EXECUTIVE INSIGHTS

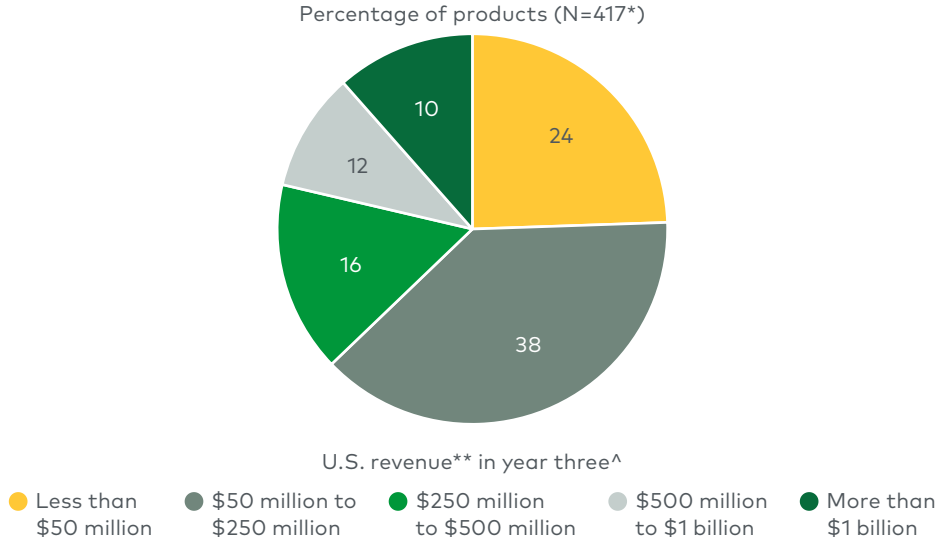
Key Indicators of a Successful Biopharmaceutical Product Launch

Blockbusters are taking more share in an increasingly challenging market

The key driver of success in the biopharmaceutical industry can be summarized very simply as finding, developing and commercializing products that address unmet patient needs *and* generate strong returns on investment (ROI). The past decade has shown that successfully bringing a drug to market has become increasingly difficult. Given the high risk involved in drug development, biopharma manufacturers seek to prioritize pipeline assets that have the potential to achieve high revenues quickly. While reaching the $1 billion threshold is a common aspiration, there is high variability in launch performance, with more than 60% of all innovative branded products approved between 2004 and 2018 generating less than $250 million in U.S. sales in their third year on the market (see Figure 1). In addition, the U.S. has the largest pharmaceutical market of any country — more than 3.5 times the size of the next largest country, China.[1]

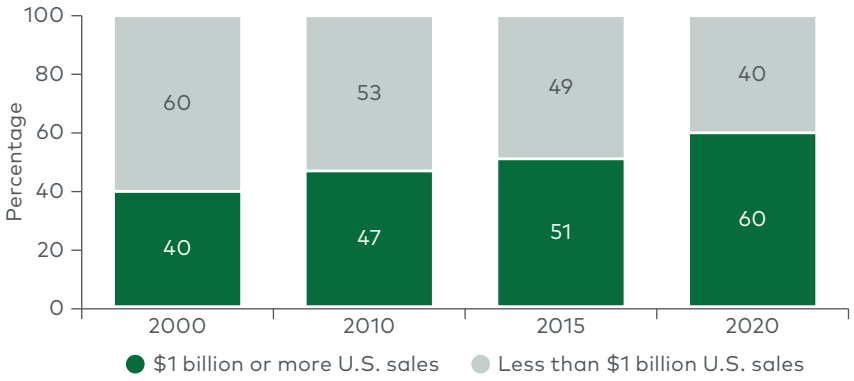
At the same time, finding and nurturing high-revenue-generating products has become increasingly important in driving top- and bottom-line growth for both the industry and individual biopharma companies. Since 2000, products with at least $1 billion in U.S. revenues have contributed to a growing proportion of the overall market (see Figure 2), with products like Keytruda, Humira and other top performers driving outsized returns for their manufacturers. Going forward, successfully identifying the right assets will be critical. The bar for differentiation is rising in many key disease areas, pricing pressure continues to increase (including the recent passage of the Inflation Reduction Act), and the industry is preparing for an unprecedented level of revenue at risk to loss of exclusivity, reaching over $100 billion (or ~7% of industry revenue) in 2028.[2]

