Open Innovation: Implementation & engagement barriers within the pharmaceutical industry

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Preface

The following content has been conducted as an academic master's thesis at Copenhagen Business School in collaboration with LEO Pharma. This study contributes to research within the field of Open Innovation. The authors have been working part time as student assistants at LEO Pharma throughout the period where the study has been conducted.

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Abstract

Drug discovery and development within the pharmaceutical industry is traditionally conducted independently in research and development (R&D) departments, based on internally developed compounds or in-licensed assets. Due to the current trends such as increasing cost of drug development, price-pressure and generic competition, Open Innovation is proposed as a less expensive and more efficient way of conducting drug development through collaboration-based innovation. Open Innovation models, based on Henry Chesbrough's framework, is thought to foster incremental innovation and the exchange of complementary know-how between actors including pharmaceutical companies, biotech start-ups and academia. Thus, facilitating reductions of fixed costs within pharmaceutical companies such as in-house R&D expenses, and generating a more agile company structure and strategy. However, a paradigm shift is required to change the current Closed Innovation mindset that is observed in many settings including the pharmaceutical industry. Implementation barriers such as Not-Invented-Here, Not-Sold-Here syndromes and appropriability issues are thought to hamper the adaptation of Open Innovation. The appropriability issue is identified as one of the main reasons for the lack of implementation of Open Innovation within the pharmaceutical industry. Top management of pharmaceutical companies might face the risk of jeopardizing internal IPR and competitive advantages when adopting Open Innovation models with permeable boundaries facilitating a bidirectional flux of knowledge. Collaboration with external partners is hampered by this mindset and operational setting, entailing losses in terms of future gains and innovative endeavors.

No recent studies have analyzed the current exploitation and implementation of Open Innovation among the key players of the pharmaceutical industry focusing specifically on compound collaboration. This study aims to map and classify the level of implementation of Open Innovation within the top 100 pharmaceutical companies worldwide through the method of web scraping. Among this target group, seven adaptations within Open Innovation models are identified as compound-specific collaborations. Based on Open Innovation models observed, the criteria and prerequisites of these platforms are analyzed based on their attractiveness for external partners.

The purpose of the study is also to identify the main barriers and concerns of collaboration for biotech start-ups. Thus, ten semi-structured interviews with CEOs of European-based biotech start-ups were included in this research. The CEOs are, in general, favorably disposed towards collaboration with pharmaceutical companies within an Open Innovation setting, despite acknowledging concerns and collaboration barriers. The ownership of data generated from the collaboration is generally identified as the biggest concern of the CEOs. However, trust and mutual benefit of the collaboration are mentioned as other important aspects.

These findings are discussed in the study based on the current perception of Open Innovation within the pharmaceutical industry. Reflections upon the future implementation of Open Innovation models within the pharmaceutical industry, including measures as the appropriability issue, are also elucidated.

Index

List of abbreviations

AI	Artificial Intelligence
CBER	Center for Biologics Evaluation and Research
CEO	Chief executive officers
COVID-19	Coronavirus Disease 2019
CRO	Contract Research Organizations
FDA	Food and Drug Administration
HIV	Human Immunodeficiency Virus
HQ	Head Quarters
IPO	Initial Public Offering
IPR	Intellectual Property Rights
IT	Information Technology
KPIs	Key Performance Indicators
MTA	Material transfer agreement
NIH	Not invented here
NSH	Not sold here
OI	Open Innovation
P&MSA	Participation and Material Supply Agreement
R&D	Research and Development
ROI	Return on Investment

1. Introduction

1.1 Innovation in the Pharmaceutical Industry

The pharmaceutical industry has, for many years, relied on drug development based on internal research and development (R&D) investments and protecting all inventions with patents, ensuring exclusive intellectual property rights (IPR). This approach aims to protect internal knowledge and prevent competitors from exploiting proprietary assets for their own benefit and by avoiding any flux of internal knowledge outside the boundaries of the company [1]. This paradigm implies considerable barriers of entry for any new players entering the market due to the extensive and increasing cost of developing and launching pharmaceutical compounds on the market [2-4].

A disruption of the traditional drug development model is triggered by erosion factors such as the rise of ventures capitalist, the need for incremental innovation and the increasing mobility of employees between companies. The evolution of the paradigm is ongoing, which makes the knowledge barriers less tangible and increases the need for scouting activity in pursuit of external discoveries [2, 5, 6]. These erosion factors combined with the current challenges in the pharmaceutical industry, have forced pharmaceutical companies to seek new approaches of openness towards drug development and collaboration with external partners. The challenges include increased competition from generic drug producers, lack of R&D efficiency and political awareness on price pressure related to drug reimbursement [7, 8].

The disruption of this silo mentality, which could be characterized as a closed innovation model [2], facilitated a separation between the value creation and value capture of the existing business model. This fact implies that employees who want to bring forward assets, which are put on hold for strategic reasons, can now create a start-up on their own with the financial support of venture capital. The value created within this new company structure can be commercialized by a new entity, which at the same time, enables acquisitions by other competitors, capturing the resultant value of the innovation breakthrough [9]. Additionally, the spillover of knowledge from company projects which cannot be efficiently commercialized upon the timeline of the breakthrough, resulting in the raise of other mechanisms to bring forward such unfinished projects with market potential [11]. This trend is observed in many industries that rely on heavy internal R&D investments to foster new products to

market, such as IT and pharmaceutical industry [10].

1.2 Alternatives to traditional models of research development

In contrast to the Closed Innovation model, the Open Innovation model offers a different mechanism of formal knowledge sharing to be exploited between companies as later explained in section 2.2. According to recent studies from Deloitte [7] [8], drugs sourced through Open Innovation initiative have a three times higher chance of late clinical phase success, compared to projects following traditional paths during the last decades. Additional studies have emphasized that biotech start-ups play a key role in the disruption of next-generation therapies in the pharmaceutical environment [11, 12]. Open Innovation models can facilitate a shorter time-to-market by utilizing resources from biotech start-ups [12]. Thus, pharmaceutical companies that solely rely on Closed Innovation might be hampered in extracting the full value in collaboration with external partners such as biotech start-ups.

Within new technologies, such as gene therapy, which already holds important implications within the pharmaceutical industry, the current traditional models of investing in R&D seem to become obsolete. According to a recent study from McKinsey [13], more than 150 investigational new drug applications were filed for gene therapy in 2018 alone, compared with a total of 800 applications to the Center for Biologics Evaluation and Research (CBER) [14]. Development of such therapies are characterized by a relatively high cost, usually targeting a small portion of the population with a high unmedical need. Thus, developing drugs within such indications might include a high-risk, limiting the profitability for pharmaceutical companies. Interestingly, an important percentage of the innovation within these indications originates from biotech start-ups, followed by a collaboration with a Big Pharma company [13].

Similarly, Artificial Intelligence has become a promising technology for *in-silico* identification of new compounds within the pharmaceutical industry. Thus, smaller companies are able to provide innovative assets without having to rely on heavy R&D investments and infrastructure for compound testing [15]. An example of a recent profitable is the agreement between the biotech start-up Excientia and the pharmaceutical companies GSK and Sanofi [16, 17].

The response of the current pandemic crisis of COVID-19 is an example of fast and collaborative approaches for vaccine development and diagnostic equipment

based on collaboration. Scientists, governments and pharmaceutical companies are collaborating and exploiting openness to accelerate the identification of vaccine candidates. This includes information sharing such as approved safety protocols for Phase I clinical trials, accelerating the timelines for drug development. Thus, the great potential of exploiting assets through external collaborations, with benefit to the companies involved and society, are key learnings from this exceptional situation [18].

These examples of current technologies and challenges within the pharmaceutical industry emphasize the need and benefits of external collaborations, which will be elucidated in this research.

1.3 Aim of research

The aim of this research is to investigate the implementation of Open Innovation collaborations between biotech start-ups and pharmaceutical companies. The theoretical concept of Open Innovation will include Henry Chesbrough's definition of Open Innovation from 2003, coupled with Alexander Schuhmacher's overview of Open Innovation implementations within the pharmaceutical industry from 2016. The research will include collection of primary and secondary data to identify the current implementation level and barriers of Open Innovation between biotech start-up companies and key players within the pharmaceutical industry.

The main research question of our project is:

1. *How does the current landscape of Open Innovation exploit the value of drug research within the 100 biggest pharmaceutical companies worldwide?*

In order to investigate the implementation level and adaptation type of Open Innovation, a subdivision of the core research question is presented in the following sub-questions:

1.a *How can the current implementation of Open Innovation platforms within the pharmaceutical industry be classified from a biotech start-up perspective?*

1.b *What are the biggest collaboration concerns for a biotech start-up when evaluating the attractiveness of Open Innovation platforms?*

Figure 1 presents a visual representation of the research questions for this study.

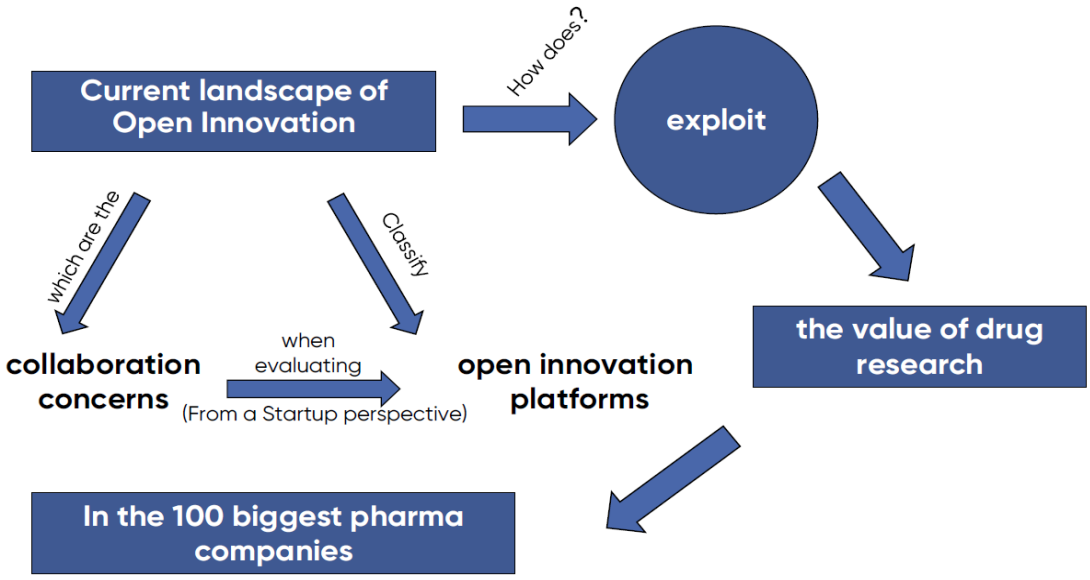

Figure 1. Visual representation of the research questions.

2. Conceptual Background

2.1 Paradigm shift in Traditional R&D

The vicious circle of drug discovery established within the pharmaceutical sector is traditionally based on the following process: internal R&D innovation, new products and technologies are further developed so that they can be commercialized. Thereby increasing the company's revenue, leveraging the existing business model and increased investments in R&D, which potentially lead to more investments in internal R&D resources.

The substantial change in this process was facilitated by the erosion factors mentioned in section 1.1. These factors include key employees leaving the company and establishing start-up companies that are built upon internal knowledge and expertise from the company. Venture capital facilitates these processes, by providing financial support for the assets to develop. Eventually the biotech start-ups can reach initial public offering (IPO) or be acquired by a bigger company. This results in a flux of knowledge from projects put on hold, which can dissipate through other processes to reach the market [5]. Additionally, companies need to consider the high attrition rate of drugs within the pharmaceutical industry. A need for a such infrastructure facilitating external projects into the pipeline of pharmaceutical companies has been addressed [2, 7].

These erosion factors have forced pharmaceutical companies to address the issue of not acting as monopolies for internal R&D innovation processes. Thus, a paradigm shift was seen, facilitating a search for external sources of innovation outside the company boundaries. This change in the existing silo-mentality also implied that external and internal knowledge should be considered equally valuable and important [6].

2.2 Open Innovation definition

Open Innovation was first introduced by Chesbrough in 2003 and defined as, *"the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation"* [2, 19]. Chesbrough reflected upon the need for company management to acknowledge the fact that "*not all the smart people work for us. We need to work with smart people inside and outside the company"* [2] and further *"valuable ideas can come from inside or outside the company and can go to market from inside or outside the company as well"*

[2]. In other words, the exchange of knowledge facilitated by Open Innovation collaborations is thought to improve R&D processes of innovation and facilitate drug development reaching existing or new markets. This type of openness will increase the business case for internal and external projects [2].

The innovation funnel or the stage-gate model are representations of the drug development process from early drug discovery to the commercialized product launched on the market. Projects are evaluated throughout the research- and development process where less promising projects are discounted. This leaves the company with only promising projects. Thus, facilitating an increased probability of success. In the Open Innovation model, the internal projects can exit through permeable company boundaries, and external projects can be internalized into the company's development process. Projects can likewise be externalized and be exploited in a different company setting or industry [2, 20]. This process is illustrated by the Open Innovation funnel diagram presented in *Figure 2*.

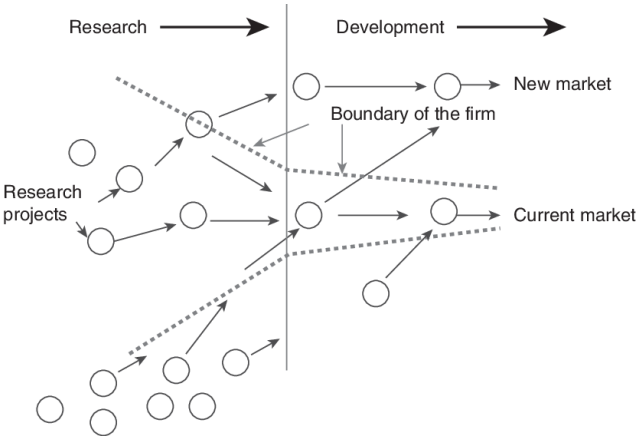

Figure 2. Open Innovation funnel with permeable company boundaries. Research projects can flow from inside the company to the outside and vice versa. Figure reprinted from [21].

