



THE REPLACEMENT ARCHITECTURE

**How biopharma
companies build beyond
the blockbuster**

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Executive summary



Replacing a blockbuster requires more than external innovation alone; sustained growth depends on balancing flagship stewardship, internal innovation, and external innovation.



Analysis of Lilly, AbbVie, Merck/MSD, and BMS suggests that companies pursue distinct approaches to external innovation, resulting in recognizable "dealmaking fingerprints."



Investor response appears to reflect not only individual transactions, but broader confidence in a company's long-term replacement architecture.



External innovation can strengthen future growth narratives, but its impact depends on how it complements internal capabilities and existing franchises.



Replacement architecture provides a practical framework for evaluating growth preparedness, portfolio strategy, and partnering opportunities.

Introduction to the Replacement Architecture Framework

A blockbuster franchise is both an achievement and a future liability.

The same product that creates extraordinary value for patients and shareholders eventually creates a replacement challenge for management teams. The larger the franchise, the larger the vacuum left behind when exclusivity expires. In that sense, every blockbuster contains the seeds of its own strategic problem.

At Healthcare at Ipsos, we increasingly see companies grappling with the same challenge: how to replace today's growth engine while simultaneously building the next one.

As **Figure 1** shows, successfully replacing a blockbuster requires more than a single strategic lever. Rather, proactive replacement architectures are built through three complementary strategic levers:

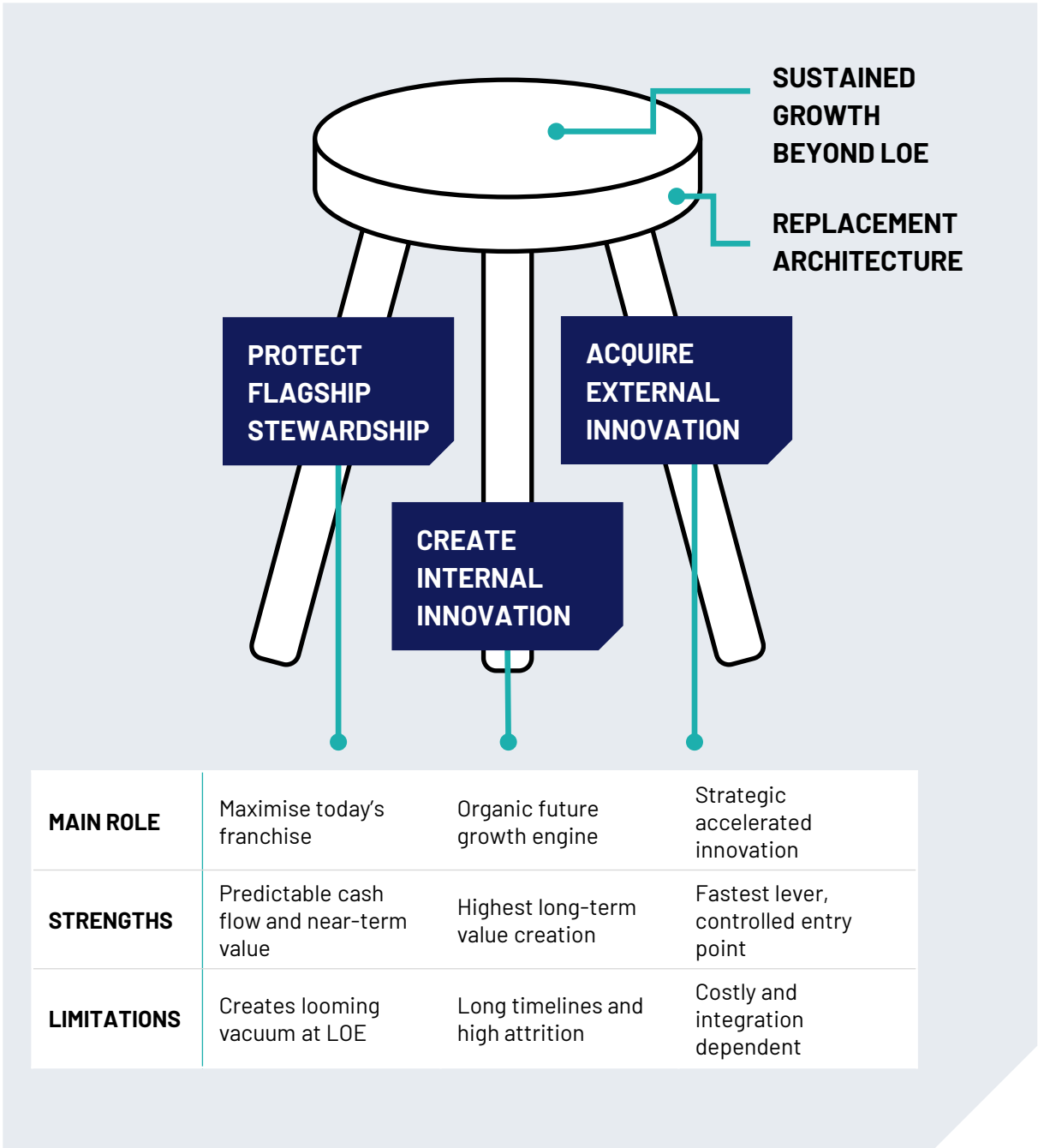
1. Flagship stewardship
2. Internal R&D
3. External innovation