Figure 1
Revenue distribution at year 3 of branded innovative drugs approved from 2004 to 2018



*Includes innovative, branded products (new molecular entity and original biological product approvals from the Center for Drug Evaluation and Research; innovative products approved by the Center for Biologics Evaluation and Research) from 2004 to 2018. Reformulations, biosimilars, and generics were excluded. Products without reported Evaluate Limited revenues for year three were excluded.
**To promote consistent comparisons across revenues from different years, revenues were adjusted for industry net price growth using published reports from IQVIA (Medicine Spending and Use in the U.S. reports) and Journal of the American Medical Association analysis of SSR Health data
^"Year three" was defined as the third full calendar year after the FDA approval date
Source: L.E.K. research and analysis; see appendix for more detailed information on methodology and sources

Figure 2
Distribution of US branded biopharmaceutical revenues* (2000-2020)



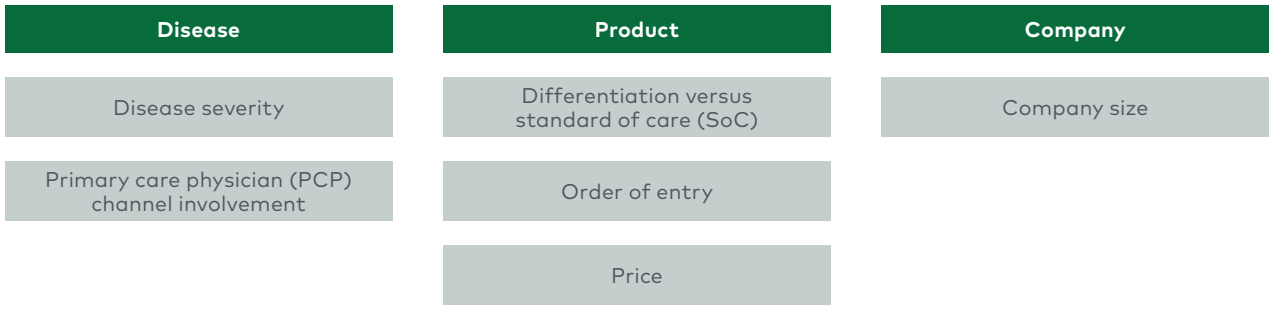
*Excludes products noted in Evaluate Limited as ex-U.S.-only sales attributed to U.S., over-the-counter products and off-patent compounds/nonproprietary products
Source: L.E.K. analysis of Evaluate Limited

Given the high cost and risk of accessing and developing innovation, it is critical for biopharmaceutical companies seeking sustainable long-term revenue growth to characterize the potential of their assets more accurately so they can focus their time and investment on the right ones.

L.E.K. Consulting analyzed the launches of all branded innovative biopharmaceutical products approved in the U.S. between 2004 and 2018 to better understand what drives products to achieve high revenue performance by their third full calendar year after Food and Drug Administration (FDA) approval ("year three"; see Appendix A for details on product inclusion and revenue measurement). We selected the three-year time frame because this period is most often critical for launch success and usually predictive of performance over a product's lifetime. However, there is some limitation to short-term performance evaluation as the short-term and outcome studies for new drugs can fail to identify certain qualities that could make a drug valuable a few years after launch when long-term data are generated.

We assessed six attributes of the disease, product or commercializing company to understand their impact on revenue performance (see Figure 3).

Figure 3
Attributes assessed in the analysis



Source: L.E.K. research and analysis

Appendix B provides detailed information on the attribute definitions and methodology.

Company size, differentiation and order of entry are key predictors of performance

Five of the six attributes led to a higher likelihood of reaching $1 billion in U.S. revenues in year three, with company size, differentiation versus standard of care, and order of entry as most important (see Figure 4 below and Appendix C for further details).

