**Supplementary information** 

# Comprehensive measurement of biopharmaceutical R&D investment

In the format provided by the authors and unedited

## Supplementary Box 1 | Developing the public company dataset

- From S&P Capital IQ, we identified 3,434 public companies with a Primary Industry Classification (PIC) Level 4 code of *Pharmaceuticals* or *Biotechnology*.
- We removed 871 companies that reported no financial results in 2021; we assume these companies had no operations.
- Two researchers independently reviewed company descriptions provided by S&P Capital IQ for all public companies (384) constituting the top 90% of total R&D expense in this population.
  - We removed 51 companies performing non-biopharmaceutical activities (which we pre-specified), such as companies primarily engaged in agriculture and animal health, contract development and contract manufacturing services, the development and supply of active pharmaceutical ingredients (APIs), medical device sales and manufacturing, the sale and manufacturing of recreational cannabis, herbal medicine, supplements and traditional Chinese medicine, and generic only manufacturers.
  - Disagreements on inclusion versus exclusion decisions were followed by a more in-depth review of publicly reported financial statements.
- For companies not included in the top 90%, we applied two approaches to remove companies performing non-biopharmaceutical activities.
  - We removed 86 companies with a Primary Level 5 PIC code related to nonbiopharmaceutical activities. Supplementary Table 1 lists all Level 5 PIC codes within the Level 4 PIC codes *Pharmaceuticals* and *Biotechnology* and identifies the Level 5 PIC codes that were used to remove companies.
  - We removed 961 companies with company descriptions including keywords associated with non-biopharmaceutical activities because S&P Capital IQ does not provide a Level 5 PIC code for all public companies. Supplementary Table 2 lists the types of activities we removed, and the associated keywords used to identify these types of activities.
- We removed 29 companies which were operating as subsidiaries of parent companies also included in the population to avoid double counting.
- The final population of public companies includes 1,436 public biopharmaceutical companies. A public company reconciliation is provided in **Supplementary Table 3**.
- While not immune from data quality concerns<sup>1</sup> the S&P Capital IQ database has been widely used in academic research on firm productivity and innovation due to its comprehensive coverage of public companies.<sup>2-4</sup>

# Supplementary Box 2 | Distinguishing between commercial- and development-stage companies

- Companies in the top 90% of R&D expense were manually classified as commercialor development-stage based on a review of company descriptions and websites.
- For companies not included in the top 90%, companies with 2021 revenue over \$1 billion were classified as commercial-stage.
- All other companies were classified as commercial-stage or development-stage using a keyword search on company descriptions and product approval/launch data provided by S&P Capital IQ.
  - **Supplementary Table 4** provides the list of keywords used to identify commercial- and development-stage companies.
  - Companies that had one or more products approved or launched in the last 10 years were classified as commercial-stage.
- Our classification results in 575 commercial-stage public companies and 861 development-stage public companies.

#### Supplementary Box 3 | Developing the private company datasets

- From Pitchbook, we identified 7,404 private development-stage companies with a primary industry group classification of *Pharmaceuticals and Biotechnology*. These companies completed 12,738 venture capital, private equity growth, and general debt deals over 2019-2021.
  - We removed 828 companies with a subindustry classification of *Discovery Tools (Healthcare), Drug Delivery*, or *Other Pharmaceutical and Biotechnology* as their activities are ancillary to the discovery and development of new drugs.
  - We removed 2,428 companies with company descriptions including keywords associated with non-biopharmaceutical activities. Supplementary Table 2 lists the types of activities removed, and the associated keywords used to identify these types of activities.
  - We removed 322 companies that are public and/or are included in the public company population.
  - We removed 1,272 deals (and 549 companies) with no reported deal value because these do not contribute to our measure of R&D investment. Pitchbook captures data on deal activity through a variety of means including self-reports from fund managers. Complete data is not available across all deals.
  - We removed 1,453 extraneous deals (and 530 companies) with irrelevant deal types. Irrelevant deal types included grants, debt refinancing, equity crowdfunding, debt repayments, leveraged buyouts and secondary public offerings.
  - We reviewed all deals over \$1 billion (and the associated company) for relevance to the biopharmaceutical ecosystem. We identified 11 total deals, all of which were removed from the population in previous steps.
  - The final private development-stage population includes 2,747 companies with 3,909 associated deals. A reconciliation of these procedures and their impact on the number of deals and R&D investment is provided in Supplementary Table 5.
- Private commercial-stage companies were manually gathered using S&P Capital IQ and manual search. We considered only private companies for which we could locate publicly reported financials. The final private commercial-stage population included 8 companies: Boehringer Ingelheim, Ferring, Leo Pharma, Les Laboratoires Servier, Menarini, Octapharma, Radius Health, and Sinovac. To the extent that our population does not include all relevant private commercial-stage companies, our measures of R&D investment and revenue among these companies would be understated.
- Due to limited disclosure requirements, data validation of private company financing data is challenging, and data completeness remains a concern.<sup>5</sup> Recognizing these data challenges, we chose to rely on the Pitchbook database which has been recognized as a strong data source by several researchers.<sup>6, 7</sup> For example, in one study utilizing several sources of data, Pitchbook had the greatest company coverage.<sup>7</sup>

