incentive enough if carrying out an OOI deal was set on the agenda of the respective department. In one case, the opportunity to work together with external scientists from renowned ivy-league universities (during early stage research projects) was also considered as an incentive for the internal staff.

Yet, overall, a lack of activity both in terms of training and incentive systems regarding OOI could be observed.

Discussion

For most dimensions investigated in this qualitative research, no common pattern could be identified across the nine different companies interviewed. Even though the companies varied in size (€1bn - €33bn annual revenues), no pattern could be distinguished that would correlate a specific preference to a specific company size. Smaller companies in the sample seemed to be equally diverse in their preferences and perceived barriers to OOI as the large pharmaceutical companies.

In fact, this lack of a unifying view could also be witnessed when more than one interview was conducted within a company. For instance there was a contradiction in two companies regarding the question whether an external player doubting asset quality represented a major barrier or not. The same contradiction was observed regarding the fear of weakening one's own competitive position due to engagement in OOI activities.

Several deductions/speculations can be drawn from this observation.
First, the lack of a unifying pattern might reflect that perception of OOI is not that much an issue of a certain company mentality or type, but rather of a personal nature. Differences in perception are most likely due to different experiences with regard to OOI activities and level of involvement. It is conceivable that a person directly involved in the transaction process of an asset might perceive different barriers more important than a person more involved with the broader strategic implications and decisions around OOI. A scientist working on a project that was de-prioritized might have more difficulties to give the asset up and convince himself that an external party is more capable of developing the asset further than a portfolio manager which is in charge of multiple projects.
In addition, personal characteristics are very likely to play a role. The more fact-based a person is, the less does the fear of delivering a competitive advantage to an external player represent a barrier to him, if he believes in the accuracy of the evaluation methods employed.
However, one must not forget that also other OOI characteristics might influence which barriers are perceived as especially hindering. For instance one interviewee made the point that the stage of development might play a decisive role in that regard. He observed that during the early research stage, people were in general more open for information exchange than with clinical projects which he attributed to the difference in cost involved.
Furthermore, as a different interviewee did not hesitate to point out, there are also different barriers according to the OOI type pursued. It is conceivable that the fear of weakening one's own competitive position is less when starting a spin-off, of which the originator company still holds a potentially high equity stake (and thus will also earn more in case of success), than with an out-licensing transaction to a direct competitor.
Last but not least, also the type of external partner could drive the dominance of certain barriers over others. As described above, some interviewees stated to have difficulties during an OOI deal, when smaller biotech companies were involved, due to the lack of alignment or differences in process standards.

Some of the observed discrepancies among the interviewed companies could also stem from the fact that OOI represents a quite novel activity among the larger companies of the pharmaceutical industry. Clearly, no unifying, dominant opinion on OOI has been established yet (following the view of 'social constructivism'), indicating that we are still in the initial phase of the OOI implementation process as no closure has been reached (Pinch & Bijker, 1984).

However, despite this observed lack of a unifying pattern and *caveats* regarding generalization of findings, there are still certain views that prevail and were alluded to by the majority of interviewees irrespective of their company's size.
Perhaps the most prominent one is connected to the importance of OOI for overall corporate strategy. The quote "*we are not here to develop value for someone else*" is really exemplary for the attitude of the vast majority of companies interviewed. For most interviewees OOI could never become part of corporate strategy as this would mean that pharmaceutical companies would deviate from their primary goal to develop and commercialize innovative assets on their own. As the pharmaceutical industry currently is facing (among other pressures) a decrease in R&D-productivity, they are more focused on ensuring pipeline viability by bringing additional assets inside, i.e. engaging in IOI. OOI on the other hand, as one interviewee put it: "*doesn't solve any of the underlying issues Big Pharma has*". Since it is the goal to increase pipeline productivity, giving away assets is seen as contra productive to the core strategy. Furthermore, the same interviewee stated that for him OOI does not represent a viable business model since he believes that no "*significant value*" could be derived from such activities. Due to the only recent engagement of pharmaceutical companies in OOI, it remains to be seen, whether this will indeed be the case. Yet, examples from other industries show that value creation from OOI is indeed possible, as for instance in the case with Xerox, where the overall value of ten spin-offs made during a period of 22 years even exceeded the value of the originating company (Chesbrough, 2002).
Moreover, considering the financial pressures pharmaceutical companies are facing, gaining additional value of unexploited assets could become more attractive for companies.