- **Scale is a critical advantage:** Company size is the top predictor of products reaching $1 billion in year three, with nearly 15% of products commercialized by large biopharmas (greater than $40 billion market cap) reaching this threshold compared to only 3% for other biopharmas. Further, more than 85% of all products reaching $1 billion were commercialized by large companies. While some of this is the result of large pharma's propensity to acquire assets with significant potential, it has implications for small and

Figure 4
Predictors of revenue at year 3

Attribute	Comparison (Bolded and underlined are characteristics where products had a higher likelihood of reaching $1 billion in year 3)	Relative likelihood* to reach $1 billion** in year 3 (N=417; ratio of percentage of products in higher likelihood group reaching threshold versus percentage of products in lower likelihood group reaching threshold)
Company size	**Large** (greater than $40 billion market capitalization in year 3) versus mid-size or small	5.0x
Differentiation versus standard of care	**Differentiated** versus not differentiated	2.6x
Order of entry	**First** within its mechanism of action/class in its indication versus second or later	1.8x
PCP channel involvement	**At least some PCP prescribing** for initial script prescribing versus none or minimal prescribing	1.6x
Disease severity	**Medium or more severe** (high likelihood of serious comorbidities or mortality) versus low	1.4x
Price	**Less than $8,000** monthly wholesale acquisition cost (WAC) versus $8,000 or greater	1.2x

*1.0x indicates equal likelihood regardless of attribute
**Revenues adjusted for industry net price growth as described in Appendix A
Source: L.E.K. research and analysis; see appendix for more detailed information on methodology and sources

midsize companies deciding whether to partner or go it alone. Leveraging the commercial experience and infrastructure of a large biopharma partner as well as its capacity to invest more broadly in life cycle indications may improve a product's revenue outlook. For smaller biopharmas to achieve similar revenue results, they will need to plan for, invest in and execute the launch and continued life cycle management of a product using the same methods as a large biopharma company.

- **Differentiation is paramount:** While not a surprise, the analysis confirmed that clinical differentiation is paramount and should be prioritized during drug development and business development. Fourteen percent of products demonstrating meaningful improvement versus standard of care, as recognized by value assessment reports and/or official treatment guidelines, reached $1 billion in year three, compared to only 6% of undifferentiated products. Achieving statistical difference on selected endpoints alone is not enough, as the selection of these endpoints and the thresholds for positive outcomes

that are clinically meaningful to physicians matter a lot. For instance, a few-week increase in progression-free survival in certain indications may represent a statistically significant difference but may not be clinically meaningful to physicians.

- **Early order of entry is important:** Products first to launch within their indication and mechanism of action were nearly twice as likely to reach $1 billion in year three than were later entrants, showing that class novelty is a clear advantage. Executives constructing clinical development programs and prioritizing internal and external investments need to strike a careful balance between best in class versus first in class, depending on each program's unique competitive situation.
- **Broad call points can still be successful:** Altogether, products targeting primary care physician (PCP) channels had a higher likelihood of reaching $1 billion in year three than those that did not. About half of products reaching $1 billion had at least some PCP involvement in prescribing decisions, including products for Type 2 diabetes, psoriasis, major depressive disorder, cardiovascular disease and vaccines. Almost all these products were commercialized by large biopharmas. Clearly, products can still drive significant revenues in call points with higher patient volume, but these products require the appropriate commercial expertise and reach.
- **Disease severity is a weaker predictor but should not be overlooked:** Interestingly, disease severity was a weaker predictor of $1 billion revenue performance compared to the other variables assessed. Nearly 80% of products reaching $1 billion addressed more-severe diseases, but more than 70% of products that did not reach $1 billion also addressed more-severe diseases. As a result, these products were only 1.4 times as likely to reach $1 billion as those addressing less-severe diseases. All else being equal, companies should still prioritize more-severe diseases with greater unmet needs; but this finding suggests that less-severe diseases should not be immediately discounted in investment prioritization decisions.
- **Price is not a key predictor for reaching $1 billion in year three:** Products costing ~$8,300 or less in wholesale acquisition cost (WAC) monthly (equivalent to $100,000 per year for a chronic treatment) were about as likely to reach $1 billion as those above $8,300 WAC per month. This price threshold was arbitrary and designed to understand the impact of potential market access restrictions on drug revenue performance, but these findings are interesting considering greater recent investment from the pharmaceutical industry in rare disease and novel modality assets with higher pricing potential.