The overall purpose of this model is to accelerate the innovation process through a dynamic exchange of knowledge [12, 22].

The traditional innovation funnel seen within the pharmaceutical industry comprising closed boundaries is thought to weed out false-positive projects, leaving the company with only viable projects that hold a promising market potential. In contrast, the Open Innovation funnel with permeable boundaries enables the recovery of false-positive projects, which eventually turn out promising, even though they initially left the company as discontinued projects [2].

Biotech start-up companies often originate as a spin-out from pharmaceutical companies and universities from projects outside their core strategy. This is the case, since projects outside of the core strategy of pharmaceutical companies and universities are often better exploited in a different

company setting. According to a recent study by Deloitte, a three times higher phase I probability of success when drugs were scoured through Open Innovation compared to traditional innovation models [8]. Small start-up companies are generally recognized as more adaptive and innovative, which might bring compounds faster to the market, compared to keeping the projects internally within the settings of big pharmaceutical companies [7, 11]. However, funding and resources are often limitations for biotech start-ups when developing and commercializing pharmaceutical compounds.

However, pharmaceutical companies can benefit heavily from internalizing projects exploited in a biotech start-up setting. As mentioned in section 1.2, biotech start-ups are thought to play an important role in the disruption of next-generation therapies such as gene therapy [11, 12]. Thus, pharmaceutical companies and biotech start-ups can mutually benefit from establishing a collaboration. This includes allocating funding and recourses to the biotech start-up, whereas new projects and knowledge are internalized into the pipeline of the pharmaceutical company.

However, a reluctant implementation of Open Innovation has been observed within the pharmaceutical industry. A strategy shift from the pharmaceutical companies are needed in order to benefit on the value proposition of Open Innovation proposed. [12, 22]. These aspects are presented in Chesbrough's work from 2003, where six Open Innovation Principles are presented, e.g.: *"If we make the best use of internal and external ideas we will win" and* stated in the 4th principle: "*companies that do not innovate die"* [2]. Dahlander *et al.*, 2008 acknowledge these aspects by stating that *"a single organization cannot innovate in isolation"* [1].

The nature of Open innovation implies disclosure of information to externals, loosening the control of internal innovation projects and IPR. This tradeoff implies the sacrifices made from a strategic perspective and the collaboration benefits gained. The barriers of Open Innovation are presented in section 2.9

Based on Chesbrough's definition and framework of Open Innovation, a platformization of Open Innovation models has been established within the pharmaceutical industry [23]. These platforms facilitate a formal infrastructure based on the value proposition of Open Innovation [23]. Such formal platforms facilitate a more structured collaboration process compared to informal collaboration approaches. Traditional innovation models are only relying on such informal collaborations, which might not extracting the full value of external collaborations including biotech start-ups.

The implementation of different Open Innovation models is explained in the following sections.

2.3 Outside-in and inside-out models

Open Innovation within the pharmaceutical industry can be conceptualized into three different flows of knowledge: "outside-in", "inside-out" and the combined "coupled process" [24, 25].

The concept of outside-in exploits the internalization of projects, compounds and knowledge into the innovation funnel of Open Innovation. Examples of outside-in processes are internalization of projects through mergers and acquisitions, in-licensing, platforms or collaborations where external knowledge are utilized internally [24, 25]. Examples of utilization of the outside-in model are Sanofi's "Innovatewith"-platform and Merck Biopharma's Open Compound Sourcing initiative.

The Inside-out model is contrary to the outside-in model, externalization of internal knowledge and projects [24]. Examples of the inside-out model are out-licensing or trade IPR as an outflow of ideas, compounds and knowledge towards the external environment. Inside-out models are utilized by big pharmaceutical companies by externalizing projects which might facilitate the foundation of a new biotech start-up. Examples of inside-out Open Innovation initiatives are Novo Nordisk Compound Sharing and Boehringer Ingelheim's OpnMe program.

The outside-in model has been studied extensively within the last years and adopted more widely than the inside-out model [25, 26]. This is likely due to the appropriability issue, which is presented in section 2.9.

The coupled process is closer towards Chesbrough's general idea of Open Innovation with permeable company boundaries, as projects and ideas flow bi-directionally into the Open Innovation funnel. This coupled process of Open Innovation is often seen in co-development projects with complementary partners where knowledge and competencies are exploited bi-directionally in internal and external flows. As proposed, this increases the likelihood of a successful project, while the participants share the risk and sunk costs of projects. These benefits are evaluated against the collaboration barriers such as the appropriability issue, which will be discussed in section 2.9 [20, 22, 24].

Open Innovation is claimed in a variety of different adaptations and there is no clear consensus on the best exploitation of the term. Implementation of Open Innovation is seen in many big companies especially

within "high-technology" industries such as Intel, IBM and Eli Lilly [2, 10, 27, 28].

2.4 Biased and unbiased Open Innovation

Pharmaceutical companies are in general prioritizing on selected core competencies and becoming specialized within a specific treatment or technology, due to the increasing competition worldwide [7]. This trend of specialization has led to a bias within pharmaceutical companies when scouting for new technologies and collaborations. Companies are searching for specific resources and knowledge within their area of specialization. This bias limits the openness and potential collaborations. Open Innovation is adopted and implemented in both biased and unbiased platforms of inside-out and outside-out models [29]. Biased Open Innovation is seen when a company is limiting collaborations to specific projects, business areas or certain acknowledged companies. Open Innovation models are not limiting the collaboration to specific areas and partners and they are consequently seen as a more open type of collaboration.

2.5 Traditional elements of Open Innovation in pharma

In this section, the traditional elements and new concepts of Open Innovation within the pharmaceutical industry will be introduced based on chapter 15 in Schuhmacher's textbook: *Value Creation in the Pharmaceutical Industry: The Critical Path to Innovation* [20]. An overview of the traditional implementations of Open Innovation and the newer concepts is listed in *Table 1.* An evaluation of selected elements will be included in the discussion section.

Table 1. Schuhmacher's overview of Open Innovation elements in the pharmaceutical industry. The different elements are divided into traditional models and newer concepts of Open Innovation. Readapted from [20].

Traditional elements of Open Innovation
Target scouting
Research Collaborations
Drug Licensing
Outsourcing
Joint Ventures
New concepts of Open Innovation
New Frontier Science
Drug Discovery Alliances
Private-Public Partnerships
Innovation Incubator
Virtual R&D
Crowdsourcing
Open Source Innovation
Innovation Camps
Fluctuating Open Teams

Target Scouting

Target scouting is exploited by big pharmaceutical companies as an adaptation of Open Innovation. The element is an example of biased Open Innovation when targeting a specific therapeutic entity by utilizing phenotypic screening and target-based screening to discover new drug development candidates from external partners. Complex technical knowledge is often required to perform phenotypic- and target-based drug screening thus Contract Research Organizations (CRO) are often included in the screening process [20].

Research collaborations

Research collaboration covers formal partnership between pharmaceutical companies and academic research institutes. This is facilitated by sharing, adapting and exploiting cutting edge knowledge from universities into the pharma industry. Often academic collaborations from universities and pharmaceutical companies are established to collaborate within a specific disease, drug discovery project or technology [20].

Drug licensing

Drug licensing is a common way for pharmaceutical companies to fill pipeline gaps by internalizing external projects and compounds. Licensing is often an integrated strategy of pharmaceutical companies through business development organizations, responsible for legal aspects. This include due diligence, negotiating of the business terms, IPR, exclusivity and therapeutic indications. Drug in-licensing and out-licensing are examples of adaptations of outside-in and inside-out models of Open Innovation [8, 30]. Thus drug licensing has been implemented to a larger extent due to the appropriability issue of Open Innovation, which is described in section 2.9 [20, 30].

Outsourcing

Outsourcing of development processes for drug discovery is a strategy for the pharmaceutical company to allocate internal resources most efficiently by relying on external expertise for certain activities. This enables companies to reduce fixed costs and thereby increase flexibility while optimizing the allocation of resources. Many CROs are offering expert knowledge and specialization within the pharmaceutical industry, which would require large amounts of resources for pharmaceutical companies to capture internally [20].

Joint ventures

Joint ventures are found in many constellations within the pharmaceutical industry when utilizing expertise across different companies in specific projects. This adoption of Open Innovation reduces the fixed costs and risks for the individual pharmaceutical company of running a drug

discovery project on its own, compared to initiating a joint venture with a partner, which already possess expertise within the specific field [20].

2.6 Novel concepts of Open Innovation in pharma

The newer elements of Open Innovation are introduced in this section based on Schuhmacher's theory. Such overview is presented in *Table 1.* An evaluation of relevant elements will be included in the discussion section.

New Frontier Science

New frontier science is an example of Open Innovation from the Japanese pharmaceutical company Takeda in how to collaborate within new technologies and innovation in projects with a 10-20-year time horizon. This includes collaborations initiated at very early state based on breakthrough innovation within projects considered as high-risk with a potential high return on investment (ROI) [20].

Drug Discovery Alliances

Drug discovery alliances are collaborations between biotech start-ups, academia and pharmaceutical companies with a 3-10-year time perspective. External knowledge and technologies are shared among the participants, which also include potential licensing and specialized resources [20].

Private-Public Partnerships

Private-public partnership is a type of Open Innovation collaboration that includes both public and private partners. Often a private-public partnership is facilitated to solve a major challenge, which could be the current COVID-19 pandemic or a consortium to develop treatments for Human Immunodeficiency Virus (HIV) [20].

Innovation Incubator

Innovation incubator is an initiative of resources provided by a pharmaceutical company to be shared and utilized by mainly biotech start-ups. When utilizing the resources provided by the pharmaceutical company such as laboratory facilities, administered help or knowhow, the biotech start-up can increase the speed and likelihood of a successful development of drug candidates [20].

Virtual R&D

Virtual R&D utilizes a small internal R&D infrastructure and relies mainly on external resources and knowledge in the drug development process. This ensures an agile and flexible company organization by lowering the fixed costs within the company [20].

Crowdsourcing

Crowdsourcing is an adaptation of Open Innovation where pharmaceutical companies request external solutions to a

defined problem on a problem-solving platform. Thereby the company can draw on external ideas and solutions from students, individuals, academic research organizations, biotech start-ups and established pharmaceutical companies [20].

Open Source Innovation

Open Source Innovation is seen when research and knowledge are shared freely into the public domain between partners including academia, biotech start-ups and pharmaceutical companies. This enables fast and efficient problem solving and advancing of science within diseases. E.g. Open Source Innovation was utilized in the exploration of the human genome [20, 31].

Innovation Camps

Innovation camps are shorter events facilitated by academia or pharmaceutical companies to solve a specific scientific challenge in teams. Often participants include students, individuals, academic research organizations, biotech start-ups and established pharmaceutical companies. The problem-solutions are then presented and evaluated by a jury. Hackathons are examples of Innovation camps [20, 32].

Fluctuation Open Teams

In contrast to the classical defined project teams and company structure, fluctuation open teams facilitate an open approach to solve challenges. This is done in temporary teams for short periods consisting of a diverse group of individuals. The team members are constantly interchanged, which facilitates new ideas and approaches to the problem-solving process [20].

2.7 Classification of Open Innovation models

The overview of Open Innovation elements listed in section 2.5 and 2.6 show the diversity of existing adaptations of Open Innovation collaborations within the pharmaceutical industry. In a recent overview from Deloitte, the most typical implementations of Open Innovation were evaluated based on their openness [7]. The overview is presented in *Figure 3.* Open Innovation initiatives such as formal outsourcing, in- and out-licensing are characterized with a low degree of openness, whereas open source initiatives are associated with a high degree of openness [7]. These aspects correlate with the appropriability issue presented in section 2.9.1.

In order to evaluate the elements of Open Innovation presented, different classifications and theoretical frameworks have been proposed [33, 34]. A classification model of Open Innovation based on accounting framework is proposed by Michelino *et al.*, 2015 [34]. This includes measures of pecuniary flows based on R&D, IPR and know-how in relation to costs, revenue, value capture and value creation. In addition, a classification system based on the degree of openness and collaboration criteria was proposed by Nilsson *et al.*, 2018 [33]. Nilsson's five-level classification framework includes aspects such as the disclosure of innovation needs, open access to resources, open science and business obligation [33]. An overview of the five-level classification system is presented in Table 2.

These frameworks are incorporated with this study as an inspiration for the selected categories of concerns for biotech start-ups when initiating an Open Innovation collaboration with a big pharmaceutical company. This ranking is presented in section 4.1. The selected concerns include ownership of the data, exclusivity rights, access to collaboration, disclosure of science and legal criteria upon collaboration. These aspects will be elucidated and discussed in the analysis- and discussion sections of this study.

