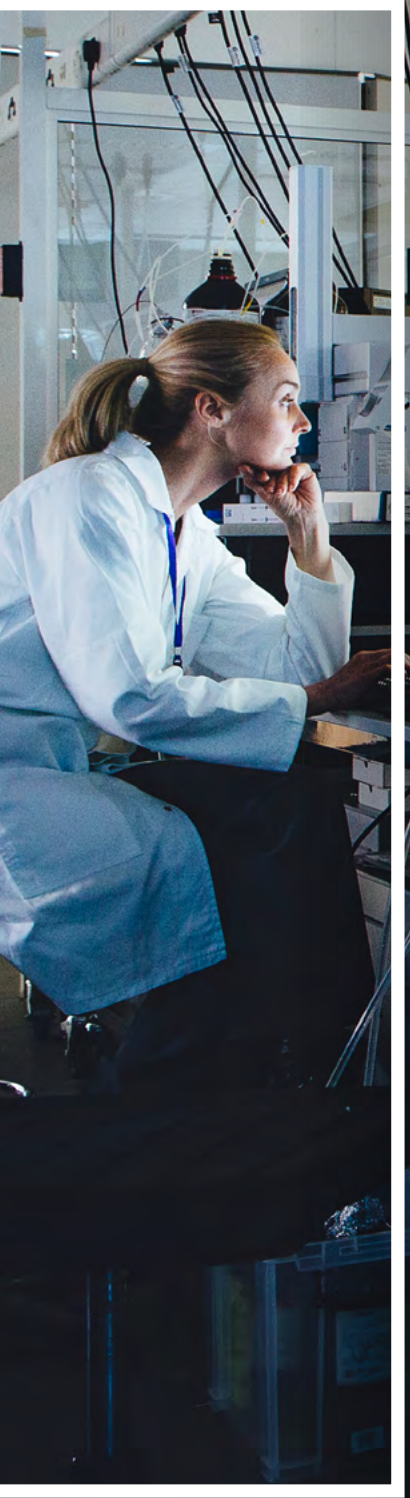
Externalizing pharma innovation is the winning strategy – now more than ever

Building a better working world



Our analysis confirms that small companies are more efficient drug developers than larger organizations, and that externally sourced products are increasingly more lucrative than home-grown ones. Biopharma leaders should embrace this trend and refocus their internal innovation efforts in favor of more aggressive business development.

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This transformation should take a deliberate, structured approach that limits internal spending on R&D to areas where the company demonstrates clear market superiority. For all other therapy areas, innovation should be sourced externally.

The patents on the cholesterol-lowering blockbuster Lipitor expired in 2011, ushering in a flood of generic atorvastatins to swiftly erode what at peak sales was a US$13.8 billion per year drug for its manufacturer, Pfizer. Pfizer had prepared for this moment for nearly a decade, investing billions on Lipitor's successor. But Pfizer scientists could neither find a successor in the dyslipidemia space, nor could they close entirely the projected revenue gap through their 2009 US$68 billion acquisition of Wyeth—despite the fact they acquired some very successful biological drugs (e.g. Enbrel) and segments (e.g. vaccines).

Of course, Pfizer isn't alone in failing to fill blockbuster-shaped holes in its top-line growth. Through different products, the Lipitor story has played out across many large pharmaceutical companies over the past decade.

But there's a better way to source new products: buy them from one of the thousands of smaller, highly specialized and more effective biopharma companies. A shift toward this kind of external innovation has been accelerating in the biopharma industry for the past two decades. Consequently, we argue that industry leaders need to lean in to this transformation even more and reduce internal research spending in favor of strengthening business development capabilities and initiatives.

The industry's largest players are less efficient at delivering new drugs to the market than their smaller counterparts, spending more per approved product, our analysis confirms. What's more, the success that these large companies do enjoy increasingly comes from externally sourced products. And the value contribution of acquired pipeline drugs has risen constantly since 2014. These trends are even more pronounced for newer modalities such as cell and gene therapies, where big pharma companies missed the initial opportunity to invest organically.

Over the past two decades, external innovation has become intrinsic to the biopharma business model. Not only do large companies highlight their partnering accomplishments, but many have started experimenting with various external innovation models. These models include the formation of corporate venture capital funds, incubators and "innovation centers" in biotech hubs. In addition, many have expanded beyond traditional alliances and acquisitions to create opt-in arrangements for eager partners, including option-based alliances and flexible co-development and co-commercialization deals. Indeed, from 2014-2018, the average annual amount biopharmas spent on M&A was roughly US$100 billion. Through 30 November 2019, the value for M&A was even higher, north of US$250 billion.