The three pillars should not be viewed in isolation: successful flagship franchises generate the resources to fund innovation, externally acquired assets typically require years of internal development before and after commercialization, and internal R&D frequently supports lifecycle management of existing franchises. The framework distinguishes strategic choices rather than mutually exclusive investment categories.



Figure 1. Replacement Architecture: A Three-legged Stool

Sustained growth beyond blockbuster loss of exclusivity (LOE) depends on balancing three complementary strategic levers: protecting today's franchise, creating tomorrow's growth engines, and acquiring capabilities that accelerate future growth.



External Innovation: The Most Visible Lever

Among the three pillars of the framework in **Figure 1**, the first, Flagship Stewardship, and second, Internal R&D, are essential to maximizing the value of established in-house assets, whereas the third, External Innovation, offers management teams the most direct opportunity to reshape their future growth profile over relatively short time horizons. It is therefore unsurprising that **business development and externally sourced innovation often become the focal point of discussions surrounding patent cliffs.**



To better understand how companies approach this third component of replacement strategy, Ipsos combined franchise lifecycle analysis, dealmaking intelligence, and investor signals across representative biopharma companies. It mapped those transactions against both flagship franchise lifecycles and subsequent stock performance.

The objective was not to determine whether any individual transaction was ultimately deemed a success. Rather, it was to explore whether recognizable patterns emerge in how companies prepare for life beyond a blockbuster and whether investors appear to reward certain approaches to future growth while ultimate outcomes remain uncertain.



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Methodology

The objective was to explore whether patterns emerge when franchise lifecycles, external innovation activity, and investor sentiment are examined together.

Four flagship franchises were selected to represent a range of replacement strategies and stages of franchise maturity: tirzepatide (Mounjaro, Zepbound; Eli Lilly and Company), adalimumab (Humira; AbbVie, originally developed by Abbott Laboratories), pembrolizumab (Keytruda; Merck & Co., Inc., known as MSD outside the United States and Canada), and lenalidomide (Revlimid; BMS). Each franchise was anchored to its commercial launch and anticipated loss of exclusivity.

Major partnerships, including mergers and acquisitions (M&A) and licensing transactions, were mapped across each franchise lifecycle and characterized by transaction type, disclosed upfront value, and development stage of the lead asset. The resulting visualization serves as a proxy for **how companies deploy external capital in anticipation of future growth needs**.

