



# Feature

## Open innovation: A paradigm shift in pharma R&D?

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Open innovation (OI) holds promise to accelerate, diversify, and innovate research and development (R&D) in the pharmaceutical industry. It remains to be assessed in which way and to what extent OI is leveraged in practice by current pharmaceutical R&D organizations. Therefore, here we comprehensively analyzed 21 research-based pharmaceutical companies and benchmarked their implementation of OI. Our data showed that OI is an integral part of R&D of all assessed pharmaceutical companies; models typically used are research collaborations, innovation incubators, academic centers of excellence, public–private partnerships (PPPs), mergers and acquisitions (M&A), licensing, or corporate venture capital (VC) funds. In addition, we conclude that the implementation of OI differs greatly across corporations and, consequently, that R&D organizations of research-based pharmaceutical companies can be classified based on their level of OI implementation into three distinct types: predominantly traditional R&D; network-based R&D; and R&D ecosystems.

**Keywords:** Pharma; R&D; Open innovation; Network-based; Crowd-based; Ecosystem-enabled R&D

### Introduction

OI was first mentioned by Chesbrough describing a shift from primarily inside-driven and vertically integrated innovation ('closed innovation') to a more holistic and open understanding of innovation.<sup>1</sup> In the meantime, it becomes evident that pharmaceutical companies need to find more effective and efficient approaches for their R&D organizations. They have increased their engagement with various OI types to tap into innovation that is created both internally and externally.<sup>2–4</sup>

We were interested to better understand the current implementation status of OI in the pharmaceutical industry. Therefore, we sought to comprehensively assess the types of OI prevailing in the pharmaceutical industry. To that end, we analyzed a group of leading research-based pharmaceutical companies and assessed their innovation processes. We differentiated between outside-in (inbound), inside-out (outbound), and coupled OI processes, and focused our analysis on inbound processes (i.e., the practice of leveraging the discoveries of others).<sup>5–7</sup>

There are various reasons for the internal use of external knowledge. For example, in academic centers of excellence, companies increasingly invest in close collaborations with premier universities and other research institutions to access complementary skills and competencies.<sup>8</sup> With innovation incubators, companies create regional hubs or networks to facilitate collaboration with academia and external scientists to enable the rapid start-up of new business ideas.<sup>9</sup> Outcubation is another inbound process that brings academia and industry together. Unlike academic

centers of excellence, outcubation is usually not reserved for selected universities but instead offers a broader group of people the opportunity to participate.<sup>10</sup> Several further new initiatives have emerged that leverage the expertise of a larger community to address specific issues, rather than sharing knowledge with just a few distinct partners, ahead of all is crowdsourcing.<sup>11,12</sup> In the same way, in open-source, innovation is encouraged because scientific outcomes are shared openly across companies, institutions, and research labs.

### Methodology

We analyzed 21 leading (as determined by global sales 2019) research-based pharmaceutical companies regarding their inbound R&D activities to establish relationships with external organizations or individuals to enrich the own knowledge base of a company.<sup>5,13–15</sup> We further included in our analyses coupled processes, such as joint ventures, because they likewise enable companies to source external knowhow for internal R&D projects.

To define the preferred innovation type, we used qualitative content analysis to identify the OI activities of the selected companies. In an effort to limit the risk of misinformation and to ensure that the status quo is presented, we narrowed our search to the information we found on the respective corporate websites. Hence, we primarily took into consideration information that was announced in either the company's press releases or corporate annual reports between 2015 and 2019 by systematically analyzing OI-related topics, words, and applications [i.e., relation(ship), collaboration, cooperation, OI, licensing, partner(ship), merger, acquisition, network, crowdsourcing, joint venture, corporate venture fund, open source, PPP, alliance). Moreover, for conglomerates, we only included the pharmaceutical segment to ensure comparability. For corporate venture funds, innovation incubators, and crowdsourcing initiatives that were initiated before January 2015, the time restriction was repealed to avoid ignoring initiatives that are still highly relevant.

We selected 13 inbound and coupled OI processes and, following the concept of external 'search breadth' in combination with the variance hypothesis, we assigned

these processes to one of three innovation categories:<sup>16–18</sup> traditional OI processes; network-based OI processes; and crowd-based OI.