The increased dealmaking activity is at least partly due to biopharma companies' desire to deepen their therapy area focus. In the 2019 EY M&A Firepower report, we predicted this trend would continue to drive deals for the foreseeable future due to evidence correlating therapy area focus and improved financial performance. That has proved to be the case in 2019. Give the current pace of technological and scientific change, one way to create the needed therapeutic depth while also devoting sufficient resources to new scientific modalities (e.g., gene and cell therapies) and digital tools is via the strategic use of deals to bolster internal initiatives.

If such capital allocation decisions signal the growing importance of externalization, other data suggest companies still have room to improve when it comes to how they allot internal research spending. Based on data from Evaluate Pharma, the industry's top 20 companies by revenue continue to spend roughly US$100 billion on R&D annually. Moreover, few of them are focused in just one or two therapeutic areas where they are truly world class. (Somewhat complicating the calculation is how companies account for their business development investments — some but not all categorize this as part of R&D.) By significantly decreasing internal spending on innovation, focusing at most on two or three therapeutic areas, and simultaneously accelerating the shift to external innovation with strategically aligned business development and licensing capabilities, large biopharmas could boost their R&D efficiencies, more intelligently tap novel platforms such as cell and gene therapies, and drive more products to the market.

This transformation should take a deliberate, structured approach that limits internal R&D spending to areas where the company demonstrates clear market superiority. Future innovation in all other therapy areas should be sourced externally. Except for those areas where a company has clear market superiority, all existing internal development activities should be spun-out, outsourced to partners or even abandoned. Companies need only to retain the minimum scientific capabilities required to adequately evaluate external assets in these other therapy areas.