#### Supplementary Box 4 | Measuring R&D investment for each population

- For public commercial-stage companies, we used the S&P Capital IQ variable "IQ\_RD\_EXP\_FN." This variable, also referred to as "Research And Development Expense From Footnotes [3168]" is a supplemental line item that represents the costs incurred by a company on the development of a new product, innovation relating to technology formulation, process development, engineering expenses, or on the process undertaken in upgrading the existing product or service line.<sup>8</sup>
  - This item includes the following: company-sponsored research and development, research and development expenses incurred for its own product, both R&D expenses sponsored by the customer and by the company, acquired or in-process R&D expenses, and the amortization /write-off of research, development, or software development costs.<sup>8</sup>
  - Under generally accepted accounting principles (GAAP) in the United States, R&D expenditures are expensed as incurred and include materials, equipment, facilities, personnel, intangible assets purchased from others, contract services, and indirect costs.<sup>9</sup> The treatment of R&D expenditures under International Financial Reporting Standards (IFRS) outside the United States are similar, except that development expenditures are capitalized and then amortized.<sup>10</sup>
- For public development-stage companies, we used the S&P Capital IQ variable "IQ\_NI." This variable, also referred to as "Net Income [15]", includes earnings from continuing operations, earnings of discontinued operations, extraordinary items, and minority interest in earnings.<sup>11</sup>
- For private commercial-stage companies, we used R&D expense as reported on each company's publicly available financial statements.
- For private development-stage companies, we used the Pitchbook Data Inc. variable "Deal Size." This variable represents the total amount of capital invested into a company by an investor or group of investors for a specific transaction.<sup>12</sup>
- Our approach assumes that all functions within development-stage companies principally support R&D efforts. However, we acknowledge that a share of companies transitioning, or close to transitioning, from development-stage to commercial-stage may incur expenses that are no longer exclusively in support of R&D activities even if they have no launched or approved products. To the extent that part of their cost structure includes marketing expenses, our approach overestimates R&D. We report on the sensitivity of our measure to this assumption for public development-stage companies in more detail in Supplementary Table 8.

### **Supplementary Box 5 | Adjustment for conglomerate operations**

- Several large, commercial-stage companies are conglomerates that perform biopharmaceutical and non-biopharmaceutical activities.
- We used business segment information provided by S&P Capital IQ to identify companies that derive a significant proportion of their total revenue from non-biopharmaceutical activities. Specifically, companies were classified as conglomerates if they derived at least 20% of revenue from non-biopharmaceutical activities as indicated by S&P Capital IQ business segment data. We limited the number of identified conglomerates to only those that could have a meaningful impact on results, defined as companies constituting the top 90% of total R&D expense and companies with 2021 revenue exceeding \$1 billion; this yielded 10 companies.
- For companies identified as conglomerates that disaggregated R&D expense by segment in their annual filings, we only included the disclosed R&D expense related to biopharmaceuticals in our measure of R&D investment.
- Three conglomerates did not disclose biopharmaceutical R&D expense in their financial statements; therefore, we included a proportion of total R&D expenses equal to the proportion of biopharmaceutical revenues as a share of total company revenues. Imputed R&D investment constituted less than 1% of aggregate conglomerate R&D investment. Imputed R&D investment is a conservative measure of R&D investment since non-pharmaceutical segments typically have much lower R&D intensity.