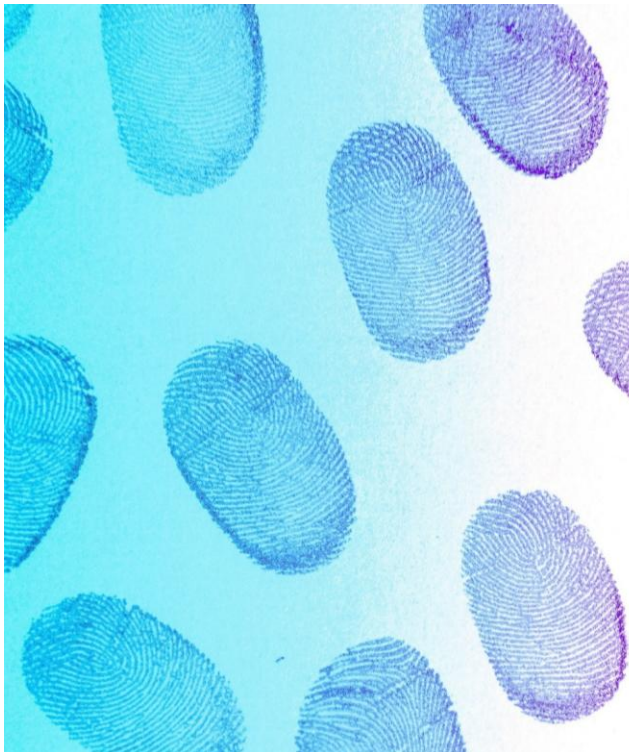
To assess investor response, each company's share price was indexed to a baseline of 100 at the time of flagship franchise launch and plotted against relative lifecycle position, allowing companies operating in different calendar periods to be compared at equivalent stages of franchise maturity.



Mapping External Innovation: The Dealmaking Fingerprint

Figure 2 maps acquisition and licensing activity across the lifecycle of each company's flagship franchise. Taken together, these dimensions form what we refer to as a dealmaking fingerprint: the characteristic pattern by which a company deploys external capital in anticipation of future growth needs. These fingerprints are intended to characterize observable patterns of external innovation activity rather than evaluate the quality or eventual success of any individual company's strategy.

Several immediate observations emerge from this analysis. First, all four companies were active dealmakers. Second, transaction volume and deal size alone do little to distinguish their approaches. More revealing are differences in when companies transacted, what types of investments they made, and how those investments were distributed across the franchise lifecycle.

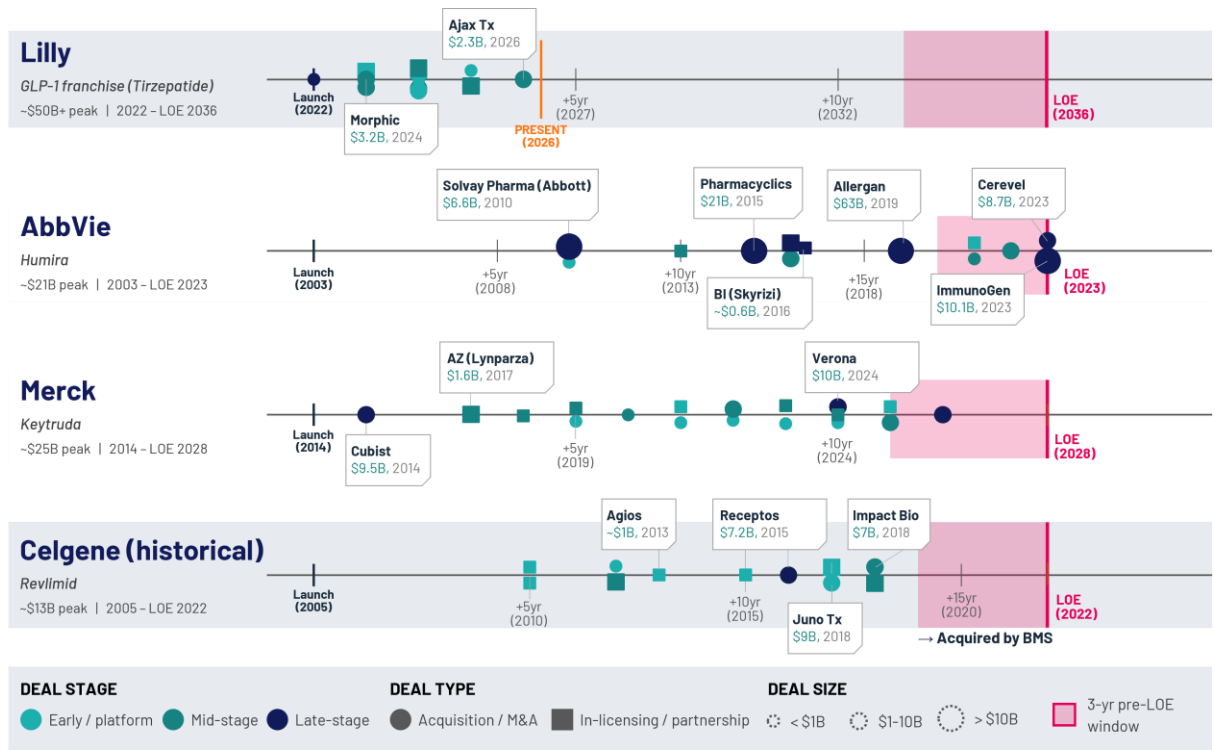


The dealmaking fingerprint is the characteristic pattern by which a company deploys external capital in anticipation of future growth needs.

