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English Edition

The Biopharma Imperative

L.E.K. Insights on Innovation, Growth, and Competitive Advantage

Foreword

This collection brings together a focused selection of L.E.K. Consulting's perspectives on the forces reshaping life sciences and biopharma. The sector continues to push at the boundaries of scientific possibility while navigating capital constraints, accelerating competition and rising expectations from patients, regulators and investors. The pieces included here examine those pressures with clarity and offer practical guidance on how leaders can respond with confidence.

Our insights highlight the strategic consequences of rapid advances in areas such as radiotherapeutics, next—generation oncology partnerships, AI and quantum computing. We also explore the commercial realities facing organisations as they compete in fast—moving therapeutic markets, reassess portfolio priorities, raise R&D productivity and operate in a more selective funding environment. Across these topics, a consistent message emerges: competitive advantage will rest with organisations that pair scientific ambition with disciplined decision—making and operational focus.

At L.E.K., we help clients interpret change and convert it into decisive action. By distilling market signals, emerging opportunities and the pressure points that matter most, this collection offers leaders a clear view of what it takes to steer successfully through a period of structural shifts.

Helen Chen
Global Sector Co-Head for Healthcare
Greater China Managing Partner

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About L.E.K. Consulting

We're L.E.K. Consulting, a global strategy consultancy working with business leaders to seize competitive advantage and amplify growth. Our insights are catalysts that reshape the trajectory of our clients' businesses, uncovering opportunities and empowering them to master their moments of truth. Since 1983, our worldwide practice — spanning the Americas, Asia Pacific and Europe — has guided leaders across all industries from global corporations to emerging entrepreneurial businesses and private equity investors. Looking for more? Visit **www.lek.com**.

EXECUTIVE INSIGHTS

Redefining Biopharma R&D Productivity: New Insights and Strategies

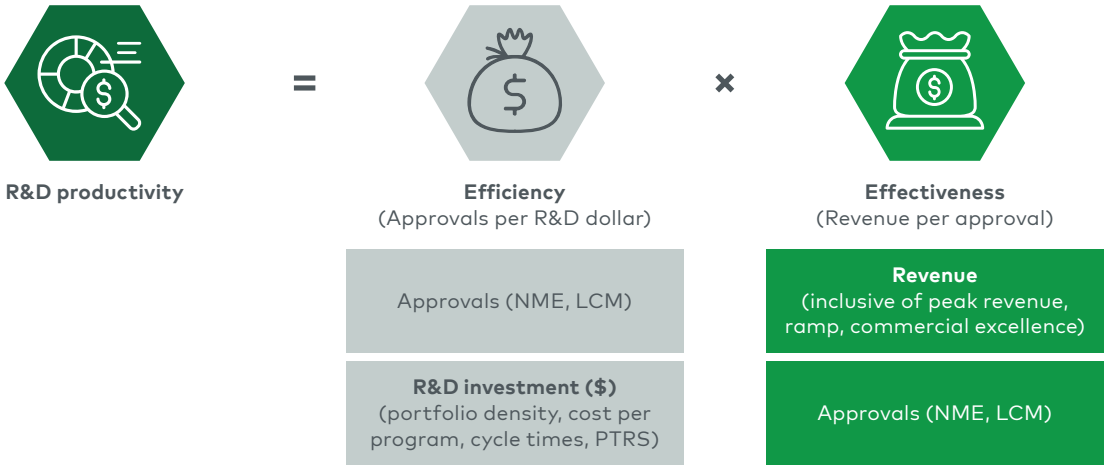
Introduction

R&D productivity stands as one of the most critical issues for biopharma executives, as it directly addresses the ability to transform pipeline investments into tangible revenue streams. Despite its importance, assessing R&D productivity is notoriously challenging due to the long innovation cycles and inherent uncertainties of drug development.

At its core, R&D productivity can be defined as the revenue generated per dollar of investment (see Figure 1). This broad concept can be further broken down into two essential components:

1. **Efficiency of the R&D engine:** This measures the number of drug approvals achieved per dollar invested in R&D. It reflects how well a company can generate successful outcomes from its research efforts within a given budget.
2. **Effectiveness of launches:** This assesses the revenue generated per approved drug. It indicates the ability of a company to maximize the commercial potential of its products through successful market entry, commercialization strategies and life cycle management.

Figure 1
R&D productivity framework



Note: NME=new molecular entity; LCM=life cycle management; PTRS=probability of technical and regulatory success
Source: L.E.K. research and analysis

Previous attempts to assess R&D productivity often suffered from outdated data, opaque methodologies or limited scope, focusing on a small subset of companies. However, with the biopharma industry undergoing significant shifts, it is more critical than ever to adopt a current and transparent approach to understanding how R&D productivity is evolving.

In this edition of L.E.K. Consulting's *Executive Insights*, we explore the two key components of R&D productivity and compares R&D efficiency and R&D effectiveness between Top 15 Biopharmas by revenue and the remainder of the industry (smaller companies).[1]

Such insights are essential to inform and optimize R&D strategies in this dynamic landscape. By understanding the nuances of R&D productivity across different segments of the industry, leaders can leverage mutual strengths to enhance productivity and navigate the evolving challenges and opportunities in drug development and commercialization.

Smaller companies surpass large pharmas in R&D efficiency

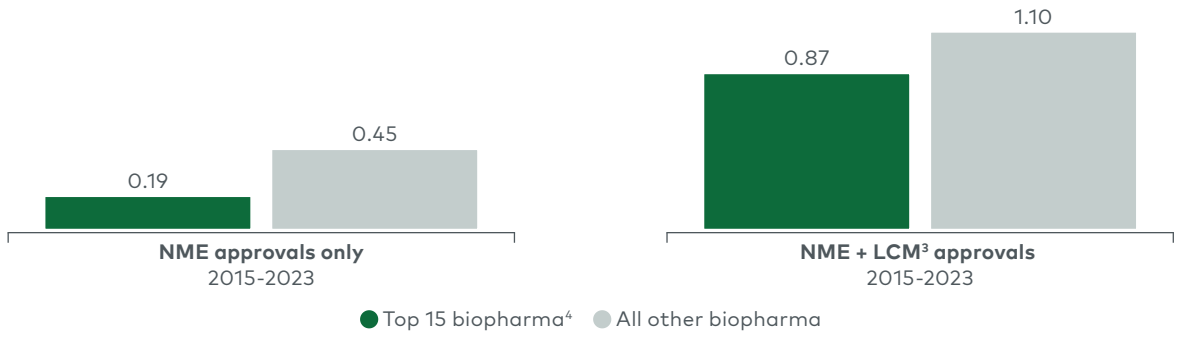
Despite remarkable advances in science, technology and operational practices, the consensus within the biopharma industry is that R&D productivity has been steadily declining. This trend is evident in the widening gap between industry R&D expenditures and revenue growth over the past decade.[2] This situation stems from a steady decline in efficiency, a trend that has persisted over the past 50 years.[3]

A major factor behind the decline in R&D efficiency is the escalating complexity of clinical trials. The scale and scope of these programs have expanded significantly, driven by evolving regulatory demands and a rapidly changing global clinical trial landscape. This has led to longer trial durations, greater enrollment challenges and higher investment costs. Consequently, the number of new approvals per R&D dollar has decreased over the past few decades.

Interestingly, large pharmas have been less efficient at converting R&D investments into new drug approvals compared to the rest of the industry (see Figure 2). Even when factoring in life cycle indications, the efficiency disparity remains evident, although less pronounced.

This is partly driven by their reliance on outliers — mega-blockbuster drugs such as Keytruda, Humira and Dupixent, among others — to drive top-line growth. To meet stringent internal revenue and return-on-investment thresholds, large pharmas concentrate their efforts on programs with the highest market potential, which typically have more life cycle management opportunities. While such drugs deliver transformative value, they also significantly raise the bar for R&D investments, demanding substantial financial resources and time to achieve market success. This heavy focus on blockbuster outcomes often leads large pharmas to prioritize effectiveness — producing high-impact, high-revenue therapies — at the expense of efficiency, limiting the number and diversity of opportunities pursued within their R&D investments and reducing the potential efficiency of their R&D portfolios in addressing broader medical needs.

Figure 2
R&D efficiency: R&D investment per approval by company type, including number of NME and NME + LCM approvals per $1B in R&D

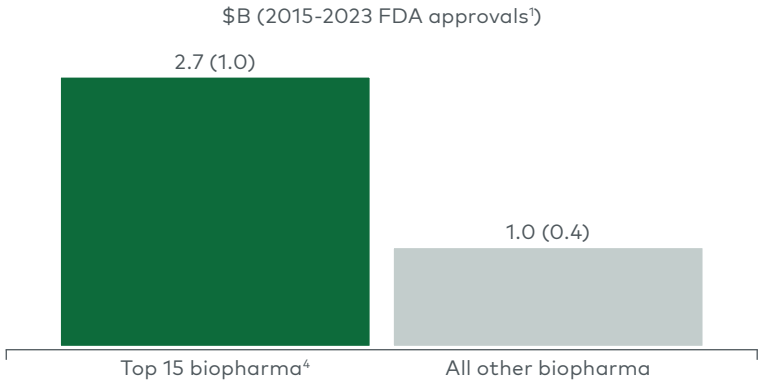


[1]Includes CDER and CBER approvals (vaccines and biologicals); [2]Approvals of acquired companies are included in NewCo company approval counts and revenues if approved after the acquisition date. [3]LCM includes new indication, new patient population, pediatric, and new route of administration; [4]Top 15 Biopharma companies were categorized based on biopharma revenues >$25B in 2024; 2024 trends show a continuing decrease in NME approvals per $1B of R&D spend with Top 15 Biopharma falling to 0.1 and All Other Biopharma pharma falling to 0.3
Source: FDA, company investor presentations and SEC filings

Large pharmas lead in effectiveness, generating more revenue per approval

Large pharmas consistently demonstrate greater R&D effectiveness than smaller companies, a difference largely attributable to their substantial commercial scale and capabilities. From 2015 to 2023, the average peak revenue for new molecular entities (NMEs) approved by large pharmas was approximately $2.7 billion, significantly exceeding the roughly $1 billion average for NMEs from smaller companies. This analysis, which includes historical and forecasted periods through 2030, highlights the revenue-generating advantage of larger organizations (see Figure 3).

Figure 3
R&D effectiveness: Average (Median) NME Peak Revenue[2] by Company[3] Type

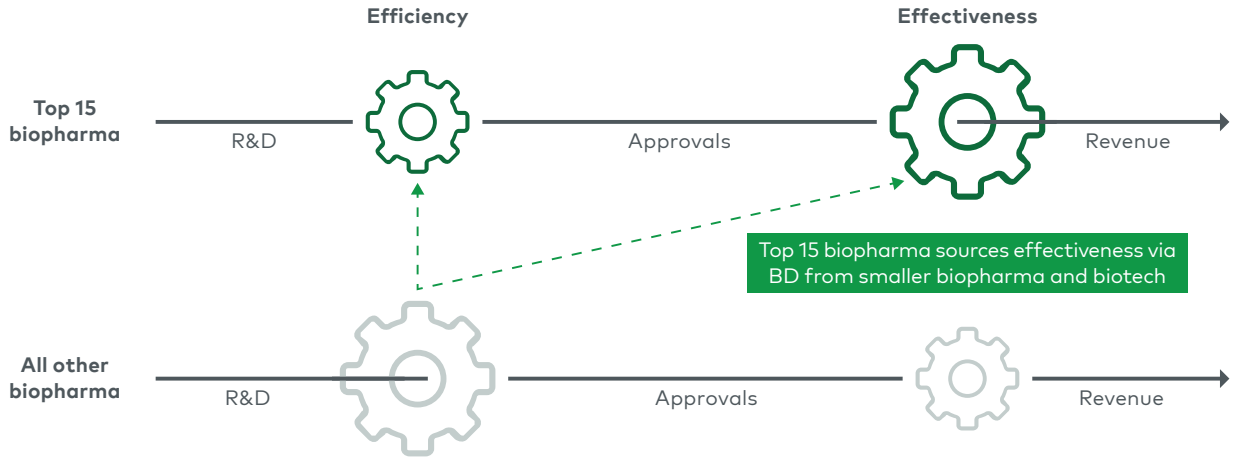


[1]Includes CDER and CBER approvals (vaccines and biologicals). [2]Revenue includes all LCM associated revenue. [3]Approvals of acquired companies are included in NewCo company approval counts and revenues if approved after the acquisition date; [4]Top 15 Biopharma companies were categorized based on biopharma revenues >$25B in 2024, All Other Biopharma is defined as all other innovative biopharma and biotech companies (excluding generics, devices, services, and platform/technology companies); When accounting for 2024 peak revenues for Top 15 Biopharma and All Other Biopharma NME approvals, Top 15 Biopharma remains constant while All Other Biopharma increases to $1.1B average peak revenue
Source: FDA, company investor presentations and SEC filings

Interestingly, large pharma drug candidates that are organically discovered or acquired at a preclinical stage, on average, generate higher revenue than those that were acquired or in-licensed during clinical development. This could be attributed to more stringent portfolio prioritization and the ability to invest earlier in lifecycle management opportunities for these assets.

Smaller companies often operate under significant financial constraints, driven by limited access to capital and a lack of scale in capabilities. As a result, they focus on advancing only those assets they can independently develop and commercialize, prioritizing R&D investments that are both cost-efficient and timely. For therapies targeting larger markets with higher barriers to entry, these companies typically lack the resources needed for full development and commercialization. This limitation often necessitates partnering with large pharmaceutical companies that can leverage their established clinical expertise and commercial infrastructure to bring these therapies to market (see Figure 4).

Figure 4
Conceptual model of R&D efficiency and effectiveness



Note: BD=business development
Source: L.E.K. research and analysis

Strategic actions for biopharma leaders

Large pharmas and smaller companies play distinct yet synergistic roles in driving innovation. Smaller companies act as incubators for novel ideas, while larger pharmas provide the scale and resources to transform these ideas into market-leading therapies. This interplay between small and large players needs to evolve to unlock new opportunities and drive greater value across the biopharma ecosystem.

Specifically, large-pharma executives should shift their R&D productivity to:

- Structuring their portfolios with sufficient shots on goal to produce outlier mega-blockbuster assets that can feed their revenue growth requirements. This requires maintaining stringent portfolio prioritization processes.
- Investing in internal innovation by optimizing for access to early science, speed in clinical development, breadth of therapeutic application and development success rate. Large pharma drug candidates that are organically discovered or acquired at a preclinical stage on average are likely to be more productive in generating returns than those accessed externally at later stages of development given transaction costs.
- Deploying business development into more selective opportunities. While business development will remain essential for larger pharmas, it can be a costly way to drive R&D productivity. Large pharmas should therefore carefully weigh the contribution of their business development activities to R&D productivity and rely on it as needed, as opposed to the default approach.