Traditional OI processes rely strongly on internal knowledge and expertise. To define what belongs to this, we first examined publications on OI in the pharmaceutical industry for 2006.<sup>19</sup> However, the topic was not frequently discussed until 2010.<sup>19</sup> Therefore, by 'traditional', we cover all OI processes that were commonly used by leading pharmaceutical companies before 2010. Therefore, we considered M&A, in-licensing, co-development, research collaborations, joint ventures, and corporate venture (CV) funds to be more traditional. These partnerships are usually narrow in scope, focused on a specific research target, and linked to a particular investigator.<sup>20</sup>

Network-based OI processes focus on building and maintaining a network of long-term relationships with a well-defined number of external partners.<sup>17</sup> Here, the value creation process changes from linear to networked.<sup>21</sup> Network-based innovation includes coupled OI processes, such as academic centers of excellence, innovation incubators, and PPPs.

Third, crowd-based OI is characterized by: (i) the integration of a large number of contributors from outside the traditional firm boundaries; (ii) the exploitation of technologies, such as social networks and peer-to-peer technologies; and (iii) the transfer of value-creating activities to a crowd.<sup>21</sup> Given that crowd-based OI does not only refer to crowdsourcing initiatives, we assigned the OI processes outcubation, crowdsourcing, open source, and virtual R&D to this category. These OI practices aim to bring the greatest possible community involvement and to make working practices transparent.<sup>22</sup>

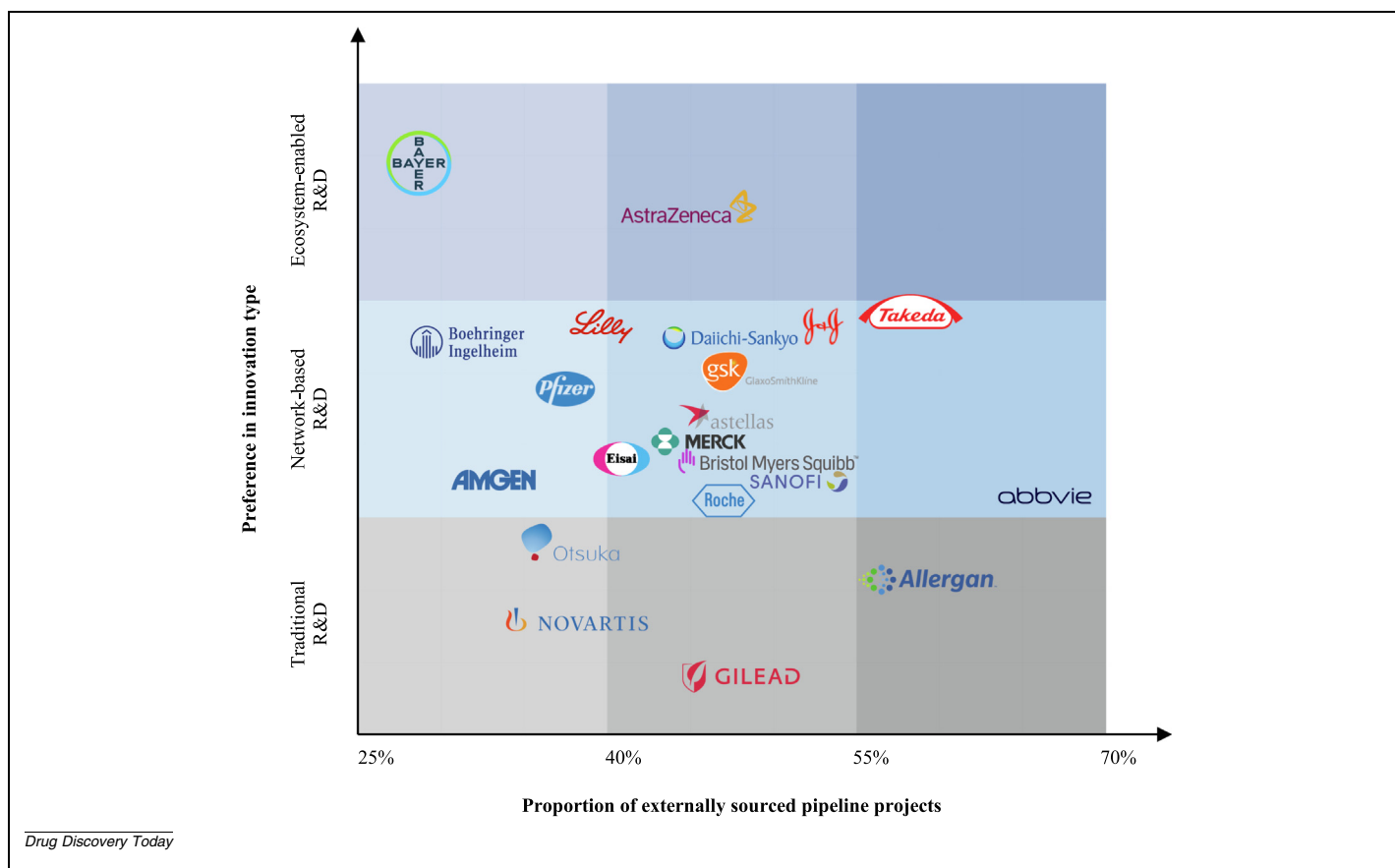
In line with these definitions and based on the qualitative content analysis, we classified the peer companies according to their predominant OI type in R&D: (i) traditional R&D: companies following a more traditional R&D type built their innovation process predominantly on internal R&D, complemented by M&A, in-licensing, CV funds, and selected R&D collaborations with academia and industry partners. Even though these companies incorporate some external knowledge

