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A case study assessing the impact of M&A and licensing on FDA drug approvals of leading pharmaceutical companies

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Despite a recent increase in FDA new drug approvals, leading pharmaceutical companies continue to face R&D productivity challenges. This highlights the need to better understand the context of their R&D concepts and related R&D outputs. Consequently, we conducted a systematic assessment of the impact of R&D expenditures, R&D intensities, mergers & acquisitions (M&A) deals and licensing agreements on new drug approvals of leading pharmaceutical companies between 2012 and 2021. Our analysis provides key insights into differentiating R&D factors: whereas R&D expenditures and the number of M&A deals correlate with the number of new drug approvals, our analysis shows no correlation with R&D intensity or the number of licensing agreements.

Keywords: Pharma R&D; R&D strategy; R&D productivity; R&D intensity; M&A; drug licensing; collaboration; FDA approvals

Introduction

The strategies of the leading pharmaceutical companies usually focus on R&D as the primary source of innovation, competitive advantage and growth. R&D strategy is defined as a 'game plan' for R&D or as a strategic framework for an R&D organization, encompassing structure, processes, core competences and a portfolio.[(p1),(p2)] R&D strategies of the leading pharmaceutical companies are typically disclosed in annual reports and have evolved over time in response to market trends, stricter regulatory frameworks and emerging technologies. Key strategic elements for gaining a competitive advantage include the level of R&D expenditures, risk tolerance, the business model of R&D (i.e., how R&D is leveraged), therapeutic focus and portfolio diversity. The need to capture new value has led to an increasing shift of R&D toward open R&D and open innovation, such as through research collaborations and licensing, strategic partnerships, as

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well as mergers and acquisitions (M&A).[p3],[p4] To balance the risks of established versus emerging technologies and disease mechanisms, leading companies often pursue multiple R&D programs simultaneously. This approach allows them to leverage a diverse range of drug targets, therapeutic modalities and therapeutic areas.[p5]

Over the past 20 years, R&D strategies of leading companies have been influenced primarily by the aim to increase R&D productivity.[p6],[p7],[p8],[p9] R&D productivity is defined as 'the total amount of innovation created for a given amount of R&D investment – a return-on-investment rate'.[p10] In this context, pharmaceutical firms face four specific challenges: (i) developing and launching a sufficient number of new drugs that (ii) are commercially successful enough to compensate the enormous R&D costs and (iii) drive corporate growth through innovation, while (iv) managing the innovation gaps that typically arise from strategic decisions made over a decade ago.[p5],[p11]

The aim to improve R&D productivity has led to various corporate initiatives, such as Bristol-Myers Squibb's (BMS) novel clinical trial designs, AstraZeneca's 5R framework or Pfizer's Signs of Clinical Activity (SOCA) paradigm.[p12],[p13],[p14] In addition, accessing external innovation and knowledge by traditional, network-based and crowd-based open innovation models is gaining increasing importance in the pharmaceutical industry.[p15] For example, 65% of 323 new drugs (2015–2021) approved for the top 20 pharmaceutical companies were externally invented, most often by biotech firms, and accessed through licensing or M&A.[p16] Consequently, the internalization of external assets has become a widely used R&D strategy to build new competence, adopt transformative technologies and access new drug candidates. This has led to the conclusion that the business model of leading companies has evolved to be that of a biotech-leveraged pharma company (BIPCO).[p16]

M&A is regarded as a key strategy for expanding R&D pipelines.[p17] Particularly, pharmaceutical companies that face drug pipeline and product portfolio gaps tend to be more active in acquisitions, with the larger firms being more likely to pursue acquisitions when anticipating low growth and excess capacity owing to patent cliffs.[p18],[p19] Notably, as in the past,[p20] in the post-COVID-19 era some major pharmaceutical companies now hold high cash reserves, while facing patent expirations of blockbuster drugs, such as Humira® (AbbVie, total sales in 2023 of US$14.4B; key patent expiration in 2023), Revlimid® (BMS; US$6.1B; 2025), Stelara® (Johnson & Johnson; US$10.9B; 2025) or Cosentyx® (Novartis; US$4.9B; 2025). Along with the relatively low financial valuations of public biotech companies,[p21] which encourage partnerships and M&A as crucial components of biotech financing, patent expirations and associated revenue losses are key drivers for biotech–pharma collaborations.[p22] For instance, to create new value after the COVID-19 pandemic and to strengthen its core competences, Pfizer reinvested its Comirnaty® surplus (worldwide total sales of US $37.9B in 2021) in acquiring the antibody–drug conjugate (ADC) specialist Seagan for US$43B in 2023, including its top-selling drug Adcetris® (brentuximab vedotin).[p23]

Despite the shift in business models of top companies toward greater external innovation, many of them have not succeeded in sustainably increasing their R&D productivity.[p16],[p24] This underscores the need to better understand the context of R&D strategy and R&D productivity. Thus, we aimed to investigate the impact of key strategic elements, such as level of R&D expenditure, R&D intensity, number of M&A deals and number of in-licensing agreements, on the R&D output (total amount of innovation) of leading pharmaceutical companies.