On the other end, small-company executives should center their efforts on:

- **Sustaining and enhancing R&D efficiency.** Small companies have historically excelled due to their lean teams, constrained capital and focus on efficiency. However, as they grow and gain access to larger pools

of capital — fueled by recent high-value financings — they risk losing this critical edge. To maintain their R&D efficiency, these companies must continue to prioritize agile and financially disciplined management of early-stage programs, as well as well-designed experiments and trials that maximize impact while minimizing resource expenditure. By staying adaptive and disciplined, they can scale without sacrificing their innovative and nimble culture.

- **Rethinking clinical development of lead assets.** Too often, small companies focus their lead asset development on niche indications to secure early clinical proof of concept. While this approach is often dictated by financial constraints, it may limit long-term potential. Executives within these companies should consider a more ambitious strategy by targeting larger, higher-value indications when possible. Bold prospecting in these areas can deliver greater valuation and drive significant shareholder value, even if it requires creative financing or partnerships to achieve.
- **Exploring value-retaining deals.** Biotech platforms often present unpredictable therapeutic applications, necessitating a strategic balance between targeting smaller, independently manageable indications and addressing larger, more competitive markets that require collaboration with large pharma. When partnerships are necessary to maximize an asset's value, executives should avoid giving away too much value too early and structure deals to retain long-term upside, such as through co-development, co-commercialization agreements or attractive milestone payments.

By prioritizing these strategies, biotech and pharma executives can effectively navigate the evolving and competitive biopharma ecosystem, combining innovation with disciplined execution to drive R&D productivity and achieve sustainable success.

The authors would like to acknowledge Jenny Mackey and Ethan Hellberg from L.E.K.'s Healthcare Insights Center for their contributions to this article.

For more information, please contact us.

Endnotes

[1]The top 15 biopharma companies were categorized based on biopharma revenues >$25 billion in 2024 (Evaluate Pharma estimates). Non-top 15 biopharma is defined as all other innovative biopharma and biotech companies (excluding generics, devices, services and platform/technology companies).

[2]Genengnews.com, "The Great Pharma Wasteland." https://www.genengnews.com/topics/drug-discovery/the-great-pharma-wasteland/

[3]Nature.com, "Breaking Eroom's Law." https://www.nature.com/articles/d41573-020-00059-3

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EXECUTIVE INSIGHTS

Radiotherapeutics on the Rise: Addressing Supply Chain Complexity

Key takeaways

1. Manufacturing of radiotherapeutics requires complex supply chain management, with unique challenges across isotope production, radiolabelling, dose production and distribution.
2. As radiotherapeutics gain momentum, supply chain is increasingly front of mind for biopharma to ensure security of supply, whether through in-house supply or CDMOs.
3. CDMOs and other providers considering entry in radiotherapeutics need to understand and assess which part of the supply chain is most attractive and how they can differentiate.
4. While the supply chain is fragmented today, this is likely to consolidate as players start to expand across the value chain.

No one-size-fits-all approach

Radiopharmaceuticals are a rapidly advancing class of radioactive compounds with diagnostic and therapeutic applications. We discussed the drivers for market growth in our previous *Executive Insights*, "From Niche to Widespread Use: The Turning Point for Radiotherapeutics." In this instalment, we focus on the supply chain and how players, current and emergent, should prepare for these complexities.

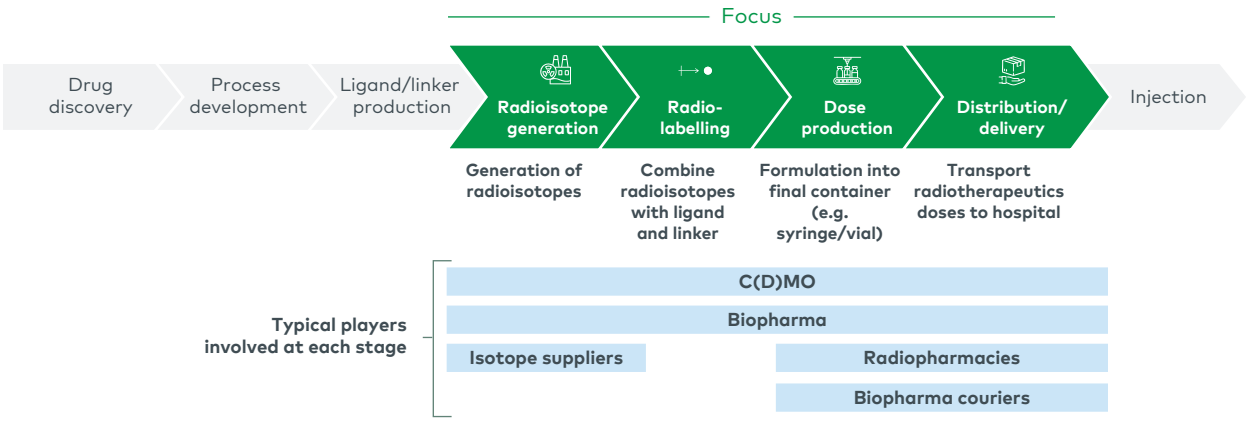
The supply chain for radiodiagnostics is relatively well established and may rely on cyclotron production of radioisotopes close to the site of administration. By contrast, radiotherapeutics manufacturing is likely to be more centralised relative to diagnostics, but it is less established and therefore likely to remain a consistent topic of discussion and focus of investment diligence. This *Executive Insights* focuses on radiotherapeutics.

Indeed, the optimal choice of radioisotope is not only dependent on clinical considerations; challenges related to supply chain, which vary depending on the radioisotope, bring with them optionality for biopharma considering in-house or outsourced manufacturing, as well as opportunities for contract development and manufacturing organisations (CDMOs) and other providers to participate and differentiate.

The radiotherapeutics value chain can be broken down into multiple steps. Here, we focus on four key manufacturing stages: radioisotope generation, radiolabelling of the radioisotope to the ligand, dose production into ready-to-administer doses and distribution/delivery. Each step involves specialised expertise and infrastructure, with different stakeholders playing critical roles (see Figure 1).

Figure 1

Radiotherapeutics value chain



Note: C(D)MO=contract (development and) manufacturing organisation
Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

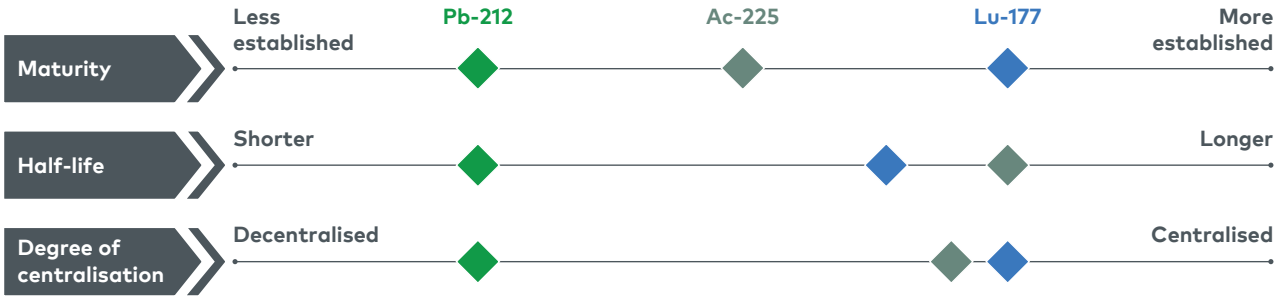
To illustrate how isotope-specific nuances impact supply chain considerations, we highlight how each step may vary for three isotopes enjoying industry interest and with varying degrees of maturity, half-life and manufacturing centralisation (see Figure 2):

- Lu-177 (half-life approximately 6.7 days), a beta-emitting isotope which has been the driver behind the radiotherapeutics resurgence through recent commercial launch successes of Novartis' Pluvicto (mCRPC, 2022) and Lutathera (GEP-NET, 2017).
- Ac-225 (half-life approximately 10 days), an alpha-emitting isotope towards which the research community had initially gravitated as the 'next wave' behind Lu-177 beta-therapies.

- Pb-212 (half-life approximately 10.6 hours), an alternative alpha-emitting isotope which has more recently been gaining development traction alongside Ac-225.

Figure 2

Comparison of key radiotherapeutic isotopes



Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

External supplier participation in radioisotope generation to de-bottleneck supply

Arguably, the step historically limiting growth of the radiotherapeutics sector is radioisotope generation. Isotopes are typically provided by isotope suppliers, even to biopharma manufacturing radiotherapeutics in-house, though integrated CDMOs can produce isotopes where production does not rely on nuclear reactor processes.

Lu-177 is typically generated through nuclear reactors, led by key commercial isotope suppliers including Shine, Nusano, ITM and NRG. The industry is transitioning to non-carrier methods, which come with fewer drawbacks. These methods use Yb-176 as starting material, historically sourced from Russia. There is a push towards alternatives that are not located in Russia, including those produced by isotope suppliers such as Shine and Nusano in the US.

To ensure consistent supply, pharma needs to coordinate with these third-party suppliers for Lu-177 generation. As Lu-177 isotope suppliers do not typically handle subsequent radiolabelling and final dose formulation, this creates an opportunity for CDMOs to offer such services by partnering with isotope producers.

Ac-225's complex raw material sourcing relates to limitations of its potential production methods. Ac-225 production through separation from Th-229 comes with scalability limitations due to supply scarcity. Cyclotron production using Ra-226 requires stringent handling procedures due to safety concerns around exposure to both Ac-225 and Ra-226. Methods like Th-232 spallation require high-energy accelerators and create side reactions.

Production complexity creates opportunities for both Ac-225 isotope suppliers and CDMOs to compete and increase integration along the value chain. Some isotope suppliers (e.g. NorthStar, SpectronRx, Eckert & Ziegler) are exploring alternative scalable options such as electron accelerator photonuclear transmutation of Ra-226. These players also provide subsequent radiolabelling services, acting as CDMOs.

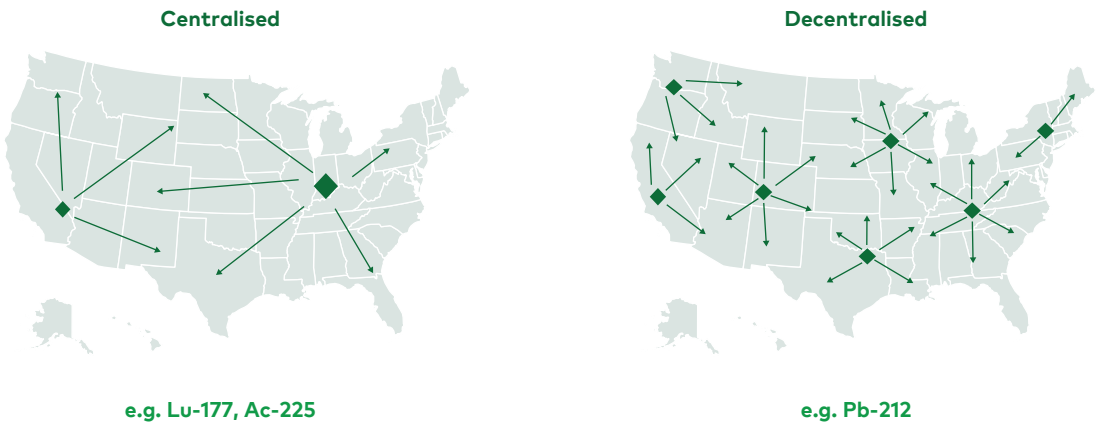
Pb-212 faces fewer supply constraints on its raw materials Th-228 and Ra-224, but it comes with a shorter half-life (approximately 10.6 hours), requiring production in decentralised generators close to the patient. To solve for this, some biotechs have chosen to become more involved in radioisotope generation.

Indeed, select companies developing Pb-212-based assets — such as ArtBio, AdvanCell, Perspective Therapeutics and Orano Med — have developed their own Pb-212 generator production capabilities. Orano Med, together with RadioMedix, have recently signed an agreement with Sanofi as part of a licensing agreement to assume manufacturing responsibility, suggesting that biopharma companies with Pb-212 generator production expertise can also act as contract manufacturers in this area.

Depending on the commercial success of Pb-212, opportunity may exist for CDMOs to position themselves as regional Pb-212 bases in a hub-and-spoke setup with large generators to be installed on-site at the CDMO, reducing the need for complex shipping logistics (see Figure 3).

Figure 3

Centralised vs decentralised manufacturing



Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

Radiolabelling at the core of CDMO offerings

Subsequent radiolabelling connects the radioisotope to the targeting ligand via chelation. For Lu-117 and Ac-225, radiolabelling can be performed in centralised facilities owing to their relatively long half-lives. The specific conditions vary based on chelator and isotope, but labelling may require high temperature and pressure requirements alongside radioactive compound handling precautions.

Whilst biopharma may want to consider in-house labelling for supply security and quality control, CDMOs can play a key role to avoid costly investment as well as complexity in infrastructure (e.g. shielded laboratories, handling systems such as hot cells, glove boxes) and procedures for biopharma. CDMOs can also bring substantial expertise in chelation and ultimate linking of targeting compound and radioisotope that are difficult to establish for new entrants (see Figure 4). Example CDMOs currently in the field include SpectronRx and NorthStar.

Pb-212's shorter half-life necessitates local radiolabelling and therefore a more widespread geographical footprint. CDMOs can play a key role in accommodating local needs for radiolabelling due to the isotope's shorter half-life.

More broadly, radioactive decay drives the need for radiopharma CDMOs to more frequently produce (smaller) batches throughout the year in contrast to the potential for larger, more infrequent batch sizes for other therapeutic modalities. The more continuous nature of production drives higher utilisation rates, which could lead to different operations and levels of profitability when compared to other therapeutic-modality CDMOs.

Extending CDMO capabilities into dose formulation and logistics

Following radiolabelling, the compound is formulated into ready-to-administer syringes or vials. This stage is specialised, as the therapeutic dose needs to be accurately measured to maximise efficacy while minimising toxicity. Dosing is complicated by the radioactive decay of isotopes, which must be accounted for in the production process to ensure that patients receive the intended radiation dose.

CDMOs can oversee this process for companies without in-house capabilities. Radiopharmacies are another player that can perform this step, though some facilities operate as both a CDMO and a radiopharmacy.