sources, they still own and control the majority of innovation tasks internally. Hence, focused attempts to apply OI and to access external innovation may be present, such as portfolio complementation, but no consistency beyond that is apparent; (ii) network-based R&D: In addition to a foundation in traditional R&D, these companies regularly use network-based OI processes on a broad basis to build and maintain long-term R&D relationships. By regularly, we mean R&D collaborations lasting several years or processes that are applied to multiple partners; (iii) ecosystem-enabled R&D: realizing that they cannot go alone and there is a need to go beyond a network-based R&D, these companies leverage all kinds of OI processes to acquire technologies and knowledge from multiple sources.<sup>38</sup> In particular, they strategically build their own R&D ecosystem by integrating a large number of contributors from outside the traditional firm boundaries and networks, and have initiated several crowd-based OI processes. In contrast to network-based R&D, the boundaries of these firms are less distinct, segmented, and categorized. Collaborations are initiated not only when there are project needs or specific work packages. Internal and external boundaries are progressively moving.

For the second dimension of the OI framework (Fig. 1), we assessed the number of externally developed drug projects that were in the company's pipelines at the end of 2019. For this purpose, we used the figures from the Pharma Intelligence report *Pharma R&D Annual Review 2020*.<sup>13</sup> For the evaluation of the proportion of externally sourced pipeline projects, we mapped the total number of drugs in the pipeline in relation to the drugs developed externally. The mean value, as well as the minimum and maximum values, were then used to determine the degree of external knowledge sourcing: (i) low, with a <40% of pipeline projects being developed externally; (ii) medium, with a respective range of 40–55%; and (iii) high, with >55% of the pipeline projects being acquired from external sources.

### Open innovation models in pharmaceutical R&D

Our results indicate that, over the past decade, OI has found its way into, and is a widely used R&D model of the research-

**FIGURE 1**

Open innovation (OI) framework. Peer companies are ranked according to their preferred innovation type as well as the proportion of externally sourced pipeline projects. The figure illustrates the extent to which different companies use external knowledge sources and, thus, helps to identify the OI strategy of each company. On the y-axis, companies are grouped according to their preferred innovation type, which was defined based on a qualitative content analysis of publicly disclosed OI practices between 2015 and 2019. The OI level increases with advanced use of external research & development (R&D) elements and with the increased exposure to diverse external innovation sources and parties. On the x-axis, the companies are further subdivided according to the proportion of external/partnered projects in their pipeline (as of 2019).

based pharmaceutical industry. However, the depth and breadth of implementation differs across major industry players. All investigated companies use M&As and selected R&D collaborations to access external knowledge. The majority (15 out of 21 companies) also uses network-based OI processes to supplement R&D. Only two firms leverage all kind of OI processes to a significant extent (Fig. 1).

According to our research, traditional R&D collaborations with either technology-based or market-based partners remain one of the most popular forms of external knowledge sourcing (Table 1).

M&A transactions are another traditional and still popular means to reach new external innovation, technologies, and patents. Allergan (22), Novartis (17), Roche (10), and Merck & Co. (10) were the companies that had completed the

most transactions between 2015 and 2019 (regardless of the transaction value).

The number of in-licensing agreements during the period under consideration ranged from 23 to 1. Companies having announced the most in-licensing agreements in that timeframe include Takeda (23), Astellas Pharma (14), and Gilead Sciences (14). However, these numbers are to be taken with caution, because they only include publicly announced agreements. Moreover, our research showed that in-licensing is closely associated with R&D collaborations, because many companies simultaneously entered into collaboration and licensing agreements with the same partner to jointly co-develop and -commercialize a drug candidate.

Partnerships with entrepreneurs and academia are having an increasingly important role in that space. As a consequence, 15

out of 21 companies run a CV fund, as well as every fourth company operating an innovation incubator (Table 1).