# Supplementary Box 6 | Rationale for including IPR&D expenses in total R&D investment

- GAAP and IFRS both acknowledge that R&D intangible assets may be acquired rather than internally developed. However, the standards for expensing versus capitalizing acquired R&D assets (in-process R&D, or IPR&D) differ slightly.<sup>13, 14</sup> Our methods recognize that R&D expense can include the amortization and write-off of IPR&D.
- We include IPR&D expenses in our calculations for two reasons:
  - First, a commercial-stage company faces a choice between investing in internal R&D to develop knowledge or purchasing it through an acquisition. From an economic perspective, whether the knowledge was acquired or developed in-house is irrelevant, and assuming a competitive market, had a drug company been able to create the knowledge in-house more efficiently, it would have done so. This assumption does not require that the company would have created the exact same knowledge in-house had it not purchased it, but rather that it would have invested equivalent resources into internal R&D efforts.
  - Second, R&D asset acquisitions add value to the biopharmaceutical R&D ecosystem when large pharmaceutical firms use their specialized knowledge to increase the value of acquisitions or to diversify risk of a decline in revenues. A large pharmaceutical company can bring a drug to market more efficiently than a small company would have been able to given scale-effects.
- Although we believe including IPR&D expenses is appropriate, we acknowledge that the accounting treatment of IPR&D expenses differs from other R&D expenses, and thus could result in the aggregation of expenditures that occurred at different times and perceived double-counting if this method is repeated for multiple years.

#### Supplementary Box 7 | Other variables used

- To measure revenue for public commercial-stage companies, we used S&P Capital IQ's variable "IQ\_TOTAL\_REV", also known as "Total Revenues [28]". For private commercial-stage companies, we used total revenue as reported on publicly available financial statements.
- To measure selling, general, and administrative ("SG&A") expenses for public companies, we used S&P Capital IQ's variable "IQ\_SGA", also known as "Selling General & Admin Expenses [23]". This variable includes all SG&A expenses, related stock-based compensation, and other expenses. **Supplementary Tables 7 and 8** use this measure.
- To measure selling and marketing ("S&M") expenses for public companies, we used S&P Capital IQ's variable "IQ\_SALES\_MARKETING" which includes advertising and marketing expenses, marketing stock-based compensation, and distribution expenses. **Supplementary Table 7** uses this measure.
- To measure total IPR&D expenses in the public commercial-stage company • population, we measured the total difference between "IQ RD EXP FN" and "IQ RD EXP" after adjusting for companies with missing "IQ RD EXP" values. "IQ RD EXP", also known as "R&D Expenses [100]" represents total R&D expenses reported on the face of the income statement, whereas "IQ RD EXP FN" is collected from the notes to the financial statements. A number of companies did not report R&D expenses on the face of the income statement, but did so in the notes. Beyond that, as described by Capital IQ client support, the primary difference between "IQ RD EXP FN" and "IQ RD EXP" is that the latter excludes all IPR&D expenses, as well as other miscellaneous items. We confirmed this difference by means of manual review for the 10 largest companies in terms of R&D. Thus, the aggregate difference between the two across our public commercial-stage population, after removing the impact of companies with missing "IQ RD EXP", allowed us to derive the sensitivity analysis discussed in the main text. We assumed that all IPR&D expenses contributed by conglomerates were related to their biopharmaceutical operations.

