EXECUTIVE INSIGHTS

Optimizing Pharmaceutical Portfolios Through M&A: Lessons From Over a Decade of Transaction Experience

Executive Summary

- Since 2010, the biopharmaceutical sector has experienced a surge in M&A, with 195 biopharma M&A deals involving over 500 acquired assets and approximately $1 trillion in total investment.
- Half of these deals have focused on commercial-stage assets. This trend is likely to persist as companies aim to acquire revenue streams in response to looming exclusivity losses for major products and pricing challenges due to ongoing Inflation Reduction Act (IRA) reforms.
- Oncology remains the leading area in public biopharma M&A, but fields like immunology, neurology/psychiatric and rare diseases have gained momentum in the past five years.
- More than half of acquired lead assets fall short of pre-deal sales forecasts by about 40% over three years post-launch due to overly optimistic commercial assumptions and execution challenges. Additionally, acquired clinical-stage assets frequently miss their anticipated launch dates, underscoring the need for rigorous clinical and commercial due diligence.
- Success in post-deal performance is commonly linked to assets that are first in class and show clinical differentiation in broad patient groups. Conversely, therapies targeting narrow patient populations or those that do not offer significant advantages over the standard of care often disappoint.

- As 2024 unfolds, pharma executives need to strengthen their capabilities in swiftly identifying, assessing, finalizing and assimilating deals. This strategy is key to leveraging the numerous prospects available in the fast-paced and evolving biotechnology industry.

Large pharmaceutical companies are investing to improve their R&D efficiency and their capacity for organic drug development. Yet they continue to rely extensively on external assets and technologies to fulfill their growth objectives. In their pursuit of innovation through external avenues, these companies have various deal options at their disposal, including product licensing, forming joint ventures for specific products or portfolios, and acquiring other companies. The differences between these deal structures are not always distinct, as the deal-making activities of large pharmaceutical companies frequently blend various types of transactions.

As the biotechnology sector continues to underperform the broader market and major pharmaceutical companies encounter significant challenges (e.g., loss of exclusivity periods for key brands, pricing pressures due to the IRA), the need for externalizing assets has intensified. The financial strength of pharmaceutical companies, evident in their robust cash flows and strong balance sheets, has provided them with substantial reserves, enhancing their inclination toward M&A more than ever before. This is further complemented by the latest wave of divestments of non-innovative pharmaceutical assets by companies like Merck, Lilly, GSK and Novartis, which has freed up capital, empowering these large pharmaceutical companies to become serial acquirers in the biotech sector.

To gain insights into how large pharmaceutical companies can thrive through M&A, L.E.K. Consulting has conducted an analysis of the public biopharmaceutical M&A deal-making landscape since 2010, defined as the acquisition of publicly traded biotech companies that are either in the clinical or commercial stage and focus on innovative therapeutics. Our analysis includes global transactions (U.S., EU, Asia-Pacific), is focused only on clinical-stage or commercial-stage acquisitions, and excludes asset licensing and partnership deals. Acquisitions of generics, over-the-counter products, medical devices, diagnostics and preclinical platform companies were excluded from this analysis.

We will examine which types of biotech companies are being acquired, who the leading acquirers are, what characteristics define a successful deal and what to expect for M&A in 2024 and beyond.