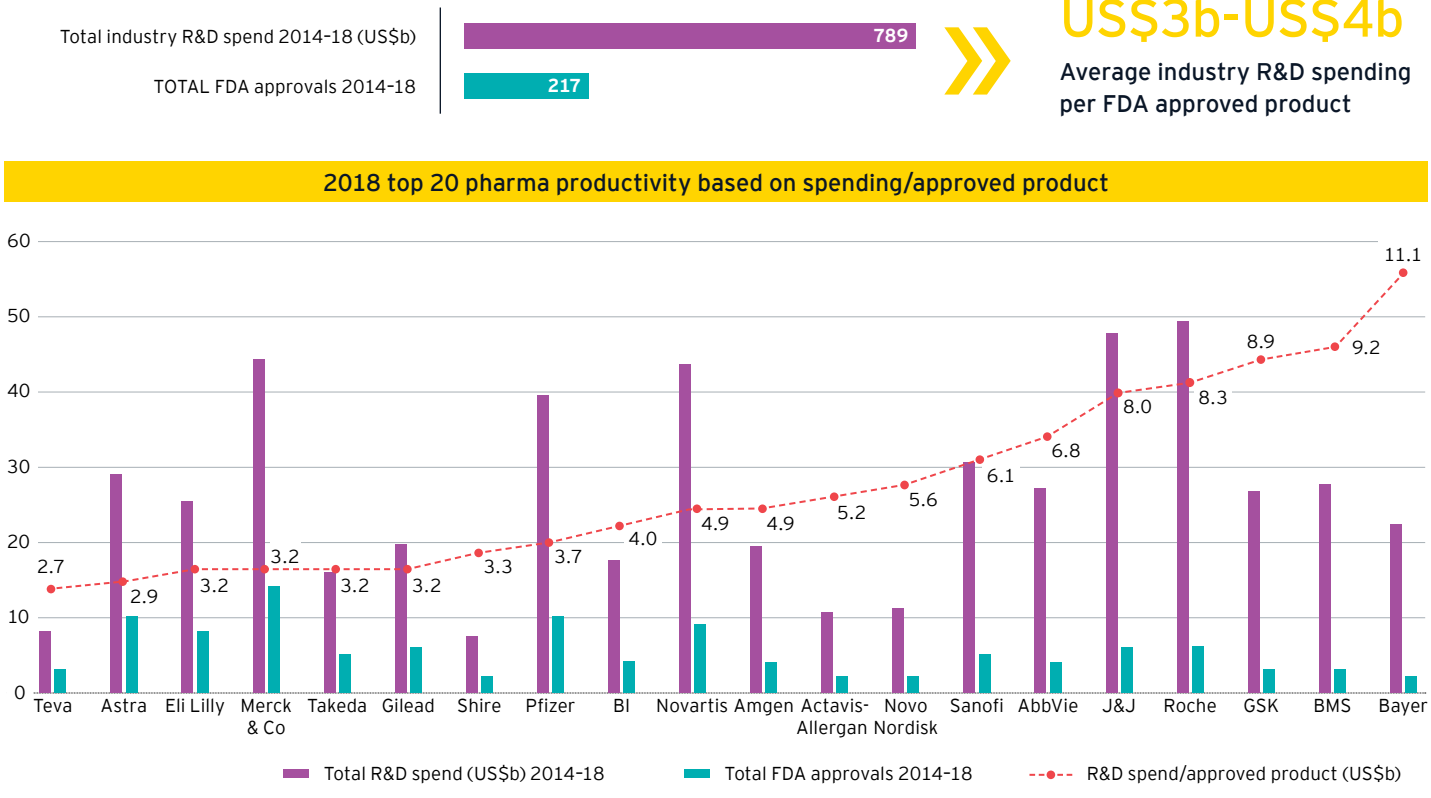
Smaller companies are more efficient

Consider the cost of getting a drug approved in the US. Between 2014 and 2018, the entire biopharma industry spent nearly US$800 billion on R&D (Figure 1). During that five-year span, the U.S. Food & Drug Administration approved 217 new molecular entities. On average — and admittedly not accounting for supplementary approvals of drugs already on the market or expenses related to drug development and registration outside the US — that's roughly US$3 billion–US$4 billion spent per FDA-approved therapy.

Looking at only the top 20 biopharma companies by revenue, the drug development cost increases significantly, jumping to US$5 billion–US$6 billion on average. In other words, the industry's biggest companies spend nearly 50% more per approval than the industry average. Compared with smaller biopharma companies that have had at least two drugs approved by the FDA from 2014–18, the contrast is even more jarring: the cohort of large companies spends on average about five to six times as much on development as the 11 smaller biotechs in this cohort.

Figure 1

R&D expenditures for top 20 biopharmas are higher than industry average, signaling a need for change in their innovation strategies