Methodology

Our analysis sought to encompass the top 20 pharmaceutical companies by sales in 2022. However, certain companies were excluded, because the study solely focused on (i) fundamentally research-driven organizations with (ii) consistent data over the past 10 years and (iii) a primary emphasis on pharmaceuticals, accounting for >50% of their revenue. For this reason, Johnson & Johnson, Bayer, Merck,[1] Sinopharm, China Resources Pharmaceutical and BioNTech[2] were excluded. As a result, our analysis focused on 14 leading research-based pharmaceutical companies: Abbvie, Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Eli Lilly, Gilead Sciences, GlaxoSmithKline (GSK), Merck & Co., Novartis, Pfizer, Roche, Sanofi and Takeda.

Our observation period covered the 10 years of 2012–2021. According to Munos,[p25] a time lag of up to 5 years should be considered when analyzing the commercial effect of R&D (R&D outcome).[p25] Because we analyzed R&D output, we did not account for a corresponding time lag. Additionally, assets are typically internalized in preclinical and clinical development phases. Given the typical R&D timelines, the effect of R&D activity can be expected within 10 years.

We analyzed five key R&D metrics: (i) R&D expenditures; (ii) R&D intensity (the ratio of R&D expenditure to revenue); (iii) M&A deals; (iv) licensing activities; and (v) the number of new drugs approved by the FDA from 2012 to 2021. Financial data were sourced from Refinitiv Eikon, with currency conversion performed using Refinitiv Eikon's embedded function. Different fiscal years were standardized by manually adjusting financial figures to align with the calendar year-end. To ensure comparability among companies, we used R&D expenditure data from Refinitiv Eikon, because it specifically reports internal R&D expenditures. These costs of in-house R&D activities do not include R&D-related costs, such as license fees, asset acquisition expenses, in-process R&D expenses (IPR&D), amortization and impairment charges (both often part of IPR&D) or restructuring costs. Additionally, Refinitiv Eikon applies a consistent definition of R&D spending, regardless of varying accounting standards and reporting practices. R&D expenditures in US$ were adjusted for inflation and indexed to 2021. The data on new drug approvals by the Center of Drug Evaluation and Research (CDER) of the FDA (2012–2021), including CDER-related approvals of new molecular entities (NMEs) and new therapeutic biologics

[1] Excluded from the analysis because of corporate structure with multiple business units, making it difficult to analyze the pharma-related internal R&D expenditures.
[2] No consistent data available for the 10 years of the analysis.

(NTBs), were sourced from the FDA's official website.

Data on M&A deals (limited to majority deals) were sourced from Refinitiv Eikon, annual company reports and investor relation information. The following deals were not considered in our M&A analysis: minority acquisitions, abandoned deals (such as the abandoned acquisition of Shire by Abbvie), non-R&D-related asset deals, joint ventures, acquisitions of already approved drugs, acquisitions of priority review vouchers, acquisitions of assets unrelated to the core business of research-based pharmaceutical companies, such as in pharmaceutical supply, health engagement, animal health, medical devices, diagnostics, generics, biosimilars, consumer health, over-the-counter (OTC) drugs, vaccines and cell and gene therapy deals.

Corporate communications were analyzed to identify in-licensing deals. The licensing data set was supplemented with information from Refinitiv Eikon and GlobalData databases. Licensing agreements were assumed to be correctly classified as distinct from other asset transactions within the sources. The following licensing deals were not included in our analysis: agreements covering gene and cell therapies, biosimilars, vaccines, generics, OTC drugs, diagnostics, medical devices and animal health. In addition, licensing deals covering already FDA-approved drugs, supplier agreements, as well as commercialization and promotion agreements, were not considered.

Our statistical analysis consisted in calculating Pearson's correlation coefficients, their respective 95% confidence intervals, as well as two-sided *P*-values. Furthermore, we calculated simple linear regression, slope, Y-intercept, X-intercept, as well as the 95% confidence intervals. All statistical analyses and respective graphs were generated using GraphPad Prism (version 9.5.1, Boston, MA, USA).

Results

Table 1 presents the descriptive results of our analysis, including total revenue, total R&D expenditures, R&D intensity, number of FDA-approved new drugs, number of M&A deals, M&A deal volume, and number of licensing agreements for the group of 14 analyzed companies (2012–2021). Collectively, these companies spent US$910.6B for (internal) R&D, with Takeda reporting the lowest 10-year R&D expenditures at US$39.7B and Roche the highest for R&D at US$119.9B. The 14 firms received FDA approval for 155 new drugs in the time-period assessed, resulting in an average R&D efficiency of US$5.9B R&D investment per new drug approval (2012–2021). The company-specific R&D output (2012–2021) ranged from a minimum of five new drugs (Boehringer Ingelheim) to a maximum of 18 (Novartis). Our analysis identified a total of 144 M&A deals and 402 in-licensing agreements (2012–2021). The average R&D intensity among the companies was 18%, which differs from the often cited 20% ratio of top-line revenues invested in R&D. This discrepancy could be attributed to adjustments made to standardize total revenues and R&D expenditures, ensuring better comparability and focusing on internal R&D.