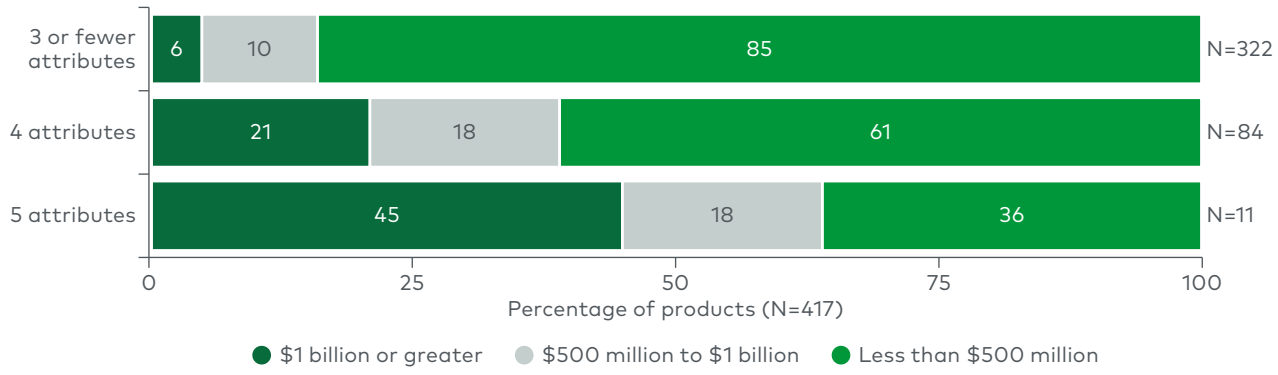
Considered individually, these findings confirm some important principles of biopharmaceutical development: Seek differentiation, execute trials as efficiently as possible to promote speed to market and consider partnering to expand commercial reach. Notably, the attributes that most strongly predict $1 billion revenue performance in year three relate to the product and the company — suggesting that execution is critical for greater levels of revenue. Companies can influence differentiation and order of entry to some degree through trial design and execution, even though some of the characteristics of the product and dynamics in the market are already set. The fact that 85% of all products reaching the $1 billion threshold were commercialized by large companies suggests that, in addition to their propensity to acquire or in-license products with high revenue potential, large companies' launch and life cycle management experience likely drive greater product performance.

But how well can individual predictors be used together to assess a product's likelihood of becoming a top performer?

Considering multiple attributes together, it is easy to predict which products will not become top performers, but more difficult to predict which will

Assessing findings across all five predictive attributes reveals a critical takeaway — revenue performance is never a guarantee. Figure 5 shows what percentage of products possessing three or fewer, four, and five predictive attributes achieved $1 billion of revenue in year three after approval.

Figure 5
Revenue distribution* at year 3 by number of predictive attributes



*Revenues adjusted for industry net price growth as described in Appendix A
Note: Lines may not total 100 due to rounding
Source: L.E.K. research and analysis; see appendix for more detailed information on methodology and sources

Between 2004 and 2018, more than three-quarters of the products possessed three or fewer predictive attributes, and only 6% of those achieved $1 billion in revenue. Another 20% of the products possessed four predictive attributes, and ~20% of them achieved $1 billion in revenue — more than three times as likely as those with three predictive attributes or fewer. Of the very few products with all five attributes, 45% reached $1 billion. While still no guarantee, having four or more of the five attributes made a product nearly four times more likely to achieve the $1 billion threshold than products with three or fewer attributes. Even at the lower threshold, only products with five attributes had approximately a 64% chance of reaching $500 million at year three. This does not even account for all the technical risk in successfully navigating clinical development.

These findings have broad implications across the product development and commercialization process

These insights have implications for portfolio prioritization, business development, partnering, clinical trial design, and launch planning and execution choices.