In order for OOI to happen more frequently though, an important barrier has to be overcome first. The majority of companies complained about the very poor effort vs. return ratio that engagement in OOI activities entails.
On the one hand this has to do with the low level of upfront payments (compared to the already spent costs for development) external parties are willing to pay currently. This situation might change if the demand for development assets will increase further. Judging from the current trends in R&D-productivity development (Munos, 2009), this might very likely be the case.
On the other hand, the effort for arranging and implementing an OOI deal could be minimized. At present, transaction costs are still quite high as some aspects of the OOI process are not yet implemented in a systematic fashion but are usually done in an *ad hoc* approach. Furthermore, even when dedicated functions were installed which should support and improve the establishment of a systematic OOI approach, the process was inefficient due to a lack of empowerment and a lack of resource allocation. Members of the dedicated function team especially had difficulties accessing the relevant documentation as employees got re-assigned to different projects immediately after de-prioritization of a project. The OOI team had to rely on the good will of the project staff to provide

them with the information they needed. As OOI has at most low priority for overall corporate strategy, no rewarding systems are in place to incentivize the scientific staff to support the OOI team in addition to fulfilling their normal in-house duties.

This **competition over resources** of OOI activities with in-house and/or IOI activities represents probably the largest barrier to OOI as it is hindering OOI at multiple stages throughout the process.
Starting with the deal objective, the potential strategic and financial benefits of engaging in OOI have to be weighed against pursuing in-house or IOI activities. Since the latter are perceived to be better aligned with the 'primary mission' of pharmaceutical companies to improve pipeline viability and increase the amount of commercializable products, OOI has a difficult standing. Upfront payments are low and long-term profitability is uncertain. With in-licensed projects on the other hand, probability of success is perceived to be higher, since the staff trusts their internal capabilities to add value to a respective project. By giving the development to somebody else (i.e. giving up control), uncertainty increases since the development capabilities of the external party are harder to assess than the internal ones. This perception is exemplified by the following statement: *"[With IOI there is] more sense of opportunity, less of a sense of catastrophic risk associated to the project*".
There are, however, a number of arguments, why this view on OOI not increasing probability of success might be wrong or could at least be challenged. Firstly, the external company could have more suitable development and commercialization capabilities than the originating company, be it in terms of scientific, manufacturing, distribution or marketing capabilities. Secondly, decision structures e.g. in a biotech environment are less complex, enabling faster decision making and acceleration of the development process. Thirdly, staff motivation to advance the project in question might be considerably higher on the licensee side as the project might be one of the few the licensee company has in development at all. Moreover, additional motivation stems from the fact that the external party sees a high potential in the licensed asset, otherwise it would not have struck the deal in the first place.
During the course of the interviews, however, it became clear that the reluctance to engage in OOI was not only due to the mistrust in the capabilities of the external party but was also due to image and reputation-related issues. Apparently it is viewed as a reputational damage or a sign of misjudgment if another company succeeds in developing a product that was de-prioritized by the originating company. If a project is just terminated and not transferred to an external party, the project assessment cannot be challenged and consequently not be proven wrong. This follows the attitude of "*if you say 'no', you're always right*" as one interviewee pointed out, exemplifying the fear of personal accountability.
This attitude not only entails the fear of misjudging the value of an asset (which is similar to giving away 'corporate crown jewels'), but also the fear of admitting the absence of certain capabilities. This fear of being perceived as incompetent is very difficult to address and will probably disappear only when through other pressures more and more companies are forced to engage in OOI, making it a more common process.

In order to build up the necessary experience and making OOI practices more common, certain deal constellations could be identified during the interviews that seem to facilitate OOI by circumventing some issues that lead to the building of barriers.