## **Supplementary Box 8 | Limitations**

- Our analysis provides only a cross-sectional estimate of R&D investment for 2021. Measuring R&D investment for a single year does not capture the changing landscape of drug development over the development lifecycle. Future research could apply our methods over time, which would further inform how the biopharmaceutical industry continues to evolve and change.
- We relied on S&P Capital IQ to provide data on public company financial results and Pitchbook to provide private company deal funding data. To the extent that these datasets are incomplete or certain data anomalies exist, we may underestimate total R&D investment and/or revenues. Similarly, while we manually collected data for several large private biopharmaceutical companies, we were unable to include all potentially relevant companies due to the lack of public reporting.
- Our results may be understated to the extent that publicly reported R&D (as gathered by S&P Capital IQ) does not capture indirect costs necessary to support or operationalize R&D (such as, relevant general and administrative expenses, training, pharmacovigilance expenses). We proxy for R&D investment at private development-stage companies using a three-year average of Pitchbook deal data because financial data is seldom accessible in the public domain. To the extent that all financing deals are not captured by Pitchbook, we may underestimate total R&D.
- Overall, due to more limited data, private company R&D is more likely to be understated relative to public company R&D. Further, data visibility in regions outside of the USA may be lower, giving R&D investment in those regions a higher probability of understatement. For example, we removed a total of 1,272 private deals with missing deal value; 68% of the removed deals involved private companies headquartered outside of the USA.
- We relied on both manual review and an algorithmic approach (for example, industry codes, keywords searches, and revenue amounts) to arrive at our populations. While we believe these methods yielded populations representative of the biopharmaceutical ecosystem, to the extent they resulted in the improper exclusion, inclusion, or classification of a company, our results would be impacted.
- We did not seek to include spending by governments or nonprofits. However, we recognize that governmental entities provided support for pharmaceutical research and commercialization during the COVID-19 pandemic. Our study does not identify or adjust for any impact of pandemic-related government funding.

#### Supplementary Box 9 | Results in context

- While the focus of this comment was to provide a transparent measurement of global biopharmaceutical R&D, it is helpful to contextualize our results with respect to prior research, relevant comparisons, and implications for current policy debates.
- **R&D Investments & Ecosystem Policy.** For example, our results align with comparative international estimates, including those by the OECD, that show the USA as the global hub for biopharmaceutical R&D.<sup>15, 16</sup> The large amount of R&D investment by US-based firms has been attributed to several factors: A large domestic market, innovation-friendly public policy, continued government investment in basic science, strong academic funding in bioscience-related fields, a highly trained workforce and comprehensive public-private R&D collaborations across competing innovation clusters.<sup>17-22</sup> While the exploration of policies affecting these factors falls outside of this study's aim, a robust, replicable measure of R&D investment and intensity is foundational for future research and informed public debate.
- **R&D Investments and Returns.** The Congressional Budget Office (CBO) calculated that publicly traded US firms reinvested a growing share of revenues into R&D from 2000-2019, with R&D intensity averaging 19% up to a peak of 25%.<sup>23</sup> Our finding of 30% R&D intensity for public US companies in 2021 suggests a continued upward trend of this relationship; adding private companies provides an even higher estimate for the entire US R&D ecosystem (34%). It has been widely noted that R&D investment in the pharmaceutical sector is contending with declining productivity, typically characterized as the ratio of R&D investment to new drug approvals or to the commercial value of new drugs over the investment period.<sup>23-25</sup> To the extent that our finding of greater R&D intensity indicates costlier drug development overall, we believe it provides a critical input for scholarly investigations and regulatory policy aimed at discerning levers to optimize R&D productivity across the ecosystem.

# Supplementary Table 1 | S&P Capital IQ Level 5 PIC Codes

Included	Excluded
Pharmaceutical Products	Veterinary Drugs
	Pharmaceutical Contract Manufacturing
Medicinal Chemicals and Botanical Products	Services
Not Specified	Agricultural Biotechnology
Non-Prescription Drugs	Orthobiological Products
	Biotechnology Research Equipment
Biological Products	Manufacturers
Gene Research and Development	Pharmaceutical Contract Laboratories
Protein and Genome Sequence Products	Microbiology
In Vivo Diagnostic Substances	Medical Device Research and Development
	Pharmaceutical Contract Research
Drug Delivery Technologies	Organization

# Abbreviations: S&P, Standard and Poor's; PIC, Primary Industry Classification Source:

[A] S&P Capital IQ.