Additionally, several companies have formed joint ventures with biotech and/or pharmaceutical companies as well as with research institutions. Joint ventures allow companies to share costs, risks, and expertise as well as increase flexibility.<sup>23</sup> However, the unstable and volatile character of joint ventures and the difficulties associated with the framework management of such alliances lead to a rather low average success rate.<sup>24</sup> Consequently, most companies have no or only one active joint venture.

Moreover, several companies have established innovation incubators to connect with entrepreneurs and provide a 'one-stop-shop' for any potential partner. This model is used particularly by Bayer, Johnson & Johnson, and AstraZeneca,

TABLE 1

Traditional OI models in the pharmaceutical industry<sup>a</sup>

Company	Major R&D collaborations (2015–2019)			CV funds			Refs/Web address
	No. of technology-based collaborations	No. of market-based collaborations	Total number	Name	Foundation year	No. of companies in portfolio <sup>a</sup>	
AbbVie	5	26	31	AbbVie Ventures	2009	24	<a href="https://www.abbvie.com/partnerships/abbvie-ventures.html">https://www.abbvie.com/partnerships/abbvie-ventures.html</a>
Allergan	2	11	13	Amgen Ventures LLC	2004	32	<a href="https://www.amgenbd.com/s/about-us#AmgenVentures">https://www.amgenbd.com/s/about-us#AmgenVentures</a>
Amgen	8	27	35				
Astellas	6	9	15	Astellas Venture Management LLC	2005	21	<a href="https://www.astellasventure.com/">https://www.astellasventure.com/</a>
AstraZeneca	12	22	34	Leaps by Bayer	2015	22	<a href="https://leaps.bayer.com">https://leaps.bayer.com</a>
Bayer	10	12	22				
Bristol Myers Squibb	10	14	24				
Boehringer Ingelheim	15	38	53	Boehringer Ingelheim Venture Fund	2010	33	<a href="http://www.boehringer-ingelheim-venture.com">www.boehringer-ingelheim-venture.com</a>
Daichi-Sankyo	5	16	21	Eisai Innovation Inc.	2019	4	<a href="https://www.eisaiinnovation.com">https://www.eisaiinnovation.com</a>
Eli Lilly	7	16	23				
Eisai	10	23	33				
Gilead	7	26	33	Action Potential Venture Capital SR One	2013	8	<a href="https://www.actionpotentialvc.com">https://www.actionpotentialvc.com</a>
GlaxoSmithKline	1	4	5				
Johnson & Johnson	0	10	10	Johnson & Johnson Innovation	1973	40	<a href="https://www.srone.com/jninnovation.com/jjdc">https://www.srone.com/jninnovation.com/jjdc</a>
				Johnson & Johnson Impact Ventures	2019	15	<a href="https://chwi.jnj.com/about/johnson-johnson-impact-ventures">https://chwi.jnj.com/about/johnson-johnson-impact-ventures</a>
				Merck Global Health Innovation Fund	2010	29	<a href="https://www.merckghifund.com">https://www.merckghifund.com</a>
Novartis	7	14	21	The Novartis Venture Fund	1997	27	<a href="https://www.nvfund.com/#OurFund">https://www.nvfund.com/#OurFund</a>
				dRx Capital	2015	19	<a href="https://www.drxcapital.com">https://www.drxcapital.com</a>
Otsuka	2	9	11	Taiho Ventures	2016	14	<a href="https://taihoventures.com/">https://taihoventures.com/</a>
Pfizer	3	13	16	Pfizer Ventures	2004	57	<a href="https://www.pfizer.com/partners/venture-investments">https://www.pfizer.com/partners/venture-investments</a>
Roche	1	1	2	Roche Venture Fund	2002	35	<a href="https://www.venturefund.roche.com">https://www.venturefund.roche.com</a>
Sanofi	2	18	20	Sanofi Ventures	1994	26	<a href="https://sanofiventures.com">https://sanofiventures.com</a>
Takeda	16	47	63	Takeda Ventures, Inc.	2001	61	<a href="https://www.takedaventures.com">https://www.takedaventures.com</a>
				DDG Fund	2018	6	55

<sup>a</sup> Table considers all major R&D collaborations defined as publicly announced R&D collaborations in company press releases and annual reports (FY 2015–2019). Collaborations announced by other parties were not considered. Definition of technology-based versus market-based R&D collaborations: external technology-based partners include academic institutes, government agencies, or organizations in other industries. The aim is to jointly conduct research, development, or clinical trial (excluded donations, co-promotion, or marketing activities). External market-based partners include pharmaceutical or biotechnology companies. The aim is to jointly conduct research, development, or clinical trials (including drug discovery alliances and strategic partnerships; excluding co-promotion, or marketing activities).<sup>54</sup> Number of portfolio companies as of July 31, 2021. For Bayer, the portfolio includes companies from the health sector and excludes companies from the agricultural sector. SR One has operated independently since 2020. Drug Discovery Gateway Investment Limited Partnership (DDG Fund) is a joint investment fund with the Japanese-based Alternative Asset Management firm, Whiz Partners Inc.

