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Investigating the origins of recent pharmaceutical innovation

Alexander Schuhmacher, Markus Hinder, Alexander Dodel, Oliver Gassmann & Dominik Hartl

Leading pharmaceutical companies have historically been engaged in all stages of the R&D pipeline, from target identification through to drug marketing, and thus have been termed fully integrated pharmaceutical companies (FIPCOs). In the past decade, externally invented assets gained through partnering or mergers and acquisitions (M&As) have become a prominent component of the pipelines of such companies. Given the long development cycles and the increasing level of collaboration between pharma companies and biotech companies, however, the precise origins of innovation are not obvious, in part as regulatory approvals for innovative drugs by agencies such as the FDA are granted to the company filing the applications, which is not necessarily the company that discovered the active pharmaceutical ingredient.

Understanding the origins of innovation provides a deeper understanding of the pharma business model and could support strategic improvements. We therefore systematically assessed the origins of innovation for all new molecular entities (NMEs) and new therapeutic biologics (NTBs) approved between 2015 and 2021 by the Center for Drug Evaluation and Research (CDER) of the US Food and Drug Administration (FDA) for the top 20 biopharma companies globally by sales in 2020 (see Supplementary information for details).

Origins of pharmaceutical innovation

The FDA approved 323 new drugs between 2015–2021, of which 138 were filed for approval by the top 20 biopharma companies (Supplementary Table 1). The majority (65%) of the new drugs originated from external sources, whilst 28% were invented internally, 5% were discovered collaboratively, and the remaining 2% include other special cases (Fig. 1a, Table 1). Classifying companies as pharma or biotech based on their foundation date, the majority of the 138 drugs (47%) were invented by biotech companies founded after 1976, whilst 38% were invented by pharma companies founded earlier (Supplementary Figure 1, Supplementary Table 2). Only a minority of new drugs originated from universities or other academic institutions (7%) or were the output of other third-party drug discovery collaborations (6%) (Supplementary Table 3).

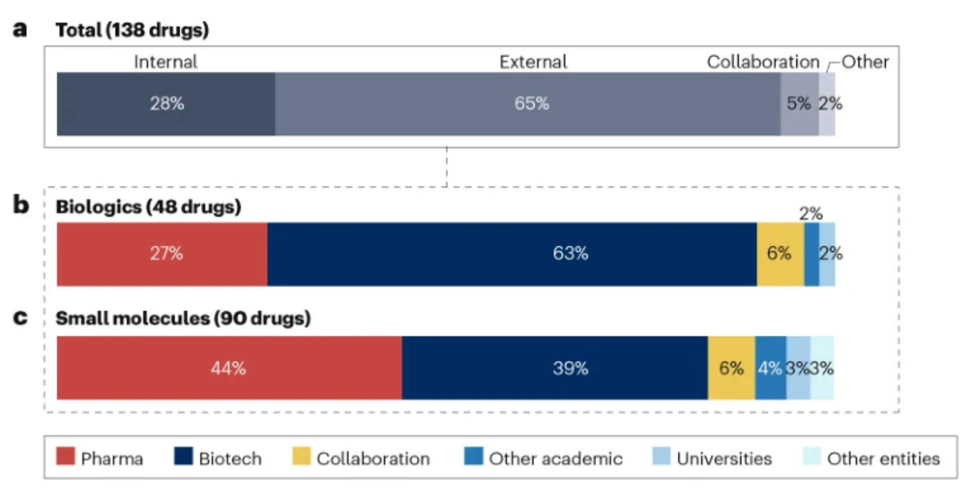

Fig. 1 | Origins of FDA-approved new drugs filed by the top 20 biopharma companies between 2015–2021. a, Overall, 65% of the new drugs originated from external sources. The majority of biologics (63%) originated in biotech companies (b), while the largest group of small-molecule drugs (44%) originated in pharma companies (c). Other academic institutions include non-profit research organizations and governmental research institutions. For details of the data and analysis, see Supplementary information.

Notably, the majority (63%) of the 48 NTBs approved for the top 20 biopharma companies had their origin in biotech companies (founded after 1976), whilst 13 NTBs (27%) were invented in pharma companies (Fig. 1b). For the 90 approved small-molecule drugs, 44% (40 NMEs) originated in pharma companies, 39% (35 NMEs) derived from biotech companies, 6% (5 NMEs) were developed in collaboration with other academic and 10% (10 NMEs) came from other sources, such as non-profit or governmental research organizations (Fig. 1c).

Finally, analysing the group of 90 drugs (65%) that originated from external sources, 56 (41%) of these new drugs were gained through M&As and 34 (25%) were in-licensed (Supplementary Table 4).

Discussion

Our analysis indicates that the business model of the top 20 biopharma companies in recent years has largely been built on external innovation, as only 28% of recently FDA approved drugs were invented and developed internally. Biotech companies were the most important origin of innovation (47% of new drugs) for the top 20 companies. In addition, the internal R&D of the top 20 companies overall has had a stronger focus on small-molecule drugs, and they have accessed the majority of their biologics from biotech companies.