Regarding the M&A activities of the companies, our analysis revealed the following information. The combined value of the 144 M&A deals was US$579.1B. However, the deal volume was not uniformly distributed among the investigated companies. BMS (US$110.6B) and AbbVie (US$92.1B) invested substantially in M&A activities, whereas GSK (US$9.2B) and Boehringer Ingelheim (US$1.4B) did not leverage much from this form of external

TABLE 1

Key R&D figures of leading pharmaceutical companies (2012–2021)

Company	Total revenue (US$B)	Total (internal) R&D expenditures (US$B)	Average R&D intensity	Number of FDA-approved drugs	Number of M&A deals	Total M&A deal value (US$B)	Number of in-licensing agreements
Roche	638.97	119.91	19%	15	16	19.92	40
Pfizer	567.17	86.43	16%	12	11	41.09	34
Novartis	557.75	95.68	17%	18	13	36.59	28
Merck & Co.	469.08	86.39	19%	15	17	38.16	31
Sanofi	465.08	69.20	15%	11	8	30.12	19
GlaxoSmithKline	456.36	58.39	13%	13	4	9.21	18
AbbVie	327.42	50.13	16%	8	6	92.13	33
AstraZeneca	287.43	60.84	21%	14	16	61.38	26
Bristol-Myers Squibb	264.82	59.64	23%	7	11	110.56	29
Gilead Sciences	254.28	38.62	16%	9	10	43.31	23
Eli Lilly	245.73	59.97	24%	12	10	13.98	41
Amgen	244.03	44.20	18%	7	10	16.46	18
Takeda	226.45	39.69	18%	9	6	64.78	34
Boehringer Ingelheim	217.82	41.46	19%	5	6	1.43	28
Total	**5222.38**	**910.55**		**155**	**144**	**579.12**	**402**
Mean	**373.03**	**65.04**	**18.1%**	**11.07**	**10.29**	**41.37**	**28.71**
Standard deviation	**146.97**	**24.99**	**3.16%**	**3.73**	**4.10**	**31.54**	**7.46**

Data source: annual reports (2012–2021), press releases (2012–2021), Refinitiv Eikon, GlobalData and FDA website (see methodology) – data normalized and cleaned. R&D intensity is calculated as the ratio of internal R&D expenditures to total revenue. Financial data originally reported in other currencies was converted to US$ by applying Refinitiv Eikon's embedded function.

innovation (Table 1). The exceptionally high M&A volumes of BMS and Abbvie can be ascribed to distinct major deals (volume > US$10B): Abbvie acquired Allergan (US$64.1B, 2019) and Pharmacyclics (US$20.1B, 2015), whereas BMS invested in Celgene (US$80.3B, 2019) and MyoKardia (US$13.1B, 2020). Other major deals in our analysis are AstraZeneca's acquisition of Alexion Pharmaceuticals (US$41.1B, 2020), Gilead's acquisitions of Immunomedics (US$20.6B, 2020) and Kite Pharma (US$11.1B, 2012), Merck & Co.'s deal with Acceleron Pharma (US$11.5B, 2021), Novartis's deal to acquire GSK's oncology business (US$16B, 2014), Pfizer's acquisitions of Array Biopharma (US$11.2B, 2019) and Medivation (US$14.3B, 2016), as well as Takeda's acquisition of Shire (US$57.2B, 2019). Amgen, Boehringer Ingelheim, Eli Lilly, GSK and Roche did not execute any deals exceeding US$10B (2012–2021). In summary, major deals (2012–2021) amounted to a total financial volume of US$372.7B, representing 64.4% of the total deal volume.

In terms of number of deals, our descriptive results reveal that there is no significant upward or downward trend during the 2012–2021 period. The number of M&A deals varied between a minimum of seven deals (in 2013 and 2017) and a maximum of 24 deals in 2020 (data not shown). Major deals (>US$10B) accounted for 9% of all transactions made between 2012 and 2021. The majority of acquisitions were valued <US$10B (Figure 1), comprising 45% minor deals (<US$1B) and 38% medium deals (US$1B to US $9.99B). For 8% of deals, the financial volume was not disclosed.

Regarding the scope of M&A deals, between 2012 and 2021, 95% of M&A deals by leading pharmaceutical companies involved biotech firms, whereas only 5% were with other pharmaceutical companies. The majority of these M&A deals focused on oncology, representing 39% of all transactions. Other key areas included inflammation (8%), metabolism (6%), rare diseases (6%) and neurodegenerative diseases (6%).