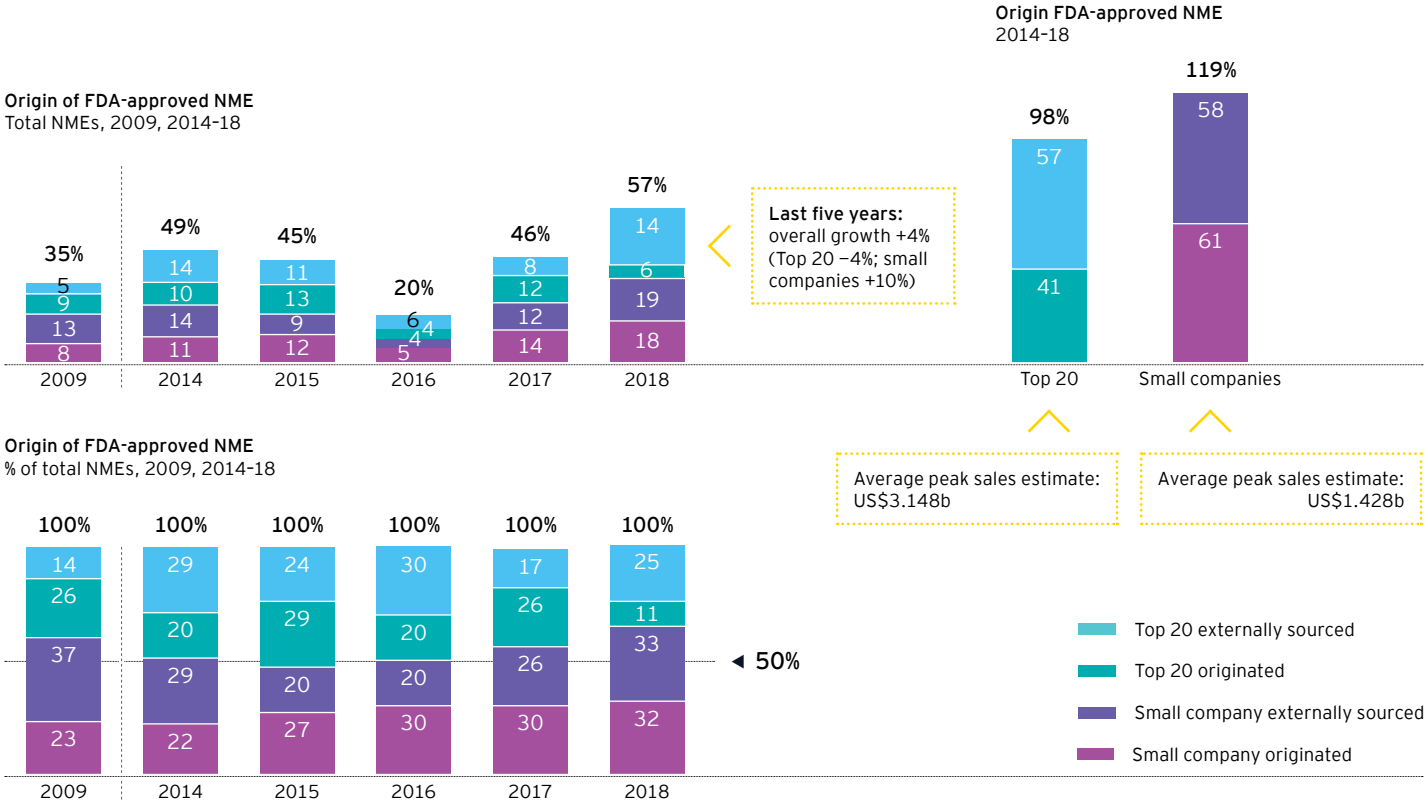


Note: Figures depend on the analyzed time period, 2014–18; Top 20 Pharma companies in 2018 based on prescription drug revenues. Shire 2018 R&D spend is estimated given the acquisition by Takeda early 2019

Source: EY-Parthenon, U.S. Food & Drug Administration, Evaluate Pharma and company reports

Figure 2

FDA NME approvals are increasingly coming from smaller companies, creating opportunities for bigger biopharmas to source innovation externally



Source: EY, U.S. Food & Drug Administration; EY-Parthenon analysis

There are complicating factors that may affect this comparison. First, this is admittedly only a five-year snapshot. What's more, large companies with global footprints are more likely than smaller biotechs or regionally focused biopharmas to develop and commercialize their assets in other major global markets such as Europe, Japan and, increasingly, China. As a result, they are likely to spend more per development program because of that expansive geographic reach.

Large companies are also more likely to build out franchises based on a single key product across many therapeutic indications. For example, the anti-TNF alpha drugs that treat multiple autoimmune diseases and the cancer drugs that are tested in several tumor types are almost exclusively the domain of large biopharma companies. That strategy results in higher development costs; however, the additional approvals in new indications tend to generate additional revenue streams that offset these development costs. (Note, these types of therapeutics may start off in the hands of smaller biotechs, but because of their potential utility — and revenue forecasts — in multiple therapy areas, they are frequently acquired or licensed by larger biopharmas.)

A third caveat that may bias the results is the tendency of larger biopharma companies to invest in primary care indications that require significant commercial infrastructures and larger, more complex, and more expensive clinical trials. As is the case for franchises based on a single product, these therapeutics have greater revenue potential or even a broader medical benefit. For example, from 2014–18 there were 41 drugs approved by FDA that were also fully developed in-house by top 20 pharmaceutical companies. These products had an average peak sales forecast of more than US$3 billion annually. In contrast, during that same period, the 61 drugs developed and approved by all other companies were forecast to bring in at most only US$1.4 billion annually.

Nevertheless, the origins of these approved drugs appear to be shifting, creating even more opportunity for large companies to acquire or in-license candidates and products (Figure 2). Between 2014 and 2018, the overall growth in FDA-approved drugs was 4%. But during that same five-year time span, the number of FDA-approved drugs from the top 20 pharmaceutical companies fell 4%, while the number of FDA-approved drugs from smaller companies increased 10%. In both 2017 and 2018, top 20 biopharma companies received 20 NME approvals each year. Those same years, small companies received 26 and 37 approvals, respectively. Over the five-year time span only 2015 saw more drugs approved from top 20 companies than their smaller competitors. What's more, of the 98 large-company drugs approved by the FDA from 2014–18, the majority (57) were externally sourced.

Interestingly, small companies didn't always push their own drugs across the finish line: 58 of the 119 drugs approved from smaller companies during this same period were externally sourced as well. (Many of these drugs were cast off by large companies — either because they were not a strategic fit or weren't expected to generate significant revenue.)

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As a greater share of new drug approvals arise from emerging technology platforms such as cell and gene therapy, larger companies that tend to be behind the adoption curve for new therapeutic modalities should use acquisitions and licensing to get access to necessary IP and avoid falling even further behind.

How does the focus on oncology across the industry affect business development strategies?