Firstly, opt-in deals with buy-back options mitigate the fear of giving away valuable corporate assets, as already discussed in detail above.
Secondly, companies seem to be far more willing to give assets away that do not originate from their own internal pipeline. Such was the case for one of the companies interviewed, where after the acquisition of a small biotech most of the assets were spun-out again and only the asset with the highest potential was kept.
Thirdly, a clear demarcation of indication areas is conducive in order to mitigate the fear of delivering competitive advantage to a competitor. In one example, as described by an interviewee, two companies pooled their early stage assets of two independent indications in order to profit from the combined discovery expertise. Any development after the discovery stage would then again be conducted by the individual companies alone. Yet, in order to compensate for the input gained in the discovery stage, the partner company would obtain royalties if a compound stemming from the pooling effort made it to the market. This is in fact an example of combined inbound and outbound Open Innovation as expertise was both given to and received from an external party. Still, it illustrates nicely that certain barriers can be circumvented when engaging in OI practices, in this case by making sure that the respective indication areas of interest to the two involved parties did not overlap.
Furthermore, companies seem to be more willing to engage in OOI if pipeline overlap occurred in consequence of a recent merger/acquisition, since resources are not sufficient to support all pipeline projects, even though there might be some promising assets among them. One could speculate that in those cases, the sense of opportunity is bigger, as the projects are perceived as being more valuable since they do not stem from the normal process of internal de-prioritization but from an excess of projects with only limited resources available.
Last but not least, the presence of a champion convinced of the benefits of OOI can enable the execution of OOI activities even if the general corporate attitude towards OOI is not supportive: "*it only happened when I myself tried to push it through*".

Coming back to the competition between IOI and OOI, an additional important issue is that teams responsible for OOI are often also in charge of performing IOI activities. Again due to the better fit with corporate strategy, the licensing teams are incentivized more to focus on bringing projects in than giving them outside. So only if they have spare capacity would they evaluate projects suitable for out-licensing and start identifying potential partners, etc. The same is true for the negotiators responsible for closing the deals. They are in charge for both the inbound and outbound licensing activities, making the deal-making step of the OOI process a further point where competition with IOI activities arises.
Last but not least, when looking at the implementation step where the actual asset and knowledge transfer takes place, processes needed for OOI projects yet again have to compete against in-house projects. As already detailed above, the gathering of necessary documentation for asset transfer has to be supported by staff that is already in charge of other in-house projects, representing a double burden for the staff involved which is not supported by incentive systems. It is thus actually more a matter of good will if the respective staff is willing to support the OOI transfer team with the required information next to pursuing its routine in-house responsibilities.

Yet, despite the problem of increased competition between OOI and IOI processes, there are also synergistic effects that can be obtained due to the similarity of these two Open Innovation types. The extensive experience accrued regarding negotiation of licensing agreements and evaluating market potential for inbound activities is also very useful for outbound activities. This is very beneficial as the relevant capabilities are already present and simply have to be adjusted but do not have to be built from scratch. The same is true for assessing which project data are relevant to evaluate the attractiveness of a given project and to facilitate the transfer process. The company can already draw from its previous experience in inbound activities to know which data will be relevant for an external party during OOI. Conversely, experiences made while engaging in outbound activities can be employed for optimizing the inbound process, as the company can now better relate to the situation of a licensor. Also the establishment of a network was mentioned as a synergistic effect applicable in both dimensions. On the one hand, the established network of parties the focal companies has in-licensed from in the past might be helpful to identify suitable partners for an OOI activity. On the other hand, partners acquired due to OOI activities might be suitable providers of assets as well.
Summarizing, the similarities of processes employed in both IOI and OOI activities represent both a barrier for OOI in terms of competition on resources but also offer positive synergistic effects with regard to network and learning curve building.

Limitations & Future research

The research work underlying this report is based on an exploratory, data-rich research design employing a multiple case study methodology (Yin, 2003). One inherent limitation when choosing this approach is that due to the limited number of cases analyzed, generalizations regarding the industry as a whole or even on company-type level are difficult to make. The results only reflect the individual and subjective perception of the chosen interviewee on the position of his company towards OOI. Since for most of the companies only one interview partner was available (except for 3 companies where two representatives were interviewed), a classic 'triangulation' on company level was not possible as this requires at least three interview partners per company. Therefore, contradictory statements could not be resolved at this level. However, the presence of three companies per company category (small, medium, large) in the sample allowed for triangulation on a company-type level.