Regarding the development stage of the lead candidate at the time of acquisition, 24% of the acquired assets were in preclinical or drug discovery phases, 39% were in early development (Phases I and IIa), 17% were in late development (Phase IIb and Phase III), 12% encompassed entire project portfolios, 5% included already approved new drugs and 3% did not specify the specific R&D phase.

Regarding the in-licensing activities of the companies, our analysis revealed that, unlike M&A, the number of in-licensing deals demonstrates a clear upward trend during the period investigated. For the 14 analyzed companies, the number of licensing agreements increased steadily from 13 deals (minimum, in 2012) to 61 deals in 2021, peaking at 73 deals in 2020 (Table 2). Furthermore, Figure 2 illustrates the key characteristics of in-licensing activities undertaken by the 14 leading pharmaceutical companies (2012–2021). Of the 402 licensing agreements analyzed, 84% were made with biotech firms, 9% with other pharmaceutical companies and 6% with universities and not-for-profit institutions. The therapeutic focus was diverse, with primary emphasis on oncology (40%), neurodegenerative diseases (10%), virology and other infectious diseases (9%), and metabolism (6%). The majority of agreements (71%) involved research collaboration and licensing in drug discovery and preclinical phases. The remaining deals were distributed between early development (22%) and late development (7%).

In addition to the descriptive analysis of M&A deals and licensing agreements, we investigated the correlation of four independent variables: (i) cumulative R&D expenditure; (ii) average R&D intensity; (iii) number of M&A deals; and (iv) number of in-licensing agreements – with the dependent variable (v) the number of FDA-approved new drugs (R&D output) for the 14 leading pharmaceutical companies included in our analysis (Table 3).

Our empirical findings provide several key insights:

- There is a positive correlation of the cumulative R&D expenditures (2012–2021) of the 14 companies and the number of FDA-approved new drugs they achieved during the same period. Increasing R&D expenditures by US $1B were associated with a higher R&D output of 0.12 new drugs (two-sided P-value: 0.0011) (see supplementary material S1 online). The coefficient of determination (R^2) implies that 60% of the variability of new drugs could hence be explained through R&D expenditures.
- Our results further demonstrate a correlation of the number of M&A deals pursued by the investigated 14 companies and the number of new drugs launched (2012–2021). Importantly, a single M&A deal led to 0.53 new drug approvals (two-sided P-value: 0.0242) (see supplementary material S2 online). The coefficient of determination (R^2) explains that 36% of the variability of new drugs is explainable by the number of M&A deals. This result is novel and indicates that M&A can serve as an effective component of the R&D strategy of the leading companies, significantly impacting their R&D output.
- Although licensing typically plays a key part in R&D strategies,[p22] with increasing importance in recent years (Table 2), there was no correlation of the number of in-licensing deals of the investigated companies and their R&D output (see supplementary material S3 online).
- Finally, there was no positive relation of R&D intensity and R&D output for the leading companies (see supplementary material S4 online).

Limitations of our analysis

Our analysis examined the relationship between R&D expenditure, R&D intensity, the number of M&A deals, the number of licensing agreements and new drug approvals. However, it did not account for specific deal structure details or commercial effects of related assets, because these cannot be reliably captured using publicly available data. Additionally, the impact of platform technologies on R&D output was not included in our analysis.

As described in a previous study, FDA approvals result from internal R&D activities as well as from the integration of external innovation.[p16] Therefore, we emphasize that individual licensing agreements can be highly successful in terms of R&D output, because in-licensed assets were further developed by leading pharmaceutical companies until FDA approval. Our analysis does not suggest that licensing agreements are inherently ineffective; rather, it highlights that there was no correlation between the number of licensing