#### Supplementary Table 2 | Keywords used to remove irrelevant companies

Keyword Category	Exact Keywords Applied
Generic	generic; otc; over the counter
Traditional Chinese Medicine /Herbal	tcm; traditional chinese medicine; herbal; botanical; supplements; food
Cannabis	cannabis; hemp; marijuana; thc; cannaboid; cbd
Contract Manufacturing	api; active pharmaceutical ingredient; cdo; contract; cro; cmo; cdmo; laboratory; laboratories; client, services; manufacturer; distributor; contract manufacturing; contract research; contract development
Agricultural	agricultural; agri; animal; veterinary; aquaculture; crop; pesticide
Medical Device	instrument; detection; device; equipment; biosurgical; diagnostics; screening; sequencing; isotope
Other Keywords	biofacturing; infrastructure; pharmacist; quantum; health tech; software; biotechnology platform; <b>beauty products; bioinformatics; cosmetics</b>

**Abbreviations**: OTC, over the counter; TCM, traditional Chinese medicine; THC, tetrahydrocannabinol; CBD, cannabidiol; API, active pharmaceutical ingredient; CDO, contract development organization; CRO, contract research organization; CMO, contract manufacturing organization; CDMO, contract development and manufacturing organization.

#### Note:

[1] Due to the larger number of companies and different nature of activities undertaken by companies in the private development-stage population, an expanded set of keywords was utilized to identify irrelevant companies. Keywords utilized to refine the private development-stage company population only are indicated in bold font. All non-bolded keywords were applied to refine both the public and private company populations.

## Supplementary Table 3 | Public company population reconciliation

\$USD Millions	_	2021		
Reconciliation Summary	Company Count	R&D Investment	Revenue	
Beginning Public Biopharmaceutical Population (per CapIQ)	3,434	\$266,926	\$1,430,028	
Exclusions				
Removal of Non-Operating Companies	(871)	\$0	\$0	
Removal of Irrelevant Companies From Manual Review	(51)	(\$10,579)	(\$158,398)	
Removal of Irrelevant Companies Using PIC Codes	(86)	(\$807)	(\$13,507)	
Removal of Irrelevant Companies Using Keywords	(961)	(\$6,821)	(\$145,419)	
Removal of Operating Subsidiaries	(29)	(\$741)	(\$1,971)	
Removal of Sandoz	0	(\$899)	(\$9,631)	
Adjustments				
Conglomerate Adjustments	N/A	(\$10,649)	(\$116,798)	
Net Loss Adjustment for Public Development-Stage Companies	N/A	\$7,985	(\$15,859)	
Public Biopharmaceutical Population	1,436	\$244,415	\$968,444	

Abbreviations: R&D, research and development; PIC, primary industry classification

Notes:

[1] The beginning biopharmaceutical population includes all public companies with a level 4 PIC code of *Pharmaceuticals* or *Biotechnology*.

[2] Non-operating companies are those that report no financial results in Capital IQ for fiscal year 2021.

[3] **Supplementary Box 1** describes each exclusion step in detail.

[4] The removal of Sandoz line is a manual adjustment made to remove the generic division of Novartis.

[5] **Supplementary Box 4 and 5** describe the adjustments made to public development-stage company and conglomerate R&D investment and revenue, respectively.

Source:

[A] S&P Capital IQ.

#### Supplementary Table 4 | Keywords used to identify commercial- and developmentstage companies in the public population

Commercial-Stage Keywords	Development-Stage Keywords
	clinical stage biopharmaceutical
commercial product; provides product	company
	clinical stage bio pharmaceutical
approved	company
	clinical stage drug development
marketed; marketing	company
offers	
distributes	
commercial stage	

#### Note:

[1] Companies with development-stage keywords must have no product approvals or launches to be classified as development-stage.