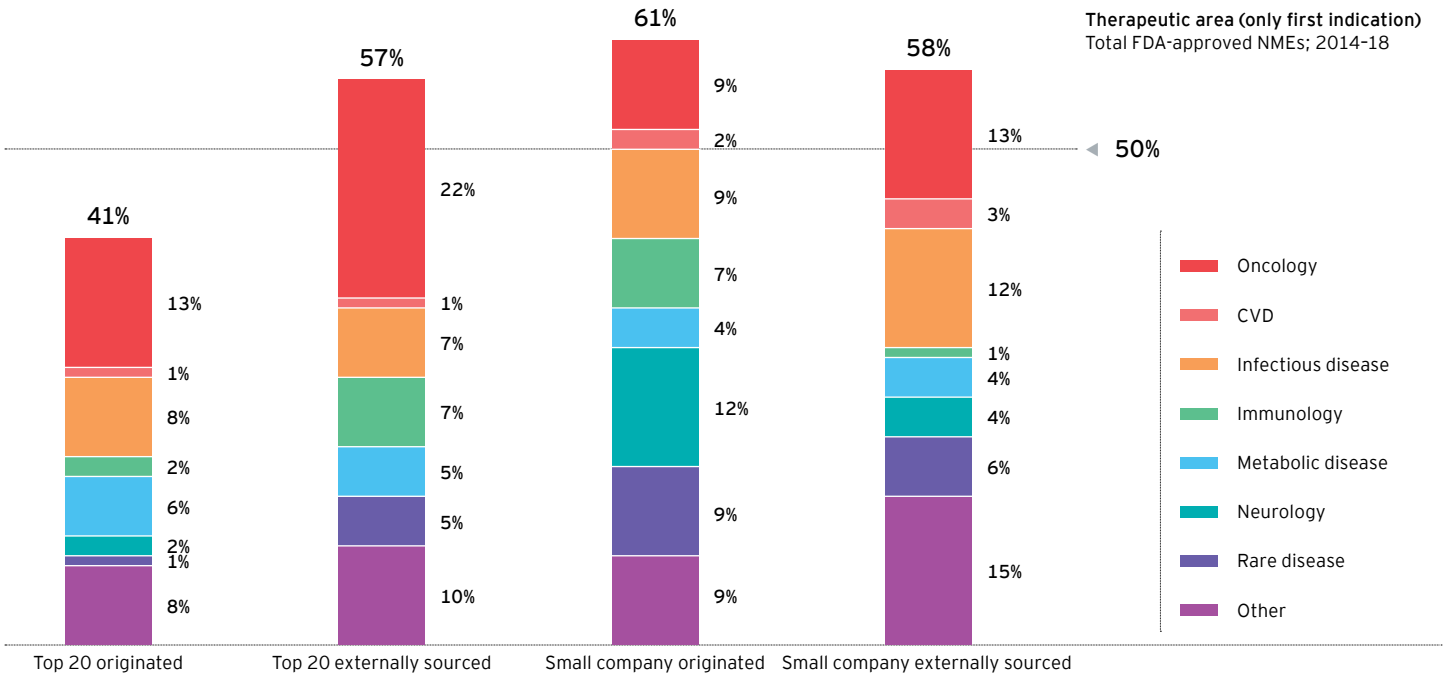
With oncology likely to be among the therapeutic areas that remain important for internal innovation and external innovation alike, how do companies balance this shift to more structured, aggressive business development in a highly saturated area where nearly all leading biopharma companies want to compete?

The oncology space is underpinned by unique dynamics. It is a therapeutic area with vast unmet need and a rapid pace of new biomedical discoveries. It's an area where biomarkers and patient- and disease-stratification have enabled more and faster FDA approvals. And it remains, along with rare diseases, an area with a relatively favorable reimbursement and pricing environment. As the top 20 biopharma companies strive to compete to develop and license oncology drugs (most of them harbor ambitions to be a leader in this important and lucrative therapeutic area), they're committing a disproportionate amount of both internal and external resources. From 2014–18, the top 20 biopharma companies received 13 oncology NME approvals from internal innovation and 22 NME approvals from external sources (Figure 3). Smaller companies also committed resources to oncologics, but had more therapeutically balanced portfolios.

It's unlikely this trend will slow any time soon, creating increasingly crowded markets. With multiple entrants in each oncology drug class vying for market share (not to mention competing for key opinion leaders and patients in clinical trials), it's only becoming more important for companies to be first-in-class or to come to market with truly differentiated product profiles. This reinforces the point that the top 20 biopharma companies will need to ramp up business development efforts to keep pace.