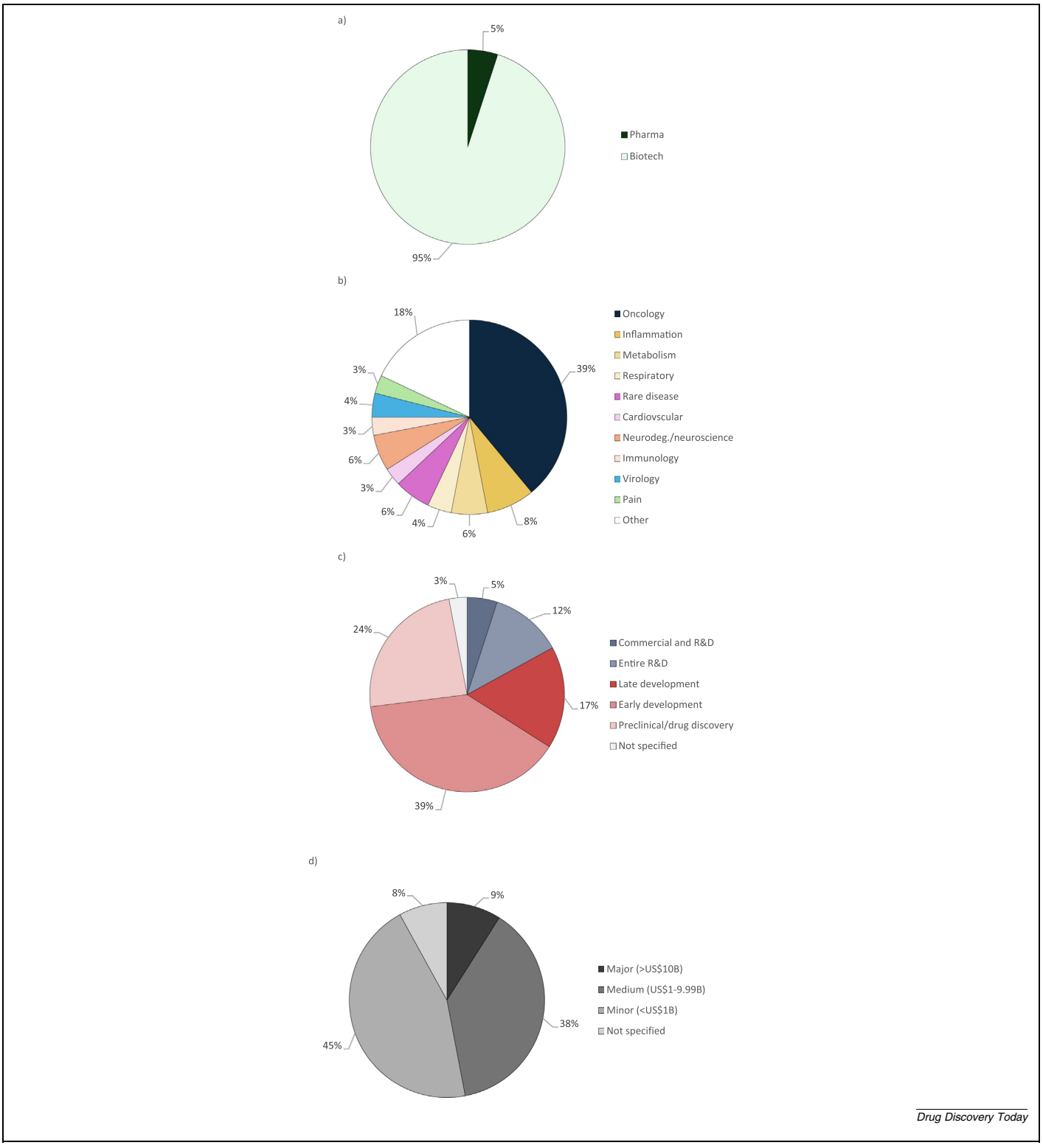

FIGURE 1

Key attributes of M&As of leading pharmaceutical companies (2012–2021). a) Deal source: source of acquisition assets. b) Deal focus: categorization resulted from the therapeutic area of deal related drug candidate. In case the deal referred to more than one candidate, the category referred to the therapeutic area of the lead candidate. c) Deal distribution: categorization of M&A deals resulted from the R&D stage of the acquired drug candidate at the time of the press release. In case the deal referred to more than one candidate, the category referred to the R&D phase of the lead candidate. In case of an entire portfolio acquisition, the deal was categorized as relating to the entire R&D phase. d) Deal size: major acquisitions are those with a transaction value of US $10B and more. Medium M&As refer to deals of a volume of >US$1B and <US$10B. And minor M&As are those with a reported value of <US$1B. N/A refers to deals with no specified transaction volume. Note: Mergers and acquisitions (M&As) were categorized according to investor relation information (see methodology). Abbreviations: M&A, merger and acquisition; DD, drug discovery; preclin., preclinical; early development, Phase I and Phase IIa; late development, Phase IIb and Phase III; entire, entire R&D value chain; commercial & R&D, M&As covering an entire project and product portfolio.

TABLE 2

Number of in-licensing deals of 14 leading pharmaceutical companies (2012–2021)

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
Abbvie	1	3	3	1	6	4	4	4	6	1	**33**
Amgen		1		2	3	5	3	1	1	2	**18**
AstraZeneca	3	2	4	2	1	2	2	1	4	5	**26**
Bristol-Myers Squibb	1		2	5	2	3	3		5	8	**29**
Boehringer Ingelheim	1			2	1	5	4	5	6	4	**28**
Eli Lilly		2	4	4	1	3	6	3	7	11	**41**
Gliead Science			1	1			4	8	7	2	**23**
GlaxoSmithKline	1			2	1			2	6	6	**18**
Merck & Co.	3	1	1	2	2	4	2	3	11	2	**31**
Novartis			1	5	3	4	5	3	2	5	**28**
Pfizer	1	5	5	3	6	3	4	2	2	3	**34**
Roche	1	3	1	6		4	5	6	10	4	**40**
Sanofi	1		1	5	3	2	1	2	1	3	**19**
Takeda		1	1	1	6	7	2	6	5	5	**34**
	13	**18**	**24**	**41**	**35**	**46**	**45**	**46**	**73**	**61**	

Data source: corporate communications, Refinitiv Eikon and GlobalData (see methodology).

agreements and the number of FDA drug approvals (2012–2021) among the leading pharmaceutical companies.