Figure 2. Representative Dealmaking Fingerprints.

Acquisition and licensing activity for Merck & Co., Inc. (MSD outside the United States and Canada), Eli Lilly and Company, AbbVie, and BMS mapped across each company's flagship franchise lifecycle, with commercial launch and anticipated LOE aligned to a common timeline to facilitate comparison. Circle size reflects upfront deal value; circles = M&A transactions, squares = licensing/partnership transactions; color indicates development stage.

Sources: Healthcare at Ipsos; company filings and press releases. Select deals shown, not exhaustive.



Four Companies, Four Distinct Approaches

This preliminary analysis suggests that companies exhibit recognizable archetypes (**Table 1**): Lilly resembles a portfolio builder archetype, AbbVie a hybrid builder archetype, Merck/MSD a franchise defender archetype, and BMS a venture builder archetype. Whether any archetype is inherently superior remains an open question, but the distinctions help explain why transaction volume alone provides an incomplete picture of replacement strategy.

Importantly, these dealmaking

fingerprints capture only one component of the broader replacement architecture. Lilly's early external activity complements an internal pipeline that includes retatrutide and orforglipron, while AbbVie's externally sourced Skyrizi was complemented by internally developed Rinvoq. BMS/Celgene – historically – may provide a useful counterexample: neither aggressive external investment nor internal efforts such as Pomalyst ultimately created sufficient confidence in life beyond Revlimid.



The same product that creates extraordinary value for patients and shareholders eventually creates a replacement challenge for management teams.

Table 1. Preliminary Dealmaking Fingerprint Archetypes

Illustrative framework categorizing distinct approaches to external innovation and replacement planning observed across Lilly, AbbVie, Merck/MSD, and BMS. Archetypes are defined by the timing, distribution, and composition of acquisitions, licensing transactions, and partnerships undertaken throughout the lifecycle of a flagship franchise.

Source: Healthcare at Ipsos, analysis.

Archetypes	Characteristics	Illustrative Example
Portfolio Builder	Early, distributed investments across modalities and therapeutic areas, creating multiple future growth options.	Lilly
Hybrid Builder	Combines internal innovation, licensing, franchise extension, and selective acquisitions to diversify future growth.	AbbVie
Franchise Defender	Prioritizes the flagship franchise while selectively adding external innovation, often accelerating as LOE approaches.	Merck/MSD
Venture Builder	Numerous early-stage, higher-risk investments emphasizing optionality and tolerance for failure.	BMS/Celgene

The Market Looks Beyond the Blockbuster

While a dealmaking fingerprint has value in its own right, a more consequential near-term question is whether investors appear to reward certain replacement architectures while the outcome remains uncertain. Share price serves not only as a real-time barometer of investor sentiment but also as a strategic asset. Companies trading at a premium enjoy greater flexibility to raise capital, fund clinical development, pursue acquisitions, and execute partnerships, creating a feedback loop in which investor confidence reinforces a company's ability to execute its long-term strategy.

Figure 3 maps stock performance for the same four companies against relative lifecycle position, indexing each company's share price to 100 at flagship franchise launch and normalizing the timeline so that companies can be compared at equivalent stages of franchise maturity regardless of when those lifecycles began.