## Supplementary Table 5 | Private company population reconciliation

\$USD Millions			2019-2021
Reconciliation Summary	<b>Company Count</b>	Deal Count	R&D Investment
Initial Private Biopharmaceutical Population	7,404	12,738	\$193,828
Company Level Exclusions			
Removal of Irrelevant Industry Codes	(828)	(1,501)	(\$15,013)
Removal of Irrelevant Companies Using Keywords	(2,428)	(4,008)	(\$59 <i>,</i> 666)
Removal of Public Companies	(322)	(595)	(\$36,023)
Deal Level Exclusions			
Removal of Deals With No Value	(549)	(1,272)	\$0
Removal of Irrelevant Deal Types	(530)	(1,453)	(\$5,696)
Private Development-Stage Biopharmaceutical			
Population	2,747	3,909	\$77,430
			2021
	<b>Company Count</b>	Deal Count	R&D Investment
Private Development-Stage Population	2,747	3,909	\$25,810
Private Commercial-Stage Population	8	N/A	\$6,176
Total Private Biopharmaceutical Population	2,755	3,909	\$31,986

Abbreviations: R&D, research and development.

Notes:

[1] The initial private company population included all companies with a Pitchbook primary industry group classification Pharmaceuticals and Biotechnology.

[2] Supplementary Box 3 describes each company level and deal level exclusion in detail.

[3] Private development-stage population 2021 R&D investment is derived from taking the population R&D investment over 2019-2021 and dividing it by 3 [77,430 / 3 = 25,810]. For development-stage company counts, we use the gross number of companies that raised capital over 2019-2021.

Sources:

[A] Pitchbook Data, Inc.

[B] Manual search on private commercial-stage company financial

statements.

## Supplementary Table 6 | Population summary statistics

	Commercial-Stage		Development-Stage	
\$USD millions	Public	Private	Public	Private
Number of Companies	575	8	861	2,747
Number of Deals	N/A	N/A	N/A	3,909
Mean R&D Investment	\$343	\$882	\$55	\$20
Median R&D Investment	\$16	\$358	\$0	\$6
Mean Revenue	\$1,887	\$6,719	\$18	N/A
Median Revenue	\$55	\$3,700	\$0	N/A

Abbreviations: R&D, research and development; USD, United States Dollar.

#### Note:

[1] We do not measure development-stage company revenue since it does not represent sales of biopharmaceutical products. Further, for private development-stage companies, public reporting is not available.

Sources:

[A] S&P Capital IQ.

[B] Pitchbook Data, Inc.

[C] Financial statements manually gathered.

#### Supplementary Table 7 | Geographic summary of the biopharmaceutical population

\$USD Millions	н	Headquarter Geographic Region			
	United	Asia /			_
Company Count	States	Pacific	Europe	Other	Total
Public Commercial-Stage	158	273	99	45	575
Public Development-Stage	463	166	163	69	861
Private Development-Stage	1,374	559	695	119	2,747
Private Commercial-Stage	1	1	6	0	8
Total	1,996	999	963	233	4,191
% of Total	48%	24%	23%	6%	
R&D Investment					
Public Commercial-Stage	\$105,077	\$27,505	\$64,048	\$749	\$197,380
Public Development-Stage	\$32,647	\$6,795	\$6,159	\$1,433	\$47,035
Private Development-Stage	\$14,827	\$6,592	\$3,815	\$576	\$25,810
Private Commercial-Stage	\$131	\$155	\$5,890	\$0	\$6,176
Total	\$152,683	\$41,048	\$79,912	\$2,759	\$276,402
% of Total	55%	15%	29%	1%	
SG&A Expense					
Public Commercial-Stage	\$91,262	\$61,146	\$88,411	\$2,024	\$242,843
Private Commercial-Stage	\$130	\$594	\$1,067	\$0	\$1,791
Total	\$91,392	\$61,740	\$89 <i>,</i> 478	\$2,024	\$244,634
% of Total	37%	25%	37%	1%	
S&M Expense (Imputed)					
Public Commercial-Stage	\$18,404	\$34,398	\$42,299	\$702	\$95,803
Private Commercial-Stage	\$0	\$8	\$694	\$0	\$702
Total	\$18,404	\$34,406	\$42,993	\$702	\$96,505
% of Total	19%	36%	45%	1%	
Revenue					
Public Commercial-Stage	\$455 <i>,</i> 480	\$183,648	\$323,490	\$5,826	\$968,444
Private Commercial-Stage	\$230	\$19,375	\$34,150	\$0	\$53,755
Total	\$455,710	\$203,023	\$357,640	\$5,826	\$1,022,199
% of Total	45%	20%	35%	0%	
Intensity Metrics					
R&D Intensity	34%	20%	22%	47%	27%
SG&A Intensity	20%	30%	25%	35%	24%
S&M Intensity	4%	17%	12%	12%	9%

**Abbreviations**: R&D, research and development; SG&A, selling general and administrative; S&M, selling and marketing; USD, United States Dollar.

