nature REVIEWS DRUG DISCOVERY

SUPPLEMENTARY INFORMATION

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The fragmentation of biopharmaceutical innovation

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https://doi.org/10.1038/d41573-019-00046-3

Supplementary Box 1 | **Data and analysis**

The state of pharmaceutical industry fragmentation was investigated using multiple analytical approaches:

***Deal-making activity*.** Merger and acquisition (M&A) deals often result in companies being acquired or merging into larger entities, thus contributing to industry consolidation. To investigate the volume of such consolidative activity in the pharmaceutical space, we analysed all M&A deals announced between January 1, 2000 and December 31, 2017 reported in the IQVIA PharmaDeals database (8706 deals classified as "M&A" according to the database's classification). Out of those, we excluded deals not relevant to innovative biopharmaceutical segment (e.g., focused on medical devices, consumer health products, generics, animal health, or pharmaceutical service providers like contract research or manufacturing organizations), resulting in 4340 relevant deals. To better understand the consolidative impact of those deals, we separated them into transactions leading to industry consolidation – those resulting in the total number of companies in the industry being reduced – and non-consolidative ones (including business unit swaps, asset acquisitions, divestments). The analysis shows that the number of consolidative deals has been oscillating between 53 and 120 deals per year (86 on average), with no upward trend to be seen over the last decade.

***Pharmaceutical revenues and R&D spend concentrated among the largest companies*.** To assess if the industry has seen increasing consolidation over time, we looked at the contribution of the 10 and 20 largest companies to the total pharmaceutical industry's revenues over the past two decades. We utilized data from EvaluatePharma® as of August 2018 (historic company-reported pharmaceutical revenues and R&D spending, supplemented with consensus analyst estimates for private companies when available; data availability for smaller private companies is incomplete, hence the share of "other" companies is probably systematically underestimated). Top companies were identified separately for each year so that the ranking is not affected by historic megamergers. The analysis shows that the proportion of revenues booked by the largest companies has been gradually decreasing (Figure S1).

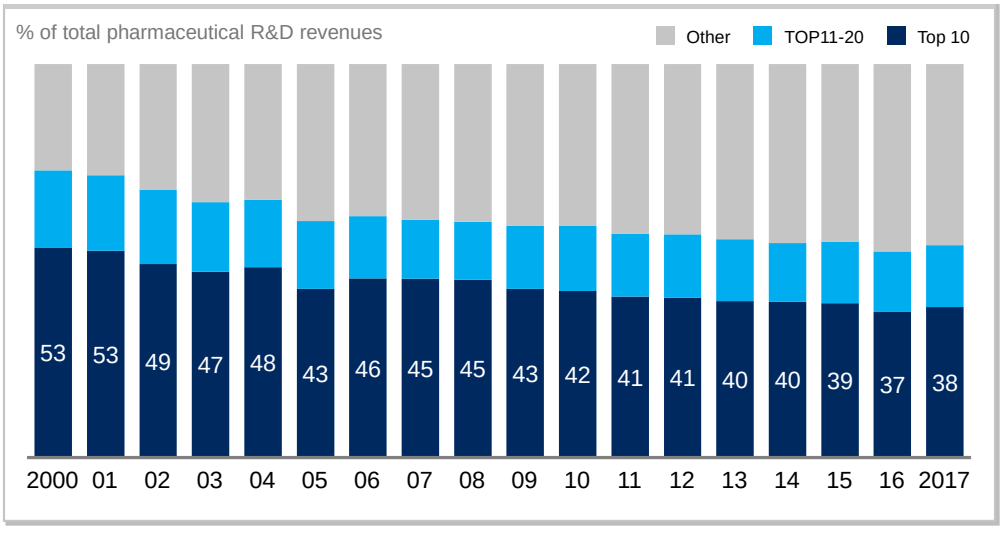

Figure S1 | **The contribution of top 10 pharmaceutical companies to global pharmaceutical revenues decreased suggesting growing fragmentation.** Source: EvaluatePharma® as of August 2018, McKinsey analysis.

Similar analyses were conducted to assess the proportion of annual pharmaceutical R&D expenditures concentrated among top companies (ranked by their pharmaceutical R&D expenditure in a given year). R&D spending concentration shows fluctuations and seems more strongly affected by megamergers – as suggested by the highest concentration (48%) observed in 2010, immediately after a wave of megamergers (Figure S2).