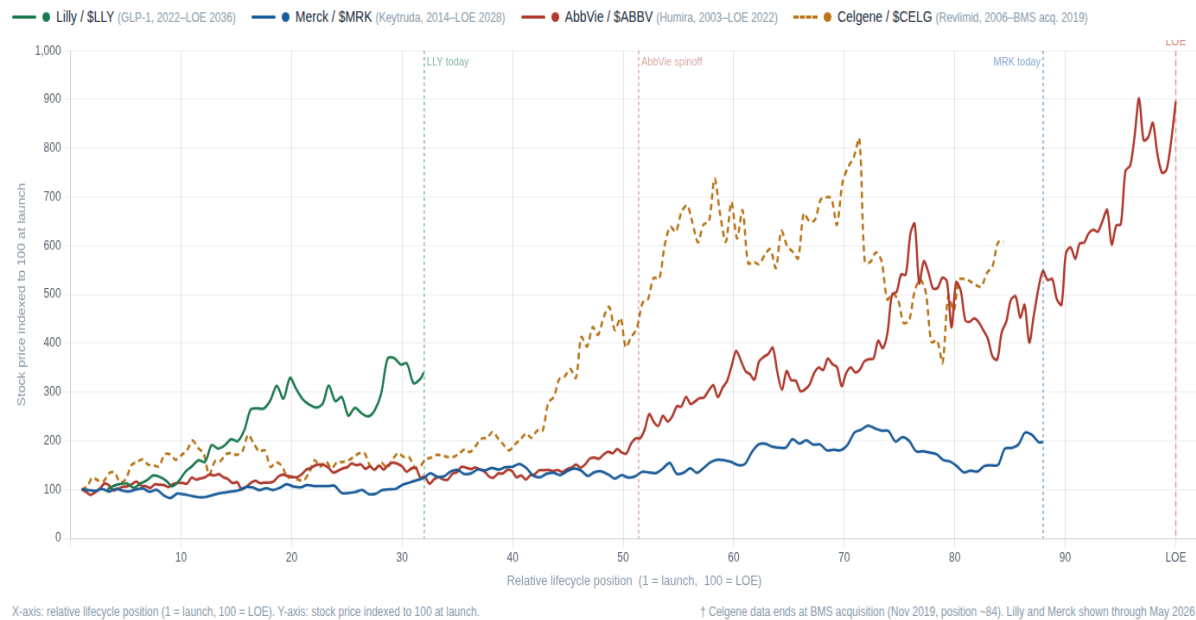
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Figure 3. Stock Performance Indexed to Launch Across the Franchise Lifecycle

Stock performance for Lilly (\$LLY), Merck (\$MRK; MSD outside the United States and Canada), AbbVie (\$ABBV, formerly \$ABT), and BMS (\$CELG), indexed to 100 at flagship franchise launch and plotted against relative lifecycle position (1 = launch, 100 = LOE). Celgene is shown through the BMS acquisition (November 2019, approximately position 84). Lilly and Merck/MSD are shown through May 2026.

Sources: Healthcare at Ipsos; Yahoo Finance.



Investors Reward Preparedness

The most obvious pattern in **Figure 3** is Lilly's divergence from the other comparator companies. Although still relatively early in the projected tirzepatide lifecycle, Lilly's stock has appreciated substantially more than other companies examined at comparable points in their franchise arcs. While it would be premature to conclude that Lilly has solved the replacement challenge, investors appear willing to recognize the company's efforts to extend leadership in obesity while constructing multiple future growth options through both internal and external innovation. Tirzepatide may be today's growth engine, but programs such as retatrutide suggest investors are already evaluating what comes next.

AbbVie's trajectory may be the most instructive. Share price appreciation suggests investor confidence emerged gradually following its spinout from Abbott in 2013 and appears tied to the progressive construction of a broader replacement architecture spanning Skyrizi, Rinvoq, oncology, neuroscience, and aesthetics.

Merck/MSD's Keytruda-era story remains unresolved. The company continues to benefit from one of the most successful

oncology franchises in pharmaceutical history. Yet investors have not rewarded the stock to the same extent as Lilly at a comparable point in the franchise lifecycle.

Whether this reflects differing expectations regarding post-Keytruda growth, differing perceptions of replacement preparedness, or simply differences in market context remains an open question.



BMS/Celgene presents an instructive contrast. For much of the Revlimid lifecycle, investors responded positively to the strength of the existing franchise and the company's willingness to invest aggressively in future growth. Yet neither aggressive dealmaking nor successful internal innovation ultimately proved sufficient to offset the scale of the approaching Revlimid challenge.

The pattern across all four companies points to the same underlying dynamic: investors appear willing to place value on credible future growth narratives before the outcome is known. Dealmaking contributes to those narratives, but so do internally developed programs, lifecycle management investments, and management teams' perceived ability to navigate an eventual LOE.