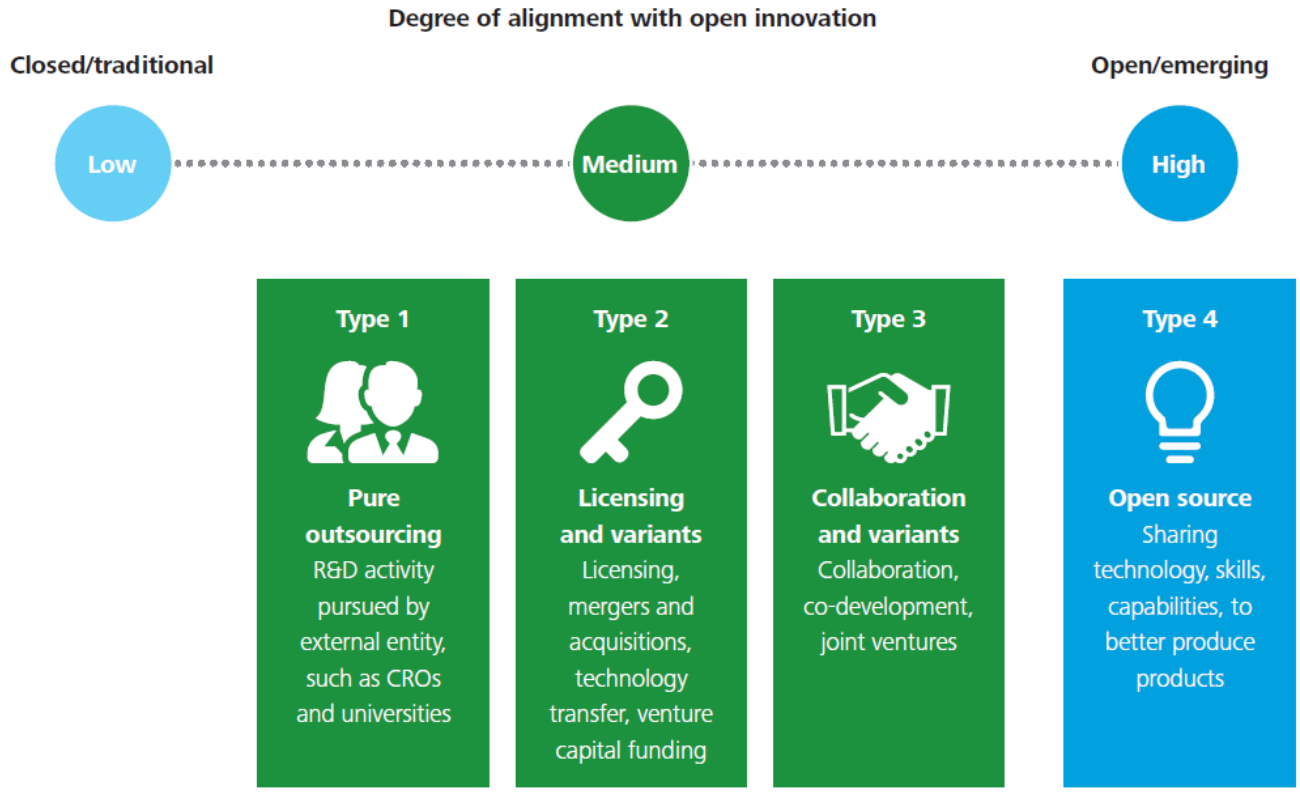

Figure 3: Categorization of Open Innovation activities within the pharmaceutical industry from "Low" to "High" based on the degree of openness. Reprinted from Deloitte [8].

2.8 Value measures of Open Innovation

No general acceptance exists of the value measures for Open Innovation activities within the pharmaceutical companies [34]. Although recent literature has focused on collaborative inventing as a source of value creation between firms, there is still an important ambiguity present in the Open Innovation literature [35].

When distinguishing the value of Open Innovation, it is important to specify between value creation and value capture. Thus, differentiating how value is generated through collaborative initiatives within the pharmaceutical industry and how the value is captured among the parties involved. Value creation is the development of inventions, which increase value, whereas value capture is defined as the process of securing financial or nonfinancial returns from value creation [35].

The four value processes by Chesbrough *et al.*, 2018 [35] can be used as a framework to investigate the elements in which value creation and value capture are divided. This concept is represented in *Figure 4*.

This matrix proposes a framework on how value is received among the different actors. For *value-in-use*, the value is received due to the fact, that the innovator benefits from its own invention. Whereas in the *value-in-exchange* category, the value is received through the exchange of knowledge in return for compensation. This compensation is based on the exploitation of the innovation. The following four elements arise from the interactions of the value creating and value capture which can be summarized as follows:

- Value realization**:** The value that is perceived by the actor of the resource application and resource utilization processes.
- Value provision: The potential value of the resources exchanged, usually knowledge-based, for later potential use.
- Value partake: The dependency on the user finding a mechanism to

Table 2. Levels of openness proposed by Nilsson et al. 2018, five levels are proposed according the fulfillment of the indicated parameters. Reprinted from [33].

Defining levels of openness in life science research collaborations					
Degree of openness	**Disclosing innovation need**	**Open access to resources**	**Open science, open source**	**No terms or commitment**	**Open data, waived rights**
Not open	–	–	–	–	–
Level 1	X	–	–	–	–
Level 2	X	X	–	–	–
Level 3	X	X	X	–	–
Level 4	X	X	X	X	–
Level 5	X	X	X	X	X

participate in other actors' value creation.

- Value negotiation (also termed appropriability): The negotiating of access and ownership over resources in return for value provision.

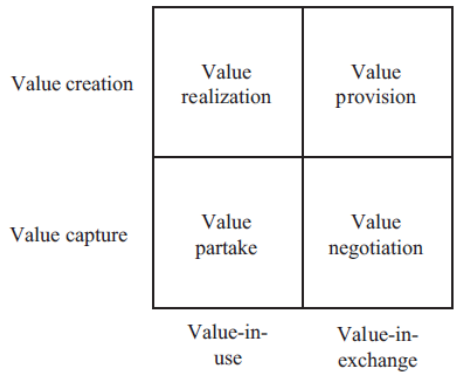

Figure 4: Illustration of the four value processes when evaluating the value perspective on Open Innovation, proposed by Chesbrough et al., 2018. Reprinted from [35].

These theoretical elements constitute a general framework on how Open Innovation constitutes to value generation processes.

It is also important to contextualize the value generated, depending on the stage of the innovation funnel presented in *Figure 2* [2]. The closer a compound is to commercialization, the higher value it represents in the pharmaceutical setting. An early-stage research project has a lower value due to the uncertainties and high risk of failing in one of the clinical development processes [35].

2.9 Implementation barriers of Open Innovation

Multiple factors are identified as barriers of Open Innovation implementation within the pharmaceutical industry. In accordance to the research questions for this study, the literature review presented in this section aims to elaborate on the different elements that arise when addressing the collaboration between the different actors within the pharmaceutical industry. These elements include barriers of IPR, adopting new R&D models, cultural and management barriers [8].

The following sections present an overview of the factors involved.

2.9.1 Appropriability issue, sunk costs and rent dissipation

The protection and flux of knowledge beyond the company boundaries are important factors to consider when evaluating the limitations of an effective Open Innovation implementation [1, 36]. Appropriability mechanisms include IPR, copyright, trademarks, industrial designs, utility models and human resource management practices [37, 38]. Appropriability can be understood as: *"the degree to which the returns from investments in R&D accrue to the innovator or other market participants"* [39].

Following this definition, a related term used to determine the ability for the company to appropriate future inventions, spawned by its current technology, is the *"generative appropriability"*, also defined as *"firm's effectiveness in capturing the greatest share of future inventions*" [40].

Big pharmaceutical companies are mitigating the appropriability issue when relying solely on outside-in adaptions of Open Innovation models. E.g. in-licensing projects at late-stage clinical development projects, when filling pipeline gaps, and in general managing a strong IPR protection by exclusively having an internalization of projects, compounds and knowledge. To protect core knowledge and inventions from being diluted and exploited by collaboration partners when adopting Open Innovation a tight appropriability regime is often implemented [1, 30, 41]. A tight appropriability regime strategy is seen when companies ensure strong patent protection around key inventions and knowledge, which lowers the risk for collaboration partners acting opportunistically and stealing the knowledge and inventions, when implementing adaptations of Open Innovation collaborations [1, 41, 42]. A trade-off and opportunity costs occur when companies implement an Open Innovation strategy with a "tight" appropriability, thereby limiting the potential collaborations significantly [30].

The sunk costs related to drug development within the pharmaceutical industry play an important role in the decision of adopting Open Innovation platforms. Due to the big investments needed in order to conduct drug discovery and drug development, top management might be concerned about jeopardizing the profitability and return on investments when entering an Open Innovation collaboration with external partners. E.g. inside-out models of Open Innovation where internal knowledge is externalized [36, 43].

Additionally, the rent dissipation referred to as *"loss of market share (…) by increased market competition generated from technology out-licensing"* [44], can affect the tendency of a company engaging in Open Innovation activities. Thus, rent dissipation would generate a negative impact on the company involved in collaborations that could arise from Open Innovation approaches.

2.9.2 *Not Invented here (NIH) syndrome and Not-sold-here (NSH) syndrome*

The NIH syndrome is an internal cultural barrier towards external sources of knowledge and inventions, often seen in outside-in models of Open Innovation. NIH was defined by Katz *et al.*, 1982 as *"the*

tendency of a project group of stable composition to believe it possesses a monopoly of knowledge in its field, which leads it to reject new ideas from outsiders to the likely detriment of its performance" [45]. Outsourcing of R&D activities can be seen as a threat for internal employees who seek to promote in-house projects and capabilities [46]. This can result in a reluctance for adopting and implementing Open Innovation models. In a recent study, the negative impact was observed on the success of projects externally incorporated including Open Innovation collaborations [47]. The NIH syndrome is related to the concept of outside-in innovation, where external knowledge and projects are internalized into the company.

The NSH syndrome relates to the NIH syndrome and refers to the external exploitation of internal assets [48]. NSH results are the inability to exploit proprietary assets that are on hold or discontinued. Employees adopting a NSH preference, prefer not to commercialize certain assets at all rather than having the commercialization done by other parties through, for instance, licensing agreements [46, 49]. NSH is an outcome of inside-out Open Innovation models, where discontinued projects and projects outside the core of the company are externalized.

2.9.3 Familiarity, awareness and understanding of Open Innovation initiatives

As presented in section 2.5 and 2.6, Open Innovation adaptations are very diverse. Thus, there is not a clear understanding of how the benefits can be tailored and exploited according to its specific needs within the pharmaceutical industry. A successful implementation of Open Innovation strategies for pharmaceutical companies, familiarity and awareness of the operational framework are required [50]. In addition, there can be a distrust towards not properly understood initiatives which represents a barrier towards a successful implementation of Open Innovation activities.

2.10 Barriers of engaging in Open Innovation platforms

When engaging at collaboration within Open Innovation, trust becomes a critical factor to achieve an efficient implementation [51]. Openness towards external knowledge represents a risk of appropriation from opportunistic actors. Therefore, the lack of trust represents an impediment to the implementation of Open Innovation platforms.

As presented in section 2.2, collaborations between pharmaceutical companies and biotech start-ups can imply a concern towards lack of internal control and ownership of projects. Such elements include autonomy, trust, vigilance and other unspecified aspects intrinsic to the collaboration [52]. A mentality change within company culture and top management are needed in order to implement Open Innovation as a core part of the business strategy. This includes a change from traditional top-down management to a more entrepreneurial and collaborative mindset when implementing a collaboration strategy [8].

These barriers of Open Innovation presented are incorporated in the concerns of collaborating with a pharmaceutical company within an Open Innovation setting. Additional implementation and engagement barriers might be present for pharmaceutical companies and biotech start-ups, which will be part of the analysis of the data collection for this study.

3. Methodology

The following sections include an overview of the philosophy of science, the argumentation of the key literature and methodology chosen for this research. Additionally, the bias, limitations and reservations for this research will be presented including an argumentation validation and generalization of this study.

3.1 Philosophy of Science

Saunders *et al.*, 2009 presents four different philosophical perspectives when conducting research: positivism, realism, pragmatism and interpretivism in *Research Methods for Business Students* [53]. The assumptions related to the different philosophical perspectives are important, as they define the way research and interpretation of the data collected are conducted. When reflecting upon the background of authors of this research, as biotechnologist, and the fact, that this research is conducted as part of an internship at LEO Pharma's headquarters in Ballerup, the bias and limitations of this study cannot be neglected. Thus, a value-free interpretation of the Open Innovation collaboration cannot be justified, as the authors will take part in the social interactions in the data collection and interpretation. The analysis and interpretation of the data will be affected by the author's background, motivation and beliefs and cannot be stated as value-free. Thus, the interpretivism stance is chosen as the philosophical perspectives for this study. Interpretivism acknowledges that we as humans act as social actors on the basis of our surroundings and the truth is often socially constructed. Interactions and variability play a key role when interpreting complex topic, such as Open Innovation collaborations within the pharmaceutical industry [53]. The interpretivist perspective strongly correlates with hermeneutics and social constructivism, as social constructivism is defined as a research philosophy *"that views the social world as being socially constructed"* [54] and *"Subjectivism holds that social phenomena are created from the perception and consequent actions of those social actors concerned with their existence" [53]*. Interpretivism acknowledges that our understanding of the world is subject to the nature of the researcher and generic patterns should not be concluded based on this research. Thus, the truth is determined by the socially constructed acceptance of elements such as Open Innovation. Interpretivism is often chosen as the philosophical perspective within the research area of business and management concepts, including topics such as collaboration and openness [53]. This is the

case since social science studies the behavior of human beings. This behavior can to some extent be defined as how humans perceive things. Thus, interpretivism in relation to social constructivism is chosen as the research stance for this study.

The authors acknowledge that through the perspective of interpretivism and social constructivism, we should not draw generic patterns on the basis of this research. Furthermore, it is unlikely to reproduce this research with identical findings and the results of this research are not to be interpreted as objective. As stated, this research is conducted as a part of an internship at LEO Pharma Open Innovation from February until May 2020. This position has provided the authors of this study with valuable insights and competent feedback in regard to the general understanding of Open Innovation within the pharmaceutical industry.

Criticism of interpretivism includes the bias occurring when conducting unstructured interviews and by interacting with the interviewees. Thus, data collection is conducted in a subjective manner. Interpretivism is used to gain insights into complex topics and findings and should not be generalized. Opposite to positivism, interpretivism does not exploit the validity and implications of validated hypothesis. By relying on a truth based on socially constructed acceptance, new findings might be hampered and neglected until the general perception is changed. Thus, by utilizing an interpretivism stance for this study, a deep insight within Open Innovation is expected as an outcome. However, new findings to in opposition to the general acceptance are not expected. Thus, the philosophical stance of interpretivism limits the outcome of this research to providing additional insights to already accepted theories, in this case, Open Innovation.

The following section will include reflections upon the choice of key literature, the methods utilized in this research, including bias and limitations.

3.2 Selection of key literature and theoretical framework

This study will foremost draw to two sources: Henry Chesbrough's general introduction of Open Innovation and Alexander Schuhmacher's perception and implementation of Open Innovation within a pharmaceutical setting.

Chesbrough's textbook: *Open Innovation: The New Imperative for Creating and Profiting from Technology* from 2003 is chosen as one of the key contributions and theoretical frameworks for this study, as it is highly cited and thus generally well respected [55]. Chesbrough's framework presents a new infrastructure on how to

exploit knowledge from external collaboration by utilizing Open Innovation. Open Innovation is facilitating a more efficient knowledge exchange, based on formal collaborations between companies. Chesbrough's conceptual framework defines Open Innovation and presents the value measurements in terms of value creation and value capture in *Value Creation and Value Capture in Open Innovation* from 2018 [35] which is included in the theoretical framework of this study. However, Chesbrough has received critique for claiming this new framework of Open Innovation which facilitates a paradigm shift between Closed- and Open Innovation [56]. The need for companies to exploit external collaboration in order to innovate was already proposed in 1985 [57].