Another potential limitation of our analysis pertains to the potentially varying timeframes needed for internal R&D, M&A and in-licensing to influence the number of approved new drugs. Thus, considering the potential practical significance of our findings, it would be beneficial to validate the analysis using an expanded dataset (e.g., covering 20 years) and incorporating additional statistical approaches.

Correlational and regression analyses cannot determine causality. A dataset of n = 14 observations is on the one hand limiting or narrow but on the other hand it is very relevant because most major biopharmaceutical companies are included. The calculated r, r^2 and P-values indicate the strength of the correlations. Correlation analyses are sensitive to outliers and therefore can suggest correlations that were caused by a high variability. Our graphs and calculated 95% confidence intervals do not suggest such a bias.

When interpreting our data, two important aspects need to be highlighted. The slope of the regression curve for incremental investments translating to 0.12 (US$1B R&D spend) or 0.53 (M&A) for a new drug approval have individual Y-axis intercepts (3.263 and 5.494, respectively), which, in turn, implies that this increment needs an upfront investment as indicated by the Y-axis intercepts. One last limitation is that we cannot make any inferences on our first data points and the origin of the regression function. As an example, it remains unclear what the R&D output would have looked like if investments below US$41B (Boehringer) or below four M&As (GSK) had been undertaken.

Concluding remarks and discussion

In our analysis, we examined the impact of key strategic elements (R&D expenditures, R&D intensity, M&A and in-licensing) on the R&D output (total amount of innovation) of 14 leading pharmaceutical companies. The results are novel, offer new insights into pharmaceutical R&D and R&D productivity, and might impact future pharmaceutical business models.

R&D expenditure is a metric that demonstrates the actual R&D effort of a firm. It typically depends on the quality of internal and external R&D opportunities.[p6] We could show that higher R&D expenditures of the leading companies were related to higher R&D output (2012–2021). Investing US$1B in internal R&D was positively correlated with 0.12 new drugs approved by the FDA. Thus, our empirical analysis confirms our previous finding that there is economy of scale in pharmaceutical R&D.[p26] By contrast, R&D intensity is an indicator to measure the relative R&D potential of a firm. In our study, the R&D intensity of the leading pharmaceutical companies was not associated with FDA new drug approvals. Hence, we substantiate the claim that a flexible investment in R&D improves R&D productivity,[p10] whereas investing in R&D on a static range (fixed R&D intensity) does not positively impact the R&D output.

Our empirical analysis provides two additional key insights with impact for the R&D strategies of the leading pharmaceutical companies:

- the number of M&A deals correlated positively with new drug approvals; while
- in-licensing was not correlated with a higher R&D output.

Regarding these two independent variables, it should be noted that the terms and conditions of M&A deals in most cases are only partially disclosed, and the specifics of licensing agreements are not consistently published. Therefore, we focused on an R&D productivity analysis based on the number of M&A deals and licensing agreements as the input factor and the number of FDA drug approvals as the output factor. This represents an R&D efficiency calculation rather than an analysis of R&D effectiveness. A subsequent analysis evaluating the input (R&D expenditures, M&A investments, licensing costs) in the context of the outcome of R&D (commercial value of FDA approved new drugs) would be particularly intriguing.

Another debatable question to be explored in future analyses is the relationship between the variables R&D expenditure, R&D intensity, M&A and licensing. In terms of R&D strategy and investments in R&D, there are strategic interconnections and potential dependencies, such as