Distribution and delivery represent the final step prior to patient administration. Due to radioisotope decay, this process must be carefully managed. Shipping requires compliance with strict (inter)national regulations, and specialised packaging is essential to ensure safety during transport. Depending on the isotope and capabilities of the players in the value chain, there could be anywhere between one and three players exchanging

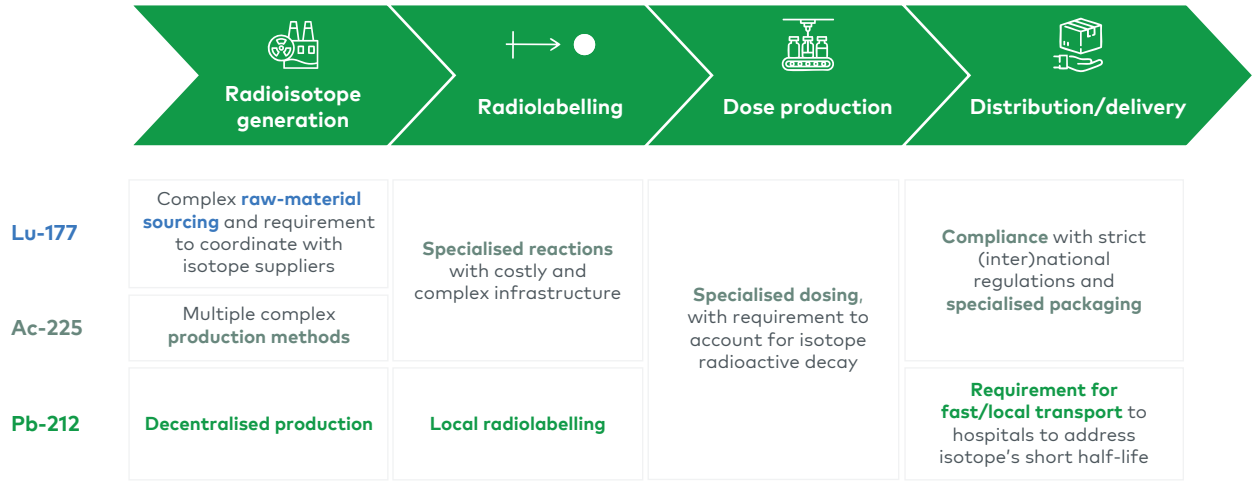
radioactive intermediates or final dose product prior to final delivery for patient administration.

The short half-life of the radioisotope is a key parameter to consider for logistics and reinforces the importance of integrated providers, as evidenced by Orano Med's specialised logistics for Pb-212. In North America, for example, Orano Med's ATLab, leveraged for large-scale production, is strategically located in Indiana next to major national and international distribution hubs and delivery companies (e.g. FedEx) to ensure fast transport to hospitals and address the 10.6-hour half-life of the isotope.

Challenges in this step may result in potential for more biopharma courier services to expand their offering into radiotherapeutics and leverage the optimisation and speed of their logistics. Companies such as Life Couriers provide logistics services for radiopharmaceuticals and may also cover other sensitive biopharma products, such as live cells, as adjacent services. Once the radioisotope is received, hospitals and treatment centres play a critical role in final correct handling, storage and patient administration.

Figure 4

Summary of value-chain complexities



Source: L.E.K. research and analysis

Implications for radiopharmaceutical supply chain participants

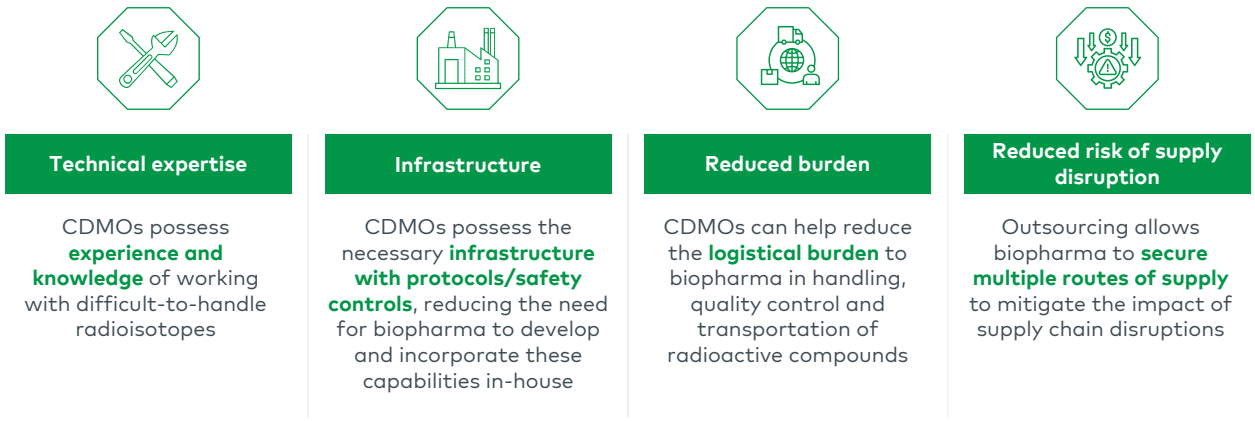
As radiotherapeutics move from niche to widespread use, an increasing number and range of players can participate in the supply chain. Some early-stage radiopharma biotechs have built manufacturing capabilities, pioneering new processes.

As the field of radiotherapeutics matures, CDMOs and other providers can play an increasingly important role; they can offer biopharma their expertise, infrastructure, logistical control and supply-risk mitigation (see Figure 5). This could be through offering

radiolabelling capabilities, or infrastructure and expertise to accommodate high-temperature/pressure chelation processes, whilst adhering to stringent requirements for radiation safety, regulatory compliance and isotope handling.

Figure 5

Value proposition of CDMOs in radiotherapeutics manufacturing



Note: CDMO=contract development and manufacturing organisation
Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

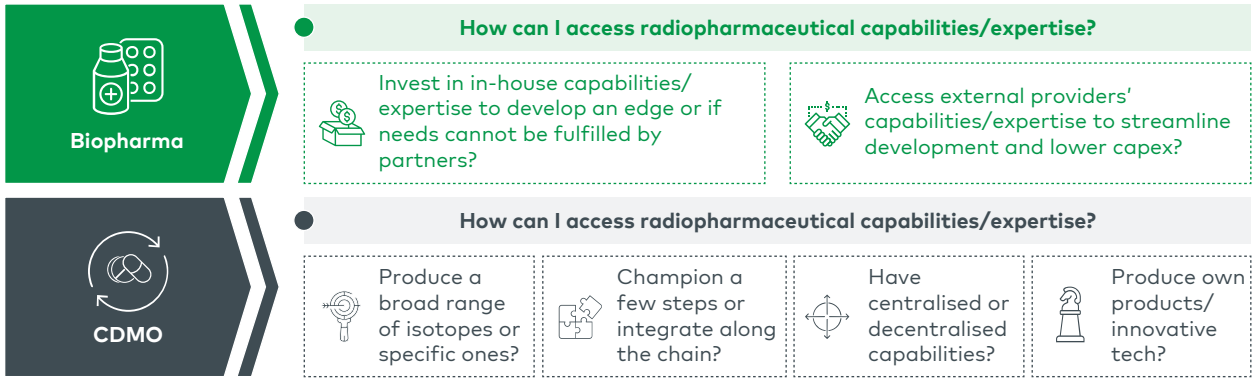
In the growing radiotherapeutics market, the supply chain is a significant complexity that companies should aim to carefully address. Biopharma exploring radiotherapeutics need to decide between investing in developing in-house capabilities and expertise or partnering with external providers to leverage their infrastructure and expertise to lower capital expenditure and focus on their own core competencies of drug discovery and development.

External providers — including CDMOs, isotope suppliers and biopharma couriers — can simplify this complex value chain, but they will need to carefully think through how they can differentiate and evolve to ensure they maintain a unique position in this fluid ecosystem where processes and technologies are not yet fully set (see Figure 6).

Over time, we anticipate that some providers will extend their offering along the value chain as consolidation takes place and as investment allows them to target adjacent areas.

Figure 6

Key radiotherapeutics chain considerations for biopharma and CDMOs



Note: CDMO=contract development and manufacturing organisation
Source: L.E.K. research and analysis

How L.E.K. can help

As radiotherapeutics grow, securing a reliable supply chain is key. Whether you're a biopharma company or a CDMO, L.E.K. can help you identify opportunities, mitigate risks and build a strategy for success.

Get in touch today to find out how to stay ahead in this evolving market.

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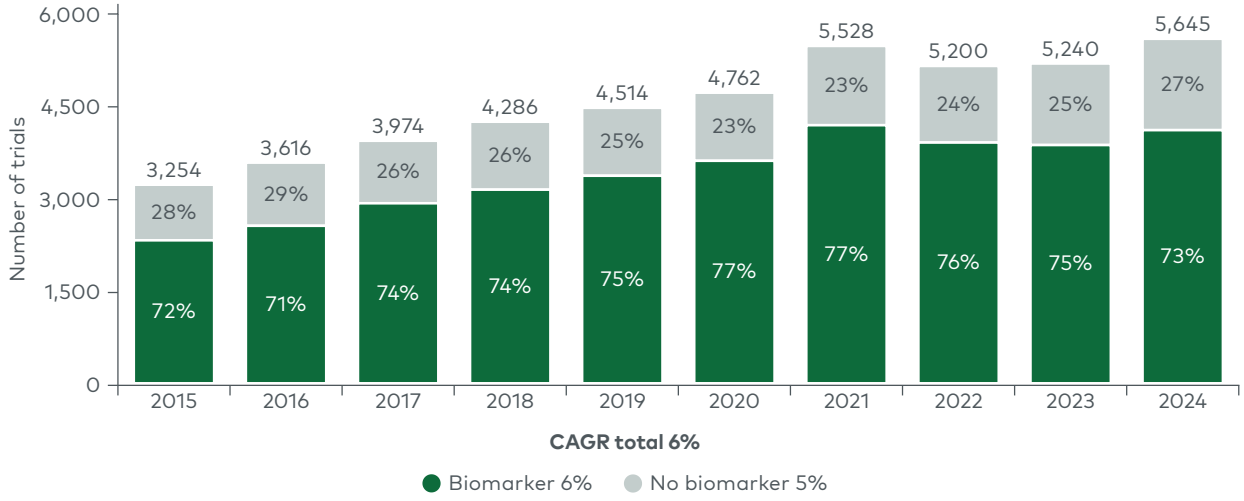
EXECUTIVE INSIGHTS

Launching Novel CDx for Oncology: 7 Strategies for Biopharma Companies

Early genetic screening, targeted therapies and other precision medicine (PM) offerings in recent years have transformed care and significantly improved outcomes for oncology patients while delivering substantial value creation that drives increased pharma investment. PM leverages biomarker (BM) strategies to successfully develop, commercialize and differentiate therapeutics by improving R&D efficiency and optionality, supporting regulatory filings, and enabling smaller and more productive clinical trials. To achieve commercial success for an oncology PM therapeutic, however, biopharma companies must also accomplish the effective launch of a companion diagnostic (CDx) that identifies eligible patients and informs ongoing treatment decisions.

Over the past decade, the proportion of oncology trials using BMs has steadily tracked overall trial growth except for a slight post-pandemic decline amid tough U.S. and Chinese macroeconomic conditions. In 2024, three-fourths of all oncology clinical trials included the use of a BM (see Figure 1).

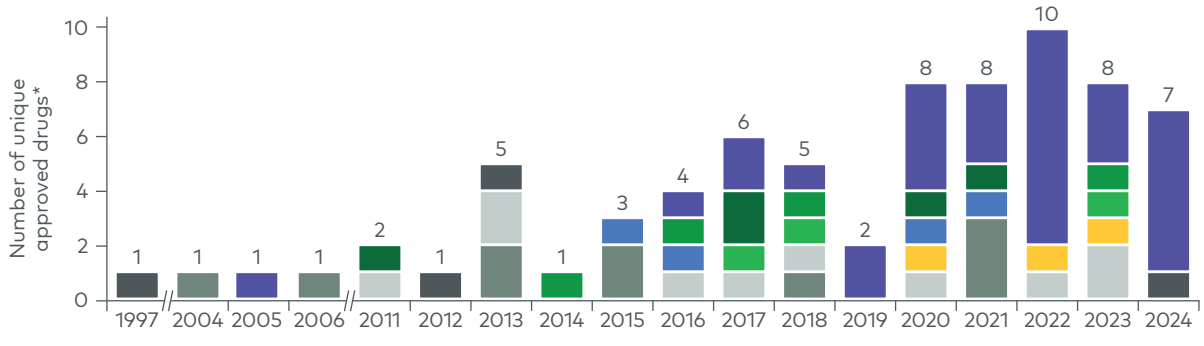
Figure 1
Biomarker use in oncology trials, by year (2015-24)



Note: CAGR=compound annual growth rate
Source: TrialTrove; L.E.K. research and analysis

Rising BM use in trials has predictably had an impact on product launches, with the U.S. Food and Drug Administration (FDA) approving seven to 10 oncology therapeutics with CDx annually since 2020 — and with an increasing focus on novel biomarkers rather than traditional ones (see Figure 2).

Figure 2
FDA-approved therapeutics with CDx, including novel oncological therapies (1997-2024)



	1997	2004	2005	2006	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Cumulative therapies	1	2	3	4	6	7	12	13	16	20	26	31	33	41	49	59	67	74
Cumulative indications**	1	2	3	4	7	8	14	15	20	26	32	42	49	69	82	100	116	132

*Count of unique companion diagnostic-therapy combination approvals
**Indication refers to broad cancer type and sample type (e.g., breast cancer or non-small cell lung cancer) rather than particular label indication, which may include factors such as age, line of therapy, other mutations or other patient/cancer characteristics
***Includes the following types of mutations or mutations in the following genes/gene classes: BCR-ABL, C-kit, dMMR, ESR1, EZH2, FGFR2, FGFR3, FOLR1, HLA, IDH1, IDH2, Ki-67, KRAS, MET, NTRK, PDGFRA, PI3KCA, ROS1, TP53
Note: FDA=Food & Drug Administration
Source: FDA list of approved companion diagnostic devices (accessed February 2025); L.E.K. research and analysis

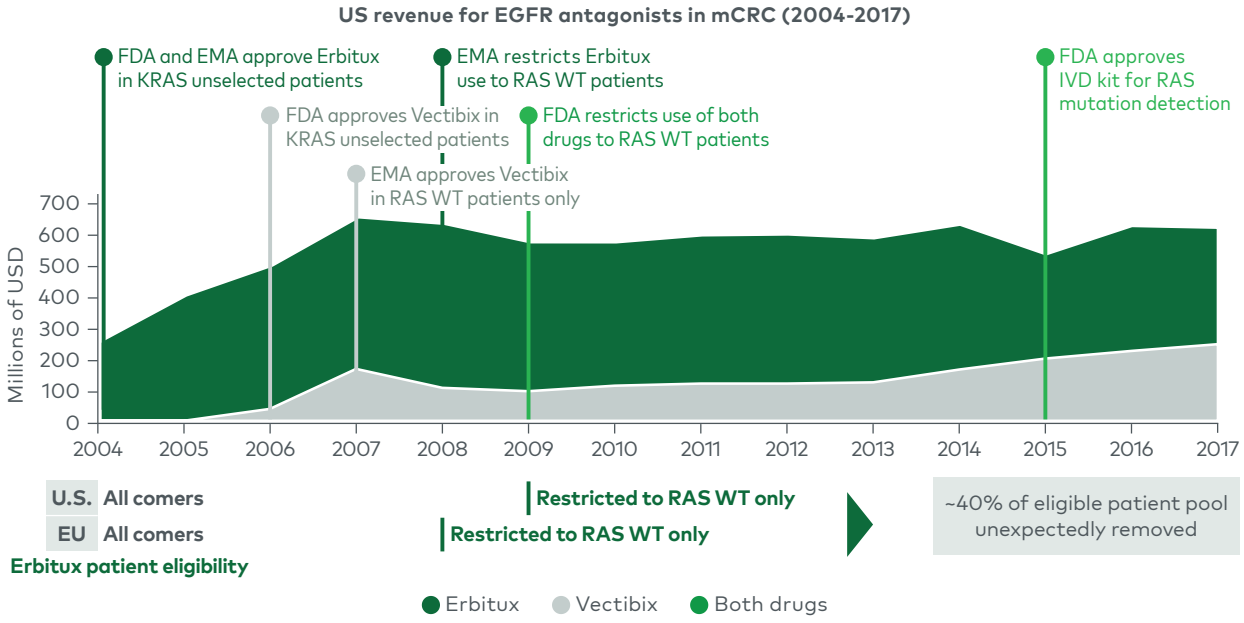
Given the advantages of launching a diagnostic (Dx) — and the many complexities involved — preparing to launch novel CDx in concert with the therapy itself is imperative. In working with biopharma companies to launch novel CDx for oncology therapeutics, L.E.K. Consulting has uncovered seven critical strategies to share.