Whether that confidence is ultimately sustained, however, depends on the architecture's ability to generate durable growth beyond the flagship franchise itself.

This naturally raises a related question. If investors appear willing to reward coherent replacement architectures over time, how do they react to the individual transactions that help build them?



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Architectures Over Transactions

Figure 4 illustrates that investors can react very differently to individual transactions. AbbVie's acquisition of Allergan in 2019 (**Figure 4A**) was met with a negative market response. In contrast, its acquisitions of ImmunoGen and Cerevel in late 2023 (**Figure 4B**), announced within days of one another, may reflect investor reactions to both transactions.

Not all transactions, however, elicit a meaningful response. Lilly's acquisitions of Morphic and Ajax Therapeutics, for example, produced little discernible share price movement (data not shown), suggesting that many transactions are too small to alter investor expectations regarding future growth materially.

The lesson is not that deals do not matter, but that investors appear capable of evaluating individual transactions on their own merits while maintaining a broader view of a company's long-term trajectory. Individual deals may be received positively, received negatively, or generate little observable investor response. Yet the longer-term patterns observed in **Figure 3** suggest that investors ultimately care less about any single transaction than whether a credible replacement architecture is taking shape. For management teams, this creates a practical challenge: distinguishing between activity and progress. Viewed through this lens, the objective of dealmaking is not simply to acquire assets, but to strengthen the broader growth story.



Figure 4. Deal Announcement and Acquirer Stock Price Reaction

Daily closing price and trading volume for AbbVie (\$ABBV) in the weeks surrounding two deal announcements: (a) the acquisition of Allergan (Jun 25, 2019, \$63B), and (b) the acquisition of ImmunoGen (Nov 30, 2023, \$10.1B) and Cerevel (Dec 6, 2023, \$8.7B). Each panel shows approximately 40 trading days centered on the announcement date; volume bars highlight the announcement day in red. The Cerevel acquisition (\$8.7B) was announced Dec 6, 2023, six days after ImmunoGen; continued price appreciation after Nov 30 likely reflects both transactions.

Sources: Healthcare at Ipsos; historical daily price data, AbbVie Inc.

Figure 4A

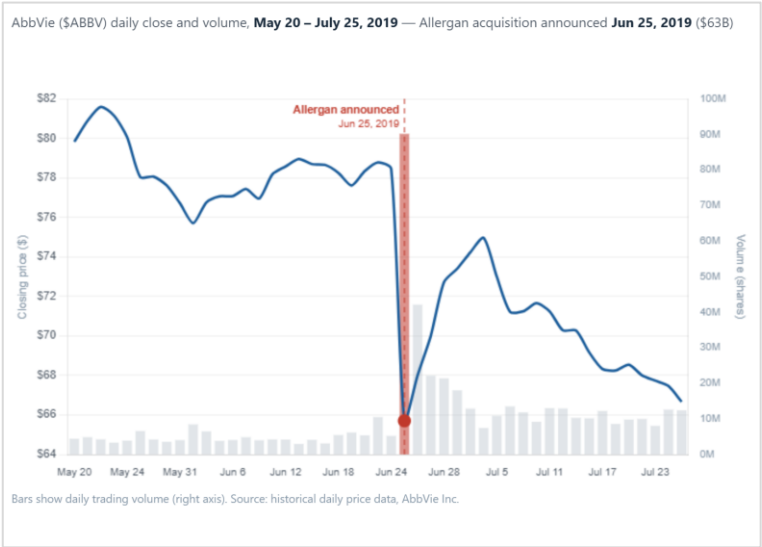
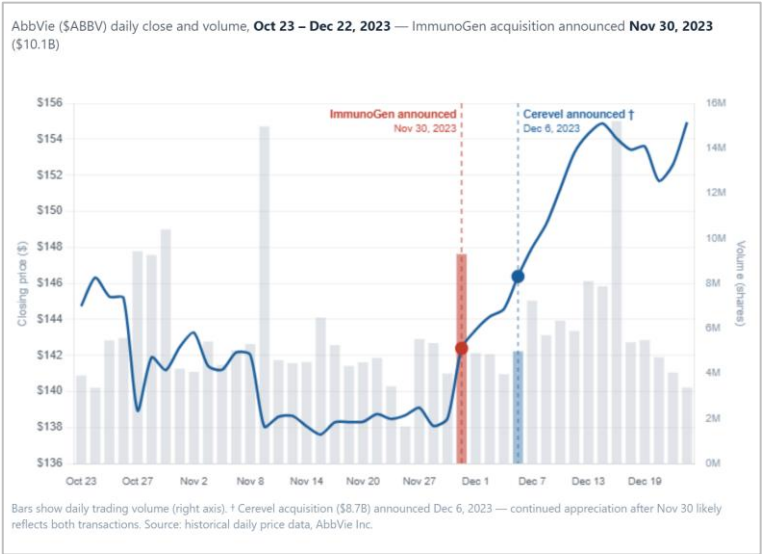