which operate numerous incubators at major life-sciences hotspots around the world, such as Bayer's entrepreneurial

CoLaborator or LifeHubs, Johnson & Johnson's Janssen Labs (JLABS), or AstraZeneca's BioVentureHubs (Table 2).<sup>25–27</sup>

Another relatively new form of academic-industry partnership, outcubation, was recently discussed in the litera-

TABLE 2

Network- and crowd-based OI models in the pharmaceutical industry<sup>a,b</sup>

Network based						Crowd based							
Innovation incubator			Academic centers of excellence			PPP			Crowdsourcing initiative			Open-source initiative	
Name	Launch year	Refs	Name	Other parties	Refs	Name	Total number	Name	Launch year	Refs	Name	Refs	
<b>AbbVie</b>						SGC, IMI, DNDi, TB Alliance, FNIH Biomarkers, ANDI, GENE Consortium	7				ORIEN Avatar Research Program	80	
											NTD Drug Discovery Booster Consortium	81	
<b>Allergan</b>						IMI, FNIH Biomarkers, ANDI	3						
<b>Amgen</b>						IMI, FNIH Biomarkers	2						
BioScienceLA	2018	<a href="https://biosciencela.org">https://biosciencela.org</a>											
<b>Astellas</b>						IMI, DNDi, TB Alliance, MMV, FNIH Biomarkers	5				Exchange of Compound Libraries	82	
			Joint research chair	Osaka University	60						Joint Open Innovation of Drug Repositioning (JOINUS)	83	
			Alliance Station	Kyoto University	61						Joint Biomarker Database	84	
			Health Mock Lab	Yokohama City University, Tokyo University of Arts	62						NTD Drug Discovery Booster Consortium	81	
<b>AstraZeneca</b>						IMI, ELF, DNDi, MMV, Human Vaccines Project, FNIH Biomarkers, GENE Consortium	7	CoSolveChallenge	2014	74	Exchange of Compound Libraries	84	
BioVentureHub	2014	<a href="https://www.azbioventurehub.com">https://www.azbioventurehub.com</a>	Functional Genomics Centre	Cancer Research UK	63								
Accelerate Cambridge Life Sciences Program	2015	56											
Gatehouse Park BioHub	2015	57									AstraZeneca's CRISPR program	85	
Shanghai AI Innovation Center	2019	58									NTD Drug Discovery Booster Consortium	81	
<b>Bayer</b>						SGC, IMI, ELF, DNDi, FNIH Biomarkers	5	Grants4-Initiatives	2009	75			
CoLaboratory	2012	<a href="https://www.colaborator.bayer.com">https://www.colaborator.bayer.com</a>	Precision Cardiology Laboratory	Broad Institute of MIT and Harvard	64								

(continued on next page)

TABLE 2 (CONTINUED)

Network based						Crowd based						
Innovation incubator			Academic centers of excellence			PPP		Crowdsourcing initiative			Open-source initiative	
Name	Launch year	Refs	Name	Other parties	Refs	Name	Total number	Name	Launch year	Refs	Name	Refs
Bayer LifeHubs	N/A	<a href="https://innovate.bayer.com/lifehub-overview">https://innovate.bayer.com/lifehub-overview</a>	Joint Research Lab	Brigham and Women's Hospital, Massachusetts General Hospital	65			PartnerYourAntibodies	2015	75		
Grants4Apps Bristol Myers Squibb	2013	<a href="https://g4a.health">https://g4a.health</a>	Center for molecular synthesis (BMS-CMS)	Princeton University	66	IMI, DNDi, MMV, FNIH Biomarkers	4				ORIEN Avatar Research Program	80
Boehringer Ingelheim			Joint Research Center for Immuno-Infection	Tsinghua University	67	SGC, IMI, DNDi, Human Vaccines Project	4				OpnMe	86
Daichi-Sankyo			Joint Virtual Research and Development Center	University of Texas MD Anderson Cancer Center	68							
						IMI, DNDi, TB Alliance, MMV, GARDP	5	TaNeDS	2011	76	Joint Biomarker Database	84
											Joint Open Innovation of Drug Repositioning (JOINUS)	83
Eli Lilly Lilly Gateway Labs	2019	59	Lilly Diabetes Center of Excellence (LDCE)	Indian Bioscience Research Institute, Indiana University School of Medicine	69	IMI, FNIH Biomarkers, ADNI	3	InnoCentive	2001	<a href="https://www.innocentive.com">https://www.innocentive.com</a>	National Cancer Institute's Blood Profiling Atlas	87
								YourEncore	2001	<a href="https://www.yourencore.com">https://www.yourencore.com</a>		
								OIDD Program	2011	77		
Eisai			Eisai-Keio Innovation Lab for Dementia	Keio University	70	DNDi, MMV, GARDP, ADNI	4				NTD Drug Discovery Booster Consortium	81
Gilead												
GlaxoSmithKline						IMI, DNDi	2					
						IMI, DNDi, TB Alliance, MMV, Human Vaccines Project, GENE Consortium	6	Discovery Fast Track Challenge	2015	78	ATOM Consortium	88
Johnson & Johnson JLABS	2012	<a href="https://jlabs.jnjinnovation.com">https://jlabs.jnjinnovation.com</a>				SGC, IMI, ELF, DNDi, MMV, Human	9	Quickfire Challenges	2017	<a href="https://jlabs.jnjinnovation.com/">https://jlabs.jnjinnovation.com/</a>		