1. Adopt an 'opt out' mentality.

Leaders in PM follow an opt-out approach: All new oncology programs start with a Dx component, consistently assessing needs and planning for them across the development life cycle. This mindset leads PM leaders to integrate Dx and therapeutic development through established Dx resources and capabilities. All-comers therapeutics can still be pursued, but this requires an active decision by leadership supported by clinical evidence.

The alternative "opt in" mindset — the assumption that an all-comers approach will work and BM development will follow — limits a company's ability to build Dx capabilities and processes, and disadvantages PM programs that require early and frequent collaboration between Dx and therapeutic teams. For example, in 2009 (after five years on the market), the FDA restricted Lilly's EGFR inhibitor Erbitux to KRAS wild-type patients (who comprise approximately 60% of colorectal cancers) based on data from a competitor's product. U.S. market adoption stagnated after the decision, and the cumulative revenue impact over the next decade reached hundreds of millions of dollars (see Figure 3).

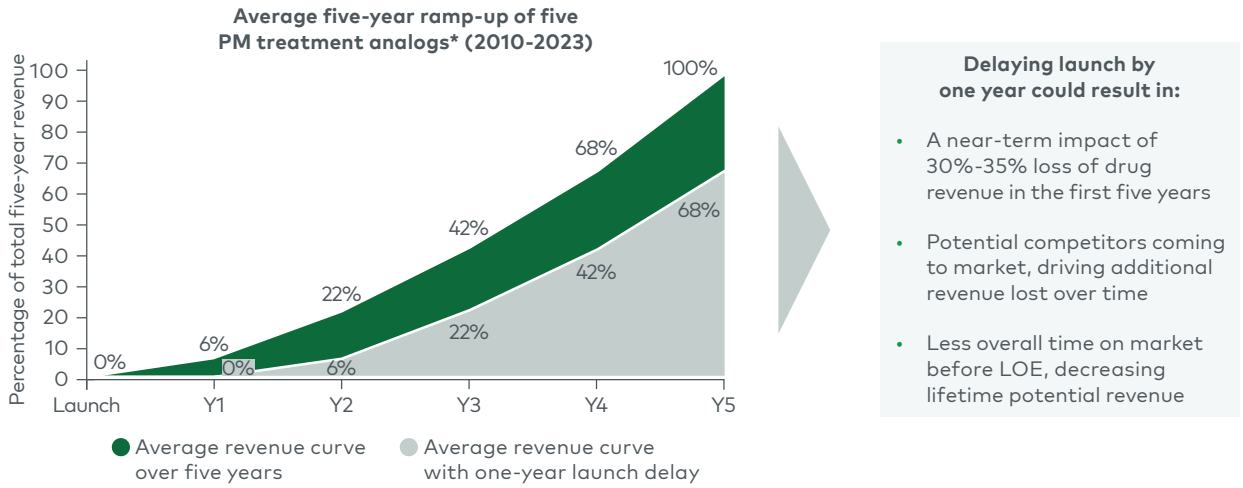
Figure 3
Case study: Erbitux in mCRC



Note: mCRC=metastatic colorectal cancer; FDA=Food & Drug Administration; EMA=European Medicines Agency; IVD=in vitro diagnostic
Source: Evaluate Pharma; FDA list of approved companion diagnostic devices; L.E.K. research and analysis

Indeed, historical averages suggest a one-year delay in launching a BM-directed drug could reduce the initial five-year cumulative revenues by 30%-35%, owing to the typical adoption ramp curve (Figure 4).

Figure 4
Revenue loss from launch delays in PM technology



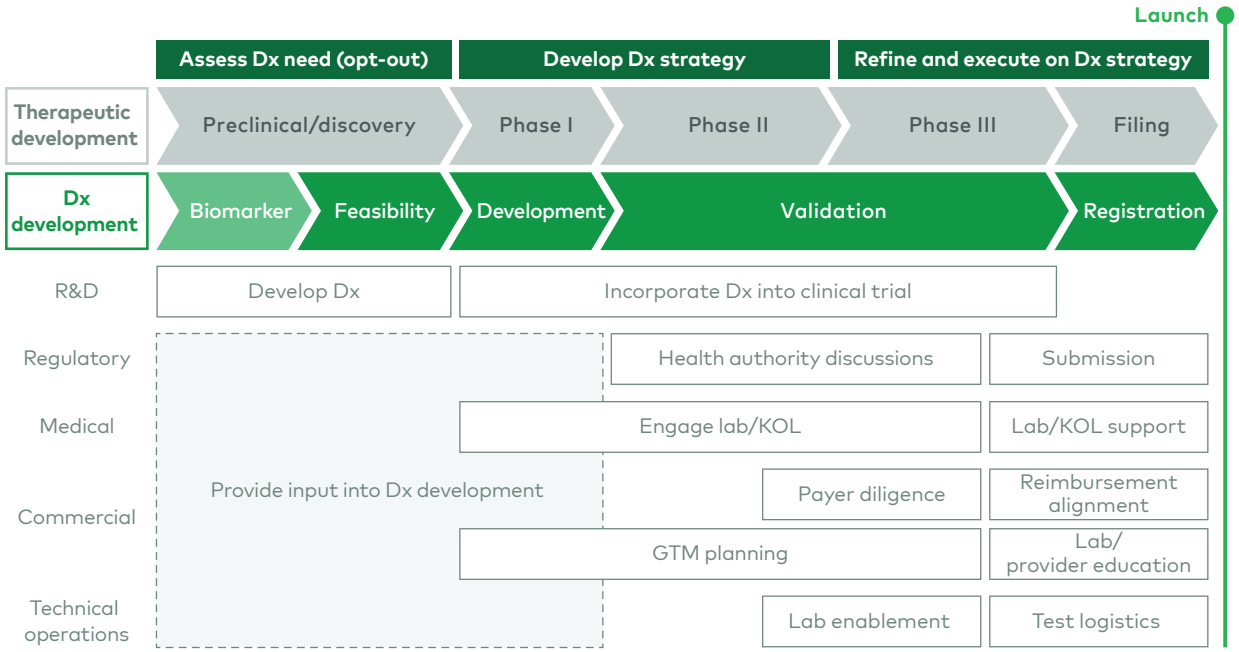
*Includes Lynparza (2015-20), Rydapt (2017-22), Vitrakvi (2020-25F), Xalkori (2011-16), Zelboraf (2011-16)
Note: PM=precision medicine; LOE=loss of exclusivity
Source: L.E.K. interviews, research and analysis; Evaluate Pharma

Dx leaders codify the opt-out mentality in their processes, requiring teams to consider Dx needs early and to continually reassess those needs throughout development — whether by adopting a proactive approach to BM discovery through comprehensive patient profiling, banking multiple bio samples and so forth; focusing on post hoc analysis to identify predictors of response; or continually optimizing by, for example, tracking molecular origins of resistance. Furthermore, they tend to organize personnel in ways that encourage dedicated focus on individual programs while maintaining centralized leadership and integrating functions and programs at the therapeutic area and enterprise levels. Embedding strategic Dx planning throughout the program drives preemptive discussion and collaboration and ensures organizationwide sharing of lessons and resources, thus increasing efficiency and institutional knowledge.

2. Start planning for CDx launch in preclinical development.

A successful Dx launch requires multifunctional support across the value chain, and companies should start planning as early as the preclinical stage. Dx development occurs parallel to therapeutic development, with key Dx launch readiness activities stage-gated by both therapeutic and Dx milestones (see Figure 5).

Figure 5
Key Dx activities by function throughout the value chain



Note: Dx=diagnostic; KOL=key opinion leader; GTM=go-to-market
Source: L.E.K. research and analysis

To drive efficiencies, R&D must incorporate cross-functional input from commercial and medical functions during preclinical development. This approach ensures that Dx addresses patient needs and that clinical endpoints support its commercialization. Commercial and medical readiness activities should focus on understanding and educating the market, developing a Dx-specific strategy and preparing the organization for Dx launch.

3. Address the unique operational challenges of adding CDx.

Companies must consider how the specific complexities of a Dx test should inform the commercial and go-to-market strategy. During development, an individual Dx faces specific commercial obstacles that differ from challenges with therapeutics — surrounding the analyte, such as protein or DNA; the testing technology, e.g., PCR or NGS; validated instrumentation such as 510(k) clearance; and the testing format, whether an in vitro diagnostic (IVD) or a laboratory-developed test (LDT) (see Figure 6). Pharma companies looking to develop a therapeutic with CDx should first understand the BM requirements for their indication. Next steps include determining whether they can support a decentralized testing model and building a robust payer strategy.

Figure 6
Considerations for Dx approach

Dx technology		
Immunohistochemistry	**PCR**	**NGS**
• Test for single protein marker/receptor • Lowest cost and fastest turnaround • Less-straightforward interpretation	• Targeted test for one to four or more genes • Medium cost and moderate turnaround • Binary result with minimal interpretation	• Broad test for 10+ genes • High cost and lengthy turnaround • Binary result with minimal interpretation

Test modality		
	In vitro diagnostic kit	**Laboratory-developed test**
Test content	**Lower complexity** Typically single analyte	**Higher complexity** Typically complex, multi-analyte
Flexibility	**Locked in** Assay is designed, developed and regulated "as is"	**Evolutionary** Can evolve as needed
Location	**Decentralized** Can be run on IVD-cleared instruments in any CLIA lab	**Centralized, single site** Site-specific assays that require extensive validation to set up
Regulatory	**FDA-regulated/CE marked (EU)** Highly regulated content/devices	**FDA (+ CE mark, until recently) not required** May operate without regulatory clearance in U.S.
Access	**Higher rate of successful reimbursement** Often inherently better trusted to provide reliable results	**Lower rates of successful reimbursement** Reimbursement may depend on the reputation of the lab

Note: Dx=diagnostic; PCR=polymerase chain reaction; NGS=next-generation sequencing; IVD=in vitro diagnostic; CLIA=Clinical Laboratory Improvement Amendments; FDA=Food & Drug Administration; EU=European Union
Source: L.E.K. research and analysis

For example, LDTs may face reimbursement issues and require extensive lab validation, yet in the U.S. they often are faster to market and support more numerous and complex BMs because regulatory clearance is not required. Alternatively, IVD kits are FDA regulated, do not support all analytes and face greater competition from other diagnostics, but any CLIA laboratory with the correct instrumentation can run them — and typically enjoy a higher rate of reimbursement. For some companies, launching and supporting, for example, both LDT and IVD versions of the same Dx adds further complexity and requires additional readiness planning and resources.

4. Build a separate Dx launch strategy.

PM leaders treat Dx launch and therapeutic launch as interconnected yet distinct processes, with different stakeholders and challenges. Because key CDx stakeholders are a diverse group that shares little overlap with therapeutics stakeholders — think pathologists versus prescribing oncologists — targeted outreach is the best way to build awareness and willingness to prescribe. Given the intricacy involved in effective testing (particularly with novel CDx), a launch strategy needs to address the necessary instrumentation or other technology; consider laboratory needs, such as LDT support and sample prep guidance; and take market access into account.

Ideally, companies should consider the interplay between Dx and therapeutic launch strategies when planning for launch. For instance, typical sales incentive structures based on the number of patients on a therapy may be unsuitable in a PM setting, where the number of patients screened for a therapy is potentially a more meaningful measure. Developing a Dx-specific launch strategy can enable widespread adoption and enhance the overall PM opportunity.

5. Leverage partner capabilities purposefully while developing internal expertise.

When empowering critical partners (internal and external) for their expertise in developing, filing and manufacturing Dx tests, biopharma companies should be intentional about expanding specific activities and achieving sufficient oversight. Depending on the organization's size and capabilities, tasks such as BM selection, test development, study result interpretation or Dx sales may be beyond internal capacity. On the other hand, activities that require close interaction with the therapeutic team (e.g., sample collection and banking) or that are strategic in nature (e.g., market access) may be better managed in-house.

Even when leveraging a partner, launching a Dx requires dedicated internal resources with Dx-specific expertise across the value chain. Specialists who understand both Dx and PM therapeutics are rare and in high demand, requiring early planning and strong retention efforts. Finding the right balance between external expertise and internal foundational knowledge will be crucial to overseeing Dx partners, who may lack the broader in-house context or may not be incentivized to optimize tests or fully invest in launch activities (see Figure 7).

Figure 7
Key development activities ownership: Dx partner vs. pharmacy team

Dx launch

Dx development	Biomarker discovery	Biomarker feasibility	Biomarker development	Clinical validation	Filing	Commercial-ization

Activities owned or co-owned by Dx partner or pharma	Dx partner vetting and selection	Determination of detection method	Test development	Stakeholder training/education and test marketing	Filing for regulatory approval
Expected role of Dx partner	• Engage with pharma and provide relevant information	• Determine detection method for use in Dx test	• Develop pilot assay and validate assay in clinical studies	• Support IVD kit field sales and stakeholder training/education	• File for Dx regulatory approval according to strategy set by pharma
Expected role of pharma Dx team	• Engage Dx partner and gather relevant input from functions	• Determine detection method for use in Dx test/coordinate supply chain	• Define strategy and manage sample collection, banking and analysis	• Drive stakeholder awareness and manage marketing for LDT	• Drive global regulatory filing strategy and ensure alignment with Dx partner
Expected role of pharma Tx team	• Provide input on Dx partner selection process	• No role	• Run clinical trials	• Tx sales represen-tatives to share basic Dx test information during detailing of oncologists • Tx MSLs to address basic Dx questions if pathologists/on-cologists contact pharma	• In market, Tx FTEs to support local filing as needed

Note: Dx=diagnostic; IVD=in vitro diagnostic; LDT=laboratory-developed test; Tx=treatment; MSL=medical science liaison; FTE=full-time equivalent
Source: L.E.K. research and analysis

Scaling a Dx ecosystem appropriately can prevent delays in Dx launch planning and execution. Overall, costs incurred when empowering an external partner or developing in-house talent should be viewed as imperative for product success — a strategic investment into that asset franchise rather than just a necessary evil to be minimized.