Chesbrough's conceptual framework of Open Innovation does not include specific implementations and adoptions within a pharmaceutical setting. Thus, Chesbrough's theory is coupled with Alexander Schuhmacher's overview of the implementation of Open Innovation within the pharmaceutical industry: *Value Creation in the Pharmaceutical Industry: The Critical Path to Innovation* from 2016 [20]. Schuhmacher's textbook presents different adaptations of Open Innovation models within the pharmaceutical industry, which the authors are investigating in this study. Thus, we find Schuhmacher's work very relevant for this research coupled with Chesbrough's generic framework.

However, the authors of this study are aware of the fact that there is a big gap between the academic qualities and acceptance of the two contributions from Chesbrough and Schuhmacher. But we do believe the fit of Schuhmacher's research to be equally important to the quality and acceptance for the research [55]. The authors of this research acknowledge that Schuhmacher's insights will provide knowledge to this study that we otherwise would not have been able to obtain. We take the necessary reservations regarding the potential lack of general acceptance of Schuhmacher's work by validating the statements with original literature and in combination with contributions from other well-respected authors such as Gassmann, Laursen and Dahlander [1, 24, 30]. However, despite the significant difference between the academic acceptance of the contributions from Chesbrough and Schuhmacher, it is noteworthy to mention the fact, that Schuhmacher's work is relatively new and less generic than Chesbrough's. This becomes then the case as Schuhmacher's work is tailored specifically towards the pharmaceutical industry. Thus, the number of citations from the contributions should not be directly compared.

3.3 Research approach

The aim of this study is to understand the perception and implementation level of Open Innovation within the pharmaceutical industry. In order to answer the research questions, an inductive or deductive research approach can be chosen. The deductive approach is used within the natural sciences and it generally utilizes quantitative data by verifying or falsifying a hypothesis [58]. The deductive approach within natural sciences is often conducted with a positivistic research philosophy [53, 58]. In opposition to this, the inductive approach is characterized as more explorative and seeks to develop a theory on the basis of the data collected, often utilizing qualitative methods such as interviews [53]. However, as reflected in section 3.1, the philosophical perspectives of this study are mainly based on interpretivism and social constructivism, which acknowledge the bias and subject nature of this topic and the author's setting within this research [53, 54].

The research approach for this study will mainly rely on a deductive approach, including both primary and secondary data collection by web scraping and qualitative methods, which will be presented in the following sections [53, 59]. The theoretical framework presented in section 2.2, 2.5, 2.6 and discussed in 3.2, introduces the general concepts of Open Innovation. Additionally, the incentives of implementing openness and collaborations within the pharmaceutical industry, biotech start-ups and academia are presented. Based on these concepts, a hypothesis consisting of a general acceptance of the benefits and attractiveness of Open Innovation collaboration within the pharmaceutical industry are deducted in this study.

For the purpose of this study, collaborations with academia or other pharmaceutical companies have been excluded. The reasoning for this approach is introduced in section 1.2. The factors justifying this approach include the presumed attractiveness for pharmaceutical companies to collaborate with biotech start-ups within formal Open Innovation models [7, 11].

3.3.1 Web scraping

In order to answer the research question; *"How does the current landscape of Open Innovation exploit the value of drug research within the 100 biggest pharmaceutical companies worldwide?"*, a web scraping approach is chosen. This web scraping data collection is conceived as secondary data collection based on publicly available descriptive information [60]. Additionally, this approach is interesting from an academic

perspective, since the authors observed an important lack of research within the field of perception and implementation of current Open Innovation initiatives within the pharmaceutical industry.

As introduced in section 2.2, the authors intend to explore digital platforms that enable a formal collaboration between pharmaceutical companies and biotech start-ups. The aim is to specifically look for website domains that can work independently, to a certain degree, from the organization's traditional means for the establishment of collaborations, i. e. general contact information.

Due to the time limitations of this research and the limitation of resources, programming including comprehensive HTML web scraping of the entire internet for all pharmaceutical companies and biotech start-ups is not possible [60]. Consequently, the secondary data collection is conducted manually by the authors without making use of programming software. The key words selected for the web scraping include "Open Innovation", "Collaboration", "Openness" and "Compound". These keywords are selected on the basis of the key literature included in this study and the Open Innovation classification presented [2, 20, 33, 34]. It is believed, that a thorough search for the chosen keywords, related to Open Innovation within pharmaceutical companies' webpages, annual reports and publicly available material, will display the perception and implementation level of Open Innovation within the key players of the pharmaceutical industry. Due to time limitations of the research, all pharmaceutical company and collaboration cannot be included in this study. Therefore, the top 100 pharmaceutical companies worldwide based on revenue sales in 2018 are chosen as the target group. Evaluate Ltd has been used to identify these companies [61]. The entire company list is presented in *Appendix 1*. This target group is chosen, as it represents the key players of the pharmaceutical industry. This fasct is emphasized as the 10 biggest pharmaceutical companies account for 41,7% of the total market share within the pharmaceutical industry [62]. As presented in section 3.4.1, the necessary reservations including the bias and limitation of this research method and approach are taken. A validation of the data collected is included in section 3.5.

3.3.2 Semi-structured interviews

In addition to the secondary data collection described in section 3.3.1, a more exploratory method is included as a key element of this research, by conducting semi-structured interviews with biotech start-ups companies [59, 63]. Semi-structured interviews are a common qualitative methodology when

investigating complex topics such as the perception of Open Innovation within a pharmaceutical setting. The data collected in a semi-structured interview is classified as primary data [53]. This approach allows the authors of this study to strengthen the validity of the findings, by aligning and triangulating the perception of Open Innovation insights identified in the two different data collections.

The semi-structured interviews are preferred for this research, as they provide a balanced explorative approach with open-ended questions, including a clear descriptive structure for the interview [59]. Thereafter, semi-structured interviews are chosen instead of the structured or unstructured interview approach. Semi-structured interviews enable the authors to understand the Open Innovation perception within the pharmaceutical and biotech setting, which enables an alignment of the results to some degree [53]. An interview guide for the semi-structured interview is designed, including the interview questions, probes and definitions of the elements included in the interviews [53, 59, 64].

The target group for this research is key stakeholders within the Open Innovation collaboration. This includes top management from big pharmaceutical companies, biotech start-ups and academia. For this study, we choose to focus on the biotech start-up companies and their concerns when initiating a collaboration based Open Innovation with a big international pharmaceutical company. The relevance for contacting biotech start-up companies is presented in section 1.2. Chief executive officers (CEO) from biotech start-up companies are selected as the target group, as they are potential key stakeholders of Open Innovation collaboration within the pharmaceutical industry. This primary data collection will be compared with the secondary data collection of web scraping described in section 3.3.1.

The biotech start-ups candidates for the interview, were identified through the Biotech Gate database, which entails more than 56.000 companies [65]. The database was filtered for European biotech start-ups with 30 full-time employees or less. Out of these, 50 biotech start-ups were selected as the target group by random selection. Based on an e-mail request for these 50 companies, seven positive replies were obtained and interviews were conducted with such candidates. Due to the limiting amount of positive answers and the time limitations of this study, we asked the seven participants for additional contacts within their network. Based on these recommendations, we conducted three additional interviews with biotech start-up companies. Limitations and bias of this method and research approach are described in 3.4.2.

The semi-structured interview was conducted to capture the perception of Open Innovation. In addition to the open-ended questions, the interview guide included predefined concerns for the participants to rank [64]. These predefined concerns were selected based on the proposed classifications and theoretical frameworks of Open Innovation within the pharmaceutical industry presented in section 2.7 [33, 34]. In addition, the findings from the web scraping data collection, including the "Highly relevant" Open Innovation platforms identified, were incorporated in the predefined concerns.

3.3.3 Predefined concerns for the semi-structured interviews

As mentioned in section 2.7, different frameworks to classify Open Innovation models have been presented. Based on the criteria established by Nilsson *et al.*, 2018 [33] and the literature review conducted for this study, the authors combined the level of openness with the identified patterns from the web scraping exercise, to select the predefined concerns for the semi-structured interviews.

The interviewed CEO's from European start-up companies were asked to rank the following elements from 1 to 5 when reflecting upon their biggest concern when collaborating with a big pharmaceutical company:

- Not having ownership of the data generated from the collaboration
- Business obligations (Exclusivity rights): The big pharmaceutical company gets the first right to negotiate when initiating a collaboration.
- Limited access to the collaboration: Review and approval upon evaluation of business case/project relevance needed.
- Not having "Open science": Non-disclosure of relevant science and scientific projects from the big pharmaceutical company that is of relevance to the biotech start-up
- Legal transparency: Upfront access to the contract or agreement with the collaboration criteria stated.

The duration of the interviews was scheduled for a duration of 10 min each. The interview was recorded and transcribed by the use of the software otter.ai on the author's smartphones. The transcripts were revised for possible automatization problems. The predefined concerns which the biotech start-up companies were asked to rank in-between did not include any mentioning of specific company names. Thus, they were designed as generic and not referring to compound or assay-specific platforms.

3.4 Method limitations and criticism

As presented in section 3.1, the philosophy of science for the research is from an interpretivism stance, by acknowledging the bias and limitations of this study. The authors of this study were operating as project interns at the headquarter of LEO Pharma for the duration of this study. As interns at LEO Pharma's Open Innovation team, the position provided the authors with valuable insights into the industrial perception of Open Innovation but bias the results of this study. However, this study approach has not been conducted from a company perspective, but from an academic point of view only, to map out the general perception of Open Innovation among the key players of the pharmaceutical industry including LEO Pharma.

3.4.1 Limitations and criticism of data scraping

The authors chose to conduct a web scraping exercise to identify Open Innovation platforms from the 100 biggest pharmaceutical companies worldwide based on their revenue sales in 2018, see *Appendix 1*[61]. The data scraping is normally conducted as a comprehensive HTML web scraping of the entire internet, by making use of programming software [60]. This method was chosen as it provides the researchers of this study with a deep insight into the implementation level and overview of Open Innovation amongst pharmaceutical companies. Due to the time and resource limitations of this research, it was chosen to conduct the web scraping by conducting common internet searching as presented in section 3.3.1. Thus, reflecting the start-up perspective when searching for Open Innovation platforms. This strongly limits the findings and possible conclusions of the data collection exercise. The results display the implementation level of the key players within the pharmaceutical industry. However, it is expected that the authors did not capture all Open Innovation initiatives, as the authors conducted the web scraping without making use of software tools. Of those 100 companies identified as the target group, multiple pharmaceutical companies did not have a publicly available website with content in English.

However, it is important to notice that the concept of Open Innovation builds upon openness and collaboration. From a biotech start-up perspective, one can argue that platforms from pharmaceutical companies need to be publicly available, in order for biotech start-ups to engage and initiate a collaboration. There are a strong bias and limitation of the chosen keywords for the web scraping exercise. It is expected, that

different keywords would result in different findings than presented in section 4.3.

3.4.2 Limitations and criticism of semi-structured interviews

The interpretivism stance of this study often utilizes explorative methods such as long semi-structured or unstructured interviews with a duration on more than 60 minutes each, to make sure the topic is discussed and answered until saturation of insights is reached [53, 63]. However, as the purpose of this study is to understand the perception of Open Innovation including the barriers and concerns related to collaboration, the authors chose to incorporate predefined concerns for the semi-structured interviews. The target group was decided to consist of CEOs from biotech start-up companies, as they are more abundant and thus more accessible than CEOs of big pharmaceutical companies. The CEOs of the biotech start-ups were asked to rank predefined concerns and explain their choice of ranking. [53, 63]. This approach facilitated an alignment on the ranked concerns between the participants in the interviews.

The participants for this study were selected through a biotech start-up database, which includes more than 56.000 companies [65]. We filtered for European based companies with less than 30 full-time employees. Based on this, the authors contacted 50 biotech start-ups through E-mail by introducing the research and the scope of the semi-structured interviews. As described in section 3.3.2, seven biotech start-ups accepted the interview with a duration of 10 min each. Additionally, references from the seven participants facilitated three additional interviews. All the participants were CEOs from the biotech start-ups. Out of the ten interviewed companies, seven were Danish, two Spanish and one Finnish.

The necessary reservations are taken for the results obtained and are emphasized for this research approach in the following. The sample size of 10 participants is too small to generalize the findings and no extrapolation of the perception of Open Innovation collaborations should be drawn. This correlates with the interpretivist stance of this research. Only European based biotech start-ups were included in this research, which limits the geographical findings to only European based biotech start-ups with less than 30 full-time employees. As Denmark accounted for seven out of the ten participants, the Danish concerns and insights are over-represented in the results, as seven out of ten biotech start-up companies are not based out of Denmark in general, which bias the findings obtained. A reason why seven Danish biotech start-ups agreed to participate in this research might be due to the fact that the authors are master students at Copenhagen Business

School. Alternatively, Danish biotech start-ups might be more positive towards Open Innovation and thus more prone to participate in this research. These might be reasons for the many positive Danish replies upon participating within this research. A different approach could have been calling the randomized target group by phone without prior acceptance. This would have eliminated the bias, that potentially only the biotech start-ups interested in Open Innovation accepted participation in this research.

Additionally, due to the fact, that we only received seven positive answers from the 50 randomly selected biotech start-ups, we relied on receiving additional participants based on references from the interviewees' network. This approach added three additional interviews to the data obtained. This approach was chosen due to the time limitations of the research. The bias and limitation of relying on additional participants within the same network might result in similar perceptions and concerns regarding Open Innovation platforms.

As described in section 3.3.2, the CEOs of the biotech start-ups were asked to rank the predefined five concerns presented. This survey-like approach was chosen despite belonging to the more structured type of interviews. The complex nature of the topic of this research might suggest an unstructured interview as the preferred qualitative methodology. However, when predefining and displaying the questions to the participant, the CEOs were forced to understand the different concerns in detail, in order to rank the different concerns among each other. In order to obtain a deeper understanding and facilitating a more explorative approach to this complex topic, follow up questions were prepared in the interview guide with an open-ended approach [53, 64].