JPOD	2018	<a href="https://jlabs.jnjinnovation.com">https://jlabs.jnjinnovation.com</a>		Vaccines Project, FNIH Biomarkers, ANDI				quickfire-challenges		
<b>Merck &amp; Co.</b>				IMI, FNIH Biomarkers, ANDI	3				ORIEN Avatar Research Program 80	
<b>Novartis</b>				IMI, DNDi, MMV, GARDP, FNIH Biomarkers	6					
<b>Otsuka</b>										
<b>Pfizer</b>			Joint research chair	Hirosaki University	71	DNDi	1			
			Innovation Target Exploration Network (ITEN)	University of Cambridge, University of Oxford, University of Texas Southwestern (UTSW) and selection of other institutes	72	SGC, IMI, ELF, DNDi, Human Vaccines Project, FNIH Biomarkers, ADNI	7	Pfizer's competitive grant program	2019	<a href="https://www.pfizer.com/purpose/independent-grants/competitive-grants">https://www.pfizer.com/purpose/independent-grants/competitive-grants</a>
<b>Roche</b>								Get Old Project	2016	79
			imCORE Network	More than 21 academic institutes	73	SGC, IMI, DNDi, FNIH Biomarkers, ADNI, GENE Consortium	6			
<b>Sanofi</b>						IMI, ELF, DNDi, MMV, FNIH Biomarkers	5			Exchange of compound libraries 84
<b>Takeda</b>						SGC, IMI, DNDi, TB Alliance, MMV, GARDP, FNIH Biomarkers, ADNI, GENE Consortium	9			INSIGHT-MM Joint Biomarker Database 83 ORIEN Avatar Research Program 80 NTD Drug Discovery Booster Consortium 81

<sup>a</sup> This table demonstrates the innovation incubators established and still active by the studied companies. BioScience is not Amgen's own initiative, but the company is a founding sponsor (Amgen, 2018). The table also demonstrates all publicly announced academic centers of excellence founded by the studied companies between 2015 and 2019. With respect to PPPs, our research was limited to 12 PPPs that are frequently mentioned in literature and/or company press releases. Given the lack of traceability, we referred to the current membership disclosure on the organization's website (as of July 31, 2021). The table also demonstrates the crowdsourcing initiatives launched and still active by the studied companies. Grants4-Initiatives includes Grants4Traits, Grants4Biologicals, Grants4Tech, and Grants4Leads. Innocentive was divested in 2005 and, since 2020, has been part of the SaaS business, and open innovation marketplace Wazoku. YourEncore was acquired by Advarra in January 2021. The table also demonstrates all publicly announced open-source initiatives launched by the studied companies between 2015 and 2019.

<sup>b</sup> Abbreviations: ADNI, Alzheimer's Disease Neuroimaging Initiative (<https://adni.loni.usc.edu>); DNDi, Drugs for Neglected Diseases Initiative (<https://dndi.org>); ELF, European Lead Factory (<https://www.europeanleadfactory.eu>); GARDP, Global Antibiotic Research and Development Partnership (<https://gardp.org>); FNIH, Foundation for the National Institutes of Health (<https://www.fnih.org>); IMI, Innovative Medicines Initiatives (<https://www.imi.europa.eu>); MMV, Medicines for Malaria Venture (<https://www.mmv.org>); SGC, Structural Genomics Consortium (<https://www.thesgc.org>).

ture as a mixture of incubation and outsourcing.<sup>10</sup> Schellekens and Moors cite the BioMedX Innovation Center at the University of Heidelberg as an example of an outcubator model.<sup>28</sup> However, because this is a specific OI model, our analysis could not identify other examples where a new biotech company is founded to act as an intermediary and employer.