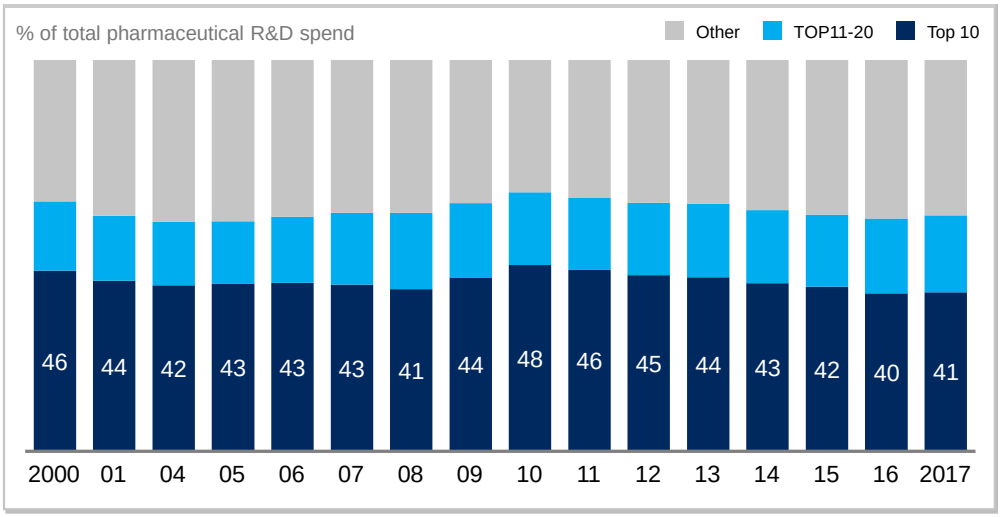

Figure S2 | **The contribution of top 10 pharmaceutical companies to global pharmaceutical R&D expenditures.** Source: EvaluatePharma® as of August 2018, McKinsey analysis.

Share of clinical trials sponsored by the largest pharmaceutical companies. Sponsorship of clinical trials is an important measure of the industry's innovation activity. To analyse the share of the top companies we focused on trials reported in the clinicaltrials.gov registry starting from 2003 (before then clinical trial disclosure was incomplete, which could lead to biased results). The analysis included interventional trials in phases 1, 2 and 3, with at least one company listed as sponsor. Top 10 pharmaceutical companies are defined as companies that most consistently ranked top 10 (based on pharmaceutical R&D revenues) across the investigated 15-year time frame: Roche, Novartis, Pfizer, Johnson & Johnson, Merck & Co, Sanofi, AstraZeneca, Eli Lilly, GlaxoSmithKline, Bristol-Myers Squibb, including any of their subsidiaries and acquired companies. For companies that underwent megamergers the pre-merger entities are included as in this case clear separation was not possible – this results in actual number of companies considered as top 10 in years 2003–2009 being higher than 10 (the dataset includes also companies that underwent megamergers within this time-frame: Aventis, Genentech, Schering-Plough and Wyeth). The analysis shows a clear decline in the share of top 10-sponsored trials (trials that include one of the top 10 or their subsidiaries as one of sponsors) – both when it comes to number of new clinical trials initiated every year and when we look at overall planned enrolment for these newly-initiated trials. This effect is in fact slightly less pronounced due to the overestimation coming from higher number of pre-merger companies included in the top 10 in the first years of the analysis.

Industry's R&D productivity index. To assess the contribution of different groups of companies to the industry's overall R&D productivity, we used the "R&D ROI vintage index" methodology (as described by Smietana *et al. Nat. Rev. Drug. Discov.* **14**, 455–456; 2015), updated using data as of August 2018. The companies were segmented into "top 10", "top 11-20" and "other" based on the average rank of the companies throughout the full timeframe of the analysis (in case of entities that merged, the higher ranking one was taken into account for the historic years).

Trend in the number of industry players. We used the EvaluatePharma® dataset (as of November 2018) to assess how the total number of active companies changed over time. A company was assumed to be active in a given year when the dataset included either reported (for public companies) or estimated (for private companies) company-level information: pharmaceutical revenues or R&D expenditures or visible pipeline assets active in that year. This methodology does not allow the overall number of industry players to be estimated, as the coverage is systematically lower for small private companies and start-ups, but allows the number of mid-sized and large players across the industry to be approximated.