Figure 3

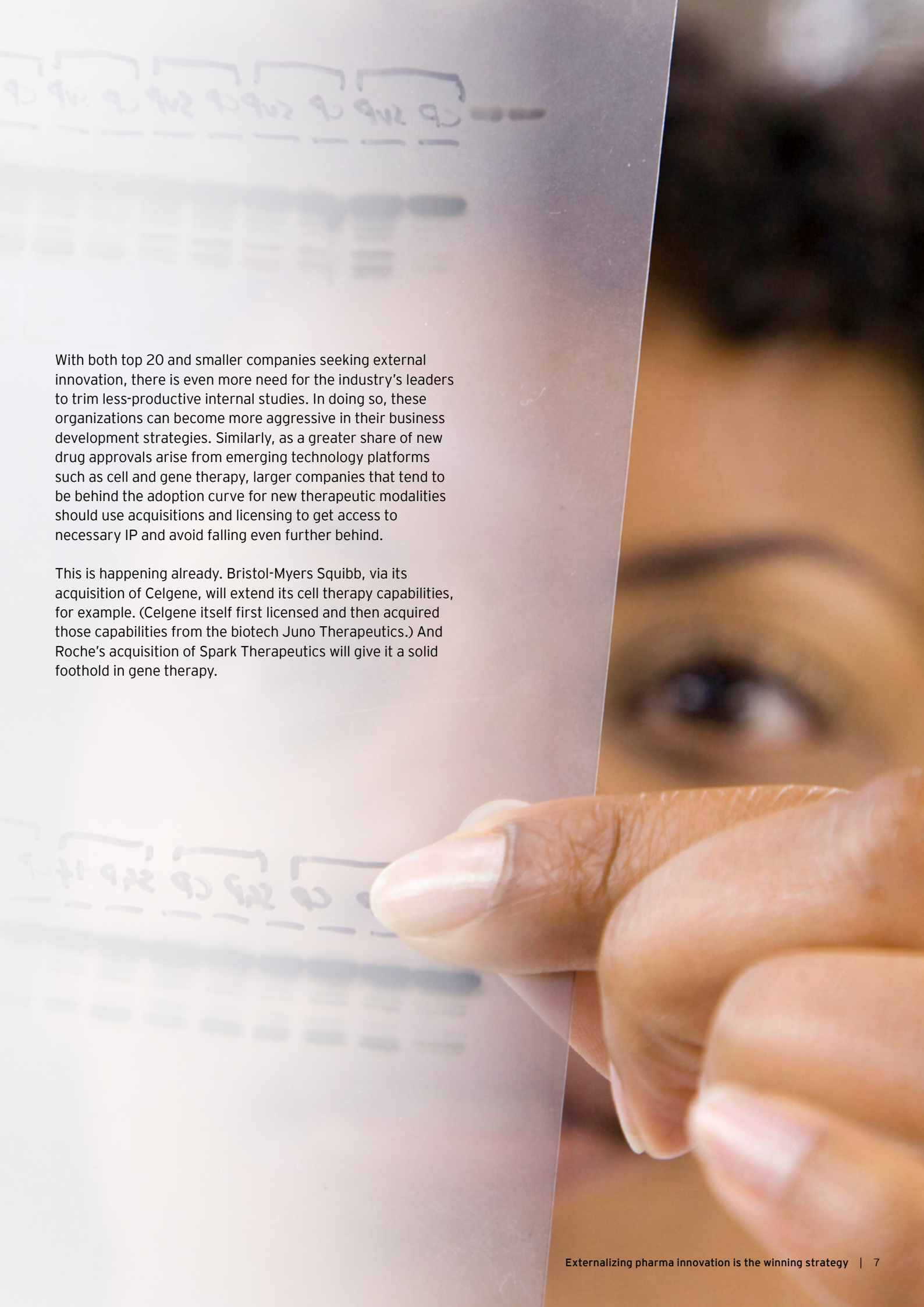
Oncology is a top therapeutic area for both top 20 and smaller companies, with more new drugs externally sourced than internally originated



Source; EY-Parthenon, U.S. Food & Drug Administration

With both top 20 and smaller companies seeking external innovation, there is even more need for the industry's leaders to trim less-productive internal studies. In doing so, these organizations can become more aggressive in their business development strategies. Similarly, as a greater share of new drug approvals arise from emerging technology platforms such as cell and gene therapy, larger companies that tend to be behind the adoption curve for new therapeutic modalities should use acquisitions and licensing to get access to necessary IP and avoid falling even further behind.

This is happening already. Bristol-Myers Squibb, via its acquisition of Celgene, will extend its cell therapy capabilities, for example. (Celgene itself first licensed and then acquired those capabilities from the biotech Juno Therapeutics.) And Roche's acquisition of Spark Therapeutics will give it a solid foothold in gene therapy.