Moreover, pharmaceutical companies can establish academic centers of excellence to strengthen relationships with scientists and young talents. Our research showed that every second company had announced at least one new center of excellence between 2015 and 2019 (Table 2).

The opening of the pharmaceutical industry has also given PPPs a big push. While PPPs initially included mainly academic and national or international public funding organizations, the membership has diversified and now includes patient organizations, health insurances, pharmaceutical companies, and partners outside the health sector.<sup>29</sup> We focused our investigation on precompetitive and proof-of-concept PPPs.<sup>30</sup> In sum, Takeda (10) and Johnson & Johnson (9) are most active in that space (Table 2).

Our research further confirmed the growing impact of crowdsourcing and open source in drug discovery and research (Table 2). Seven out of 21 companies have initiated some sort of crowdsourcing approaches and 13 companies apply at least one open-source approach. Among them excels Eli Lilly, which founded the two crowdsourcing platforms InnoCentive and YourEncore in 2001, both operating independently today. Encouraged by the success, Eli Lilly launched another crowdsourcing platform in 2011 called Open Innovation Drug Discovery (OIDD).<sup>31</sup> Bayer followed with its crowdsourcing platforms Grants4Targets (G4T), Grants4Traits, Grants4Biologicals, Grants4Tech, and Grants4Leads, as well as PartnerYourAntibodies, to develop ideas for novel solutions. Other pharmaceutical companies having established their own Internet portal for crowdsourcing include Daiichi Sankyo, GlaxoSmithKline, AstraZeneca, Johnson & Johnson, and Pfizer. Moreover, some companies, such as Boehringer Ingelheim, work together with the help of specialist brokers that have plat-

forms, such as InnoCentive, Kaggle, or NineSigma.<sup>32</sup> However, in our research we focused on company-owned platforms because these require larger strategic investments.

Open source is another emerging OI model, used by several pharmaceutical companies. Especially during the early stage of drug discovery, an open community approach can bring numerous advantages to pharmaceutical R&D stakeholders. However, the challenge is that, following the open source philosophy, all potential solutions and discoveries are public domain.<sup>22</sup> This contradicts the intellectual property (IP)-driven traditional pharma R&D model, in which only exclusive ownership leads to differentiation and reliable sources of income. As a consequence, so far, the open source model has only had a significant role in the field of poverty-related infectious diseases and neglected tropical diseases, where substantial public and philanthropic funds are available.<sup>22</sup>

Finally, our research confirmed that virtual R&D organizations have not yet established themselves in large pharmaceutical companies.<sup>2,33</sup> Despite some prominent examples, such as Chorus, launched by Eli Lilly in 2000, or Protodigm, a purpose-built virtual pharma company created by Roche in 1996, no recent example was identified.<sup>34–36</sup>

### Open innovation framework

Based on our in-depth analysis, we ranked each of the peer companies according to their preferred innovation type and the proportion of external acquired R&D projects to capture the current innovation landscape in the pharmaceutical industry (Fig. 1). The resulting OI framework illustrates the extent by which leading research-based pharmaceutical companies leverage external innovation sources for R&D. Accordingly, most companies follow a network-based R&D model that is built on internal R&D in combination with a network of long-term R&D partnerships. Two companies, Bayer and AstraZeneca, have realized that they cannot go alone and have opened their R&D in a significant way and built their own R&D ecosystems, while four pharmaceutical companies (Novartis, Otsuka, Gilead, and Allergan) rely more on traditional R&D.

Comparing these results with our previous investigations,<sup>4</sup> our analyses do not support an industry-wide paradigm shift from predominantly closed to open R&D models when comparing 2010 with the current situation. It further illustrates that leading pharmaceutical companies continue to rely on traditional OI practices, such as in-licensing, M&A, R&D collaborations, and CV funds, because they want to retain control over their research process and limit their collaborations to distinct selected partners. For example, we found that Gilead Sciences is among the companies that rely most heavily on traditional innovation processes. Although Gilead Sciences has acquired many external pipeline projects through R&D collaborations and in-licensing agreements, the projects are primarily developed based on internal resources and expertise. This conclusion was reached because Gilead Sciences did not disclose any network- or crowd-based innovation practices, with the exception of its membership of two PPPs. However, companies no longer need to launch their own crowdsourcing or open-source platforms because there are several commonly used platforms, such as Kaggle, InnoCentive, and DREAM, that can facilitate the interaction with the crowd.<sup>37</sup> Nevertheless, our analysis aimed to identify companies that leverage crowd-based OI models to a significant extent and, thus, incorporate them actively in their OI strategy.