Notes:

[1] R&D intensity represents R&D investment as a share of total revenue. SG&A intensity and S&M intensity are also calculated as a share of total revenue.

[2] Headquarters as reported by S&P Capital IQ (Public companies), Pitchbook (Private development-stage companies), and manual search (Private commercial-stage companies).

[3] Other includes Canada, Africa, the Middle East, Latin America, and the Caribbean.

[4] While only a fraction of imputed S&M expense is directly related to consumer advertising, the aggregate measure of S&M expense may not capture all non-advertising S&M items for all companies. For some companies, such items may instead be reported elsewhere, such as within SG&A. As captured by S&P Capital IQ, it appears more common that S&M data for companies following International Financial Reporting Standards (IFRS) contain a broader range of non-advertising items within reported S&M – for example, commercialization expenses such as commissions to distributors or trade bad debt – compared to US based

companies operating under Generally Accepted Accounting Principles (GAAP). In part, regional differences in S&M therefore reflect variations in reporting standards and the representation of reported S&M items in the S&P Capital IQ dataset we used.

[5] We imputed S&M considering that not all companies reported this metric separately (39% of public commercial-stage companies that reported SG&A did not report S&M expenses). S&M as a percentage of SG&A for companies that reported both metrics was on average 39.5%. We used this percentage to impute total S&M for public companies that only reported SG&A. **Sources**:

[A] S&P Capital IQ.

[B] Pitchbook Data, Inc.

[C] Financial statements manually gathered.

		[1]	[2]	[3]
\$USD Millions	Net Loss Method	Adjust Transitional Companies	Net Loss Adding Back SG&A Expense	R&D Expense
Public Development-Stage R&D Investment	47,035	45,842	29,383	39,050
% Reduction from Net Loss Method		-3%	-38%	-17%

# Supplementary Table 8 | Public development-stage R&D investment sensitivity analysis

#### Abbreviations:

R&D, research and development; SG&A, selling, general, and administrative.

#### Notes:

[1] Companies transitioning, or close to transitioning, from development-stage to commercial-stage may incur expenses that are not in support of R&D activities, such as selling and marketing activities. We identified 76 development-stage companies that had revenues increase by more than \$10 million from 2021 to 2022, suggesting that these companies may have been transitioning to commercial-stage in 2021. Had we measured R&D for these companies using R&D expense (as we do for commercial-stage companies), rather than the total net loss (as we do for development-stage companies), our estimate of total R&D investment among public development-stage companies would have been approximately \$1 billion lower (or 3%). This results in a less than 1% decrease in global R&D investment. It is important to note that these companies did not have launched or approved products in 2021, which supports our initial conclusion that these companies should be treated as development-stage.

[2] Removal of SG&A expenses from net loss results in a reduction of \$18 billion (or 38%) of total R&D investment among public development-stage companies. This results in a 6% decrease in global R&D investment. See **Supplementary Box 7** for more detail on the S&P Capital IQ variables used to measure SG&A expenses in the public development-stage population. This sensitivity was performed to understand the level of SG&A incorporated in net loss across the public development-stage population.

[3] Use of reported R&D expense instead of net loss results in a reduction of \$8 billion (or 17%) of total R&D investment among public development-stage companies. This results in a 3% decrease in global R&D investment.

#### Sources:

[A] S&P Capital IQ.

[B] Pitchbook Data, Inc.