Thus, the identification of common patterns or the lack thereof across all interviews analyzed can give a valid initial indication of the general perception of OOI dominating in the pharmaceutical industry. Yet, no quantification is possible due to the limited number of cases analyzed.

A further limitation of the reliability of this research occurred due to practical matters. Even though the employment of interview guidelines is a means to ensure reliability (Yin, 2003), for some interviews the allocated time was not sufficient to go through all the points of the questionnaire, resulting in some missing data points for the analysis (marked as 'n.a.' in the result overview table).
On the one hand this was due to a limited time slot the interviewees were able to provide. On the other hand – being the case for the majority of missing data points – depending on the degree of expertise of the respective interviewee, some points were discussed more extensively than others, resulting in an uneven distribution of time devoted to particular questions. Consequently, certain details could not be accounted for as extensively. A better time management on the part of the interviewer would have been warranted to prevent such uneven distributions. Yet, due to the open-ended and only semi-structured nature of the interviews, this does require a certain established experience of the interviewer. In order to compensate for those missing data points, follow-ups on the missing questions were done where possible. Yet, due to a tight working schedule this was not possible for all interviews, representing a major drawback with regards to reliability.

In terms of the generalizability and validity of the results, a further *caveat* to be considered is that the interview questions were guided towards identifying barriers to the OOI process in general. Yet, during the course of the interviews it became apparent, that according to the different OOI practices considered, different barriers can also arise. For instance the potential barrier of an external player doubting asset quality is not so much applicable to the situation of a strategic alliance as in an out-licensing activity, since in a strategic alliance the originator company still holds a considerable stake in the asset, and thus has to connect a commercial potential to this asset.
It is thus difficult to judge from the experience from an interviewee on one OOI-activity-associated barrier on overall associated OOI barriers. The interview question would have had to be better differentiated between the individual OOI activities.

However, since this study was of an exploratory kind, the primary intention was to gain a first impression of potential barriers associated to OOI activities which have been presented and discussed in detail in the previous sections of this report.

In order to avoid the limitations present in this study, future research on OOI barriers should follow a quantitative approach in order to increase the validity of the results through a higher case number and thus broader applicability.
Considering the still quite novel appearance of this business model in the larger pharmaceutical companies, next to more detailed quantitative approaches, further qualitative research will be advantageous for describing particular characteristics of each individual OOI activity and contributing to a better understanding of OOI implementation as a whole. In that respect, for instance further evaluation of the observation made in this report that barriers towards OOI apply both to large and smaller companies alike would provide valuable insights. Furthermore, future research should differentiate clearly between the particular OOI activities under investigation in order to obtain a more fine-grained picture on the OOI process and its associated barriers. The same is true for the distinction between OOI barriers related to non-strategic or strategic assets respectively. A more detailed investigation could shed more light into the specific benefits obtainable with each asset type and the associated requirements necessary to guarantee successful implementation.
From a managerial point of view, it would be interesting to further assess which structural approach is more productive and efficient considering that two types of managerial structures (dedicated function and inline functional design) were found to be employed by the interviewed companies.

Whereas future research will presumably provide a better and more reliable basis to devise specific managerial measures tailored to the particular OOI activities, still some general managerial advice can be deduced from the results obtained in this study, which will be described in detail in the following section.

Managerial advice

Since competition of IOI and OOI activities for internal resources was found to be a main barrier impeding OOI implementation in large pharmaceutical companies, managerial measures should especially focus on this aspect in order to mitigate the negative consequences for OOI engagement. In this context, two interviewees proposed the involvement of a third external party to take over the coordination of the OOI process, being in charge of finding partners and maximizing the value of the respective asset. In line with the definition of Sieg *et al.* (2010), the third party would assume the role of an 'innovation intermediary' which "create[s] value for clients by identifying, accessing, and transferring solutions to problems in various stages of the innovation process to their clients" (*idem*, p. 281). This way, most of the competition for internal resources could be avoided and the external party would run the risk of finding suitable partners and closing the deals. Since it would be their sole activity to facilitate OOI deals, the relevant processes could be optimized and carried out in a systematic fashion, thereby increasing the probability of OOI success. An additional factor contributing to a better OOI result is the higher degree of motivation for reward to be expected from the third party compared to the internal staff who lacks incentives for engaging in OOI.