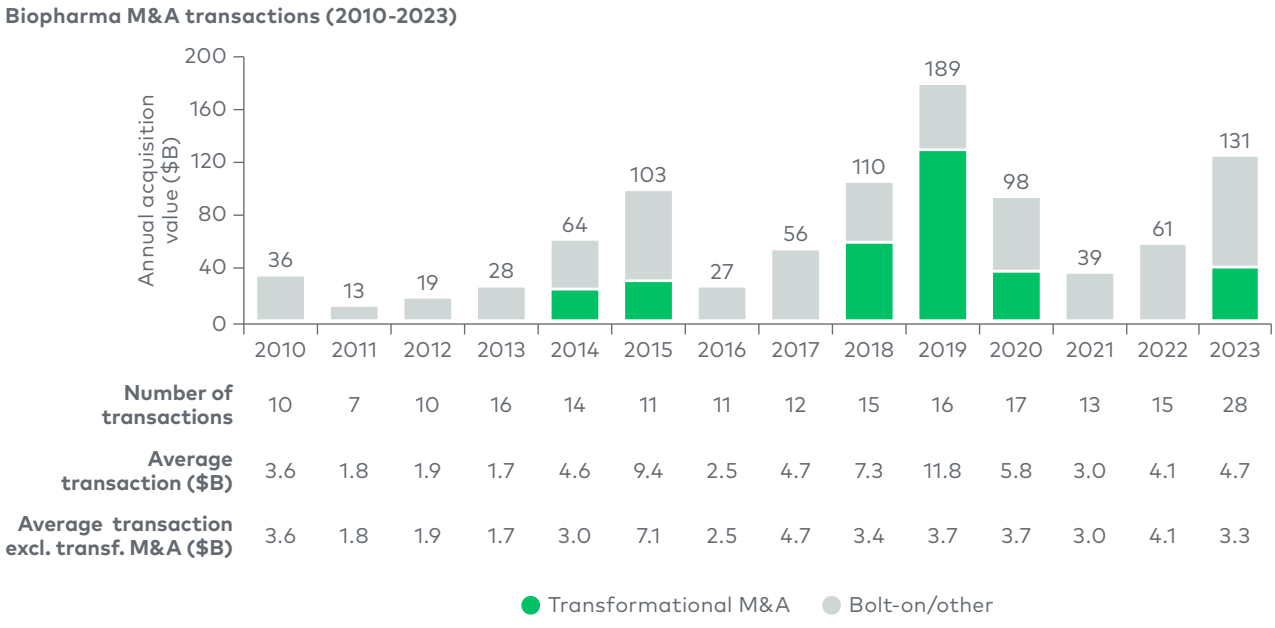
Biopharma consolidation since 2010

From 2010 to 2023, there were 195 public biopharmaceutical M&A transactions, totaling around $1 trillion in M&A investments with an average of $70 billion invested yearly. When adjusted for inflation in today's value, this amounts to $1.2 trillion in M&A investments with an average of $83 billion invested yearly. To put this volume of transactions in perspective, the combined equity value of the top 20 global biopharmaceutical companies stood at $3.6 trillion at the close of 2023.

M&A activity has been cyclical since 2010, reaching its peak in 2019 with 16 deals amounting to $189 billion. Notably, there was a decrease in M&A transactions in 2021 and 2022, attributed to economic uncertainties and the COVID-19 pandemic. Yet a notable rebound occurred in 2023 with 28 biotech M&A transactions, totaling $131 billion in deal value (see Figure 1).

Analyzing these figures when excluding transformational M&A, defined as transactions exceeding $25 billion in equity value and surpassing 20% of the acquirer's market capitalization, the past year stands out as one of the most active in the past decade. This surge in recent M&A activity is likely attributable to an improvement in the macroeconomic environment and the pressures resulting from imminent drug pricing negotiations impacting pharma revenue covered by CMS Part D.