- **Portfolio prioritization and business development:** Optimizing R&D investments and making business development decisions across multiple assets and/or indications are critical to maximizing ROI. In addition to revenue forecasting and product valuation, companies should consider evaluating programs across the key attributes and recalibrating expectations if products do not meet some of them.
- **Proactive and strategic clinical development:** When a company believes it has a product with attractive revenue potential, it needs to invest sufficiently in trials to demonstrate its differentiation from standard of care. It is important to understand which endpoints and performance thresholds will result in meaningful clinical differentiation and then design trials accordingly. This will only become more important as the Inflation Reduction Act is implemented, since clinical differentiation is a critical way to support pricing decisions.
- **Launch planning and execution:** Pre-launch activities need to include early engagement with customers to co-develop the product value proposition and its differentiation along the predictive attributes identified in this analysis. Small to midsize companies that plan on self-commercializing need to invest sufficiently in the launch, starting before pivotal trials are designed or at least three years prior to first market authorization. Those that opt for a commercial partnership need to identify the right time in their product's development to maximize partnership deal terms, while leaving sufficient time to prepare for the launch.

L.E.K. helps companies with critical choices at all inflection points along the product development and commercialization process. We leverage learnings from our proprietary Launch Monitor tool and our experience from working with many small-, mid- and large-cap biopharmas, including more than half the companies that launched their first innovative product in the past two decades, to guide our approach. We will be happy to discuss this analysis further as you weigh its implications on your efforts to maximize the probability that internal and external innovation and investments can help as many patients as possible and support your future organizational success.

Note: While these findings are specific to the U.S. market, they may also broadly apply to other markets.

For more information, please contact lifesciences@lek.com.

Appendix

Appendix A

Products included in the analysis and methodology for revenue in year three

Inclusion and exclusion criteria for 417 products analyzed

- FDA approval date between 2004 and 2018
- Branded and patented
- Innovative product (new molecular entity and original biological product approvals from the Center for Drug Evaluation and Research; innovative products approved by the Center for Biologics Evaluation and Research)
- Not a reformulation, biosimilar or generic
- Evaluate Limited revenue data available for the third calendar year after launch (as of November 2022; note some revenues for 2021 are still not marked as "actual" in Evaluate Limited data)
    - Note: Evaluate Limited revenue data is not available for more than an additional 100 products, which tend to be lower-revenue products or those commercialized by private companies

U.S. revenue as reported by Evaluate Limited was used for the analysis

- "Year three" was defined as the third full calendar year after the launch date; for example, 2007 revenue was used for products launched in 2004, and 2020 revenue was used for products launched in 2017, regardless of when during the year the product was approved
- To promote consistent comparisons across revenues from different years, revenues were adjusted for industry net price growth using published reports from IQVIA (Medicine Spending and Use in the U.S. reports) and a Journal of the American Medical Association analysis of SSR Health data
- 2018 was selected as the cutoff year for the analysis as it represents the last cohort of products with actual revenue data for three full years on the market at the time of publication