6. Infuse dedicated Dx expertise throughout the organization.

Successful Dx launch planning requires an environment where Dx needs are supported, integrated across functions, scaled appropriately and prioritized across the value chain. Essential strategies such as adopting an opt-out Dx mindset and investing in early Dx development and launch planning (as discussed earlier) can be up against an inertial mindset around an all-comers approach. Overcoming pushback from various levels of the company and other headwinds — such as the high costs associated with Dx development and the relatively low direct revenue from Dx versus therapeutic investment — will require unequivocal and sustained support from leadership. In prioritizing Dx investment, savvy PM leaders must also

expedite alignment of activities and incentives across Dx and therapeutic teams to generate the cross-functional collaboration needed for a successful launch.

7. Incorporate a thoughtful LCM strategy.

To become leaders in the PM space, companies must adopt a dedicated life cycle management (LCM) strategy that supports continuous evolution and improvement. Early and proactive planning is crucial for a biopharma company's ability to create sustained impact of BM oncology therapies, but Dx strategy does not end at launch. A meaningful LCM strategy will empower the organization to anticipate next-generation technologies, expanding indications, real-world evidence planning and continuous engagement with key stakeholders — all of which advances the ultimate goal of maximizing therapeutic potential.

L.E.K. continuously monitors pressing issues throughout the biopharma industry landscape in order to deliver innovative lessons, cutting-edge insights and actionable support and strategies that enhance our clients' ability to achieve their goals.

For more information, or to explore strategies that can unlock new possibilities for your biopharma business, please contact us.

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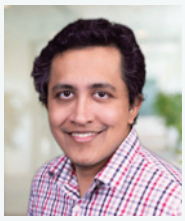

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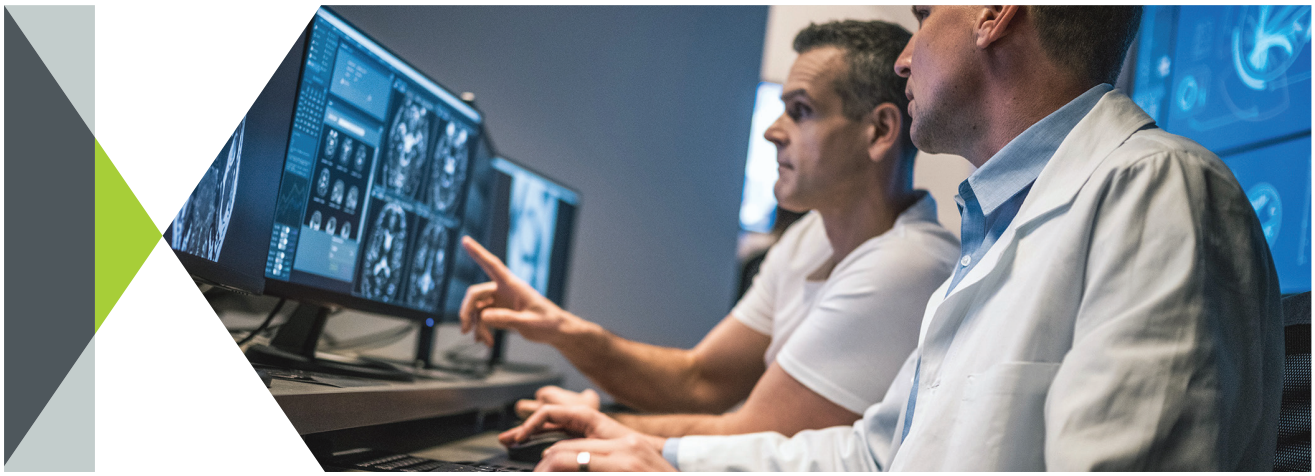


EXECUTIVE INSIGHTS

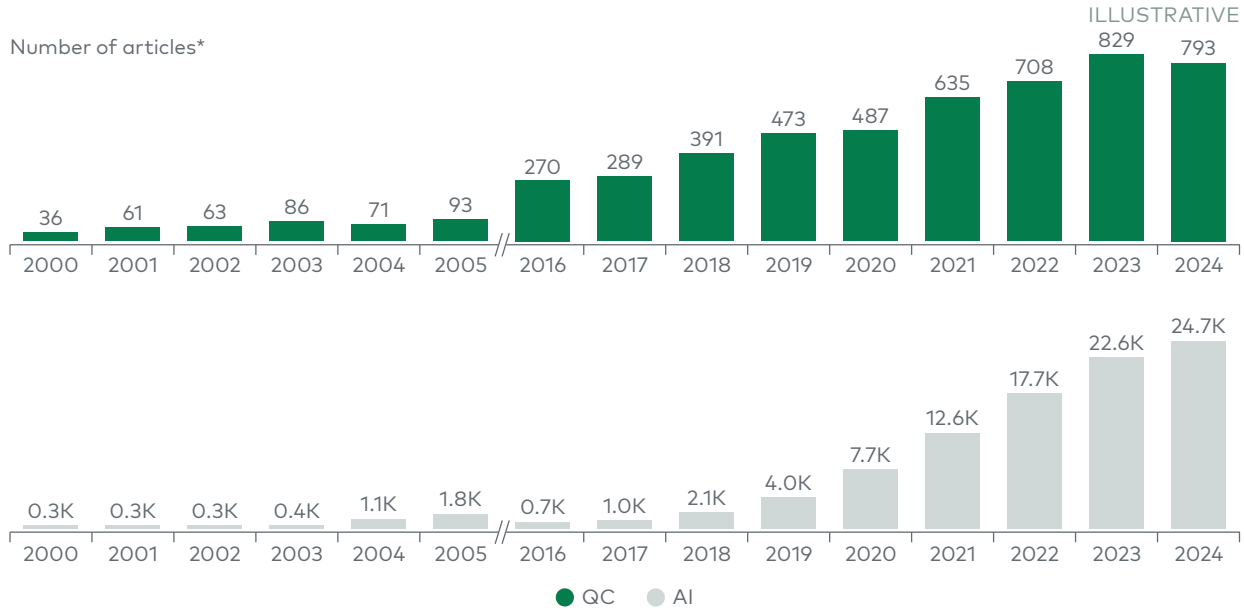
Quantum Computing in Biopharma: Future Prospects and Strategic Insights

Quantum computing — what can it do for biopharma?

Rising clinical thresholds, the growing need for complex drug modalities and extended development timelines are making novel molecular entities (NMEs) increasingly difficult to develop. The annual R&D spend per NME, from discovery to launch, is estimated at $1.5 billion-$3.5 billion,[1] with annual R&D spend across the top 15 pharmaceutical companies (PharmaCos) growing roughly one and a half times since 2010 and projected to reach up to $18 billion by 2030.[2] Compounding this challenge, biopharma faces mounting pressure to accelerate innovation due to compressed product life cycles under the Inflation Reduction Act, and more than $200 billion in biopharma revenue is potentially at risk from loss of exclusivity by 2030.[3]

Could technological advances in artificial intelligence (AI) or quantum computing (QC) help address biopharma's throughput and spending challenges? AI has seen explosive growth in the past five years, and QC is following suit, as evidenced by increasing publication trends (see Figure 1). QC leverages principles from quantum mechanics to process information exponentially faster than classical computing. The potential for QC and AI to revolutionize the biopharma industry together by offering unprecedented computational power and problem-solving capabilities is enormous.

Figure 1
PubMed mentions of QC and AI (October 2000-2024)



*Includes search terms "quantum computation," "quantum computational," "quantum computer," "quantum computers" or "quantum computing" anywhere in the article
Note: QC=quantum computing; AI=artificial intelligence
Source: PubMed; L.E.K. research and analysis

To date, AI has seen significantly more investment due to its relative maturity, accessibility and market readiness. However, AI's gain is not QC's loss. QC and AI are complementary. QC can enable faster training of and inference from AI systems and brings an ability to process data in ways classical computers cannot. Through this it can unlock computational possibilities that are currently unobtainable.

Investment in QC has grown globally. Cumulative investment in the QC market is fueled by both the public and private sectors, totaling around $8 billion in the U.S., approximately $15 billion in China and about $14.3 billion across the U.K., France and Germany through 2024.[4] While private investments in quantum technology have declined from COVID-19 highs due to tightening funding environments and higher interest rates ($2.3 billion worldwide private investment in 2022 versus around $1.3 billion in 2023),[5] quantum intellectual property (IP) development over the past 10 years has increased significantly.

Beyond growth in investment and IP development, the capacity of quantum computers via qubits — the fundamental units of quantum information — has expanded dramatically. IBM progressed from a 5-qubit processor in 2016 to a 433-qubit processor in 2022, with plans to achieve more than 1,000 qubits in 2025.[6] This advancement extends across the industry, with

companies such as Google, IonQ and QuEra also demonstrating remarkable improvements in qubit capacity.[7]

What is quantum computing?

Quantum computing (QC) harnesses the principles of quantum mechanics to solve complex calculations beyond the capabilities of classical computers, representing a branch within the broader field of quantum science.

QC compared to quantum science and quantum mechanics

QC applies principles from quantum mechanics to process information in fundamentally new ways, enabling exponentially faster problem-solving for certain tasks compared to classical computers. It is an interdisciplinary field within quantum science, which broadly studies quantum phenomena across physics, chemistry and engineering.

Quantum interference

A fundamental principle that enables QC to be successful is quantum interference, which emerges due to the wavelike nature of quantum particles. By combining the probability amplitudes of these waves to create patterns, quantum computers can process information uniquely.

Key aspects of quantum interference include:

- Computational parallelism: Enables simultaneous evaluation of multiple solutions, making certain problems tractable
- Precision enhancement: Amplifies correct solutions while suppressing errors, improving quantum sensing accuracy
- Coherent control: Facilitates precise manipulation of quantum states for advanced quantum logic and circuits

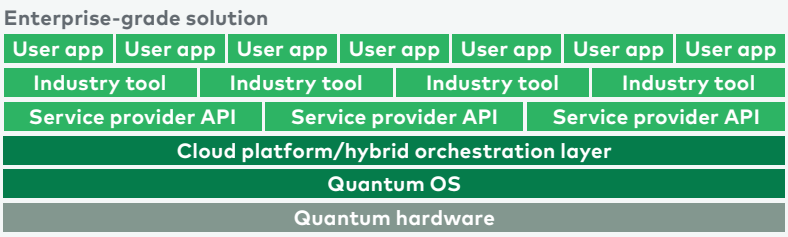
Quantum interference underpins quantum advantage across computing, communication and sensing, offering new insights into information processing.

Quantum stack

Integrating quantum interference into quantum networking requires a structured quantum stack, which defines the hardware and software layers essential for scalable QC.

(continued)

Quantum stack overview



- Production grade is **reliable**, **flexible** and **secure**
- Integrates **seamlessly** with customer's production workflow
- **Rapid** customer development and deployment

Note: API=application programming interface; OS=operating system
Source: L.E.K. research and analysis

Quantum networking

Quantum networking connects quantum computers using quantum mechanics to surpass classical communication. By transmitting quantum states instead of binary data, these networks enable secure, high-performance distributed computing.

Potential benefits to biopharma from quantum networking include:

- Secure transmission of clinical trial data/real-world data
- Interoperability across pharma entities for collaboration

Pioneering QC applications in drug discovery and clinical trials

QC has the potential to revolutionize the biopharma value chain by overcoming classical computing's limitations in handling complex datasets and simulations (see Figure 2). The most impactful areas are expected to be in drug discovery and research. QC directly addresses the inherent limitations of classical computing in computer-aided drug design because molecules operate by quantum rules — their behavior fundamentally involves dealing with exponentially large-state spaces, which classical systems can only approximate at great computational cost. Quantum-enhanced generative models can also explore vast chemical spaces faster than classical techniques can, leading to the discovery of more novel drug candidates previously inaccessible for many years with classical computing, reducing R&D timelines, lowering costs and improving success rates.

In clinical design and operations, QC can enhance patient stratification and trial optimization by analyzing complex genomic, biomarker and real-world patient data. Quantum machine learning can identify optimal patient subgroups for personalized medicine, reducing trial failures and improving efficacy predictions. Quantum optimization can also refine trial site selection and adaptive trial designs, increasing efficiency and reducing costs.

Beyond R&D, QC can drive efficiencies across other areas of the value chain. QC can help optimize manufacturing and supply chain processes, improve predictive analytics for commercial functions, and increase efficiency of operations to improve sustainability.

While still evolving, QC's ability to tackle biopharma's most computationally challenging problems could lead to groundbreaking efficiencies and transformative advancements.

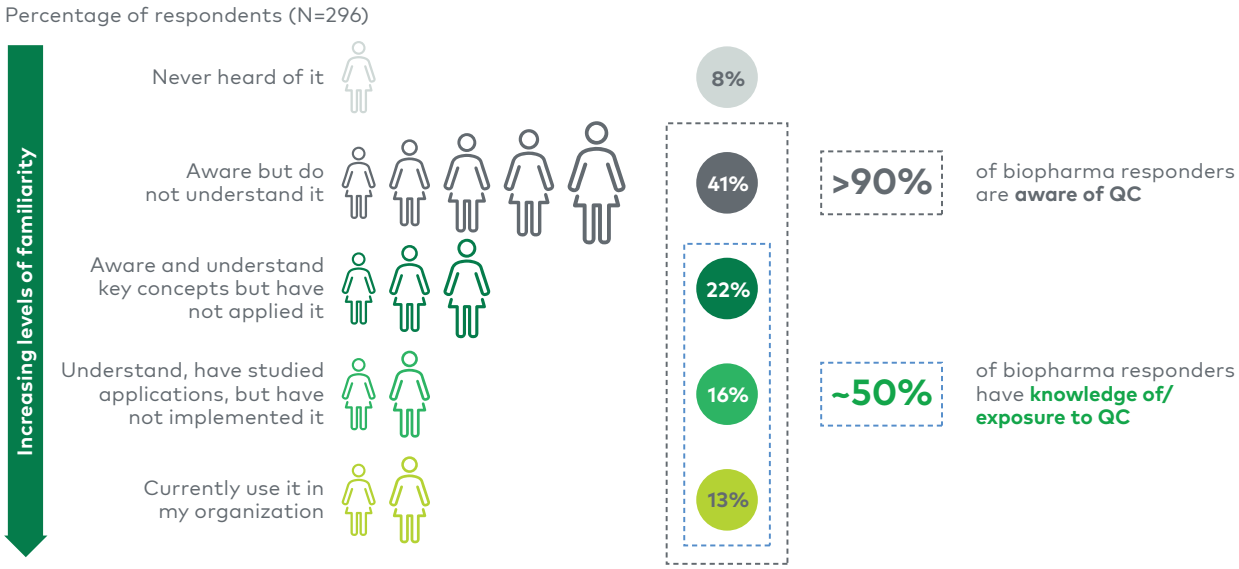
Figure 2
Six areas of biopharma capabilities for quantum technology use cases

Note: ADME=absorption, distribution, metabolism and excretion; DMPK=drug metabolism and pharmacokinetics; LCM=life cycle management
Source: L.E.K. research and analysis

Emerging interest is driving QC into a pre-utility phase in biopharma

With these high-value QC use cases, it is not a surprise that an L.E.K. Consulting survey of roughly 300 U.S. and EU biopharma stakeholders indicated that over 90% of them are aware of QC and its potential. Additionally, about 50% of respondents, representing 110 unique biopharma companies, stated they understand key concepts and have had exposure to QC or have experience studying its applications (see Figure 3).