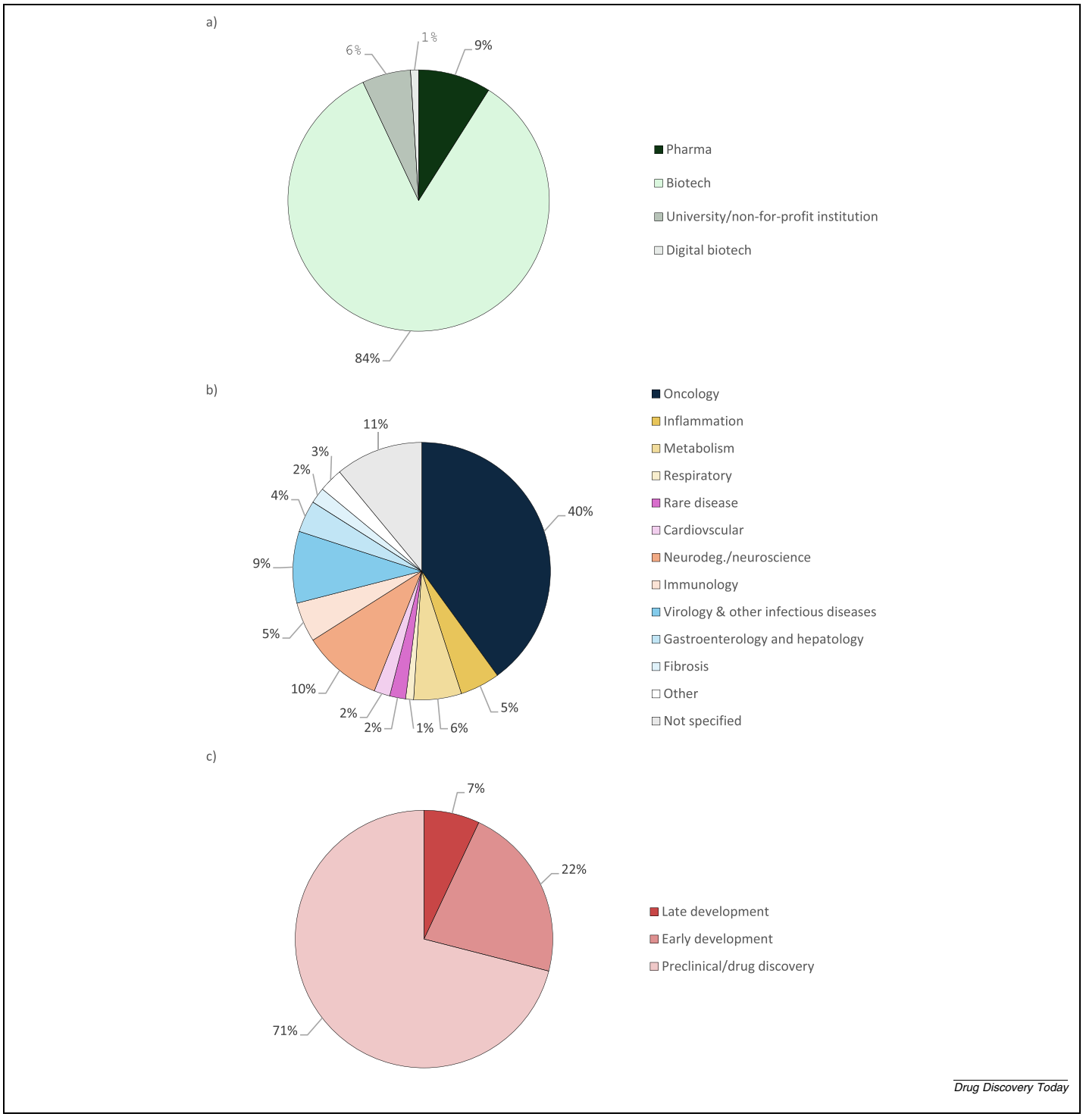

FIGURE 2

Key attributes of in-licensing deals of leading pharmaceutical companies (2012–2021). a) Deal source: source of license right. b) Deal focus: categorization resulted from the therapeutic area of deal related drug candidate. In case the deal referred to more than one candidate, the category referred to the therapeutic area of the lead candidate. c) Deal distribution: categorization of license deals resulted from the R&D stage of the licensed drug candidate or technology at the time of the press release. In case the deal referred to more than one candidate, the category referred to the R&D phase of the lead candidate. Note: License deals were categorized according to investor relation information (see methodology).

in portfolio decisions. Nevertheless, our analysis (see supplementary material S5 online) shows that the individual variables in our statistical analysis do not display any correlations.

Our results provide a first, yet well-supported, insight with practical relevance, challenging the prevailing R&D model of the leading companies that often relies on a combination of (i) internal R&D, (ii) acquisition of external assets and (iii) collaboration with biotech firms through drug licensing.[p16] Specifically, the finding that there is no correlation between the number of licensing agreements and FDA drug

TABLE 3

Correlation of R&D strategy elements and R&D output of 14 leading pharmaceutical companies (2012–2021)

	R&D expenditure vs R&D output	Number of M&A vs R&D output	Number of in-licensing deals vs R&D output	Average R&D intensity vs R&D output
Observations	14	145	405	14
Pearson r				
r	0.7756	0.5970	0.1918	−0.08251
95% confidence interval	0.4163 to 0.9254	0.09724 to 0.8563	−0.3772 to 0.6557	−0.5874 to 0.4686
R^2	**0.6015**	**0.3564**	**0.0368**	**0.0068**
P value				
***P* (two-tailed)**	**0.0011**	**0.0242**	**0.5113**	**0.7792**
P value summary	**	*	ns	ns
Significant? (alpha = 0.05)	Yes	Yes	No	No
Number of XY pairs	14	14	14	14

Data source: annual reports (2012–2021), press releases (2012–2021), Refinitiv Eikon, GlobalData and FDA website (see methodology) – data normalized and cleaned. R&D expenditures (US$B) are inflation-adjusted to 2021. Financial data originally reported in other currencies was converted to US$ by applying Refinitiv Eikon's embedded function. Standard errors in parentheses: *, $P < 0.05$; **, $P < 0.025$; ***.

approvals should make pharma executives challenge their R&D strategies. This is becoming particularly relevant as licensing has gained increased importance in recent years, at least among the 14 leading companies analyzed.