Figure 1
Trends in public innovative biopharmaceutical M&A since 2010



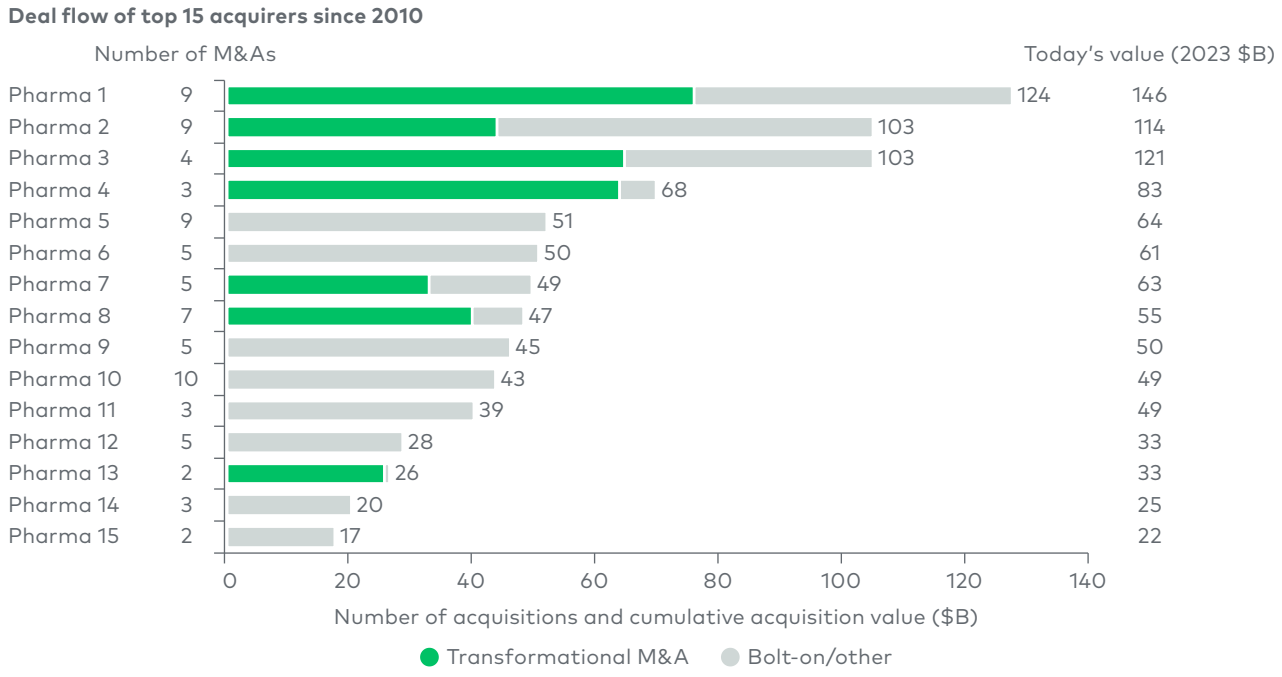
Note: Includes clinical- and commercial-stage public M&A transactions only
Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, S&P Capital IQ

A detailed analysis of the acquirer ecosystem reveals that the top 15 acquirers have been particularly active, responsible for approximately 80% of the total roughly $1 trillion transaction value since 2010. These top acquirers have completed on average five acquisitions since 2010. Impressively, their M&A activities have significantly ramped up in the past five years, with an average annual M&A investment of $6 billion since 2019. This marks a substantial increase, doubling from the previous annual average of $3 billion.

Since 2010, four prominent pharmaceutical companies have collectively invested over $60 billion in public M&A (approximately $80 billion today, accounting for inflation). This significant investment accounts for 40% of the total transaction value in the sector. During this period, each of these M&A leaders completed a significant transformative acquisition. Noteworthy examples include Bristol Myers Squibb's merger with Celgene, AbbVie's acquisition of Allergan, Takeda's purchase of Shire and Pfizer's merger with Seagen.

The rest of the notable M&A players have been more opportunistic acquirers. Since 2010, these companies have been involved in a string of acquisitions ranging from $15 billion to $50 billion total per company (roughly $20 billion to $60 billion when adjusted for inflation in today's value). These firms generally target companies with more-streamlined portfolios, often focusing on those with an average of one to five clinical assets, rather than a broad and diverse product range (see Figure 2).

Figure 2
Top 15 acquirers in public biopharma M&A (2010-2023)



Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, S&P Capital IQ

Predominant focus in mergers and acquisitions

The majority of acquisitions since 2010 have been strategically directed at acquiring commercial-stage these acquisitions represent about 50% of the total deal volume (94 out of 195 transactions) and approximately 75% of the transaction value, amounting to $850 billion of the overall $1.2 trillion today, adjusted for inflation. This significant focus on commercial-stage targets underscores the buyers' inclination to secure risk-free revenues, a strategy driven by the need for greater certainty in managing the challenges of portfolio maturity and imminent patent expirations. The rest of the transaction activities have centered around clinical-stage assets, evenly divided between pre-proof of concept (POC), with 52 deals worth $105 billion in today's value) and post-POC stages (comprising 49 deals worth a total of $208 billion in today's value).