Figure 4B



Turning Replacement Architecture into Strategy

Replacement architecture provides an actionable lens for companies on both sides of the partnering equation. For pharmaceutical companies, it can reveal portfolio gaps, benchmark preparedness, and identify where external innovation could strengthen future growth. For biotechnology companies, the same lens can reveal where an asset or platform may have greatest strategic value to prospective partners or acquirers.

FOR PHARMA

Where should we build, buy, or partner?

- 1. Diagnose the architecture**
Assess the balance of flagship stewardship, internal R&D, and external innovation against future growth needs.
- 2. Benchmark preparedness**
Compare dealmaking fingerprints, portfolio gaps, and replacement strategies with relevant peers.
- 3. Prioritize external innovation**
Identify where specific assets, technologies, or partnerships could most meaningfully strengthen the future growth story.

FOR BIOTECH

Where do we fit, and for whom?

- 1. Identify strategic need**
Determine which potential partners face portfolio gaps or future growth challenges your asset can address.
- 2. Understand the buyer**
Assess prospective partners' dealmaking fingerprints, priorities, timing, and preferred transaction patterns.
- 3. Strengthen the partnering strategy**
Prioritize counterparties and position the asset or platform within the context of each company's strategic needs.

How Ipsos Can Help

Ipsos combines proprietary healthcare data, therapeutic expertise, competitive intelligence, investor perspectives, and advisory capabilities to help clients evaluate replacement preparedness, prioritize external innovation opportunities, and identify future growth scenarios. We apply these frameworks on a company-specific basis, combining portfolio, competitive, investor, and dealmaking perspectives to support external innovation and partnering decisions.

Conclusion: Why Replacement Architecture Matters

The analysis suggests that successful preparation for life beyond a blockbuster depends not on any single transaction or strategic lever, but on a credible replacement architecture spanning flagship stewardship, internal innovation, and external innovation. Investors may reward that architecture before its ultimate success is known, but credibility is not the same as sufficiency. BMS illustrates the distinction: substantial internal and external investment generated confidence for much of the Revlimid lifecycle, but ultimately failed to convince investors that future growth could offset the scale of the approaching challenge.

The framework may become even more relevant as the industry evolves. China has become an increasingly important source of external innovation for global pharmaceutical companies. In contrast, companies such as Belgium-based Argenx, BridgeBio, and Alnylam demonstrate that emerging biopharma companies can increasingly commercialize independently, potentially strengthening their negotiating leverage. Advances in AI and computational drug discovery may further accelerate

scientific progress and competitive crowding, increasing the value of identifying future growth opportunities before they become obvious.

In increasingly complex healthcare markets, replacement planning can no longer rely on any single source of information. Competitive activity, scientific innovation, investor expectations, and partnership dynamics must be interpreted together.

The companies best positioned for life beyond a blockbuster may therefore not be those doing the most deals, but those constructing credible replacement architectures across all three dimensions of growth. Counterintuitively, the most informative question may not be how large today's franchise can become, but whether a credible successor architecture is already taking shape.

Three implications for biopharma leaders:

01

Patent-cliff management begins long before LOE.

02

External innovation is most effective when integrated into a broader replacement architecture.

03

Investors appear to evaluate future growth readiness, not just current franchise strength.



Investors appear willing to reward credible future growth narratives before the outcome is known. Dealmaking contributes to those narratives, but so do internally developed programs, lifecycle management investments, and the perceived ability of management teams to navigate an eventual LOE.

OCTOBER 2026

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