Share of new molecular entities coming from top 10 pharmaceutical companies. The US FDA new molecular entities (NMEs) and biologics license applications (BLAs) can be used as a proxy for novel pharmaceutical products coming to the market (i.e., the biopharmaceutical industry's innovation output). We evaluated the sponsor applicants for the novel molecules approved by the FDA's CDER and CBER divisions between 1990 and 2018, and found that the share of approvals coming from top 10 pharma companies has declined from 54% in 1990-92 to 26% in 2016-18 (3-year averages were used to avoid potential bias related to small sample size in individual years) (Figure S3). Top 10 companies were defined as the companies that were most frequently present in the top 10 ranking by pharmaceutical revenues over the past 20 years (AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck & Co, Novartis, Pfizer, Sanofi and Roche) and their subsidiaries. The analysis includes companies that were predecessors of these top 10 players through megamergers (e.g., Wyeth and Aventis) if they were large enough to be among top players at the time of the merger (therefore products launched by biotechs like Genzyme or Genentech prior to their acquisitions are not attributed to top pharma companies).

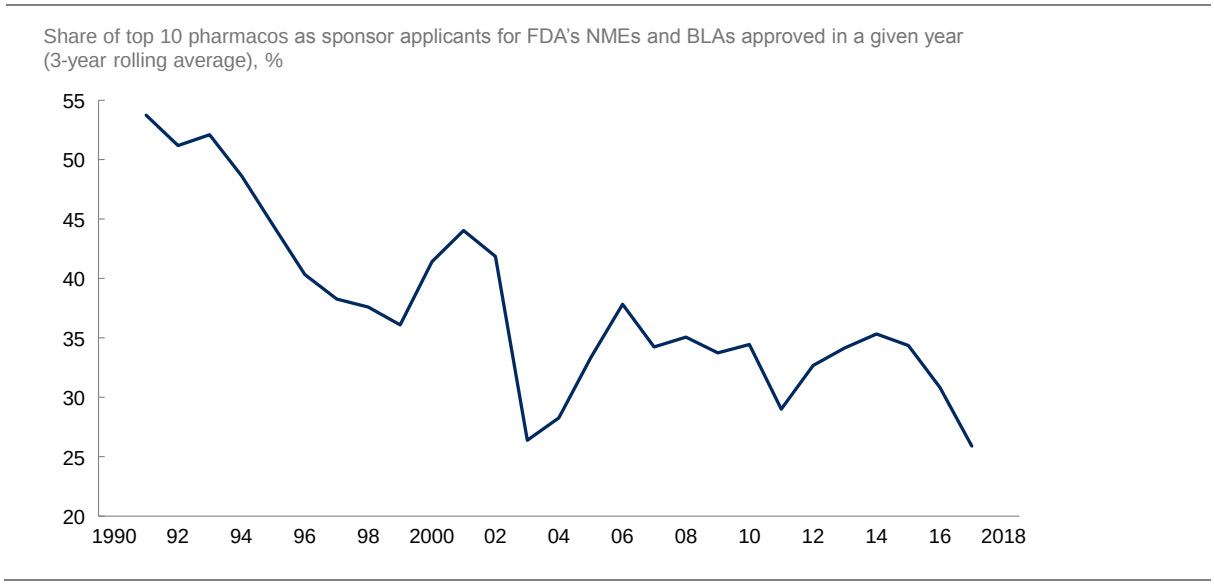

Figure S3 | **The contribution of top 10 pharmaceutical companies to novel pharmaceutical approvals.** Source: FDA, EvaluatePharma® as of November 2018, McKinsey analysis.

***Proportion of pharmaceutical NME revenues coming from organic vs. externally originated assets*.** To assess if the pharmaceutical industry has become more reliant on partnering in bringing innovation to the market, we calculated the share of total pharmaceutical revenues by their source of origin using annual product-level net revenue data from EvaluatePharma® as of September 2018, using Evaluate's "strategy" classification to determine the sourcing mechanism of individual products. This analysis is restricted to innovative pharmaceutical products, and excludes generics, OTC and biosimilars. Revenues categorised as "organic" are generated by the company in whose labs the product was originated (including products originated as early R&D partnerships between pharma companies and academia). Revenues classified as "acquired" reflect products originated outside of the current owner company and sourced through either company or product acquisition. Revenues classified as "partnered" reflect products in-sourced by the company using in-licensing or joint venture transactions. Products that are marketed by multiple companies can have their respective portions of revenues attributed to different categories, e.g., part of revenues generated by the initial developer can be in the "organic" category while part that is partnered out (e.g., as part of a region-specific marketing deal) can be reported as "in-licensed".