As expected, the average acquisition value correlates strongly with the development stage of the primary asset. This value, adjusted for inflation, ranges from an average of $1.2 billion for portfolios for lead assets in phase 1, escalating to $9 billion for acquired portfolios led by a single asset or multiple commercial-stage assets (see Figure 3).

Figure 3
Number of transactions and value by stage of lead asset (2010-2023)

Biopharma M&A transactions by stage of lead asset

	PHASE 1	PHASE 2	PHASE 3	APPROVED
Number of M&As	11	41	49	94
Average transaction size ($B)	1.2	2.2	4.2	9.0

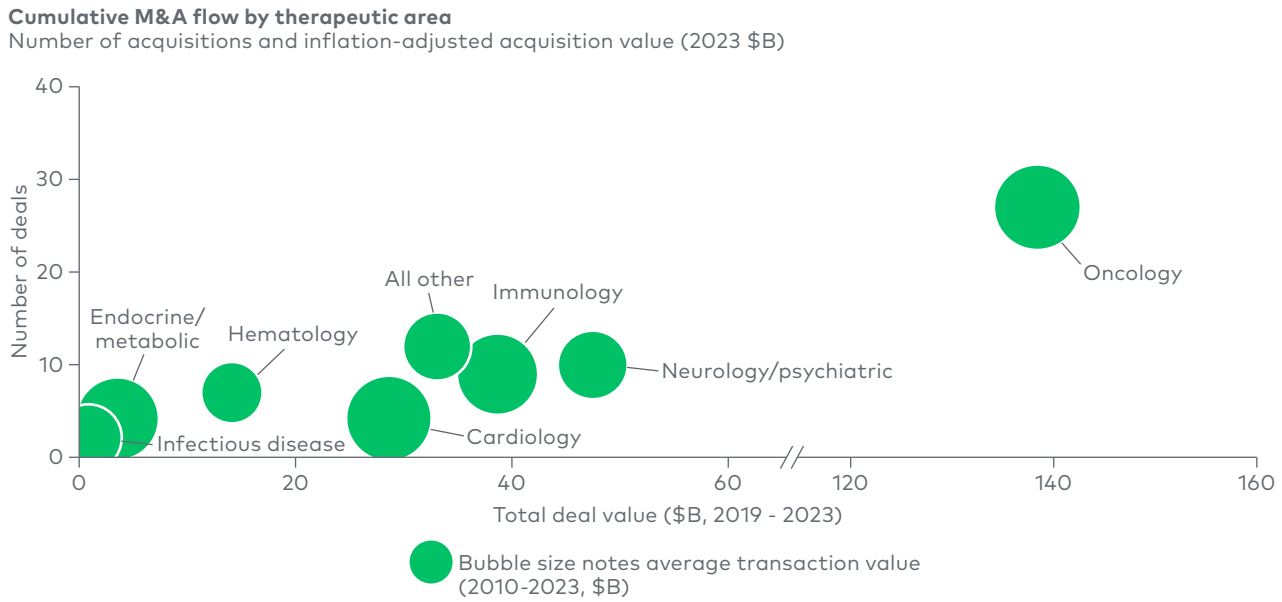
Number of acquisitions and average inflation-adjusted acquisition value (2023 $B)

Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, S&P Capital IQ

In examining the breakdown of deals by therapeutic area, oncology continues to dominate biopharmaceutical M&A activity (see Figure 4). Since 2010, the total transaction value in oncology has surpassed the combined value of the next three therapeutic areas. More recent trends, since 2019, further underscore this dominance, with oncology constituting approximately 25% of the overall deal value and 30% of the deal volume in the sector.