Whereas this proposed business model of employing an innovation intermediary seems to address major barriers to OOI such as competition on internal resources and the internal incentive problem, there are still some *caveats* and managerial challenges to be considered.
In order to identify suitable partners, the third party has to have full access to confidential internal data relevant for the project. The originating company might be reluctant to disclose this kind of information to a third party. Furthermore, even if the originating company agrees to disclose the information, the relevant documentation must again be compiled by the internal staff, as only they have the required insights into the project details. Due to the problems outlined above (discussion section), problems will arise during this step due to a potential lack of resources and a lack of incentive. However the third party could, as one interviewee pointed out, support the documentation process by putting forward an action plan to organize and optimize resource allocation internally.
Yet it remains to be seen whether the internal staff would follow the third party's instructions and would support the OOI process without adequate incentives.

Furthermore, none of the measures concerned with 'outsourcing' OOI activities are likely to be successful if there are no changes in OOI management and attitude internally as well.
Most importantly the staff involved has to be better incentivized to perform and support OOI activities. This includes better information and education on the potential benefits of OOI for the company and in what way each employee can contribute. Furthermore, the staff involved or division has to be able to profit from the outcome of a successful OOI activity. If "*royalties are invisible*" as in the case of one interviewed Big Pharma-representative, meaning that royalties do not come back to the originator divisions of the out-licensed asset but to the general treasury, then incentives to pursue OOI are understandably low.
However, these measures will be difficult to implement as long as OOI does not gain more importance for overall corporate strategy. As long as it is not seen as an activity worth pursuing

because it can bring substantial benefit to the company, neither the resources nor the incentive systems will be put in place to support OOI accordingly.
Therefore not only the lower scientist and management levels have to be properly educated regarding OOI, but also top management has to be aligned regarding their attitude towards OOI. In some cases in the past it has been sufficient that one member of the top management acted as a champion and pushed the OOI process through. Yet, in order to make OOI engagement more systematic and thus more efficient, the whole company has to be aligned in terms of supporting OOI. Only by improving the supporting tasks associated with the OOI process and by aligning top and lower management on the respective OOI strategy will an efficient and effective balance of strategic and operative decision making be possible in line with the OOI management framework as proposed by Lichtenthaler (2008) and Bianchi (2009).
In addition, considering the competition between IOI and OOI but also the synergistic effects resulting from engaging in both forms, installing of a controlling function on corporate-level might be beneficial as suggested by Lichtenthaler (2010b). Such a central coordination function could have the oversight on all OI-related processes and allocate resources accordingly and ensure that the beneficial effects from both OI dimensions are captured in an optimal manner.

In addition to increasing the corporate awareness for OOI benefits, another major issue will be to ensure systematization in order to optimally benefit from OOI activities (Lichtenthaler, 2008). In this respect, installing a dedicated function might represent the best approach in order to build the required 'multiplicative capabilities' (Gassmann & Enkel, 2004) to ensure successful knowledge transfer. By allocating specific resources to OOI and systematizing the process, the amount of effort can be reduced compared to *ad hoc* approaches as the involved personnel can build up a learning curve and thus optimize the process. This would lead to a decrease in the high effort currently associated with OOI activities.
Yet, current fluctuations in OOI frequency compared to the more continuously pursued IOI activities impose special challenges to the dedicated function structure. What will the dedicated team do in the periods when no OOI deals are ongoing? One of the interviewed company-representatives therefore assigned dedicated OOI responsibilities to certain staff members which only exert their function on a temporary basis; if no OOI project is ongoing, they are fulfilling other functions (mostly connected to inbound activities). This might, however, lead to competition issues again if the respective functions are not clearly prioritized.
This might be the reason why interviewees from all but 2 companies chose an *ad hoc* approach for OOI coordination. Yet, also here process systematization has to be ensured. However, only the asset selection and deal making steps were carried out in a predominantly systematic fashion, whereas partner search, asset transfer and most importantly the decision to perform OOI was carried out in an opportunistic manner. Management should therefore concentrate on implementing routines for the three latter process steps identified in order to ensure a systematic continuous OOI process flow.
In addition, it has to be made sure that those *ad hoc* or designated OOI functions are endowed with a sufficient degree of empowerment by corporate management in order to fulfil their functions appropriately. Currently, the degree of empowerment is still too low according to the statements of interviewed members of dedicated functions.