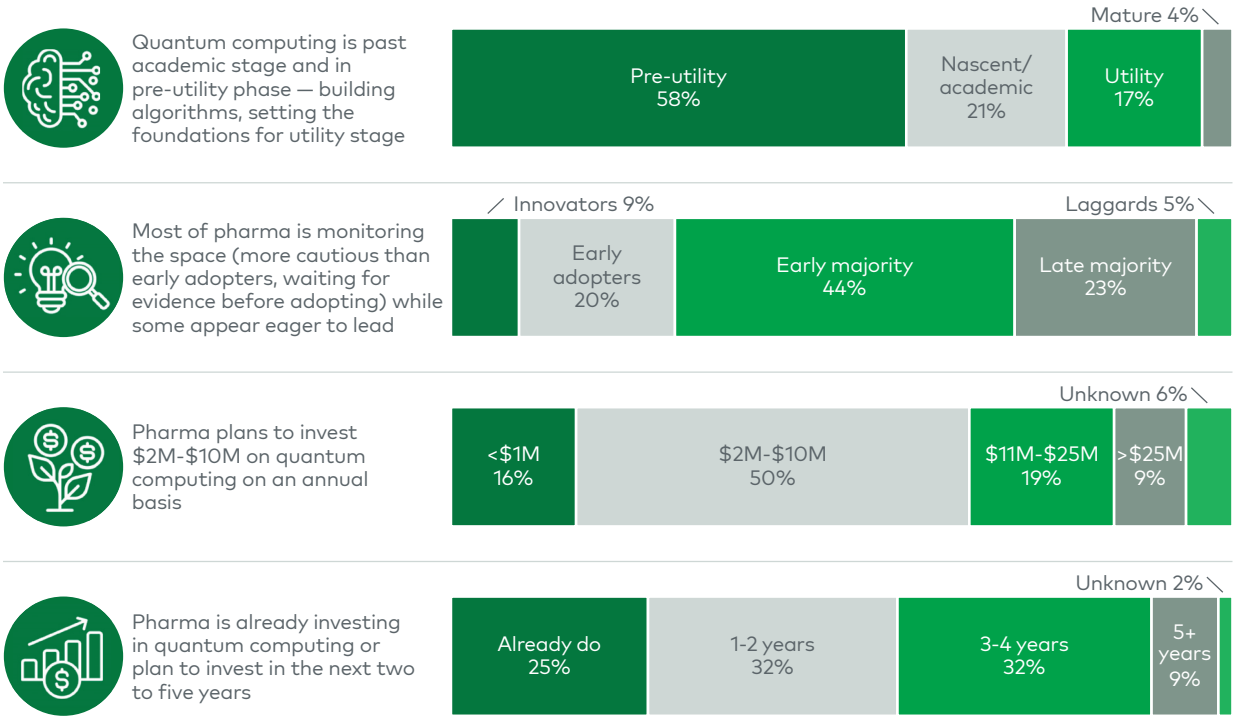
Figure 3
Biopharma familiarity with QC



Note: QC=quantum computing
Source: L.E.K. survey of U.S. and EU biopharma stakeholders across R&D, commercial, manufacturing, medical and business development functions (L.E.K. biopharma quantum survey)

Biopharma participants suggest that QC is making significant early strides, transitioning from academic research to a specialist, pre-utility phase.[8] In this phase, there is a focus on developing practical algorithms and applications to lay groundwork to drive commercial value. Approximately 44% of biopharma stakeholders are in the "early majority," awaiting evidence before integrating QC, while 30% are innovators or early adopters eager to drive innovation. Investment in QC is set to grow, with 50% of PharmaCos planning annual budgets of $2 million-$10 million and 20% expecting $11 million-$25 million over the next five years. This reflects a growing recognition of QC's benefits (see Figure 4).

Figure 4
Biopharma expects to develop quantum capabilities by leveraging partnerships



Source: L.E.K. biopharma quantum survey

PharmaCos are experimenting with QC applications across the pharmaceutical value chain, first focusing on drug discovery and clinical trials (see Figure 5).

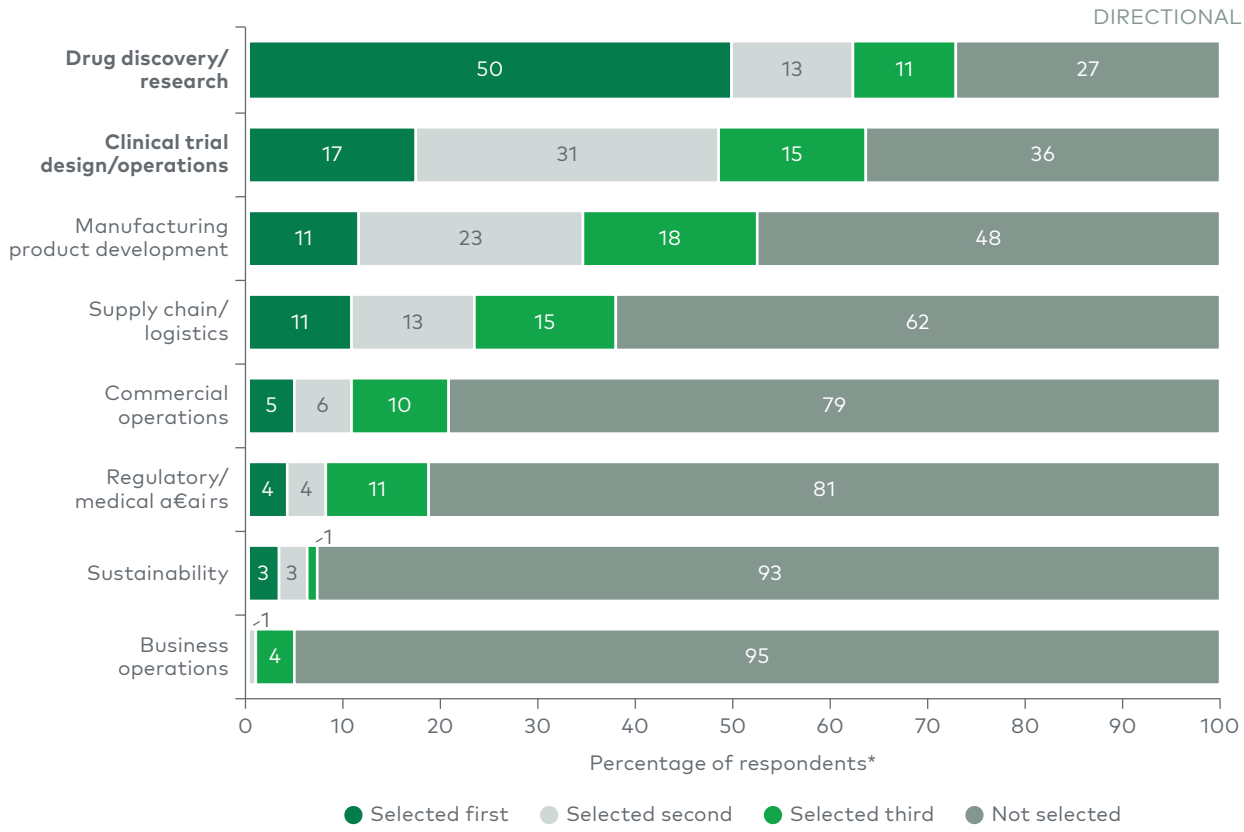
Expansion of capabilities within sustainability, commercial operations, manufacturing and product development may also be enabled by QC technology. However, the exact impact and best-suited QC modalities for each use case are still being defined.

Recent key advances in QC lead to the need for biopharmas to engage with quantum processing units and enablers

Given the excitement and investment in the space, the landscape of QC is quickly evolving, marked by significant technological advances across the ecosystem. Major milestones from large tech players in 2024 include:

- IBM's launch of Quantum Heron, its most advanced quantum computer with 156 logical qubits[9]
- Google Quantum AI's new Willow chip, which enables exponential error reduction and enhanced performance in superconducting quantum systems

Figure 5
QC benefits across the value chain



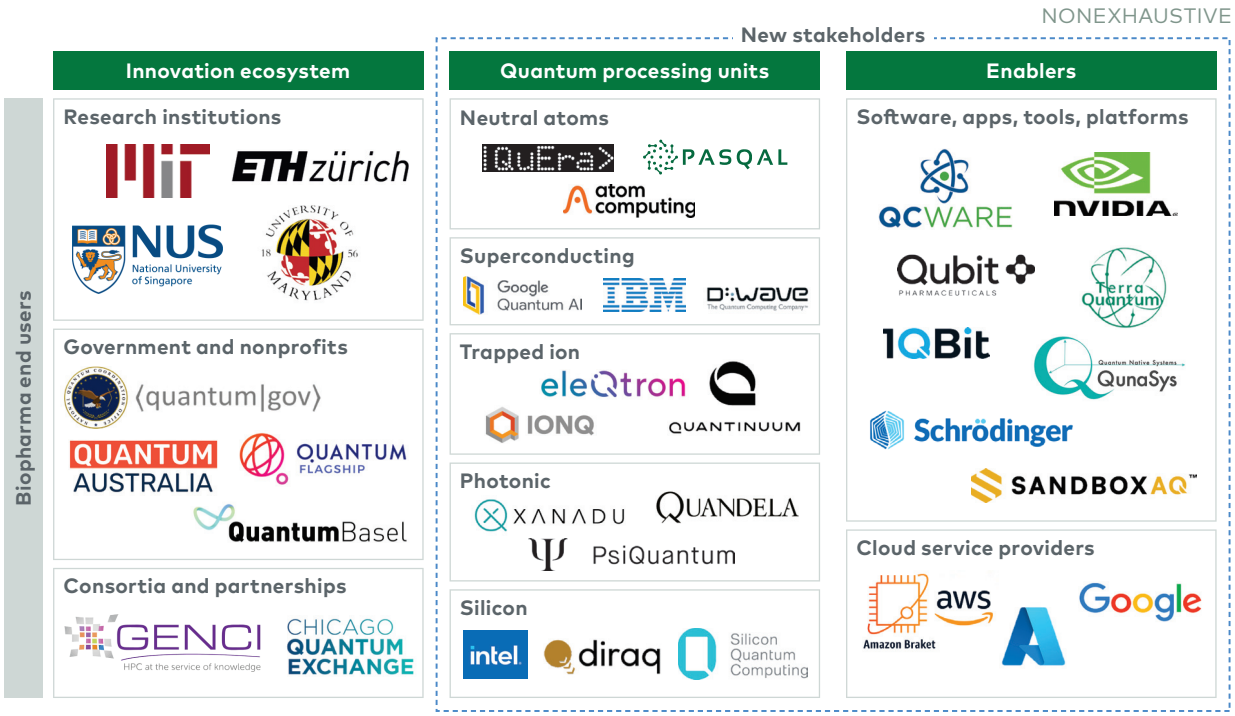
*Survey questions: Where along the value chain do you see the greatest benefit of leveraging quantum computing in your organization? (select up to three in order of importance) Where along the value chain do you believe lie the biggest hurdles or challenges to adopting quantum computing in your organization? (select up to three in order of importance)
Note: Other challenges include insufficient quantum processing units/software stack, information technology and financial investment; QC=quantum computing
Source: L.E.K. biopharma quantum survey

Pure-play QC players have also made substantial strides, including:

- IonQ's Tempo quantum computer achieving 99.9% 2-qubit gate fidelity, positioning the company as a leader in trapped-ion technology
- Quantinuum's achievement of 12 logical qubits with its system model H2, a threefold advance over previous models

With these advancements in QC, two key stakeholder groups are emerging: the quantum processing unit providers and the enablers that facilitate access to QC. These stakeholders drive momentum and funding for QC. Like engaging with AI players, biopharma stakeholders should proactively collaborate with these diverse QC ecosystem players to fully harness these technologies and stay competitive in this evolving field (see Figure 6).

Figure 6
Growing number of new stakeholders in the evolving QC ecosystem



Note: QC=quantum computing
Source: L.E.K. research and analysis

Strategic partnerships needed to compete within a specialized market

Due to the growing complexity of the QC ecosystem, successful integration of workflows depends on building capabilities through strategic partnerships. Notable collaborations include:

- **IBM Quantum with GSK, Moderna and AstraZeneca:** Optimizing messenger RNA research and clinical data imputation using IBM's Quantum Heron and Condor processors
- **Google Quantum with Boehringer Ingelheim:** Exploring molecular simulation algorithms to aid in drug discovery with Google's Sycamore processor

Partnerships underscore the industry's commitment to integrating QC into pharmaceutical workflows, highlighting the collaborative efforts needed to overcome technical challenges and achieve utility (see Figure 7). Building in-house expertise and fostering external partnerships will be crucial to leverage necessary talent quickly. Companies that act swiftly will gain a competitive advantage, positioning themselves as leaders in this emerging field.

Figure 7
Major pharma companies have established relationships with QC organizations

NONEXHAUSTIVE

Note: QC=quantum computing
Source: Company press releases

The near-term impact: Intersection of QC, AI and classical computing

The most promising near-term advancement is combining QC with AI and classical computing in hybrid workflows. This combination leverages the strengths of all technologies, enabling more accurate simulations of complex systems, enhanced machine learning models and improved process optimization for larger datasets at significantly faster speeds. More than 70% of biopharma stakeholders anticipate that QC will augment classical computing and AI, offering more precise and efficient solutions, especially in navigating breakthroughs in drug discovery and development.