While the focus on oncology is likely to remain steady, the fields of neuroscience and psychiatry saw a significant surge in late 2023, particularly with recent deals like AbbVie's acquisition of Cerevel and BMS' purchase of Karuna. This makes it the second-most-valuable area in cumulative acquisition value since 2019, with a staggering $30 billion in M&A in 2023 alone.

Figure 4
Cumulative acquisition of public biopharma companies by therapeutic area (2019-23)



Note: "All other" includes nephrology, gastrointestinal, ocular, respiratory, dermatology, hepatology, genitourinary/sexual function and musculoskeletal; deals for multiple therapeutic areas were not included, as they are mainly driven by large-scale transformational M&A with broad commercial and development portfolios across therapeutic areas; rare/orphan/genetic was not included, as it applies across therapeutic areas and is not mutually exclusive with therapeutic area categories
Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, S&P Capital IQ

Immunology is also gaining momentum. Of the 12 deals in the immunology sector since 2010, nine have taken place in the past five years. This therapeutic area now claims the third-highest average deal value.

Additionally, there has been a growing trend among buyers to pursue acquisitions of companies specializing in rare and genetic diseases, within any therapeutic area. Since 2010, there have been 47 deals in this disease archetype, with 28 occurring in the past five years. Acquisitions of rare and genetic disease assets are attracting notably high valuations (median of $3.5 billion today).

A final yet critical factor in assessing key drivers of M&A is the scale of the acquisition. Over the past five years, strategic bolt-on acquisitions — defined as deals with an equity value below $30 billion and/or less than 20% of the acquirer's market capitalization — have been markedly more common, making up over 95% of all deals, than the transformational M&As that occurred during the same period.

The preference for bolt-on acquisitions over transformational mergers appears to be influenced by two main factors:

- First, the value creation from transformational acquisitions has shown variability. Although these transactions can significantly boost the acquirer's scale, evidenced by increased revenue, a more robust pipeline and greater financial leeway, their impact on shareholder value creation has not been consistent. An analysis of the buyer total shareholder return (TSR) for five of the seven transformative acquisitions included in this analysis shows an average decline of 5% in TSR one year after the transaction and a 10% decline three years after, when compared to the Pharmaceutical Index.[1] In stark contrast, the AbbVie-Allergan deal stands out, significantly outperforming the index over the three-year period with increases of 45% and 114%, respectively.
- Second, the increasing vigilance of the Federal Trade Commission (FTC) regarding mergers and acquisitions has become more apparent, as seen in high-profile instances such as Amgen's proposed acquisition of Horizon and Pfizer's pursuit of Seagen. Recently, this has extended into early-stage licensing deals, with the FTC seeking an injunction against Sanofi's licensing agreement of a phase 1 asset in Pompe disease from Maze Therapeutics. This intensified regulatory oversight has brought a degree of caution into the market, thereby moderating the appetite for large-scale deals as companies contemplating major M&A moves now have to navigate a more complex regulatory landscape, consider the likelihood of antitrust challenges and evaluate the possibility of having to make significant concessions to gain regulatory approval.

Hallmarks of M&A performance

A key driver of valuation in clinical-stage and commercial-stage acquisitions is the projection of future sales. We analyzed how reliable sell-side projections are before an acquisition to better understand the limitations of such guidance in deal-making.