#### References

- 1. Liu G. Data Quality Problems Troubling Business and Financial Researchers: A Literature Review and Synthetic Analysis. *Journal of Business & Finance Librarianship*. 2020:1-47.
- Satta G, Parola F, Penco L, Esposito de Falco S. Insights to Technological Alliances and Financial Resources as Antecedents of High-tech Firms' Innovative Performance. *R&D Management*. 2016;46(S1):127-144.
- 3. Unsal O, Rayfield B. Institutional Investors and Medical Innovation. *The Quarterly Review of Economics and Finance*. 2019;74:190-205.
- 4. Lev B, Radhakrishnan S, Yixing Tong J. Earnings Component Volatilities: Capital Versus R&D Expenditures. *Production and Operations Management*. 2021;30(5):1475-1492.
- 5. Kaplan SN, Lerner J. Venture Capital Data: Opportunities and Challenges. University of Chicago Press; 2017. *Measuring Entrepreneurial Businesses: Current Knowledge and Challenges*.
- 6. Lerner J, Nanda R. Venture Capital's Role in Financing Innovation: What We Know and How Much We Still Need to Learn. *Journal of Economic Perspectives*. 2020;34(3):237-261.
- 7. Burton MD, Cole S, Dev A, et al. *The Project on Impact Investments' Impact Investment Database*. 2021. *Harvard Business School*. Accessed April 25, 2024. https://www.hbs.edu/impact-investments/Shared%20Documents/Impact%20Investing%20Database.pdf
- 8. Capital IQ. As described by Capital IQ client support services. n.d.;
- 9. Accounting Standards Codification 730-10-25-1 and 730-10-25-2.
- 10. International Accounting Standard 38.54 and 38.57.
- 11. S&P Capital IQ database. S&P Capital IQ. n.d.;
- 12. Pitchbook database. *Pitchbook Data, Inc.* n.d.;
- 13. Accounting Standards Codification 350-30-35-17A and 805-20-30-1.
- 14. International Accounting Standard 38.33 through 38.37.
- 15. Editor. US Biomedical R&D Spending Declines, Asian Spending Soars. *Nature Reviews Drug Discovery*. 2014;13:91.
- 16. OECD. Pharmaceutical research and development. https://www.oecd-ilibrary.org/sites/6e38c622en/index.html?itemId=/content/component/6e38c622-en
- 17. Cleary EG, Beierlein JM, Khanuja NS, McNamee LM, Ledley FD. Contribution of NIH Funding to New Drug Approvals 2010–2016. *PNAS*. 2018;115(10):2329-2334.
- Baily MN, Montalbano N. Clusters and Innovation Districts: Lessons from the United States Experience. 2018. The Brookings Institution. Accessed April 25, 2024. https://www.brookings.edu/wpcontent/uploads/2018/01/es 20180116 bailyclustersandinnovation.pdf
- Kyle MK. The Alignment of Innovation Policy and SocialWelfare: Evidence from Pharmaceuticals. *Innovation Policy and the Economy*. 2020;20(1):95-123.
- Pressman L, Planting M, Moylan C, Bond J. Economic Contributions of University/Nonprofit Inventions in the United States: 1996 – 2020. 2022. Biotechnology Innovation Organization (BIO) and AUTM. Accessed April 25, 2020. https://autm.net/AUTM/media/About-Tech-Transfer/Documents/BIO-AUTM-Economic-Contributions-of-University-Nonprofit-Inventions\_14JUN2022.pdf
- 21. Wessner CW. Entrepreneurship and the Innovation Ecosystem Policy Lessons from the United States. Springer; 2005. *Local Heroes in the Global Village. International Studies in Entrepreneurship.*
- 22. Research America. U.S. Investments in Medical and Health Research and Development: 2016-2020. 2022. Research America. Accessed April 25, 2024. https://www.researchamerica.org/wpcontent/uploads/2022/09/ResearchAmerica-Investment-Report.Final .January-2022-1.pdf
- 23. Congressional Budget Office. *Research and Development in the Pharmaceutical Industry*. 2021. *Congressional Budget Office (CBO)*. Accessed April 25, 2024. https://www.cbo.gov/publication/57126
- 24. Schuhmacher A, Hinder M, von Stegmann Und Stein A, Hartl D, Gassmann O. Analysis of Pharma R&D Productivity A New Perspective Needed. *Drug Discovery Today*. 2023;28(10)
- 25. Paul SM, Mytelka DS, Dunwiddie CT, et al. How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge. *Nature Reviews Drug Discovery*. 2010;9:203-214.