For example, Qubit Pharmaceuticals leverages QC for advanced target characterization and molecular dynamics within small-molecule drug discovery while simultaneously utilizing AI-driven generative modeling, virtual screening and predictive analytics. Additionally, Qubit has partnered with Pasqal to leverage both classical computing and QC to model proteins, NMEs and water molecules at high levels of accuracy.

Further, IonQ's collaboration with AstraZeneca includes the creation of an applications development center within AstraZeneca's BioVentureHub to advance QC for drug discovery and development. In addition, IonQ has collaborated with NVIDIA, AstraZeneca and AWS to advance drug development using computational tools — achieving 20x speedups in molecular simulations versus AWS' previous implementation — and paving the way for quantum-accelerated biopharma and materials science.

Further advancements, including running AI on quantum computers, are exciting but not expected to be seen for longer periods of time.

The path forward for QC in biopharma

The integration of QC into the pharmaceutical industry holds immense potential to revolutionize drug discovery and clinical trials. While QC represents a longer-term (five-to-10-year) strategic investment requiring scalable hardware, advanced error mitigation and correction, and specialized algorithms, the opportunities it presents are significant. QC can enhance predictive analytics, optimize clinical trial designs and expedite the discovery of novel therapies, ultimately accelerating drug development and reducing time to market for new treatments.

Despite current challenges such as talent acquisition and a steep learning curve, strategic investments, partnerships and AI integration can enable the industry to harness QC's transformative power. Continued collaboration and innovation will be crucial.

Biopharma stakeholders should address the following key questions to effectively utilize QC's benefits and remain competitive:

- Does my organization have a clear plan on how to experiment with and deploy QC within key functions, especially R&D?
- Within R&D, are there specific use cases that would be most appropriate for QC? On what basis should these be identified?
- How do I balance external partnerships and collaborations alongside internal capabilities to accelerate realization of the potential from QC in R&D?
- To implement QC effectively, what key internal operating model requirements must be met, specifically regarding talent, hardware, data infrastructure and software?
- To what extent should QC be leveraged alongside AI? Is there a benefit from integrating early (e.g., hybrid workflows) or operating independently prior to integration? What is the optimum roadmap for my organization?

By considering these questions and investing strategically in QC, the pharmaceutical industry can harness new opportunities and achieve remarkable progress across drug discovery, clinical development and operation, the supply chain, and manufacturing.

Note: L.E.K. conducted a number of interviews with both AI and pharma experts including Google, IONQ, Qubit and others to help triangulate and inform the findings.

For more information, please **contact us**.

Endnotes

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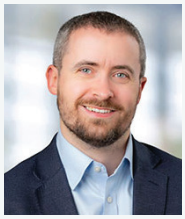

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CASE STUDY

Optimizing Biopharma Operations for Strategic Growth

Background and challenges

The client in this case was a clinical-stage biopharma company specializing in the development of therapeutics using antibody-drug conjugate (ADC), with operations spanning multiple sites including dedicated process development and Good Manufacturing Practices (cGMP) facilities. The company was facing a pivotal strategic shift after recently deciding to outsource key capabilities.

To align with this evolving strategy, the client sought to evaluate cost-efficient operating models that aligned with its longer-term strategy. Key challenges included realigning cGMP manufacturing operations to meet future needs, assessing the financial implications of structural changes to improve cost-effectiveness and creating a roadmap for effective implementation of changes.

Approach

The L.E.K. Consulting team undertook a comprehensive diagnostic to evaluate and align the cGMP manufacturing facilities with the client's evolving strategy. The approach included the following key steps:

Phase 1: Establishing a baseline and strategic options

The team first established a baseline low-cost scenario, externalizing key manufacturing processes while maintaining the facility's existing structure. This served as a cost-efficiency benchmark for comparison. Next, a range of strategic options was developed to realign the operational footprint with the client's growth objectives while ensuring regulatory compliance and efficiency.

Phase 2: Quantifying and prioritizing scenarios

Each option was assessed based on its financial impact, operational feasibility and degree of strategic alignment. A prioritization framework highlighted the most feasible paths to cost savings and sustainable growth.

Phase 3: Financial and operational impact analysis

Our team identified key operational changes including workflow redesign and optimized resource use. A detailed financial analysis estimated savings, efficiency improvements and five-year financial impacts.

Phase 4: Business case and implementation roadmap

For the top strategic options, business cases were developed to quantify benefits and inform leadership decision-making. A high-level implementation roadmap provided key milestones and risk management strategies for execution.

Results

L.E.K.'s analysis enabled the client to adopt a strategic plan that optimized its cost structure and streamlined operational focus. Through the transition from in-house cGMP manufacturing to a more flexible external supply model, the client significantly reduced fixed costs and labor-related costs while reallocating resources to higher-value activities such as new product development and process improvements. The new approach enhanced financial performance, scalability and the client's ability to innovate and remain competitive in a rapidly evolving market.

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EXECUTIVE INSIGHTS

The Race is On: Winning Smart in the Intensifying GLP-1 Market in China

Introduction

The global glucagon-like peptide-1 receptor agonist (GLP-1) market has experienced significant growth and is projected to expand further. China's GLP-1 market is similarly expected to grow substantially, with analysts estimating it could reach RMB 100 billion (US$14 billion) by 2030. GLP-1 therapies, which effectively regulate blood glucose levels and support weight loss, have gained widespread acceptance among healthcare providers (HCPs) and patients.

In 2024, leading GLP-1 molecules reached top positions in global pharmaceutical revenues. Semaglutide (including Ozempic, Wegovy and Rybelsus) ranked second globally with sales of $29.3 billion, while t irzepatide (including Mounjaro and Zepbound) ranked fourth with $16.4 billion in sales.

Leading players such as Novo Nordisk and Eli Lilly are expanding production capacity through acquisitions and outsourcing to meet rising GLP-1 demand. Other multinational corporations (MNCs) are also active; for example, Roche has strengthened its pipeline through the acquisition of Carmot Therapeutics and a partnership with Zealand Pharma. Meanwhile, Chinese companies are rapidly advancing through fast following, innovation and licensing, with key developments including Innovent's mazdutide, Innogen's supaglutide, Hengrui's oral candidate HRS-7535, United Laboratories' licensing of its first-in-class "triple-G" (GLP-1, gastric inhibitory polypeptide (GIP) and glucagon) a gonist to Novo Nordisk and Ascletis' positive Phase 1 results for its "oral + injection" candidate, ASC30.

China — the world's second-largest pharmaceutical market and home to the largest diabetic (164 million by 2030) and overweight (200 million to 250 million by 2030) populations — has become a critical strategic battleground for both global pharmaceutical giants and local players. Consequently, competition in the Chinese GLP-1 market is expected to become increasingly intense.

1. Key drivers of GLP-1 market growth

1.1 Expanded indications and increasing disease prevalence

In addition to type 2 diabetes and weight management as key battlegrounds today, GLP-1 therapies have shown clinical promise in treating a wider array of conditions, including Alzheimer's disease, cardiovascular risk reduction , MASH (metabolic dysfunction-associated steatohepatitis) and chronic kidney disease (CKD). (F or example, see in Table 1 the status of indications for semaglutide.) This broadening of indications has opened new patient segments and strengthened clinical appeal. Simultaneously, the rising global prevalence of obesity, diabetes and associated conditions has fueled growing demand for effective therapeutic solutions.

Among emerging indications, MASH represents a particularly promising opportunity. As of March 2025, the U.S. Food and Drug Administration has approved only one pharmacologic treatment (i.e., resmetirom) specifically for MASH or its precursor, NASH (nonalcoholic steatohepatitis), while the European Medicines Agency and China's National Medical Products Administration have approved none. GLP-1 agents — the leading candidates being studied in advanced clinical trials — show substantial potential in this area. Additionally, GLP-1 therapies are gaining recognition as a novel approach to Alzheimer's disease due to their anti-inflammatory and neuroprotective characteristics.

Table 1
Indication status of Novo Nordisk's semaglutide in the US

Semaglutide approved and pipeline indications as of January 2025	Pre-clinical	Phase 1	Phase 2	Phase 3	Pre-Registration	Approved
Type 2 diabetes mellitus						◆
Obesity						◆
Cardiovascular risk reduction						◆
Diabetic nephropathy					▲	
Alzheimer's disease				▲		
Chronic kidney disease (CKD)				▲		
Diabetic retinopathy				▲		
Knee osteoarthritis				▲		
Metabolic dysfunction-associated steatohepatitis (MASH)				▲		
Prediabetes				▲		
Peripheral artery disease				▲		
Acute ischemic stroke			▲			
Chemotherapy-induced gastrointestinal toxicity			▲			
Liver cirrhosis			▲			
Type 1 diabetes mellitus			▲			
Intermittent claudication	▲					

Source: L.E.K. analysis

China's massive and growing population of individuals with type 2 diabetes and overweight conditions further elevates the relevance of GLP-1s. In 2021, China had 141 million people with diabetes, projected to rise to 164 million by 2030 — the highest globally, according to the International Diabetes Federation. Furthermore, 200 million to 250 million Chinese are expected to be overweight (body mass index >27) by 2030, according to the World Obesity Atlas and the Chinese Center for Disease Control and Prevention, positioning the country as the largest potential patient base for overweight treatment. China also has the largest patient base for the expanded indications such as MASH and Alzheimer's disease, most of which are currently under investigational studies in China.

1.2 Rising awareness through education and word of mouth

Historically, obesity has been viewed as a behavioral issue. This perception is gradually shifting due to the government's increasing attention to and emphasis on public weight management and the increasing visibility and efficacy of GLP-1 therapies.

In June 2024, the National Health Commission (NHC) and 16 government ministries jointly released the "Implementation Plan for the Year of Weight Management Initiative"(《"体重管理年"活动实施方案》), calling for a scientific understanding of weight management and appropriate medical intervention. As of April 2025, the NHC had further issued the "Notice on the Establishment and Management of Weight Management Clinics,"(《关于做好体重管理门诊设置与管理工作的通知》). In the same month, the commission officially included weight management as one of the key actions under the Healthy China initiative, marking the elevation of weight loss to a national strategic priority. These efforts are reframing public understanding, highlighting obesity as a treatable chronic illness rather than a perceived failure of individual willpower.

In China, public and clinical awareness of GLP-1 therapies for overweight and obesity had emerged prior to the approval of Wegovy and Mounjaro and was further strengthened following the drugs' mid-2024 approvals for chronic weight management. The publication of standardized treatment guidelines in 2024 — i.e., the "2024 Edition of the Clinical Guidelines for the Diagnosis and Treatment of Obesity" (《肥胖症诊疗指南(2024年版)》) — formally endorsed GLP-1 therapies as a recommended option for weight management. With these official approvals and guideline recommendations, pharmaceutical companies are now able to conduct legitimate direct-to-consumer (DTC) education and outreach campaigns, accelerating the expansion of public awareness, acceptance and adoption of GLP-1 treatments in China.

1.3 Evolving GLP-1 therapeutic development

Innovation in molecular structure and delivery methods is another key driver of growth. Currently approved GLP-1 therapies are primarily peptide-based injectables, with once-weekly administration being the main approach. Although these therapies provide significant clinical benefits, substantial unmet needs remain, creating opportunities for further innovation. The emergence of oral GLP-1s, once-monthly injectables, dual- and triple-receptor targets and combination therapies has enhanced patient convenience, improved adherence and broadened clinical utility, bringing healthcare practitioners more options for individualized treatment. In China, domestic companies are closely aligning with these global trends, and leading players are actively advancing in this direction. For example, Hengrui is developing the oral GLP-1 HRS-7535 alongside dual- and triple-receptor targeted therapies, focusing on the GIP/GLP-1 and GCGR /GIP/GLP-1 pathways. Similarly, Gan & Lee is progressing GZR18, a biweekly injectable, as well as GLP-1 + insulin candidates.

As R&D investment continues, next-generation GLP-1 products will reinforce the class's role as a transformative force in the treatment of metabolic diseases, including diabetes, obesity and related conditions.

2. Escalating competition and the need for differentiation

2.1 Brand differentiation beyond GLP-1 class

The molecules landscape in China is expected to become even more competitive than in developed markets, where the GLP-1 category is primarily dominated by leading multinational pharmaceutical companies. As of February 2025, China already had 60-70 late-stage (Phase 2 or later) pipeline assets, directly competing with semaglutide, tirzepatide and other candidates in diabetes and weight loss. Additional early-stage pipeline assets and global candidates that have not started clinical trials in China yet can further intensify the competition in the future.

Within the late-stage pipeline assets (around half of which are targeting weight management), eight are oral ones, aiming to solve the inconvenience of injections, and approximately 20 are dual-target or triple-target, aiming to achieve superiority in clinical effectiveness.

In China, beyond the in-market products such as semaglutide and tirzepatide and promising global pipeline assets including orforglipron (oral), MariTide (monthly injectable) and retatrutide (triple agonist), a range of China-only molecules is also emerging with strong competitiveness (see Table 2). These candidates demonstrate clinical differentiation and innovation, moving beyond traditional biosimilar or fast-follower strategies.

Table 2
Examples of in-market and pipeline molecules in China (nonexhaustive)

Molecule types	Global MNC	Chinese pharma
Oral GLP-1 small molecules	• Orforglipron (Lilly)	• HRS-7535 (Hengrui) • HDM1002 (Huadong) • VCT220 (Vincentage)
Biweekly/ monthly injectables	• MariTide (Amgen)	• Supaglutide (Innogen) • RAY1225 (Zhongsheng) • GZR18 (Gan & Lee) • ZT002 (Zhitai)
Dual- and triple-receptor targets	• Tirzepatide (Lilly) • Survodutide (Boehringer Ingelheim) • CagriSema (Novo Nordisk) • Retatrutide (Lilly)	• Mazdutide (Innovent) • HRS9531 (Hengrui) • RAY1225 (Zhongsheng) • MWN101 (Lepu)

Note: MNC=MultiNational Corporation; GLP-1=Glucagon-Like Peptide-1 receptor agonist
Source: Trial database, public release, L.E.K. analysis

This rapidly diversifying market will shift the focus from general awareness of the GLP-1 class to the evaluation and selection of dozens of differentiated options. Pharmaceutical companies must clearly define and articulate their advantages in efficacy, safety, delivery and overall value to earn patient and HCP trust in an increasingly crowded market.

2.2 Imminent generics entry

Semaglutide, the biggest blockbuster product in the GLP-1 market today, is expected to lose patent protection in China in 2026, earlier than in most developed markets. Given its popularity and clinical reputation, interest from biosimilar manufacturers is already high. Some 15-20 semaglutide biosimilar/generic pipeline assets are already racing for the first abbreviated new drug application approval.

The introduction of biosimilars will increase pricing pressure and challenge the market share of originator brands. Additionally, semaglutide may be subject to volume-based procurement (VBP) as the biosimilars/generics entry could be as early as 2026, potentially impacting the pricing of Ozempic and Wegovy. This will force other GLP-1 originators, such as tirzepatide and mazdutide, to reevaluate their pricing and market entry strategies and compel pipeline developers to recalibrate their China launch plans accordingly.