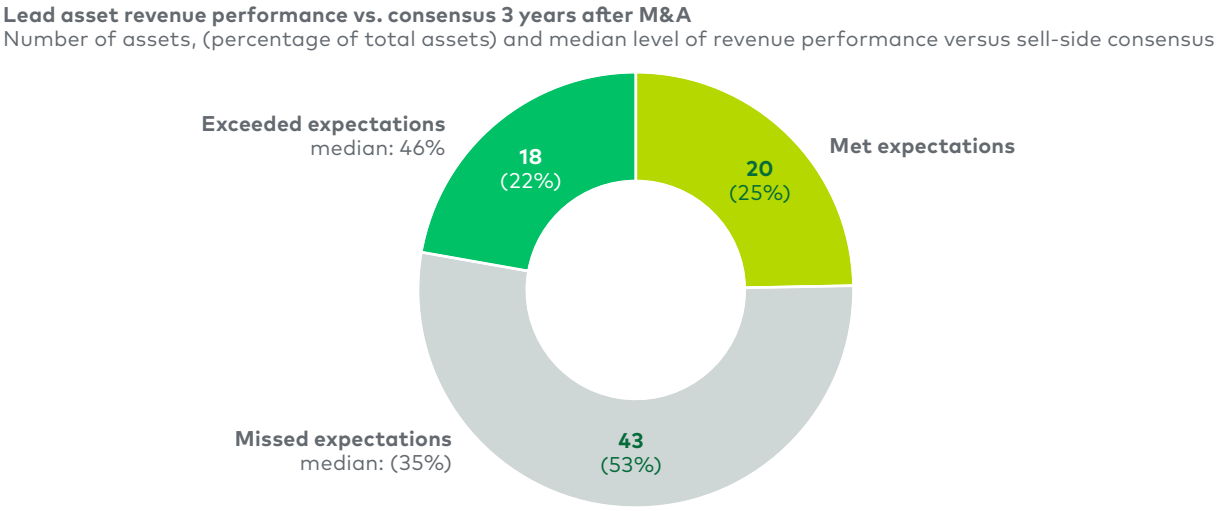
Many of the acquired lead assets in our analysis failed to meet their preacquisition launch timelines and revenue forecasts. This hindrance often resulted from a combination of overly optimistic commercial forecasts, which may arise from an inclination toward false precision to justify the acquisition premium, coupled with unforeseen hurdles encountered during the clinical development of these acquired assets.

In our analysis of 195 M&A transactions, data for reliable three years post-launch revenue was available for only 81 lead assets. The first insight is that acquirers are proficient at progressing assets through the different phases of clinical development, with their clinical and regulatory

success rates aligning with industry norms. However, approximately half of these acquired assets experienced launch delays compared to their initial projections before the transaction. On average, these delays amounted to about two years.

In terms of commercial performance, a significant portion (53%) of the acquired lead assets fell short of the revenue expectations set by sell-side analysts, underperforming these forecasts by a median of 35% in the three years post-M&A. Conversely, only 22% of these assets exceeded the projected estimates, surpassing them by a median of 46% (see Figure 5). While it is important to understand that these projections are derived from the consensus of sell-side analysts, as opposed to the buy-side consensus usually mirrored in the acquiree's stock price at the transaction time, many acquired lead assets often failed to deliver the expected value. This shortfall has, at times, weakened the fundamental strategic justification for these acquisitions.

Figure 5
Comparison of 3-year post-launch commercial performance for lead assets acquired in public biopharma M&A (2010-2023)



Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, Evaluate Pharma (accessed July 2023)

Our analysis highlights two primary characteristics that contribute to the commercial success of acquired assets: their strategic positioning within the lead indication and being first in class in their mechanism of action.

- Assets that target patient populations in the early stages of the treatment pathway (e.g., first-line therapy) of their lead indication generally exceed expectations. For instance, Takeda's Takhzyro disrupted the prophylactic standard of care in hereditary angioedema, becoming the preferred first-line treatment. Similarly, BMS' Reblozyl represented a new approach to treating anemia in beta-thalassemia as an alternative or supplemental option versus red blood cell transfusions, which were a suboptimal standard of care.

- Innovativeness is another key determinant of success. Assets with a novel, first-in-class mechanism often surpass expectations. Examples include Novartis' Zolgensma and Roche's Esbriet, both first-in-class lead assets acquired from biotech companies that significantly outperformed analyst projections. These pioneering assets saw both a rapid uptake and a higher-than-anticipated adoption level, which analysts had initially underestimated. On the other hand, "me-too" assets entering an already saturated market face more significant challenges in gaining traction and adoption.

Surprisingly, there was no marked difference in the proportion of assets underperforming projections between those acquired at a clinical stage and those already on the market at the time of acquisition. It might be presumed that uncertainties in regulatory outcomes and product labeling for assets still in development could lead to less accurate prelaunch revenue projections.