Multiple of the CEOs acknowledged, that the concerns would be very specific, depending on each case of collaboration and type of information flux. They would have preferred more context in terms of the specific collaboration when ranking the concerns. In addition, a concern that was not part of the five predefined questions was the element of trust. The authors realized this lack when analyzing the first interviews conducted. However, in order to align and compare the different results obtained, the authors chose to utilize the original interview guide throughout the remaining interviews. Additional open-ended questions were added at the end of each interview in order to capture the trust concern when small biotech start-ups are to collaborate with a big pharmaceutical company within Open Innovation.

Due to the time limitations of this study and the lack of positive responses from the distributed E-mails, the final sample size of

ten interviews impacts heavily the bias of the results obtained. The authors of this research take the necessary reservations of the data collected and acknowledge the data should not be generalized. However, the findings of the perceived concerns and the open-ended questions related to Open Innovation, did in general provide the authors of this study deep insights into the topic. The authors would not have been able to obtain these insights from the web scraping method only, due to the complexity of this research topic.

3.5 Data validation and justification

The authors of this study acknowledge that the methodologies utilized, and data collection conducted in this research should be perceived with cautiousness, as described in section 3.4.1 and 3.4.2. However, despite acknowledging the necessary reservation from bias and limitations presented, we believe the data is valid for the purpose of this exercise. By utilizing two different methodologies as the semi-structured interviews and web scraping data collection, a triangulation of data collection is conducted, which strengthens the reliability of the data obtained.

In order to strengthen the validation of the data collected by the web scraping approach, the data collected and presented in section 4.1 and 4.2 were aligned with industry experts. Niclas Nilsson, Head of LEO Pharma Open Innovation and Helen Frost, Liaison Scientist at LEO Pharma Open Innovation were asked to validate the findings. They were asked based on their general expertise and insights within the Open Innovation landscape of pharmaceutical industry. Niclas Nilsson states that: *"The findings of this research are indeed in line with our expectations of the general implementation and perception of Open Innovation within the pharmaceutical industry*". In addition, Helen Frost added: *"Although the pharmaceutical Open Innovation field may be perceived differently by different users, and is evolving, the data gathered and presented here align with the picture of the industry as I have experienced it in recent years".*

The perception and implementation level of Open Innovation within the pharmaceutical industry captured by this data collection is used to bolster the discussion on how Open Innovation is currently utilized within the pharmaceutical industry. Additionally, the data collected will be analyzed and interpreted, in order to compare the theoretical benefits of Open Innovation with the practical industry setting. Therefore, the authors will evaluate to what extent the perspectives from biotech start-ups resonate with the openness that is being pursued in the pharmaceutical industry.

4. Results & Analysis

In this section, the results obtained from the web scraping and the semi-structured interviews are presented.

First, results from the web scraping were categorized according to the criteria presented in section 4.1. Thereafter, each of the identified platforms adopting compound specific collaboration of Open Innovation were analyzed extensively. Finally, the insights obtained from the semi-structured interviews were correlated with the Open Innovation platforms identified from the top 100 pharmaceutical companies.

4.1 Categorization of Open Innovation platforms

The Open Innovation landscape was identified, based on Schuhmacher's framework of Open Innovation models presented in section 2.5 and 2.6.

The authors ranked the platforms strictly related to compound research from a biotech start-up perspective, considering factors such as attractiveness, visibility and openness. This compound approach was chosen, as the IPR and specific compound properties are the most vital assets within the pharmaceutical industry. When evaluating Open Innovation initiatives within the pharmaceutical industries, the platforms established upon compound research are categorized as the most attractive to biotech start-ups.

The authors focused on the platforms that specifically aimed to accelerate innovation in drug research. Thus, leading to drug discovery or drug characterization, which ultimately contributes to value creation for the actors involved.

This research aimed to identify the Open Innovation platforms facilitating a formal exchange of assets between a biotech start-up and the pharmaceutical company for collaboration purposes. Therefore, several initiatives were excluded. These include grant funding, venture capital, incubators, hubs, hackathons, facility sharing, case competitions, partnership programs, crowdsourcing and submission of research proposals, which were not specifically linked to the exchange of compounds. Thus, these types of initiatives were not classified as highly relevant Open Innovation adaptation for the purpose of this research.

The three assessment categories chosen are listed below and characterized in *Table 3*.

"Low" relevance for biotech start-ups: No information about Open Innovation found or a brief mentioning of Open Innovation

without any formal collaboration platform available.

"Medium" relevance for biotech start-ups: Formal Open Innovation platform established based on compound collaboration with some information disclosed. The platform facilitates collaboration with academia and/or biotech start-ups to some degree but does not facilitate a formal engagement process for collaboration.

"High" relevance for biotech start-ups: Platform available based on compound/assets collaboration e.g. drug screening and compound sharing with a high degree of information disclosed on the collaboration process. A formal agreement or terms and conditions are available. Information regarding the relevant assets or assays is disclosed.

4.2 Key stakeholder identification

The identified Open Innovation platforms are described in the following section according to the available information. In addition to the limitations of the research mentioned in section 3.4.1, the descriptions of the platforms do not include information that is obtained after login or further acceptance within the collaboration process.

Based on the criteria mentioned in section 4.1, the platforms were identified and analyzed. The platforms identified as highly relevant for biotech start-ups are listed in *Table 4*. The full list of pharmaceutical companies including their activities within Open Innovation is presented in *Appendix 1*.

Out of the 100 pharmaceutical companies analyzed, the authors identified a total of 143 different website domains leading to potential Open Innovation activities. Seven were identified as highly relevant, 48 as medium relevant and 88 as low relevant according to the categorization presented in section 4.1 and *Table 3*. Thus, this study will mainly focus on compound specific adaptations of Open Innovation when evaluating the "highly relevant" platforms as they create the biggest business value for biotech start-ups.

As presented in section 2.3, the outside-in model has been adopted more widely than the inside-out model within the

Table 3. Categorization overview of the different Open Innovation platforms according the selected criteria. Low relevance corresponds to websites in which Open Innovation is mentioned to a limited extend, without a formal platform created or where no information is found. Medium relevance corresponds to platforms identified where no further information on the collaboration process is detailed. High relevance corresponds to platforms with well-defined information on the characteristics mentioned before.

	OI mentioned	Platform available	Process disclosed
Low	-/x	-	-
Medium	x	x	-
High	x	x	x

pharmaceutical industry [25, 26]. This is likely due to appropriability issues, which have been presented in 2.9. The majority of inside-out adaptations of Open Innovation within the pharmaceutical industry are characterized as out-licensing, presented in section 2.5. Reasons why inside-out implementations of the Open Innovation are less adopted, excluding out-licensing, are because they mainly facilitate scientific research. Thus, creating limited business value for external partners such as biotech start-ups.

As presented in section 2.5 and 2.6, several adaptations of Open Innovation initiatives have been proposed by Schuhmacher. Thus, it is possible to correlate the current landscape identified among the key pharmaceutical players corresponding to the common approaches mentioned in section 2.5 and 2.6. Therefore, it is possible to corroborate the landscape identified among the key pharmaceutical players corresponding to the common approaches mentioned in the theoretical framework.

In the following, the seven compound specific Open Innovation platforms of high relevance to biotech start-ups are presented.

Sanofi, Innovatewith. Sanofi's Open Innovation platform offers a specialized team divided according to the research area of interest and aims to create partnerships through submission forms. The site is managed by yet2. This third party is responsible for reviewing the applications on behalf of Sanofi.

The "Innovatewith"-platform indicates the clinical area of interest, as well as the type of compound that are of interest to Sanofi. It is possible to submit a specific solution to one of the specific problems addressed on the webpage. The proposal is reviewed and if found appealing, further contact is initiated in order to start a potential collaboration.

Legal disclaimers containing the submission terms and conditions are available after a first registration process. Such information is available prior to submission of any information regarding the compound [66].

AbbVie, Open Innovation Portal. Activities include a compound sharing toolbox, based on a library of compounds, providing free shipment upon request of submission. Out of the 63 compounds available on the platform, a maximum of 20 compounds can be requested. The compounds are characterized and can be utilized for preclinical research.

After selecting the compounds, the user is required to create an account, sign a Material Transfer Agreements (MTA) and to submit a non-confidential description of how the compounds are intended to be used [67].

AstraZeneca, Openinovation.astrazeneca. The Open Innovation platform is divided into

multiple collaboration opportunities including; compound sharing, proposal submission, molecule testing on assays and additional delivery/clinical opportunities.

Similar to AbbVie's "Open Innovation Portal", the preclinical toolbox from AstraZeneca offers the possibility to request a maximum of two to three compounds out of 51 available compounds from multiple therapeutic areas. After the submission of a non-confidential proposal, a review is conducted. If accepted, an MTA is signed in order to further progress on the project proposal. Reporting is required within six months of study completion.

The platform includes a drug target validation section, which enables participants to do compounds screening throughout proprietary libraries. If results are found relevant, further collaboration or other potential rewards such as publications and royalties (if IPR licensed) are mentioned on the webpage [68].

Novo Nordisk, Novo Nordisk Compound Sharing. Novo Nordisk's Open Innovation compound platform offers participants access to peptides and antibodies at a preclinical stage. The compound library includes 17 characterized assets. Ownership of the data is retained by the applicant and discussion of future collaboration is encouraged. All the relevant information regarding the assets is disclosed in advance. The process requires a non-confidentially purpose description including terms and conditions, but no reporting is required [69].

Boehringer Ingelheim, OpnMe. The OpnMe Open Innovation is a compound sharing platform, offering a total of 46 compounds. The compound related activities are divided into the following categories:

- Molecules for order:
  Preassembly for early research purposes. The compounds are sent after registration and ownership of the data is retained by the applicant.
- Molecules for collaboration:
  Compounds from ongoing drug discovery projects, which can be accessed upon submission of collaboration proposal. If approved, the further collaboration is discussed.

Login is required to assess further application process [70].

Merck KGaA, Biopharma Open Innovation Portal. Merck's Open Innovation platforms include multiple activities, including "open compound sourcing", which allows potential partners to submit compounds proposals. Accepted compounds are included in a High-Throughput Screening library for the identification of new therapeutic compounds. Disclosure of the chemical structure of the compound is required for an in-silico screening before the laboratory assays are initiated. Signing of a

Participation and Material Supply Agreement (P&MSA) is required and information regarding the next steps is provided if accepted.

Merck's Open Innovation platform includes a compound sharing system for research. "Biopharma Mini Library" provides access for scientists and researchers to a library of former research and development compounds. If the application is accepted, the next step of the collaboration is signing of a MTA [71].

LEO Pharma, LEO Pharma Open Innovation. The platform is based on providing specialized assays exclusively within dermatology and skin inflammation. IPR and data ownership are retained by the applicant. If the compounds are found interesting, further collaboration might be initiated. The mechanisms of relevant assays are publicly disclosed as well as the collaboration agreement. After signing the agreement, vials are provided to participants, in order to ship molecules free of charge for testing. Once testing is conducted, the data generated is disclosed to the participant. No description of the research purpose or molecule characteristics is required from the participants.

As part of the Open Innovation platform, an Artificial Intelligence (AI)-driven *in silico* testing of molecules is offered. This enables LEO Pharma to screen the proposal without requiring the physical compounds [72].

4.3 Interview analysis

In order to understand how biotech start-ups perceive the Open Innovation platforms from the pharmaceutical companies, the authors conducted ten semi-structured interviews. The limitations and bias of these interviews are discussed in section 3.4.2. Raking of predefined collaboration concerns, as mentioned in section 3.3.3., was a main part of the interview. The results are summarized in *Figure 5*.

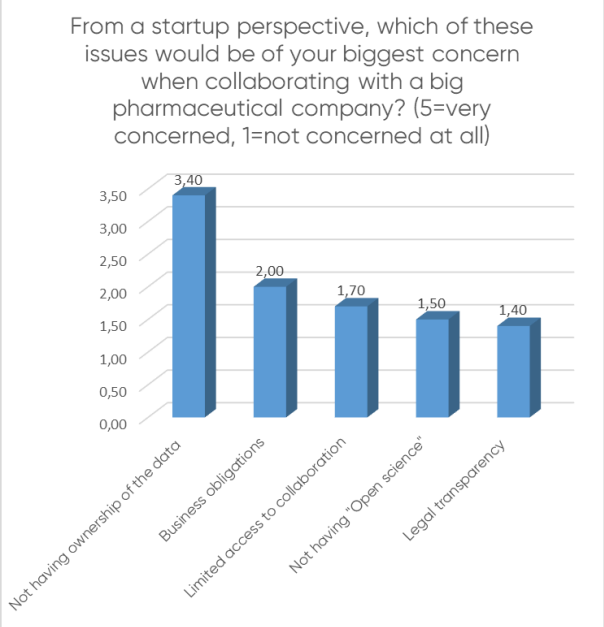

Figure 5: Average ranking of pre-defined collaboration concerns from the CEOs of biotech start-ups. The sample size of the study corresponds to 10 interviewed CEOs of biotech start-ups. The participants were asked to rank the indicated from 1 to 5.

Despite taking the necessary reservations stated in section 3.4.2 of bias and limitations for the semi-structured interviews, the overall ranking of the concerns by biotech start-ups indicates, that ownership of the data is the biggest concern.

Interview quotes:

In order to understand the perception of Open Innovation collaborations within the pharmaceutical industry, the authors asked the CEOs of the biotech start-ups to explain their choice of ranking. Selected quotes for the specific predefined concerns are presented in the following. The full transcript of the ten interviews can be accessed in the complementary material of this project [73].