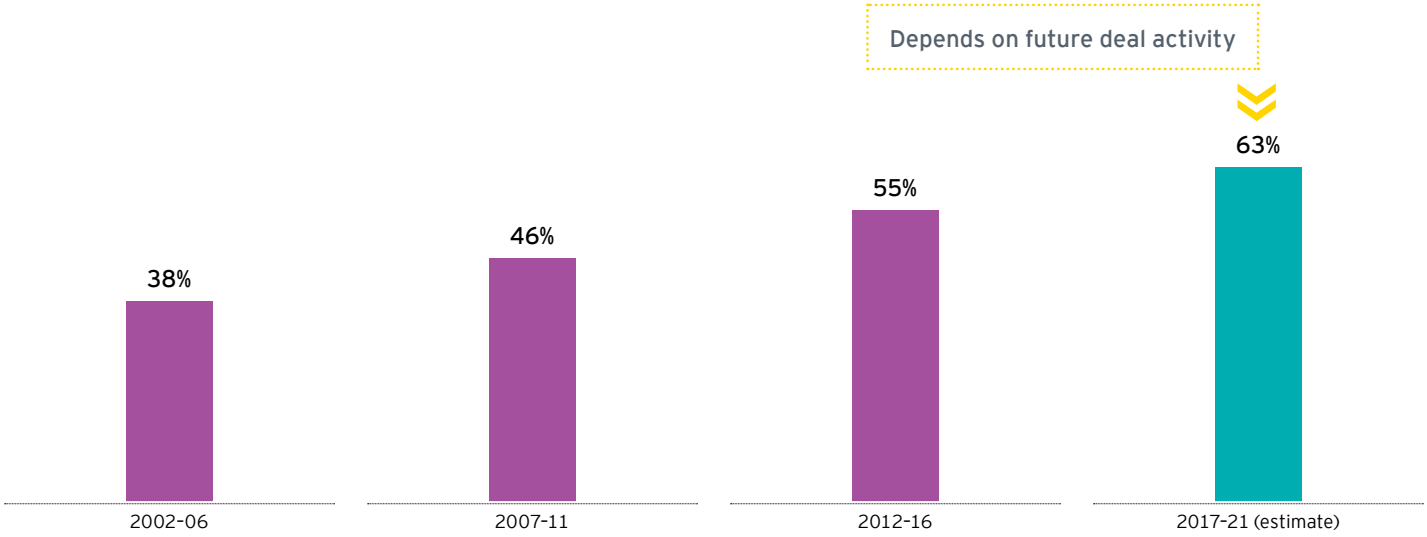


Buying innovation

Looking at a slightly narrower cohort of large biopharmas over a longer time horizon we can see the steady growth in the proportion of revenue that is generated by externally sourced products (Figure 4). The average revenue contribution of external innovation at the top 12 biopharma companies has grown from only 38% of all sales in the five years from 2002–06 to an estimated nearly 66% of sales in the 2017–21 timeframe — and this excludes products that were already on the market at the time they were acquired or partnered by a top 12 biopharma company. Looking at the top 50 products from this subset of companies, 66% of sales came from externally sourced assets.

Figure 4

Buying innovation is an increasing focus of top 12 pharma companies' deal strategies, which can be seen in the increasing market share of acquired drugs



Source: EY-Parthenon analysis

Dealmaking across the dozen leading biopharmas appears to be increasingly focused at either end of the spectrum. That could be because of the relative cost and risk associated with buying assets that are in Phase 2 development relative to discovery-stage deals that have large potential deal values but smaller upfront payments. Alternatively, it may be due to the dearth of available clinical-stage assets compared with discovery and preclinical opportunities. (The lack of Phase 2 alliances may also be due to the rise of combination therapy in areas like oncology — companies are just as likely, if not more such as, to ink a non-exclusive clinical trial collaboration instead of an alliance until it's clear that the combination actually works.) Along with securing a position in new and quickly growing therapeutic modalities, adding near-market or recently approved therapies to a pipeline or portfolio has been a consistent driver of top biopharma's so-called "bolt-on" acquisitions.

These deals, including Pfizer's recent acquisition of Array BioPharma, Roche's proposed acquisition of Spark, Novartis' acquisition of AveXis and Sanofi's acquisition of Ablynx, tend to be expensive, given the near-market and transformative nature of some of the assets involved. Roche's US$4.8 billion deal for Spark, for instance, gives the big pharma ownership of Luxturna, a therapy for inherited forms of blindness that is the first directly administered gene therapy approved in the US. Novartis's US$8.7 billion acquisition of AveXis secured Zolgensma,

another gene therapy that the FDA recently approved to treat spinal muscular atrophy. Sanofi bought Ablynx for US$4.8 billion just prior to the approval of Cablivi, the first domain antibody to win US regulatory approval for a rare blood disorder, acquired thrombotic thrombocytopenic purpura. And Pfizer's US$11.4 billion Array acquisition gives it the recently approved metastatic melanoma combination therapy Braftovi/Mektovi.