We also examined the correlation between the disease indication of acquired lead assets and the buyer's existing therapeutic footprint to determine the potential impact of established clinical and commercial proficiency on the accuracy of revenue projections and the overall performance of the product post-acquisition. In our analysis, we define an acquirer's core therapeutic areas as those where they have established commercial capability, evidenced by the presence of at least one product already in the market, and a depth of clinical knowledge, evidenced by at least one asset in mid-to-late-stage development.

More than three-quarters of the M&A transactions evaluated in this analysis focused on a primary asset that targets a core therapeutic area of the acquirer. Lead assets integrated within an acquirer's core therapeutic area generally fare better. About 50% of these assets meet or exceed pre-transaction consensus projections, while 63% of assets in noncore adjacent therapeutic areas fall short of pre-deal expectations. Furthermore, when lead assets outperform consensus, those targeting the acquirer's core therapeutic areas tend to surpass expectations by a larger margin compared to those in adjacent areas. This pattern does not hold true in terms of launch timing of acquired lead assets — they are similarly delayed in both assets targeting core and adjacent therapeutic areas.

Unleashing the full potential of M&A

Despite the challenging funding landscape faced by biotech companies, they remain at the forefront of biomedical innovation and continue to contribute about two-thirds of the industry's clinical-stage pipeline.

This extensive biotech innovation pool offers a significant range of attractive M&A prospects for pharmaceutical companies. Over 130 publicly traded biotech companies, each with a

market capitalization ranging from $1 billion to $30 billion today, are poised to become potential acquisition targets within the next two years, excluding the recent trio of acquisitions of Ambrx, Harpoon and Calypso early in this year. These companies hold valuable assets that are either already in the market or in advanced stages of development, with major clinical milestones expected before the end of 2025, making them appealing for strategic acquisitions.

For biopharmaceutical executives aiming to navigate this M&A landscape successfully, it is essential to focus on the following five strategic priorities:

1. **Establish defined M&A objectives:** To ensure sustained growth, pharmaceutical companies must regularly refresh their R&D pipeline and existing in-line product mix. This involves internal portfolio prioritization and external strategic acquisitions. Senior leaders must set distinct goals regarding the scale, frequency and timing of M&A needs for their business development teams. These objectives should focus on establishing criteria for disease indication selection for acquisition, assessing the expected revenue impact and timing of acquisitions, and appraising the degree of novelty of assets involved in these transactions. With these guidelines, M&A practitioners can then construct detailed business development roadmaps, outlining an optimal sequence of acquisitions needed to fill internal growth gaps.

   Business development leaders must consistently ensure that their actions are in sync with the company's broader strategic vision. Such alignment helps avoid the frequent problem of reevaluating a deal's strategic rationale during the advanced stages of due diligence. Establishing and following clear, specific objectives from the beginning enable companies to conduct their M&A activities in a strategically sound and efficient manner, leading to successful deal closures. This strategy also promotes seamless acquisition integration and optimizes the value obtained from each transaction.

2. **Enhance value with in-depth insights:** In the world of mergers and acquisitions, it is imperative for deal makers to conduct a thorough evaluation of potential acquisition targets, paying close attention to the ramp of projected revenue and anticipated launch timelines, especially within the first years following the acquisition. This time frame is crucial as it is frequently marked by variances between the anticipated investor returns and the actual post-deal performance.

   To ensure a realistic assessment, deal makers should adopt a comprehensive approach that includes both internal market insights and external benchmarks. This should involve an analysis of the past performance of similar assets in comparable markets, considering factors like pricing and access barriers, competitive dynamics, and operating investment requirements to win. In doing so, they should also recognize the potential for revenue uplift

when an acquired asset is integrated into the expansive network and the deep-rooted expertise of a leading pharmaceutical company. While our analysis did show that many acquired assets fall short of expectations, high-quality assets tend to thrive within a larger, more scaled commercial organization, benefiting from its unencumbered infrastructure. Conducting this level of in-depth and balanced analysis is important for unlocking greater performance and value from promising assets while de-prioritizing those M&A candidates with poor and risky prospects.