Data ownership:

" You don't want to be a service provider. So, you really want to get a lot of value out of the collaboration. And typically, the value is in some sort of IP, which you can then leverage to raise more funds or to develop commercially." ***– CEO of Cirqle Biomedical***

"we would never go into a collaboration, without having mutual ownership of that data, that's the whole point." ***– CEO of Clinical Microbiomics***

"if it's for pure development purposes, I would say, it's very important to have the ownership and maybe full ownership of the data." - ***CEO of PrOxi Biotech***

"If we collaborate with Big Pharma, and they pay the R&D activities they would also have ownership of foreground data and foreground IP. But if we pay the R&D activities, we should have the ownership and if we pay them shared it would be split. Also, I mean one thing is ownership of the data and another thing is to get ownership of the IP." – ***CEO of MonTa Bioscience***

The insights obtained from the interviews reveal that ownership of the compound and the data are perceived as the most valuable elements for the biotech start-ups. As pointed out in the quotes, data ownership does not necessarily translate into IPR ownership. IPR is obtained if the invention resulted from the collaboration patented by one of the parties. Therefore, the data generated can be retained and exploited without necessarily being protected by patent protection.

According to these findings, a collaboration is not attractive for biotech start-ups, unless they can retain total or partial ownership of that data. The importance of compound and data ownership correlates with the classification presented in section 4.1 and 4.2. Thus, compound-related platforms of Open Innovation where participants retain

total or partial ownership of that data for the biotech start-ups are perceived as the most attractive initiatives.

Legal transparency:

> *"That will depend on how good your lawyers are" – **CEO of CreatSens***
>
> *"the legal transparency, that's most important so I put one, I mean it would be it would be a definite showstopper not to have that fully disclosed upfront." – **CEO of Clinical Microbiomics***
>
> *"the legal transparency is for sure like the biggest concern I would have. I mean, if that's not in place, I would never enter into a collaboration with a big pharma company. Because ensuring your rights, and know that you have is key, otherwise they're going to steal science for the data from you and develop it themselves. I mean it's everything basically before entering a partnership." – **CEO of PrOxi Biotech***
>
> *That's very critical. Okay, I would never go into the process if I don't have a complete overview of the legal process and how that's put together. **– CEO of MonTa Bioscience***

The condition of having the legal terms disclosed upfront seems to be of high importance according to the interviewed participants. As pointed out, it is important to consider how the legal process is established. This ensures that big pharmaceutical companies cannot compromise the success of the project if the collaboration does not continue. The legal terms can relate to the ownership of IPR.

As presented in section 2.10, this legal aspect correlates to the concept of trust. This includes the risk of appropriation and opportunistic behaviors, that could arise from conflicts in legal aspects of the contract; if one of the parties obtains more benefit than the other and it is not perceived as a "fair" deal. In other words, from these highlights, it is stressed how both parties need to address the issue of generative appropriability, explained in section 2.9.1. This is required in order to define a distribution of the value captured from the compound-based collaboration. As stated in section 2.2, biotech start-ups are often in lack of resources required to protect themselves in a legal conflict against big pharmaceutical companies. Hence, the response from the legal framework was expected. As presented in *Figure 5,* however, the legal transparency was not perceived as the most important concern for biotech start-ups.

Business obligations:

"Business obligation will tell us how honest the company we are going to work with is and how ready they are in front of you. So, I think that's a behavior that the pharmaceutical company has in front of you, and the power that they have over you. So that will rule the collaboration in the next years. So, for me, that would be the first concern because this negotiation and this kind of business obligations will tell you who is going to be the collaboration in the future." ***– CEO of CreatSens***

"business obligations; I don't see that as a big problem because it's all comes down to how you draw up the contract (…) It's good for you because you can show it to third parties; that could be in investors, or that could be other pharma companies to show them that someone is actually already interested in this.
(…) They'll still have to pay you something for that, because that has restricted you from going into a dialogue with other parties like potential customers, and so on. So, I think actually that if you play it right it can also be to your advantage. Of course, it can restrict you in some ways, but I really don't see this as a problem at all. I think it can be okay and it can make your case stronger, actually ***– CEO of PrOxi Biotech***

" So, if you have a pipeline of five different products (…) I would be happy to do that, because it would trigger other companies to also make partnerships." ***– CEO of MonTa Biosciences***

In the case of business obligations, we found that interviewed participants had more diverse opinions. As indicated, it can be perceived as a matter of attractiveness from the pharmaceutical company towards the biotech start-up, triggering by partnerships for other projects or because it can attract potential investors. However, observing *figure 5* business obligations are also perceived as a limiting factor for initiating a collaboration with a pharmaceutical company.

Access to the collaboration:

"the value (of participation) is to have access to the team that we collaborate with (…) That is a value that you cannot almost buy. So, when we started this project it was mainly to get into the network, get into the pharma and build out the network in there. And because that is something that we will have, not only in this project, but many years ahead. So, for me, that is the crucial thing, as I understand it." ***– CEO of COBO***
"that would be my first concern when engaging with pharma companies. That is

that they take a lot of your time" ***– CEO of ProteoDesign***

"I would say that is definitely not a concern at all to me. I understand that they want to evaluate it, and I think it can potentially also strengthen the collaboration and the platform. To take in projects that fit into the program, so I don't see that as a problem at all" ***– CEO of PrOxi Biotech***

Similarly, to the concern of business obligations, the access to the collaboration did also generate a variety of opinions among the candidates interviewed. From the quotes mentioned above, it can be noticed how the time constraints play an important role when evaluating the need for establishing a new collaboration with a pharmaceutical company.

Nevertheless, access to the team and the network is perceived as a valuable gain beyond the possibilities of the project. Overall it does not seem a big concern for biotech start-ups when initiating a collaboration with pharmaceutical companies.

Open Science:

"Otherwise you're developing something that you don't really know if you fit into that lifecycle (…) So it is difficult to map that and this would really restrict the success of any project. ***– CEO of PrOxi Biotech***

"honestly, we don't care about open science really, we know big companies are not very open which is annoying, but we know that" ***- Claus, CEO of Glycodisplay***

*"It would be great to have open access to all of that and of course the pharma company would also benefit from sharing what would be relevant to the collaboration so they would probably do that. "****– CEO of Clinical Microbiomics***

Open science is in this context related to disclosure of relevant scientific projects and scientific information owned by the pharmaceutical company. This aspect seemed to be of some concern to the interviewed candidates.

Open science is relevant for the biotech start-ups, as it provides the participants with insights into a potential fit between their project and the interest of the pharmaceutical company. Thus, the biotech start-up can exploit collaborations that are of interest in terms of assets or technologies, which are of interest to potential pharmaceutical company partners.

Hence, by having relevant science disclosed in advance can be an important factor for biotech start-ups when deciding whether to

initiate the collaboration. However, as observed from the interviewed candidates in *figure 5,* the importance of such concern might not be crucial compared to the other factors involved in the collaboration.

In addition, it was also stated some of the CEOs that disclosure of relevant scientific information, could be of mutual benefit to both actors. Interpreting this view, one could claim that both parties would benefit by having information disclosed in advance, to assess the potential of a mutual fit of the innovation in regard to the collaboration.

5. Discussion

In the previous sections, a theoretical background of the value proposition of Open Innovation is presented subsequently with the methodology, results and analysis of this research. These findings will provide the basis of the following discussion on Open Innovation implementation within the pharmaceutical industry.

5.1 Perception and adaptation of Open Innovation within the pharmaceutical industry

Based on the definition and value proposition of Open Innovation presented in section 2.2, an extensive implementation of Open Innovation within the pharmaceutical industry is expected. As presented in section 2.2, pharmaceutical companies can leverage on collaborations with external partners such as biotech start-ups, by advantaging on their smaller size and thus more agile company setting. Biotech start-ups are thought to be more innovative and incorporate a less strict management structure, which facilitates a company culture prone towards a more explorative approach [74]. These attributes can bolster the existing internal R&D processes of pharmaceutical companies, facilitating increased competitiveness and exchange of complementary knowledge [8]. However, biotech start-ups are often hampered by a lack of funding and expertise when conducting clinical trials and commercializing drugs on the market.

According to the findings of this research presented in section 4.1 and 4.2, only seven key players within the pharmaceutical industry are pursuing a compound specific adaptation of Open Innovation according to the definitions of Chesbrough, which relies on the flux of knowledge related to compound research and development. Reasons for this reluctant adoption are explained in the implementation barriers mentioned in section 2.9.

In most cases, the Open Innovation collaboration implemented from the pharmaceutical companies can be characterized as "Drug licensing" and "Outsourcing" based on Schuhmacher's framework presented in section 2.5 and 2.6. The platforms categorized with a low and medium relevance in this study, are in general adopting a licensing and out-sourcing implementation of Open Innovation. According to *Figure 3*, these activities represents a low degree of openness and do not exploit the full value proposition of Open Innovation. Out of the platforms corresponding to low and medium relevance, multiple restrictions and criteria are found as prerequisites for external

partners such as biotech start-ups to initiate the collaboration.

Among the seven platforms of high relevance found, denominators are identified to reveal strategic features prevalent in the current landscape of Open Innovation. All the platforms are utilizing their Open Innovation platform to filter potential external projects, which they otherwise might not have identified or would have required considerable time constrains using traditional scouting means. All the platforms identified is facilitating collaboration within specific therapeutic areas or technologies. Thus, the platforms identified are all characterized as biased Open Innovation according to section 2.4.

According to the medium-relevance platforms identified in sections 4.1 and 4.2, the authors identified 48 initiatives, which implies a low-risk adaptation of Open Innovation. Most of these platforms rely on the outside-in adaptation of Open Innovation, where knowledge is solely internalized, and data is owned by the pharmaceutical company. These in-flows of knowledge can be characterized as adaptations with a low-risk for big pharmaceutical companies. However, according to the findings in section 4.3, it might bring limited value for the participants such as biotech start-ups, as the ownership of data is often retained within the pharmaceutical company. This implementation of Open Innovation does not resonate with Chesbrough's definition of Open Innovation, where the full potential collaborations are exploited when the company borders are truly permeable, and the flux of knowledge is bi-directionally.

Five out of the seven platforms presented in section 4.2 originate from the 20 biggest companies worldwide based on revenue. A reason why the biggest companies might be more prone towards Open Innovation, are due to their size and brand attractiveness. The top 10 companies capture more than 41% of the total market share of the pharmaceutical industry [62]. Due to their big revenue, facilitation of initiatives such as Open Innovation is feasible, even though Open Innovation is not implemented as an essential part of the company's business model [62].

Open Innovation is a well-known initiative and represents, consequently, a highly sought-after branding value for the pharmaceutical companies. By implementing Open Innovation initiatives based on compounds outside of the core business or internally run assays, the big pharmaceutical companies can brand themselves facilitating Open Innovation at a relatively low cost with a low risk of knowledge flux. This allows the companies to expand their external scouting activities of external projects by facilitating an infrastructure with formal collaboration for

external partners such as biotech start-ups. This might lead to a gain of complementary knowledge and discoveries of compounds, in which companies would not have been able to capture otherwise. However, these platforms, based on compounds outside the core business of the pharmaceutical companies or already well-known assays, might not create attractiveness and value from the biotech start-up. This issue will be elaborated in section 5.5.

The biggest pharmaceutical companies can exploit their strong brand value in terms of collaborations within Open Innovation. This allows them to draw more attention and eventually benefit from their Open Innovation activities, compared to smaller and less well-known companies.

The majority of the "highly relevant" Open Innovation platforms are found within the biggest pharmaceutical companies. Thus, the authors do not expect to have left out a substantial number of platforms, by limiting the scope of this study to the 100 biggest companies worldwide.

5.2 Limited implementation of Open Innovation within the pharmaceutical industry

The reason for the reluctant implementation of Open Innovation within the pharmaceutical industry is likely due to the implementation barriers presented in section 2.9. One barrier to highlight is the appropriability issue. Appropriability is seen as a factor that governs the ability to profit from an innovation and strengthen the business model with IPR. Drug development is known to include tremendous sunk costs. As presented in section 2.9.1, top management of pharmaceutical companies is facing the risk of jeopardizing internal knowledge and IPR without ensuring a sufficient return on investment. This might be the case when initiating Open Innovation collaborations without ensuring protection of knowledge flux and IPR. This is believed to be the reason why licensing is the most widely implemented adaptation of Open Innovation based on Schuhmacher's overview presented in sections 2.5 and 2.6. In order to adopt an Open Innovation strategy closer to Chesbrough's definition and a high degree of openness according to *Figure 3*, a strategic paradigm shift is required to change way IPR and licensing is managed today.

A reason why top management of pharmaceutical companies is reluctant to accept the value of Open Innovation models might be due to limited success stories of collaborations within this field. Eli Lilly was pioneering the implementation of Open Innovation within the pharmaceutical industry [75, 76]. In 2009, they were among the first to adopt an Open Innovation

platform named "Open Innovation Drug Discovery" [27, 75, 76]. However, Eli Lilly did recently discontinue its platform. Reasons for this might be the aforementioned appropriability issues and the lack of return on investment. One can argue that Open Innovation, in its very basic adaptation without licensing, might be an effective way for pharmaceutical companies to create value. However, is it difficult to ensure capture value when sharing the IPR rights with one or more external partners. Additionally, the ROI is very difficult to determine for Open Innovation implementations, comparing the increased network and collaborations with external partners compared to the outflow of knowledge to externals. Due to the large sunk cost related to the pharmaceutical industry and appropriability issue, Open Innovation collaborations are more common and accepted within other industries such as the software industry [75].

To exploit the full potential of Open Innovation presented by Chesbrough, the authors of this study, suggest a stronger strategic focus of Open Innovation with a high degree of openness from top management of pharmaceutical companies.

5.3 Collaborations between pharmaceutical companies and biotech start-ups

In the semi-structured interviews conducted with CEOs of biotech start-up companies, the ownership of data generated is the greatest concern, when ranking the five predefined concerns. This concern is related to the outside-in adaptation of Open Innovation where external compounds are internalized, and the ownership of the data is often captured by the big pharmaceutical company solely. This type of collaboration is the most abundant adoption of Open Innovation when analyzing the implementation of Open Innovation platforms in the web scraping exercise.

According to the interviewed CEOs of the biotech start-ups, the data generated from the Open Innovation collaboration needs to be mutually owned otherwise, the lack of data ownership is considered as a "showstopper". This is reflected in the interview quote by the CEO of Cirqle Biomedical: *"You don't want to be a service provider. So, you really want to get a lot of value out of the collaboration. And typically, the value is in some sort of IP, then which you can leverage to raise more funds or to develop commercially".* And by the CEO of Clinical Microbiomics: *"we would never go into a collaboration, without having mutual*

ownership of that data, that's the whole point."