Importantly, each of these deals also comes with a product engine – in the cases of Spark and AveXis, gene therapy capabilities; with Ablynx, a domain antibody platform; and Array's demonstrated talent for developing small molecule cancer drugs is nearly unrivaled.

An analysis of the top 100 drugs by revenue shows the proportion of revenue derived from externally sourced products is growing steadily after plateauing at 46% from 2007 through 2011. This trend is driven by growing revenue from Bristol-Myers Squibb's Opdivo and Merck's Keytruda. Each of these anti-PD-1 checkpoint inhibitors were secured as part of large acquisitions (Medarex and Schering-Plough, respectively) and were at first overlooked. Keytruda was actually acquired twice – first when Schering Plough bought Organon, then a division of the conglomerate Akzo Nobel, and again when Merck merged with Schering Plough. The molecule was somewhat famously deprioritized at Organon, shut down at Schering-Plough, and nearly out-licensed by Merck before its enormous potential was recognized. In 2018, Keytruda revenue was more than US$7.1 billion.

Large-scale transactions remain rare. But the recent acquisitions of Celgene by Bristol-Myers Squibb, Shire by Takeda, and most recently of Allergan by AbbVie are likely to drive up the portion of revenue that comes from external products that were already on the market at the time of an acquisition. These deals may also uncover some hidden pipeline gems.

Figure 5

Increasing percentage of revenues originates from externally sourced pipeline products

Note: Analysis is based on top 100 products based on cumulative revenues from 2007 to 2016

Source: 2016 IMS data; EY-Parthenon Analysis

- Proportion of revenues from internally generated molecules is declining
- Many products that were already launched at the time of transactions were part of mega-transactions (e.g., Pfizer/Wyeth, Merck/Schering-Plough. Pfizer/Pharmacia)
- As these types of transactions have been less frequent recently and the corresponding products have lost exclusivity, sales from externally marketed products have declined
- The increase in revenues from externally sourced pipeline products is substantial
- The jump in 2014–15 was driven by highly successful new product introductions, such as Keytruda (originally from Organon) and Sovaldi (originally from Pharmasset)

Conclusion

For companies that choose to strengthen and expand their partnering initiatives and reduce internal innovation footprints there are many options. Clear-eyed strategic reviews of internal scientific strengths and a willingness to exit certain areas of R&D are the bare minimum required.

Reinforcing the necessary tools for successful business development and licensing strategies will be even more critical as internal innovation shrinks. Among these are effective valuation mechanisms; a world-class ability to scout new opportunities from a variety of academic, biotech and pharmaceutical sources; a redoubled focus on alliance management and partnering; a nose for risk analysis; and properly incentivizing scientists so external and internal assets are on equal footing.

These capabilities can reside within a leading biopharma organization and can be buttressed with ad hoc external support. What's more, the business development function should be represented at the board level. Such board representation helps to ensure key decisions can be made with alacrity and reflects not only business development's importance, but the company's mandate to source innovation wherever it resides.

Beyond building necessary skill sets within business development organizations and elevating business development within the organization, large companies must also seek out innovation where it lives — both in a geographic sense, and along the valuation continuum from academic laboratories through peer pharmaceutical firms. Over the past decade, several large biopharmas have implemented innovation-hub models in key biotech hotspots. We view these outposts as key to being able to compete for the most differentiated assets and, gather intelligence and build the best scientific and business development teams. Building company incubators and deploying corporate venture capital are also crucial elements for accessing innovation and, in areas where the biopharma company is a scientific and development leader, steering it in the appropriate direction and smoothing its path from intriguing academic science to biopharma asset.

Innovation in the biopharma industry as measured by new molecular entity approvals increasingly resides within smaller organizations. This is where large biopharma company resources need to be focused: outside the walls of their own labs. The value contribution of acquired pipeline drugs has risen and will continue to rise. We argue that the successful large biopharma companies of the future will be those that accelerate the transformation to increased reliance on external innovation and significantly curtail internal innovation activities.

> “The business development function should be represented at the board level. Such board representation helps to ensure key decisions can be made with alacrity.

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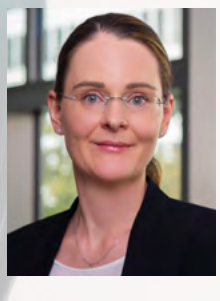

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