Breaking down these analyses on a single company level (Supplementary Table 5), 15 of the evaluated 20 biopharma companies relied largely on external innovation, with Johnson & Johnson, Sanofi, Takeda and Biogen focusing fully on externally invented new drugs (Table 1). Among companies that leveraged external innovation, in-licensing versus acquisition was further compared, revealing that Pfizer, Gilead, Takeda, and Daiichi Sankyo executed external innovation primarily by M&As, whereas Bayer, Amgen, Novo Nordisk and Biogen focused on in-licensing (Table 1).

Table 1 | Origins of drugs marketed by the top 20 companies between 2015–2021

Company	Internal	Collaboration	External: in-licensing	External: acquisition	Extern other
Novartis	Cosentyx, Piqray, Entresto, Mayzent, Scemblix	Rydapt, Kisqali	Tabrecta, Leqvio	Netspot, Lutathera, Xiidra, Beovu, Adakveo	Egaten
Roche	Alecensa, Hemlibra, Enspryng	Evrysdi	Cotellic, Xofluza, Gavreto	Tecentriq, Ocrevus, Polivy, Rozlytrek	
AstraZeneca	Tagrisso, Imfinzi		Koselugo, Tezspire	Strensiq, Kanuma, Calquence, Fasenra, Lokelma, Ultomiris, Saphnelo	
AbbVie	Rinvoq	Venclexta	Mavyret, Orilissa, Skyrizi	Avycaz, Kybella, Viberzi, Vraylar, Ubrelvy, Qulipta	
Merck & Co.	Zepatier, Pifeltro, Recarbrio		Zinplava, Prevymis, Steglatro, Verquvo	Bridion, Welireg	
Eli Lilly & Co.	Taltz, Verzenio, Emgality, Reyvow		Olumiant	Portrazza, Lartruvo, Retevmo, Tauvid	
Pfizer	Vizimpro, Lorbrena, Daurismo			Ibrance, Eucrisa, Besponsa, Talzenna, Vyndaqel	
Johnson & Johnson			Yondelis, Darzalex, Tremfya, Erleada, Balversa, Rybrevant	Uptravi, Ponvory	
Sanofi			Praluent, Adlyxin, Kevzara, Sarclisa	Cablivi, Fexinidazole, Nexviazyme	
GSK	Nucala, Blenrep			Zejula, Rukobia, Jemperli	Krintafe Cabenu
Gilead Sciences	Genvoya, Biktarvy, Veklury			Epclusa, Vosevi, Trodelvy	
Bristol Myers Squibb	Daklinza		Empliciti	Idhifa, Inrebic, Reblozyl, Zeposia	
Takeda				Ninlaro, Alunbrig, Takhzyro, Motegrity, Exkivity, Livtencity	
Bayer	Aliqopa, Lampit, Kerendia		Vitrakvi, Nubeqa		
Amgen	Repatha, Aimovig	Evenity, Lumakras	Corlanor		
Novo Nordisk	Tresiba, Ozempic, Sogroya		Macrilen		
Daiichi Sankyo	Savaysa, Enhertu			Turalio	
Astellas		Xospata	Cresemba	Padcev	
Biogen			Zinbryta, Spinraza, Aduhelm		
Boehringer Ingelheim	Praxbind				

Only approvals from the FDA's Center for Drug Evaluation and Research are included. Additional information on the approved drugs, including the dates of approval, therapeutic area and partner companies, if applicable, is provided in Supplementary Fig. 1.

Although the top 20 biopharma companies in general cover the entire R&D pipeline, from drug discovery to commercialization, and thus are 'fully integrated' per se, the finding that the majority of new drugs launched by the companies were invented by biotech companies suggests that the term 'biotech-leveraged pharma company' (BIPCO) could be a suitable way to characterize the business models of these companies, albeit to differing extents.

Predicting the future based on the past is fraught with uncertainty. However, there are cross-industry trends that will shape the pharmaceutical R&D landscape in the coming decade. For example, emerging therapeutic modalities such as gene therapies and cell therapies have shown transformational efficacy, yet scalability and reimbursement remain challenging. In the coming years, bear markets could limit access of biotechs to public markets and may intensify early biotech–pharma interactions, thereby feeding into the BIPCO model. How to flexibly leverage these evolving dynamics across therapeutic modalities and disease areas will be a key challenge for the leading biopharma companies.

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SUPPLEMENTARY INFORMATION

1. Supplementary information
2. Supplementary Fig. 1

COMPETING INTERESTS

A.S. and O.G. declare no competing interests. M.H. is an employee of Novartis and a former employee of Roche and Sanofi. D.H. is a former employee of Roche and Novartis. A.D. is an employee of Johnson & Johnson. This study did not receive external funding and was undertaken independently.

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