### Concluding remarks and outlook

Our research shows that most leading pharmaceutical companies build their R&D organizations on traditional OI processes in combination with external networks. Crowd-based OI is still rare or often limited to a closely defined group, because it is hard to manage and incorporates high uncertainty and risk of misuse of IP-relevant and sensitive company information.

This triggers the question why traditional and, to some extent, network-based R&D are more favored than an ecosystem-enabled R&D that is built on a 'large R&D ecosystem' of internal scientists as well as open and collaborative partnerships.<sup>82</sup> Several reasons are impeding the industry to use the full potential of OI, such as practical, legal, and regulatory issues in handling a large group of collabo-

rators, or the general challenges of how to deal with the paradoxes of OI enactment.<sup>39–42</sup> Companies might also struggle with negative attitudes toward inbound OI (not-invented-here syndrome) or outbound OI (not-sold-here syndrome).<sup>43,44</sup> These negative attitudes are often embedded in the corporate culture and are further intensified by cultural and organizational tensions that arise when companies start to interact with external parties.<sup>45</sup>

Moreover, the coordination–autonomy dilemma is a well-known challenge for large organizations that want to integrate smaller, innovative firms after their acquisition.<sup>46–48</sup> Nowadays, cultural barriers pose a challenge for not only M&A transactions, but all types of OI process, because large pharmaceutical companies usually have fundamentally different cultures, values, and attitudes compared with academia or small biotechnology companies. Therefore, leading pharmaceutical companies need to find a way to bridge the gap between their own culture and that of their partners. This problem could be solved by creating new internal R&D structures similar to those of smaller biotech companies or academic partners.<sup>20</sup> Good examples are the Innovative Medicines and Early Development (IMED) Biotech Unit of AstraZeneca or Chorus, a subsidiary of Eli Lilly.<sup>49</sup>

Finally, the implementation of OI can be constrained by operational barriers. Consequently, the ability of the pharmaceutical industry to mitigate business-relevant operational risks and to manage decentralized processes is crucial. Particularly, as operational and collaborative network complexities increase, there are more stakeholders and related tasks to coordinate. Companies that are unable to manage and crossfertilize such complex knowledge networks might struggle to apply OI effectively. In addition, OI requires strong leadership and a clear vision.<sup>50</sup> In that sense, most of the companies assessed here have not articulated a clear mission statement of how to implement and leverage OI in R&D. However, the examples of Bayer and AstraZeneca illustrate that OI can be effectively implemented with a well-defined strategy.<sup>51,52</sup>

A limitation of our present analysis is that it relied exclusively on publicly available corporate information. Although pub-

licly available corporate releases are legally controlled and supposed to cover what is considered substantial, we might have missed OI activities that companies undertake without reporting them in the media or that are more seen as company secret rather than a strategic initiative that is publicized. In fact, traditionally strong bonds between companies, employees, academic institutions, and alumni might be subject to such under-reporting. Furthermore, it appears important that the categories used in this paper (traditional R&D, network-based R&D, and ecosystem-enabled R&D) do not imply a judgement on the impact of such OI types in terms of R&D efficiency and effectiveness. Follow-up analyses, based on broader and more long-term data sets, should include in particular the potential impact of OI on these pharmaceutical R&D metrics.

Collectively, the goal of our research was to present the current state in OI in R&D in the pharmaceutical industry. However, this state might change and evolve as a consequence of the Coronavirus 2019 (COVID-19) pandemic, which acts as a catalyst for transformative collaboration. Besides giving digitalization a push, the search for a vaccine and therapeutic drugs stressed the power of multi-lateral R&D collaborations, such as the COVID Moonshot project (<https://covid.postera.ai/covid>) or the COVID-19 host genetics initiative (<https://www.covid19hg.org/>). The prime example of the mRNA technology space, exemplified by the Pfizer-BioNTech vaccine Comirnaty, demonstrates how innovation can happen when combining existing ideas and technologies in an open manner.<sup>53</sup> COVID-19 vaccines and also, in the meantime, therapeutics could not have been developed so quickly if governments, academia, and industry had not have collaborated so closely and shared knowledge, resources, and competencies in such unprecedented ways. Inspired by these unique ways of collaborative R&D, the challenge remains to leverage innovation frameworks, such as OI, to design and develop drugs in a faster, smarter, and more agile manner.

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