What should be known about this, and what possible explanations are there? In most cases, licensing agreements are linked with research collaborations between pharmaceutical companies and biotech firms. This form of pharma–biotech collaboration allows pharmaceutical companies to gain new insights, acquire scientific knowledge, build new technological competences and access innovation, whereas biotech firms view licensing as a commercialization strategy.[p27],[p28]

The lack of correlation between the number of licensing agreements and new drug approvals is somewhat understandable, because licensing, often combined with collaboration, typically occurs during the early development stages (early focus), where success rates tend to be lower. Additionally, agreements at this stage are often structured to align with the licensee's more cautious risk appetite. However, it could also be argued that in-licensing should demonstrate a measurable impact that goes beyond knowledge transfer and competency building. Pharma executives should carefully evaluate the purpose, scope and content of licensing agreements, particularly when they do not only involve the licensing of drug candidates with associated royalties and milestone payments but also include research collaborations. Important questions to ask in this context are: what measurable contributions do they offer? What added value do they provide beyond acquiring knowledge and building competencies? What is the tangible R&D output? These questions are crucial, because the financial scale of in-licensing agreements often parallels with that of M&A deals, particularly when all milestones are met.

Conversely, and in contrast to previous findings of a negative impact of M&A on R&D results,[p29],[p30] our insights provide strong indications of a positive effect of M&A on the R&D output of major pharmaceutical companies. This result, especially in the context that M&A can have positive impact on corporate performance,[p31] provides a rationale why pharma executives should be more selective when recognizing, assimilating and integrating external assets to commercial ends and possibly focus more on M&A rather than on in-licensing. A good example of a productive M&A is the acquisition of Celgene by BMS in 2019. The M&A deal did not only strengthen BMS's long-term capabilities in oncology and immunology but also included five new drugs (approved by the FDA between 2013 and 2020), including the two blockbusters Pomalyst® (pomalidomide, total sales 2023 of US$3.44B) and Reblozyl® (luspaterzept, US$1.01B). Another very productive deal was the US $46.8B acquisition of Genentech by Roche in 2009, which generated 13 FDA new drug approvals (2012–2020) for Roche and provided competitive advantage in the oncology and immunology field.

Empirical evidence shows that competitive advantage can be linked to technology, economies of scale and scope, processes, competencies or a firm's business model.[p32] Nowadays, the end-to-end integrated and R&D-driven business model of the leading companies is increasingly organized on a complementary combination of internally discovered and externally accessed innovation.[p16],[p33],[p34] Asset acquisitions fill pipeline gaps, increase R&D output, produce impactful innovation and enable firm growth.[p35] M&A allow companies to dynamically adapt to the changing technological, legal and economic environment and, hence, to provide sustainable competitive advantage.[p36]

What is necessary to positively leverage from M&A? According to Prabhu et al.,[p37] "deep internal knowledge provides firms with a superior ability to generate innovations from external sources such as acquisitions". This phenomenon is referred to as absorptive capacities and aligns to Cohen's and Levinthal's concept that a firm's R&D organization does not only create new information but also enhances a firm's ability to assimilate and exploit external knowledge.[p38] Because the integration of external assets allows a company to leverage its own (existing) knowledge as a valuable resource for strengthening R&D (leveraging what they know),[p39] absorptive capacity impacts a firm's ability to innovate.[p40]

In conclusion, our analysis shows that internal R&D and M&A activities significantly enhance R&D productivity of leading pharmaceutical companies. To fully benefit from this, pharmaceutical companies need to build pre-acquisition knowl-

edge in the field of the acquired asset. Therefore, pharma executives should design their R&D models around strong internal R&D that (i) dynamically adapts to new scientific and technological advancements and (ii) is strategically expanded through M&A rather than licensing.

CRediT authorship contribution statement

Alexander Schuhmacher: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kyrylo Grinchenko:** Methodology, Investigation, Formal analysis, Conceptualization. **Oliver Gassmann:** Writing – review & editing, Writing – original draft. **Dominik Hartl:** Writing – review & editing, Writing – original draft. **Markus Hinder:** Writing – review & editing, Writing – original draft, Formal analysis.

Data availability

Data will be made available on request.

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Appendix A. Supplementary material

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[1] Excluded from the analysis because of corporate structure with multiple business units, making it difficult to analyze the pharma-related internal R&D expenditures.