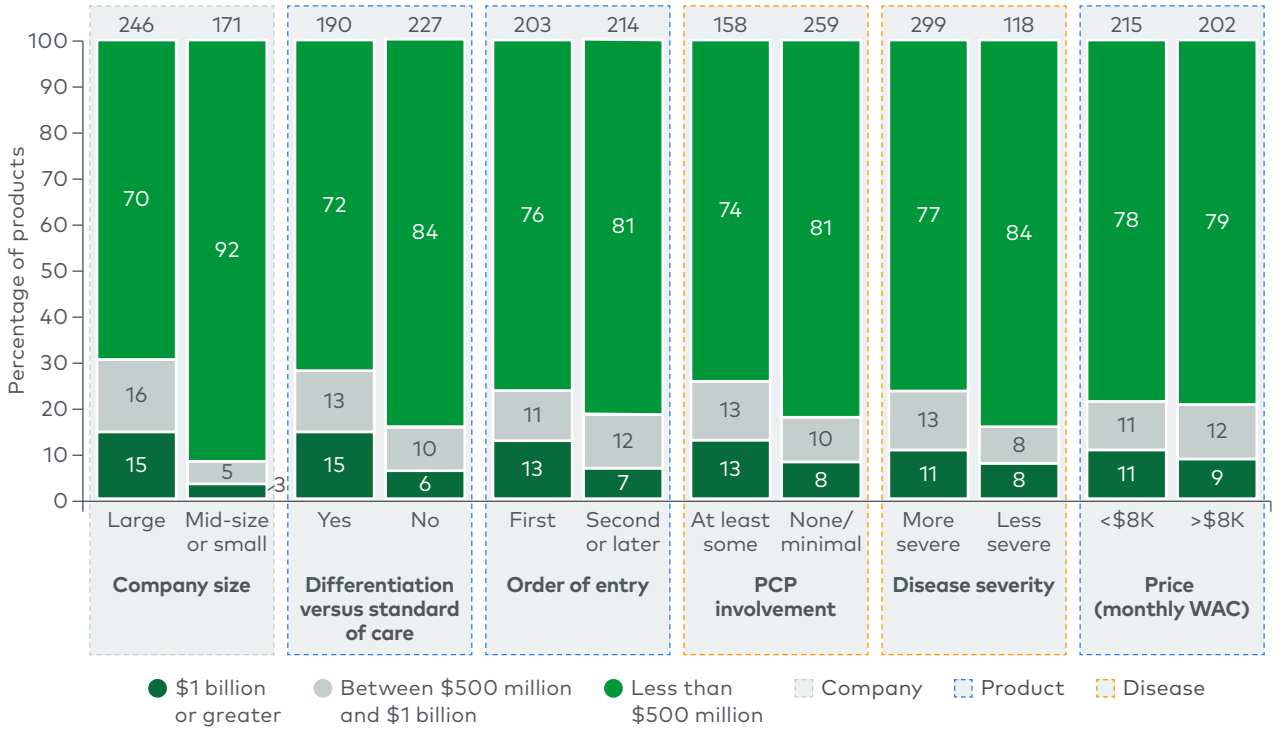
Appendix B

Attribute definitions

For each attribute, products were grouped into one of two categories, and performance of products was compared between each category

Attribute type	Attribute	Definition and sources
Disease-specific	Disease severity	Disease impact on mortality, morbidity, and quality of life • **High severity:** Diseases with a high likelihood of short-term mortality • **Medium severity:** Diseases with less direct risk of mortality but high likelihood of serious comorbidities • **Low severity:** Diseases primarily impacting quality of life Sources include the Centers for Disease Control and Prevention, World Health Organization, PubMed and other secondary data on disease mortality and morbidity, as well as U.S. and EU value assessment reports
	Primary Care Physician (PCP) involvement in call point	Relative level of involvement of PCPs in treatment decision • **At least some PCP prescribing:** PCP is a low, medium, or high prescriber for the disease • **No or minimal PCP prescribing:** PCP has little to no involvement in treatment decisions for the disease Sources include articles, patient association websites, company statements, and Medicare claims data
Product-specific	Differentiation versus standard of care (SoC)	A product's comparative clinical performance versus the SoC, leveraging published value assessment reports and treatment guidelines in the U.S. and EU • **Improvement:** Minor through major improvement on efficacy and/or safety endpoints relative to the SoC at launch (may include some products' directly comparative studies, if published value assessment reports deemed a product) • **No improvement:** Non-inferiority or inferiority relative to the SoC at launch, or no comparative data Primary source (when available) was Haute Autorité de Santé (France)'s Amélioration du Service Médical Rendu (ASMR; improvement in medical benefit). Other sources referenced include the Institute for Clinical and Economic Review, National Comprehensive Cancer Network, Federal Joint Committee (Germany), and other value assessment organizations and journals.
	Order of entry	A product's order of entry within its mechanism of action for its primary disease. Sources include Pharmaproject, Citeline and L.E.K. research and analysis.
	Price	Monthly wholesale acquisition cost (WAC) Source: SSR Health, Centers for Medicare & Medicaid Services, L.E.K. research and analysis
Company-specific	Company size	USD market capitalization of commercializing company in the third year after product's FDA approval • **Large:** Greater than $40 billion • **Mid-size:** $5 billion-$40 billion • **Small:** Less than $5 billion Private companies were assigned to company size tiers based on total revenue relative to large-cap biopharmas. Source: S&P Global Market Intelligence, company disclosures, L.E.K. research and analysis

Appendix C
Revenue distribution* at year 3 by attribute



*Revenues adjusted for industry net price growth as described in Appendix A
Source: L.E.K. research and analysis; see appendix for more detailed information on methodology and sources

Endnotes

[1]L.E.K. analysis of IQVIA

[2]Evaluate, "Evaluate Pharma World Preview 2022 – Outlook to 2028." https://www.evaluate.com/thought-leadership/pharma/world-preview-2022-report

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About L.E.K. Consulting

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