3. **Understand the risk of unrelated diversification:** Pharmaceutical companies continually seek to refine and expand their therapeutic footprint to drive sustainable growth. Diversifying revenue streams has its advantages, but assessing the value of M&A targets that venture into new or unrelated therapeutic areas poses unique challenges. Our analysis shows that acquired assets tends to perform worse the more distant they are from the acquirer's existing operational expertise, current sales force channels and established provider relationships. Deal leaders need therefore to engage with external advisors who possess up-to-date expertise in the target's disease areas. These specialists can provide invaluable insights, helping construct fair and precise valuation estimates, and uncover even the smallest potential synergies.

   Additionally, deal makers must factor in the possible depreciation in value of acquired assets after integration. This entails recalibrating the expected growth of these assets, particularly in situations where key talents from the acquiree, who were essential to the target's success, leave the company. Conducting a comprehensive risk assessment in this context allows for a more judicious decision-making process. It helps in weighing the advantages of diversification against the risks associated with expanding into new therapeutic areas.

4. **Uphold objectivity and be willing to walk away:** In the demanding final phase of deal evaluation, where diverse stakeholders including bankers and legal advisors are involved, it is imperative for deal leaders to maintain both accuracy and objectivity. They should avoid the trap of using misleading accuracy or engaging in false precision to justify and close a deal.

   Despite the noticeable increase in acquisition premiums over recent years (rising from an average of 59% before 2015 to 94% after 2018, as per our analysis), it is critical for acquirers to avoid overpaying. A meticulous, unbiased assessment is key, coupled with a strategic focus on uncovering potential commercial upsides and significant synergies. By adopting this approach, decision-makers can ensure that their investment choices are not merely a response to the prevailing trend of high acquisition costs but are grounded in a thorough understanding of the target's true potential value.

5. **Cultivate superior M&A capabilities:** Executives in the biopharmaceutical industry need to go beyond investing in deal sourcing and evaluation. It is critical that they substantially increase their resources and refine their processes to attain mastery in deal integration, a key to post-merger operational excellence. Proper acquisition integration is vital to avoid delays in launch and to adeptly handle the operational complexities that arise post-merger. This encompasses a wide array of integration tasks, such as defining governance and decision rights along the M&A process, effectively communicating across teams, identifying and addressing potential issues early on, and ensuring a seamless blending of cultures and systems between the two companies. By doing so, companies can not only enhance the effectiveness of their M&A activities but also maximize the value and growth opportunities presented by each acquisition.

   In the increasingly competitive M&A landscape, the frequency and magnitude of transaction experience are becoming key elements that set apart potential buyers. A consistent track record in deal-making markedly bolsters a company's proficiency in M&A. Regular engagement in acquisitions, even at a modest pace of one transaction every two years, has the potential to develop and evolve an organization into a proficient and systematic serial acquirer.

   Furthermore, the ability to efficiently manage and execute multiple acquisitions in rapid succession over a short period of time is poised to become a crucial factor for success when facing simultaneous opportunities. Recent deal flows clearly underscore this observation, such as AbbVie's completion of two acquisitions within a single week and BMS' completion of three acquisitions in just 11 weeks. These cases underscore the urgent need for biopharmaceutical companies to scale their business development capabilities to handle multiple due diligences and integrations simultaneously.

When implemented successfully, these five strategic priorities will empower M&A professionals to more effectively and efficiently identify, assess and integrate deals, thereby securing a competitive advantage in the market. By concentrating on developing strong and scalable M&A capabilities, acquirers will not only streamline the acquisition process but also guarantee maximum value extraction from each transaction.

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[1]The VanEck PPH index was used as reference. This analysis excludes Pfizer-Seagen and Shire-Baxalta in Year 3, and excludes Actavis-Forest in all years due to data limitations.

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