In addition to addressing overall issues like awareness and process systematization, the major individual barriers identified have to be also considered in order to enhance the engagement in and the performance of OOI activities. These consisted in competition of IOI with OOI activities, a too high effort vs. return ratio, the fear of weakening one's own competitive position, and external players doubting asset quality.
The first two barriers are addressable with the measures regarding awareness and systematization as presented above.
In terms of addressing the barrier of the fear of weakening one's own competitive position, potential managerial measures could entail installing a rigorous internal due diligence process to make sure that the asset in questions has been characterized and evaluated properly. Also the preference for making opt-in deals in which the originator company can under certain requirements still buy the asset back might help mitigate this fear, as alluded to by several interviewees.
Yet, most importantly, a change in attitude is warranted that OOI represents an opportunity to gain additional value rather than a threat to the company. These changes in mentality, however, require thorough information and time to sink in and be accepted.

Finally, the barrier of external players doubting asset quality could best be mitigated by providing the external party with all the relevant information required for an external due diligence and by disclosing all the potential disadvantages the asset in question might have. With this provision of information the external party can judge the quality of the asset by itself. In the course of time, after a company has done several such OOI deals with assets of adequate quality, they are likely to build a reputation within the industry. In addition, this external barrier might decrease in the future when the OOI process is more established and no longer represents a rare event.

Conclusion & Outlook

OOI implementation within Big Pharma companies is still at its beginning stage. Many of the barriers currently associated with OOI practices are likely to disappear in the future once OOI activities are fully established and accepted by the larger pharmaceutical community. By building up their learning curves, and by step-by-step systematizing and optimizing processes, barriers such as too high effort vs. return, fear of giving away competitive advantage and external players doubting asset quality will decrease, as both companies and the surrounding community gets increasingly familiar with OOI.

As already apparent today, the dynamics of the innovation value chain are changing, moving away from the traditional fully integrated business model of pharmaceutical companies (Gilbert *et al.*, 2003). Due to the cost pressures exerted by payors and competitors and the increasing complexity of the drug development process, large pharmaceutical companies are moving away from doing everything by themselves towards a more focused approach as exemplified by the increasing specialization in which whole therapy areas are abandoned and focus on a few selected indications only. In addition, companies have become more open for external inputs reflected in the high number of collaborations and licensing activities pursued in this sector (Hagedoorn, 2002). Outbound Open Innovation is just a further logical step in the development of the new innovation value chain dynamics, since focusing necessarily leads to an excess amount of un-utilized assets which can serve as a basis for OOI activities in order to exploit company's portfolio. In addition, the huge financial losses Big Pharma will be facing in the near future due to patent expirations, will make additional revenues stemming from OOI activities even more attractive, even though OOI is currently still regarded as financially 'insubstantial' by the majority.

New times warrant new measures. And due to the strongly changing environment surrounding the pharmaceutical industry, new innovative approaches are absolutely necessary if Big Pharma wants to maintain its competitive advantage in the market place.
However, with regards to innovating the drug development process and devising new business models, large pharmaceutical companies might again turn to look at biotech companies in search of a suitable new role model.