In addition, the establishment of trust upon collaboration was in general mentioned as a key element from the CEOs. Thus, big pharmaceutical companies need to ensure co-ownership of the data generated and sufficient trust within the collaboration. This is required to establish a platform, which creates attractiveness and exploit the full potential of Open Innovation. Trust was not included as one of the predefined concerns for the CEOs to rank in-between, but the trust concern was stated by the participants in the more explorative follow-up questions of the interviews. As stated by the CEO of Herantis Pharma: *"Big Pharma are often very clever in somehow getting around the IPR".* Chesbrough incorporates the aspect of trust in regards to Open Innovation collaboration on Rousseau's consensus: *"Trust is a psychological state comprising the intention to accept vulnerability based upon positive expectations of the intentions or behavior of another"* [35, 77].

5.4 Value assessment

According to Chesbrough *et al.*, 2018, when measuring value creation and value capture in Open Innovation [35], the authors of this study examine the value of the identified platforms according to the subcategories within the value measurement proposed in section 2.8.

According to the proposed foundations for a successful implementation of Open Innovation, aspects of value assessments are analyzed in the following.

Value realization.

This study does not include the perception of a fair resource utilization, since the perception occurs after the Open Innovation collaboration is finalized.

Despite being outside of the scope for this specific research, Chesbrough *et al.*, 2018 [35] indicate that a way to avoid an unfair value realization across contributors is through transparency in regards to the development and commercialization process [35]. Chesbrough indicates that an unfair value realization across contributors can be avoided through transparency in regard to the development and commercialization process [35]. Thereafter, the platforms described in section 4.2 should be evaluated during and after the completion of the collaboration to assess the value realization.

Value provision.

The initiatives listed in section 4.2 are selected according to the ability to optimize the exchange of resources with potential value realization through the platforms for external collaboration.

These platforms engage the provision of resources by exchanging compounds or characterizing them, which will have a potential benefit. This is the case if the collaboration results in a mutual benefit for both participants. Despite the different prerequisites for engaging in the specific platforms, they all facilitate the concept of value provision.

Value partaking.

As highlighted in the study of Chesbrough *et al.*, 2018 [35], an important consideration is the perception of value through value partaking. Whether the participants are engaging or not in Open Innovation initiatives is decided upon evaluating if anticipated benefits overcome the anticipated sacrifices.

In this context, and as perceived from the interviews included in this study, time constraints and the opportunity cost represent important factors. These contribute to the ex-ante considerations when deciding to pursue an Open Innovation collaboration. Among the Open Innovation platforms identified, the prerequisites and workload required differ a lot. Due to the time limitations of these study, the authors have not been able to evaluate the time required for each platform from a participant perspective beyond the official webpage statements.

Value negotiation.

The important aspect of compound and data ownership has been widely addressed within this study. The CEOs stressed the concerns regarding data ownership and open science. Thus, disclosure of knowledge plays an important role when achieving value creation through knowledge sharing collaborations such as formal Open Innovation initiatives.

Protection of knowledge and being able to extract profit is identified as key elements from both biotech start-ups and pharmaceutical companies. However, this is highly subject to the outside-in or inside-out adaptation of Open Innovation.

In general, the platforms identified in section 4.2 have different degrees of knowledge disclosure. Noticeably, initiatives including compound sharing offer a favorable negotiation position based on the platform descriptions. A larger degree of disclosed information related to these assets is observed, likely due to the inside-out approach. At the same time, however, the overall value capture obtained by the pharmaceutical company in compound sharing approaches does not appear to generate a direct business value. This is the case since it is generally targeting researches in the academic setting rather than start-ups. Therefore, value is expected to be obtained in the long term through scientific engagement of assets presumably not further developed and commercialized

due to strategic reasons such as internal review of business cases.

5.5 Reflections upon future Open Innovation adaptations

Despite Chesbrough's generally accepted definition of Open Innovation, the term seems to be exploited foremost as a branding strategy for many companies, which for most parts if a diluted adaptation of the concept including licensing collaborations. This is the case as many of the identified Open Innovation initiatives require extensive prerequisites from the external partner and offer little business value, as the data ownership is retained by the pharmaceutical company. The different adaptations of Open Innovation initiatives are captured in Schuhmacher's overview of Open Innovation elements in sections 2.5 and 2.6.

For big pharmaceutical companies to pursue a successful and attractive Open Innovation implementation, support from top management in terms of strategic focus and resource allocation is needed. Mentality barriers such as NIH and NSH, described in section 2.9.2, are common obstacles for a successful internal implementation of Open Innovation. To adopt an appealing Open Innovation platform, the big pharmaceutical companies need to loosen their appropriability focus. Thus, facilitation flux of knowledge and data ownership related compounds to a greater extent than implemented today. However, it is important to acknowledge the high sunk costs related to drug discovery and development, which can be seen as a big concern when adopting an open approach to collaboration and knowledge outflow such as Open Innovation. As reflected in the interview with the CEO of Monta Bioscience and in the work of Chesbrough [25], a successful implementation of the Open Innovation model needs to be aligned with the organization business model within the pharmaceutical company [20, 32]. Implementation of an attractive Open Innovation model from a biotech start-up perspective does not correlate with a very tight appropriability strategy, where no knowledge or resources are shared externally.

Open Innovation is acknowledged as an attractive way of creating value within the pharmaceutical industry, as it facilitates collaborations based on openness. Thereby, complementary knowledge and compounds can leverage on the permeable company boundaries by discovering and developing assets in a faster and cheaper manner, facilitating disruptive innovation and increased competitiveness [2, 8]. According to a recent study by Deloitte, a three-times higher phase I probability of success is found when drugs were scoured through Open

Innovation compared to the traditional innovation model [8].

Open Innovation holds the potential to solve current challenges such as the COVID-19 pandemic. However, due to barriers such as the appropriability issue, a reluctant adaptation of Open Innovation models among the key players of the pharmaceutical industry is observed. Borgers, Chesbrough and Moedas reflect upon the value growth of Open Innovation implementation within the pharmaceutical industry: "*Even though many would argue that the impact of innovation on growth has been somewhat disappointing, the current trends in innovation give ample grounds for optimism"* [6].

6. Conclusion

This study presents a recent investigation of the Open Innovation implementation within the key players of the pharmaceutical industry. The overall purpose of this master's thesis project was to investigate ***How does the current landscape of Open Innovation exploit the value of drug research within the 100 biggest pharmaceutical companies worldwide?***

To answer this question, the authors collected data from the 100 biggest pharmaceutical companies, selected by revenue, in order to perform a web scraping analysis.

Despite the limitations and bias of this web scraping methodology presented, the perception of the Open Innovation landscape was validated by industry experts. Thus, the authors of this study find the data obtained valid for the purpose of this exercise.

Seven Open Innovation platforms were identified within the category of high relevance, which includes the features described in section 4.1. This number was surprisingly low, considering the presumed intrinsic benefits of Open Innovation presented by Henry Chesbrough and described in section 2.2.

The main reasons for this reluctant implementation of Open Innovation include aspects as NIH, NSH and the appropriability issue. In- and out-licensing are still the most widely accepted types of Open Innovation collaborations within the pharmaceutical industry. A paradigm shift is required for top management of pharmaceutical companies to focus on collaborations based on openness, facilitating permeable boundaries with a bi-directional flux of knowledge.

The inherent sub-questions of the study were answered as follows:

1.a: How can the current implementation of Open Innovation platforms within the pharmaceutical industry be classified from a biotech start-up perspective?

As observed from the web scraping exercise, Open Innovation is a widely used as a branding strategy, showcasing the companies' interest in collaborations towards external partners. Considering Schuhmacher's overview of Open Innovation adaptations presented in this study, a diverse range of Open Innovation models are claimed and implemented within the pharmaceutical industry.

In order for pharmaceutical companies to facilitate an attractive Open Innovation platform, implementation of a compound-specific collaboration is suggested. This will bolster the processes of drug discovery,

development and commercialization by reducing time-to-market, costs and increase competitiveness. The Open Innovation initiatives presented by Schuhmacher do not all provide equal value for biotech start-ups based on the concerns presented in section 4.3. This is the case as most of the initiatives presented are not classified as compound-specific collaborations. Additionally, most Open Innovation platforms identified are characterized as In- and out-licensing adaptations, which imply a low degree of openness according to *Figure 3*.

The authors established a classification of the identified Open Innovation initiatives, ranking them according to the criteria mentioned in section 4.1. This evaluation of platforms presents their presumed attractiveness from a biotech start-up perspective according to their focus on compound-specific collaboration strategies and degree of openness. Common denominators were identified for the Open Innovation platforms, as they all facilitate collaboration with a specific therapeutic focus from the pharmaceutical company. Thus, the highly relevant platforms are all characterized as biased Open Innovation models according to section 2.4. This latter finding is further discussed in the perspective section.

The perspective of compound-specific collaboration was chosen as a classification measure along with a high degree of openness as the compound represents the most valuable asset within the pharmaceutical industry. Thus, collaborations based on these aspects are expected to facilitate attractive platforms from the perspective of a biotech start-up.

1.b: What are the biggest collaboration concerns for a biotech start-up when evaluating the attractiveness of Open Innovation platforms?

Based on the findings from the Open Innovation adaptations on the web scraping exercise, the authors interviewed ten biotech start-up companies regarding their interests and concerns relating to collaboration with pharmaceutical companies. Based on the identified platforms from the web scraping exercise, five predefined concerns were presented for the CEOs of the biotech start-ups, in order to identify the biggest collaboration concerns. Ownership of the data generated from the collaboration was ranked as the biggest concern among the participants. The semi-structured interviews revealed additional concerns to the predefined questions. These aspects include the aspect of trust and the importance of building a strong network within the pharmaceutical industry, facilitating a strong relationship.

Altogether these findings suggest that strong support from top management is needed including a stronger strategic focus

and resource allocation towards external collaboration. This support is required in order to improve the attractiveness of the already established platforms, as many medium and highly relevant platforms identified retain the data ownership solely within the pharmaceutical company.

Platforms including a higher degree of openness, based on *Figure 3* and closer to Chesbrough's definition of Open Innovation, are more attractive for external partners such as biotech start-ups. A paradigm change is required, changing the focus from securing IPR and appropriability, towards the benefits of open collaboration and the concept of knowledge exchange. According to a recent study, a three-times higher phase I probability of success was found when drugs were observed from Open Innovation collaboration compared to traditional innovation models [8]. Thus, a paradigm shift will facilitate an increase of incremental innovation, including a more efficient drug discovery and development process, which will benefit companies involved and society.

6.1 Perspectives

Based on the findings of this study, the authors suggest additional research to be conducted related to implementation of Open Innovation within the pharmaceutical industry. Based on the literature review of this study, the value measurement of Open Innovation is a complex topic that requires more academic attention within collaborations between pharmaceutical companies and biotech start-ups. This includes the definition of appropriate Key Performance Indicators (KPI) for pharmaceutical companies when evaluating the success of Open Innovation tailored to compound-based collaborations. These additional measures can help to determine whether externally developed projects truly bring more incremental innovation contributions, as indicated in some areas of the literature reviewed, and clarify aspects such as ROI.

Open Innovation can play a crucial role in order to solve current challenges such as the urgent need for a COVID-19 vaccine and large investments required for incremental inventions within technologies such as gene therapy.

As previously mentioned in section 3.4, the limitations of this study implied a target group strictly included the top 100 pharmaceutical companies based on revenue. The authors did not make use of specific software for this data collection. Additional studies elucidating the entire pharmaceutical landscape by making use of such software is suggested. This will capture a broader picture of the implementation

level of Open Innovation within the pharmaceutical industry.

An additional approach for this type of secondary data collection could have been data collection of patent- and co-patent data. By analyzing the patent and co-patent data from the past years, an unbiased overview of the most active pharmaceutical companies, biotech start-ups and academic institutions can be established.

In order to capture additional barriers for implementing and engaging in Open Innovation collaborations, the authors interviewed ten CEOs of Biotech start-up companies in Europe with fewer than 30 full-time employees. It is suggested to conduct additional studies including the perspectives from CEOs of the pharmaceutical companies, representatives from academia, including geographical areas outside of Europe.

In this study ten semi-structured interviews were conducted with a duration of approximately 10 minutes. The interviews included predefined concerns for CEOs of biotech start-ups to rank in-between. As for the complexity of Open Innovation, the authors suggest additional research to be conducted including longer interviews without addressing predefined concerns on Open Innovation collaborations. A more exploratory methodology might capture additional barriers and attractiveness towards Open Innovation. These interviews could, for instance, be conducted as focus group interviews in order to capture additional reflections of the complexity of Open Innovation in additional studies.

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8. Appendix

Appendix 1. Top 100 pharmaceutical companies, according to their total worldwide prescription sales in 2018. Source: Evaluate Ltd.