The observed trend of 'biotechization' of the large pharmaceutical companies already indicates that Big Pharma has understood that and is acting upon it. For instance Big Pharma began to reshape its 'monolithic structures' into more 'nimble' biotech-like business units as exemplified by GSK and their introduction of centers of excellence and drug performance units (Senior, 2009; Owens, 2007). By breaking down hierarchies, scaling down team size and changing development team composition they tried to speed up the decision making process and to provide an environment that better facilitates innovation. Furthermore, Big Pharma is now heavily relying on in-licensing assets from biotech companies in order to enhance the innovative potential and quality of their development pipeline.
A further capability that biotech companies - in contrast to Big Pharma - already have established is that of pursuing both inbound and outbound Open Innovation in parallel. Biotech companies in-license assets from Academia or other biotech companies, develop them to a certain stage and then

out-license them to pharmaceutical companies. This exemplifies that both inbound and outbound activities can be performed by the same company. Moreover, it shows that the combination of internal and external capabilities according to the respective development and commercialization requirements of an asset can represent a viable business model, as proposed by Gilbert *et al.* (2003).

As with any big transition from one model or paradigm to the next, outbound Open Innovation will also take some time to get established within the Big Pharma community.
Although many interviewees stated that they do not consider OOI as relevant for Big Pharma now or in the foreseeable future, it will be interesting to see if this attitude will change, once more examples of successful OOI become available and a new generation less accustomed to the 'traditional' fully integrated pharmaceutical model takes over the top management levels.
Still this change process will represent a considerable managerial challenge due to the particular characteristic of innovation, which industry expert Bernard Munos so aptly put during the interview:

"Innovation is not a by-product of organization; it is a by-product of culture. And culture is a lot more difficult to change than organization."

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Appendix

Interview questions addressing large pharmaceutical enterprises:

A. Facts/Overview on OOI activities pursued:

1. How often is your company involved in the following outbound OI activities?

OOI activity\Frequency	Never	Rarely	Often	Constantly
Out-licensing				
Spin-off				
Joint Venture				
Participation in a public-private partnership				
Alliance for exploitation				

2. In which stages of the drug development do you typically engage in the following outbound OI activities?

OOI activity		Research/Discovery	Preclinical	Clinical	Marketed
Single asset	**Out-licensing**				
	Co-development				
	Co-promotion				
Multiple assets / therapeutic areas	**Spin-off**				
	Joint Venture				
	Participation in public-private partnership				

3. Which are your preferred partners for engaging in the respective outbound OI activities?

OOI activity		Big Pharma	Small/Mid-sized Pharma	Biotech	Other (e.g. academia)
Single asset	**Out-licensing**				
	Co-development				
	Co-promotion				
Multiple assets / therapeutic areas	**Spin-off**				
	Joint Venture				
	Participation in public-private partnership				

B. Reasons/Objectives for pursuing OOI

4. Has engagement in outbound OI practices delivered value to your company? If so, in what way?

Strategic	**Financial**
Access to niche markets	Improvement of financial returns
Disposal of assets of low strategic importance	
Other: _____	Other: _____
Exploitation of un-utilized assets	

5. Did you experience synergistic effects (1+1=3) due to outbound OI activities? If yes, could you give some examples?
6. Do outbound OI activities represent a relevant part of your corporate strategy?
7. Is the practice of engaging in outbound OI activities done opportunistically or do you have a formal, systematic way to doing so?

C. Drivers for asset selection

8. Based on which criteria do you decide to involve an internal asset in outbound OI activities?
    - Strategic:
        - Market access
        - R&D capabilities
        - …
    - Attractiveness:
        - Costs
        - Quality
        - …

D. Internal and external barriers

9. Which internal barriers do you experience with regard to outbound OI activities?
    - Selecting suitable asset(s)
    - Risk of weakening own competitive position
    - Bringing projects in-house has higher priority than OOI activities
    - Identification of suitable partners
    - Transferring the asset
    - …

10. Which external barriers do you experience with regard to OOI activities?
    - No demand
    - External players doubting asset quality
    - Cultural/Organizational differences
    - Negotiation difficulties
    - Transferring the asset
    - …

E. Management Processes

11. Do you have formalized criteria [routines] for performing
    - o Asset selection?
    - o Partner choice?
    - o OOI deal implementation?

12. Is there a dedicated OOI team in place?
13. Is there an incentive system in place?
14. Are the involved employees specifically trained for OOI activities?