(Rx) Sales Rank	HQ	Company	Link ID	OI platform	Relevance
1	US	Pfizer	1	Centers for therapeutics innovation	Medium
1	US	Pfizer	2	(Accenture)	Low
2	CH	Roche	3	N/A (?)	Low
2	CH	Roche	4	N/A (?)	Low
2	CH	Roche	5	N/A (?)	Low
2	CH	Roche	6	N/A (?)	Low
3	CH	Novartis	7	Novartis Biome Innovation lab - Finished	Medium
4	US	Johnson & Johnson	8	JLABS Resident	Medium
4	US	Johnson & Johnson	9	JLABS Events	Medium
5	US	Merk & Co / MSD	10	MSD Innovation Factory	Medium
6	FR	Sanofi	11	Innovatewith	High
7	US	Abbvie	12	Compound Toolbox	High
7	US	Abbvie	13	"Other Open Innovation Concepts"	Low
8	UK	GSK	14	Open access to compounds 2010-2015 - Appears discontinued	Medium
8	UK	GSK	15	Tres Cantos Open Lab	Medium
8	UK	GSK	16	Centre for Excellence in External Drug Discovery (CEEDD)	Medium
9	US	Amgen	17	Amgen Ventures. Partnering With Amgen	Medium
9	US	Amgen	18	N/A (?)	Low
10	US	Gilead Sciences	19	N/A (?)	Low
11	US	Bristol Myers Squibb	20	International Immuno-Oncology network	Low
11	US	Bristol Myers Squibb	21	N/A (?)	Low
11	US	Bristol Myers Squibb	22	N/A (?)	Low
12	UK	AstraZeneca	23	Openinnovation.astrazeneca	High
13	US	Eli Lilly	24	YourEncore	Medium
13	US	Eli Lilly	25	Innocentive, ArthritisHack	Medium
13	US	Eli Lilly	26	Open Innovation Drug Discovery (ODD) - Discontinued	Medium
14	DE	Bayer	27	Grants4targets (G4T)	Medium
15	DK	Novo Nordisk	28	Novo Nordisk Compound Sharing	High
15	DK	Novo Nordisk	29	INNOVO - Novo Nordisk Open Innovation in China	Medium
15	DK	Novo Nordisk	30	Innocentive (challenge 9933823)	Low
16	JP	Takeda	31	World Without Disease (Shonan iPark)	Medium
16	JP	Takeda	32	COCKPI-T + Rare Disease Hackathon - Finished	Medium
16	JP	Takeda	33	Shonan iPark	Medium
16	JP	Takeda	34	T-CiRA	Medium
17	US	Celgene	35	N/A (?)	Low
18	IR	Shire	36	N/A (?)	Low
19	DE	Boehringer Ingelheim	37	OpnMe	High
19	DE	Boehringer Ingelheim	38	N/A (?)	Low
19	DE	Boehringer Ingelheim	39	N/A (?)	Low
19	DE	Boehringer Ingelheim	40	Innocentive	Medium
20	US	Allergan	41	N/A (?)	Low
20	US	Allergan	42	N/A (?)	Low
21	IL	Teva Pharmaceutical Industries	43	N/A (?)	Low
22	US	Mylan	44	N/A (?)	Low
23	JP	Astellas Pharma	45	a cube program	Medium
24	US	Biogen	46	N/A (?)	Low
25	AU	CSL Behring	47	N/A (?)	Low

(Rx) Sales Rank	HQ	Company	Link ID	OI platform	Relevance
26	JP	Daiichi Sankyo	48	OiDE (Open Innovation for the Development of Emerging technologies)	Medium
26	JP	Daiichi Sankyo	49	N/A (?)	Low
26	JP	Daiichi Sankyo	50	TaNeDS - Finished	Medium
27	DE	Merck KGaA	51	Biopharma Open Innovation Portal	High
27	DE	Merck KGaA	52	N/A (?)	Low
28	JP	Otsuka Holdings	53	Horizontal collaborations	Medium
29	BE	UCB	54	Technology Platform Access Programme (TPAP) - Appears Discontinued	Medium
30	FR	Les Laboratoires Servier	55	Golden Ticket awarded, WeHealth by SERVIER + LabCentral	Medium
31	CA	Bausch pharmaceuticals	56	N/A (?)	Low
32	US	Abbott Laboratories	57	N/A (?)	Low
33	JP	Eisai	58	Collaboration with WIPO for NTD, 2011	Medium
34	DE	Fresenius	59	N/A (?)	Low
35	ES	Grifols	60	Fundació Grifols	Low
36	US	Alexion pharmaceuticals	61	N/A (?)	Low
36	US	Alexion pharmaceuticals	62	N/A (?)	Low
37	US	Regeneron Pharmaceuticals	63	N/A (?)	Low
37	US	Regeneron Pharmaceuticals	64	N/A (?)	Low
38	IN	Sun Pharmaceutical Industries	65	N/A (?)	Low
39	CN	Yunnan Baiyao Group	66	N/A (?)	Low
40	JP	Chugai Pharmaceuticals	67	N/A (?)	Low
40	JP	Chugai Pharmaceuticals	68	N/A (?)	Low
41	JP	Symioto Dainippon Pharma	69	Realize Innovative Seeds and Medicines (PRISM)	Medium
41	JP	Symioto Dainippon Pharma	70	N/A (?)	Low
41	JP	Symioto Dainippon Pharma	71	N/A (?)	Low
42	IT	Menarini	72	N/A (?)	Low
43	US	Vertex Pharmaceuticals	73	N/A (?)	Low
43	US	Vertex Pharmaceuticals	74	N/A (?)	Low
44	CN	Sino Biopharmaceuticals	75	N/A (?)	Low
45	IR	Endo International	76	N/A (?)	Low
46	JP	Mitsubishi Tanabe Pharma	77	N/A (?)	Low
46	JP	Mitsubishi Tanabe Pharma	78	Shonan iPark	Medium
47	FR	Ipsen	79	SPINLEAP	Medium
48	CN	Jiangsu Hengrui Medicine	80	N/A (?)	Low
49	IR	Mallinckrodt	81	N/A (?)	Low
49	IR	Mallinckrodt	82	N/A (?)	Low
50	CN	Tasly Pharmaceutical Group	83	N/A (?)	Low
51	DE	STADA Arzneimittel	84	N/A (?)	Low
52	US	Ferring Pharmaceuticals	85	Ferring Innovation Grants Portal	Medium
52	US	Ferring Pharmaceuticals	86	Ferring Innovation Grants Portal	Medium
52	US	Ferring Pharmaceuticals	87	Ferring Innovation Grants Portal	Medium
53	CN	Shanghai Pharmaceuticals Holding	88	N/A (?)	Low
54	SA	Aspen Pharmacare	89	N/A (?)	Low
55	JP	Kyowa Kirin	90	N/A (?)	Low
56	IN	Aurobindo Pharma	91	N/A (?)	Low
57	IN	Lupin	92	N/A (?)	Low
58	US	General Electric	93	N/A (?)	Low
59	IN	Cipla	94	N/A (?)	Low
60	CH	Octapharma	95	N/A (?)	Low
61	CN	CSPC Pharmaceutical Group	96	N/A (?)	Low
62	IT	Chiesi	97	WeSTART	Medium
63	UK	Hikma Pharmaceuticals	98	Hikma Innovation Competition (HIC)	Medium
64	DK	Lundbeck	99	X HEALTH - Case competition - Finished	Medium
64	DK	Lundbeck	100	Open Innovation X (Oi-X) DTU - Finished	Medium
65	CN	China Resources Sanjiu Medical & Pharmaceutical	101	N/A (?)	Low
66	JP	Santen Pharmaceutical	102	N/A (?)	Low
67	JP	Ono Pharmaceutical	103	N/A (?)	Low
67	JP	Ono Pharmaceutical	104	Discovery Alliances	Medium
68	IR	Jazz Pharmaceuticals	105	N/A (?)	Low
69	CN	Fosun International	106	Protechting	Medium
70	IN	Zydus Cadila	107	N/A (?)	Low
71	CA	Apotex	108	N/A (?)	Low
72	CH	Nestlé	109	N/A (?)	Low
73	IN	Dr. Reddy's Laboratories	110	N/A (?)	Low
74	JP	Sawai Pharmaceutical	111	N/A (?)	Low
75	US	United Therapeutics	112	N/A (?)	Low

(Rx) Sales Rank	HQ	Company	Link ID	OI platform	Relevance
76	JP	Meiji Holdings	113	N/A (?)	Low
77	US	Amneal Pharmaceuticals	114	N/A (?)	Low
78	DK	LEO Pharma	115	LEO Pharma Open Innovation	High
78	DK	LEO Pharma	116	Hackathon events in DK, US and JP	Medium
79	CN	Chongqing Taiji Group	117	N/A (?)	Low
80	DE	Grünenthal Gruppe	118	Collaboration - IMU Leiden Hub Innovation HUB	Medium
80	DE	Grünenthal Gruppe	119	NeuRoWeg	Medium
80	DE	Grünenthal Gruppe	120	PainVis	Medium
80	DE	Grünenthal Gruppe	121	Dual2PET	Medium
81	JP	Nichi-Iko Pharmaceutical	122	N/A (?)	Low
82	US	Incyte	123	N/A (?)	Low
83	US	Baxter International	124	University collaborations	Medium
84	NL	Teijin	125	Open Innovation	Medium
85	US	BioMarin Pharmaceutical	126	N/A (?)	Low
86	HU	Gedeon Richter	127	N/A (?)	Low
87	SI	Krka Group	128	N/A (?)	Low
88	JP	Kowa Company	129	N/A (?)	Low
89	JP	Shionogi	130	N/A (?)	Low
90	IN	Glenmark Pharmaceuticals	131	N/A (?)	Low
91	IT	Recordati	132	N/A (?)	Low
92	US	Purdue Pharma	133	N/A (?)	Low
93	IR	Horizon Therapeutics	134	N/A (?)	Low
94	CH	Vifor Pharma Group	135	N/A (?)	Low
95	IT	Alfasigma Group	136	N/A (?)	Low
96	IT	Bracco	137	N/A (?)	Low
97	ES	Esteve	138	"Esteve's Open Innovation model"	Medium
97	ES	Esteve	139	ESTEVE-ICIQ Mixed Unit (with the Catalan Institute for Chemical Research)	Medium
97	ES	Esteve	140	ESTEVE-USC Mixed Unit (with the University of Santiago de Compostela)	Medium
98	IN	Torrent Pharmaceuticals	141	N/A (?)	Low
99	IT	Gruppo Angelini	142	N/A (?)	Low
100	PL	Polpharma Group	143	N/A (?)	Low
76	JP	Meiji Holdings	113	N/A (?)	Low
77	US	Amneal Pharmaceuticals	114	N/A (?)	Low
78	DK	LEO Pharma	115	LEO Pharma Open Innovation	High
78	DK	LEO Pharma	116	Hackathon events in DK, US and JP	Medium
79	CN	Chongqing Taiji Group	117	N/A (?)	Low
80	DE	Grünenthal Gruppe	118	Collaboration - IMU Leiden Hub Innovation HUB	Medium
80	DE	Grünenthal Gruppe	119	NeuRoWeg	Medium
80	DE	Grünenthal Gruppe	120	PainVis	Medium
80	DE	Grünenthal Gruppe	121	Dual2PET	Medium
81	JP	Nichi-Iko Pharmaceutical	122	N/A (?)	Low
82	US	Incyte	123	N/A (?)	Low
83	US	Baxter International	124	University collaborations	Medium
84	NL	Teijin	125	Open Innovation	Medium
85	US	BioMarin Pharmaceutical	126	N/A (?)	Low
86	HU	Gedeon Richter	127	N/A (?)	Low
87	SI	Krka Group	128	N/A (?)	Low
88	JP	Kowa Company	129	N/A (?)	Low
89	JP	Shionogi	130	N/A (?)	Low
90	IN	Glenmark Pharmaceuticals	131	N/A (?)	Low
91	IT	Recordati	132	N/A (?)	Low
92	US	Purdue Pharma	133	N/A (?)	Low
93	IR	Horizon Therapeutics	134	N/A (?)	Low
94	CH	Vifor Pharma Group	135	N/A (?)	Low
95	IT	Alfasigma Group	136	N/A (?)	Low
96	IT	Bracco	137	N/A (?)	Low
97	ES	Esteve	138	"Esteve's Open Innovation model"	Medium
97	ES	Esteve	139	ESTEVE-ICIQ Mixed Unit (with the Catalan Institute for Chemical Research)	Medium
97	ES	Esteve	140	ESTEVE-USC Mixed Unit (with the University of Santiago de Compostela)	Medium
98	IN	Torrent Pharmaceuticals	141	N/A (?)	Low
99	IT	Gruppo Angelini	142	N/A (?)	Low
100	PL	Polpharma Group	143	N/A (?)	Low

Appendix 2. Related webpage domains in reference to the Link ID presented in Appendix 1.

Link ID	Link
1	https://www.pfizercti.com/, https://www.hackathon.io/pfizer
2	https://www.ideaconnection.com/pdf/pfizer.pdf
3	https://www.uppsalabio.com/about-uppsalabio/about-bio-x/
4	https://sciencebusiness.net/news/75423/Roche-seals-its-first-open-innovation-agreement-in-Europe
5	https://www.roche.com/partnering/external-innovation-james-sabry.htm
6	https://www.roche.com/partnering/about_partnering_at_roche.htm
7	https://www.novartis.com/our-science/novartis-biome, 2020 Academic-to-Industry Hackathon
8	https://jlabs.jnjinnovation.com/about-us/equipment
9	https://jlabshub.splashthat.com/
10	https://www.msdinnovationfactory.com/
11	https://www.innovatewith.sanofi/?gclid=EAIaIQobChMI16jG0puu5wIVyueaCh2Y7gMDEAAYASAAEgLrqvD_BwE
12	https://www.openinnovation.abbvie.com/web/compound-toolbox
13	https://www.abbvie.com/our-science/therapeutic-focus-areas.html
14	https://au.gsk.com/en-au/behind-the-science/patients-and-consumers/diseases-of-the-developing-world/
15	https://www.openlabfoundation.org/Collaborate
16	http://www.bioendeavor.net/CommonData/NewsFiles/GSK.pdf
17	https://www.amgenbd.com/contact/
18	https://www.amgenbd.com/specific-article?Id=05776A79-AD37-4B70-80D2-696B0F1E7253
19	https://www.gilead.com/
20	https://www.bms.com/assets/bms/us/en-us/pdf/Disease-State-Info/ii-on-infographic.pdf
21	https://www.bms.com/life-and-science/science/the-international-immuno-oncology-network.html
22	https://www.bms.com/assets/bms/us/en-us/pdf/partnering-to-speed-transformational-medicines-to-patients.pdf
23	https://az-portal-ex.idea-point.com/
24	https://www.yourencore.com/
25	https://www.innocentive.com/
26	https://investor.lilly.com/news-releases/news-release-details/lilly-launches-open-innovation-drug-discovery-platform-help-find
27	https://innovate.bayer.com/programs/grants4targets-pharmaceuticals
28	https://www.novonordisk.com/research-and-development/partner-with-us/compound-sharing.html
29	https://www.novonordisk.com.cn/RandD/INNOVO_EN.html
30	https://www.innocentive.com/ar/challenge/9933823
31	https://www.shonan-health-innovation-park.com/siteassets/pdfs/services--initiatives/incubation-center/wwd_cfp-rule-document_eng_jpn.pdf
32	https://www.takeda.com/en-au/what-we-do/research--development/cockpi-t/
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