3. The winning formula: A patient-and customer-centric strategy

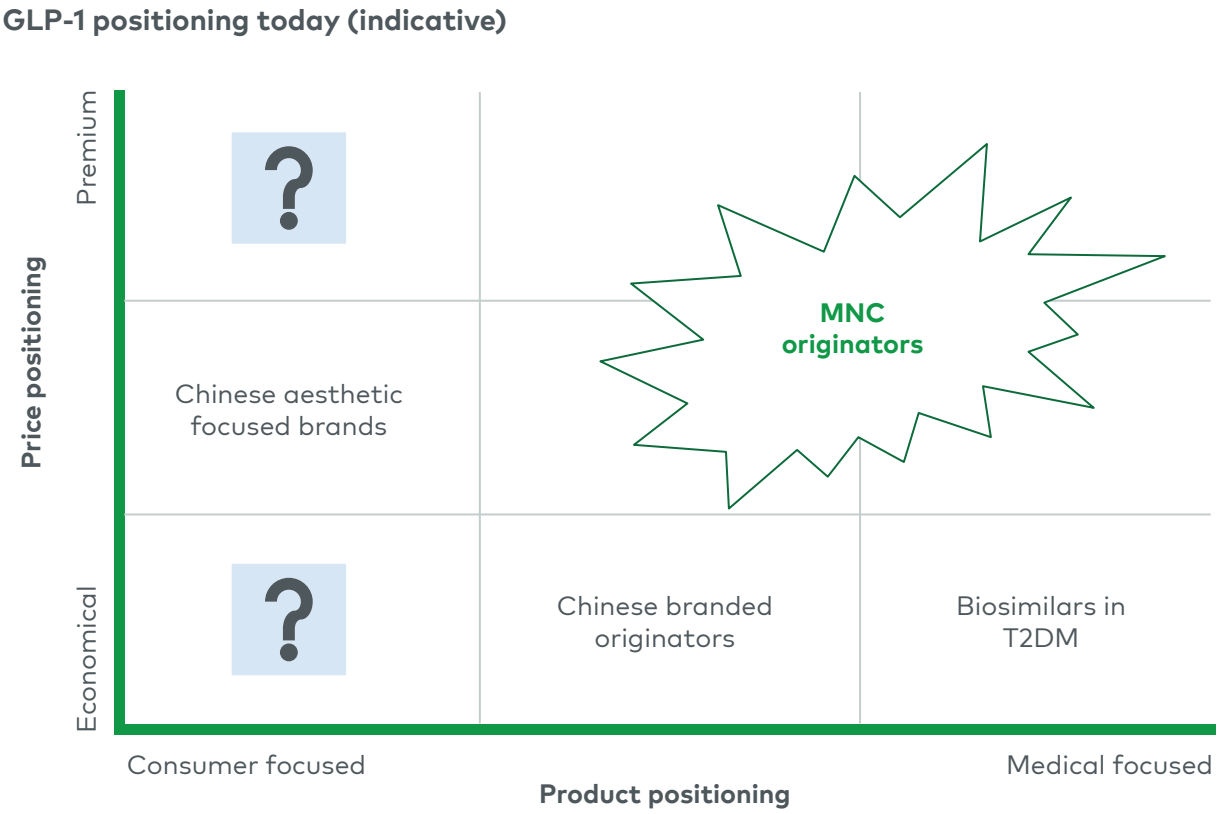
In China, the national reimbursement system typically covers treatments for chronic diseases such as diabetes, cardiovascular conditions and kidney disorders, reflecting both the long-term health burden of these illnesses and their priority in public policy. In contrast, weight management therapies — including GLP-1–based treatments for obesity — are explicitly excluded from reimbursement. This regulatory divide creates a dual-track market for GLP-1 therapies that compels the careful calibration of branding, pricing and access strategies.

To participate in a fast-growing but competitive and complicated market, GLP-1 originators will need to adopt a differentiated patient- and customer-centric strategy — leveraging both internal and external resources to optimize product positioning, building brand equity, integrating software and device solutions beyond the drug itself, and exploring innovative channels. New-indication exploration ahead of competitors is the best way to work around direct competition in a crowded market.

3.1 Optimizing product positioning in competition

In this increasingly crowded environment, direct price competition is inevitable — particularly in the self-pay weight management segment. For GLP-1 players looking to sustain market position and capture long-term value, strategic differentiation beyond pricing thus becomes essential. A simplified framework based on price and product positioning can help originators map out their direct competition and tailor value propositions accordingly. For companies with broader ambitions in GLP-1s, a multibrand portfolio strategy may enhance overall competitiveness (see Figure 1).

Figure 1
GLP-1 price x product positioning



Note: GLP-1=Glucagon-Like Peptide-1 receptor agonist; MNC=MultiNational Corporation; T2DM=Type 2 Diabetes Mellitus
Source: L.E.K. experience

When considering product positioning of each brand, a wide range of dimensions can be considered to fit the positioning within a company's portfolio and the competition (see Table 3).

Table 3
GLP-1 product positioning dimensions

Efficacy	5% weight loss	10% weight loss	15% weight loss	20% weight loss	>30% weight loss
Safety and side effects	Nausea	Muscle wastage	Weight rebound	Hypoglycemia	...
Route of administration	Subcutaneous	Oral (peptide)	Oral (small molecule)	...	...
Duration of treatment	Chronic	Cyclic	Acute	Maintenance	Induction
Body mass index	<25 (healthy)	25-29.9 (overweight)	30-39.9 (obese)	>40 (severely obese)	...
Comorbidities	0	1	2	>3	...
Brand positioning	Premium	Economical	...	...	...
Partnering	Go alone	Codevelop	Licensing	Cocommercialize	...
Dosage and administration	100% of dosage	75% of dosage	50% of dosage	25% of dosage	Flexible
Lifestyle	Metabolic syndrome	Busy sedentary professionals	Social media influencers	Health-conscious individuals	...
Call-point specialization	Endocrinology	Obesity clinic	Medical aesthetics advisers	Social media influencers	...
Distribution channels	Public hospitals	Private hospitals	Medical aesthetics institutions	Pharmacies	Online
Monotherapy vs. combination	Monotherapy	Double	Triple	...	...
...	...	...	...	...	...

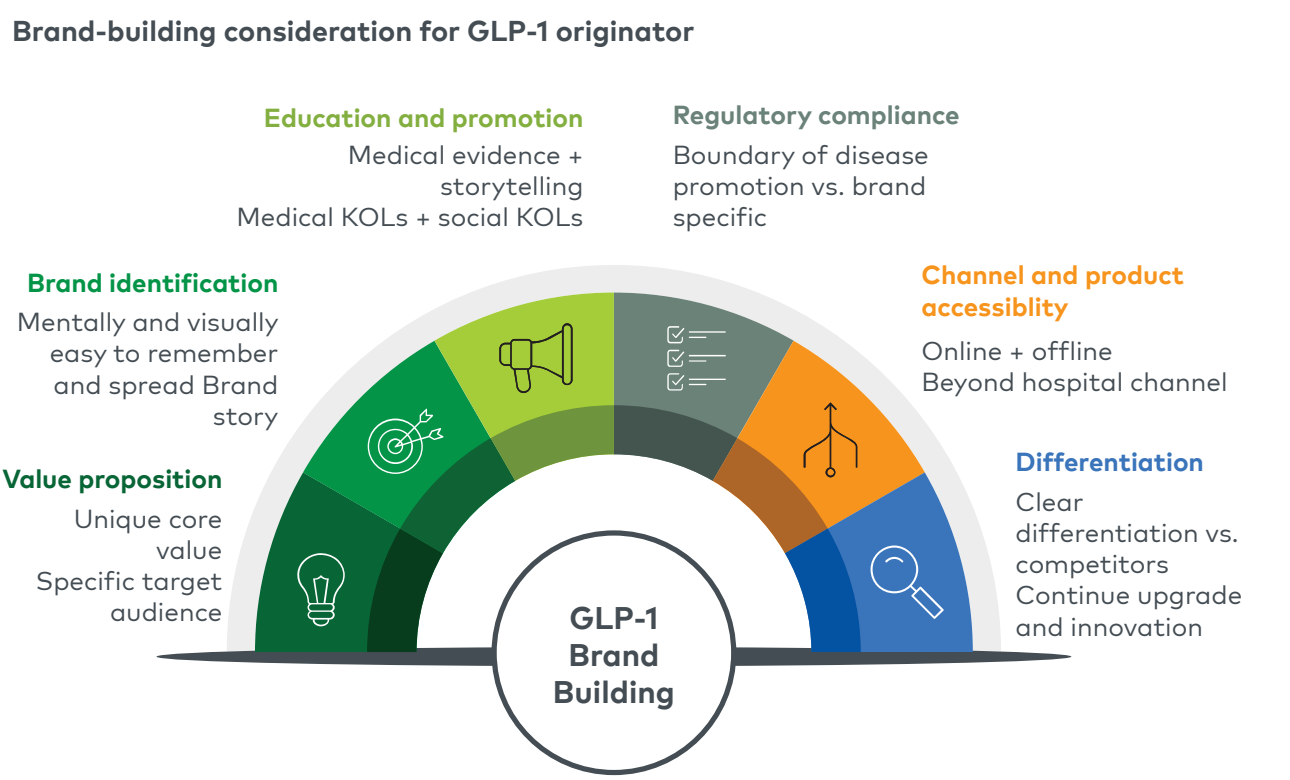
Source: L.E.K. analysis

3.2 Branding as a competitive edge

GLP-1s' consumer-oriented nature makes branding unusually important for such prescription therapy. For example, despite superior efficacy in head-to-head trials, tirzepatide lags semaglutide in public awareness today in China. Moreover, the public often struggles to distinguish between Ozempic and Wegovy and between GLP-1 monotherapy and combination agents.

L.E.K. Consulting has developed a proprietary branding framework for prescription products — highly applicable to GLP-1 therapies — emphasizing value propositions that are identifiable, memorable, sensible and shareable (see Figure 2). A DTC model with sustained innovation is critical to communicate this effectively.

Figure 2
GLP-1 branding framework



Note: GLP-1=glucagon-like peptide-1 receptor agonist; KOLs=key opinion leaders
Source: L.E.K. experience

In addition, GLP-1 players in China often face a complex strategic decision between a single-brand approach (such as Mounjaro for tirzepatide) and a dual-brand approach (such as Ozempic and Wegovy for semaglutide) across different indications.

The choice is clear: Should GLP-1 originators maintain a dual-brand strategy, which allows for premium pricing in the self-pay weight management segment while enabling reimbursement for Type 2 diabetes, but also requires greater investment in brand differentiation and market education? Or should GLP-1 originators pursue a single-brand strategy, which may support broader hospital access and unified brand equity but comes with the trade-off of lower reimbursement pricing across all indications? These are critical, nuanced decision points for all GLP-1 players operating in China to consider.

3.3 'Beyond drug' integration

GLP-1 therapies offer a unique opportunity to build ecosystems beyond the drug itself. Integrating software and smart devices for personalized monitoring and adherence can increase loyalty and improve outcomes especially in self-pay contexts.

These digital ecosystems are emerging as a key differentiator, fueled by excellent integration with the following examples of software and smart devices.

- **Software:** telehealth (including artificial intelligence chatbots and virtual assistants), digital engagement, personalized patient treatment and management, gamification , and big data and predictive analytics for drug usage, etc.
- **Smart devices:** fitness and medication trackers, continuous biometric monitoring, medication reminders, smart pens and evidence generation (with compliance restrictions to be considered)

3.4 Innovative channel strategy

The patient journey is no longer confined to hospitals, especially for self-pay weight management patients. A multiple-touchpoint omnichannel approach is essential for broad market penetration. Companies should identify the most influential stakeholders for their brand — whether HCPs, influencers and/or digital platforms — and build partnerships that enable scalable awareness and adherence.

Examples of potential influencers along a consumer-oriented patient journey:

- **Awareness and interests:** health checkup centers, wellness clubs, social platforms
- **Research and consultation:** aesthetics hospitals, medical social platforms and internet hospitals
- **Diagnosis and treatment selection:** hospitals, private clinics, internet hospitals, online-to-offline testing service providers
- **Follow-up purchase:** retail pharmacies, online pharmacies
- **Chronic management and behavior change:** commercial insurance companies and third-party administrators, digital patient management platforms

3.5 Horizontal and vertical partnership

No single company can succeed alone. Pharma players should explore both horizontal (e.g., biotech in-licensing, M&A) and vertical (e.g., contract development and manufacturing organizations (CDMOs), device suppliers) partnerships to enhance capabilities.

- **Horizontal:** Late-stage GLP-1 assets from Chinese biotechs may complement global portfolios; companies specialized in GLP-1s/endocrinology can also be potential acquisition targets for large pharmas with ambitions in such therapeutic areas

- **Vertical:** Collaborations with local active pharmaceutical ingredient/CDMO providers, injection pen manufacturers and injection needle suppliers can improve cost-efficiency and user experience

4. Next-steps thinking

With rising innovation and increasingly sophisticated stakeholder behavior, China's GLP-1 space has become both high potential and highly contested. Success will depend on a combination of strategic vision and flawless execution.

As you are continuously refining and evolving your China GLP-1 strategy, consider the following critical questions:

Pharma companies

- How can we differentiate our GLP-1 product beyond clinical efficacy — through branding, patient experience or ecosystem solutions?
- How can we sufficiently prepare for the upcoming pricing pressures from other innovative pipelines and from VBP with semaglutide biosimilars?
- What is our strategy to expand indications (e.g., obesity, MASH, CKD) ahead of the competition?
- How can we build a sustainable omnichannel presence, efficiently reaching patients beyond traditional hospital settings?
- Should we pursue horizontal (pipeline acquisition) or vertical (supply chain) partnerships to enhance our GLP-1 competitiveness?

Investors

- Which GLP-1 assets or innovators are best positioned to defend or grow market share in an increasingly crowded Chinese market?
- What pricing and reimbursement risks (e.g., VBP, biosimilar entry) could impact revenue forecasts after 2026?
- Are China-originated assets (oral GLP-1s, multitarget agonists) positioned for regional or global expansion opportunities?
- What postacquisition initiatives (e.g., development, go to market) are required to accelerate the realization of full potential?

Channel players

- With what capabilities (e.g., digital engagement, adherence programs) can we differentiate ourselves as the key enabling partner for leading GLP-1 players?
- What types of partnerships with which pharma or healthtech companies should we pursue now to secure a leadership position?

In a GLP-1 market poised for rapid expansion and fierce competition, now is the critical moment for every stakeholder — from pharma companies to investors to channel players — to rethink their strategies, partnerships and competitive edge.

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EXECUTIVE INSIGHTS

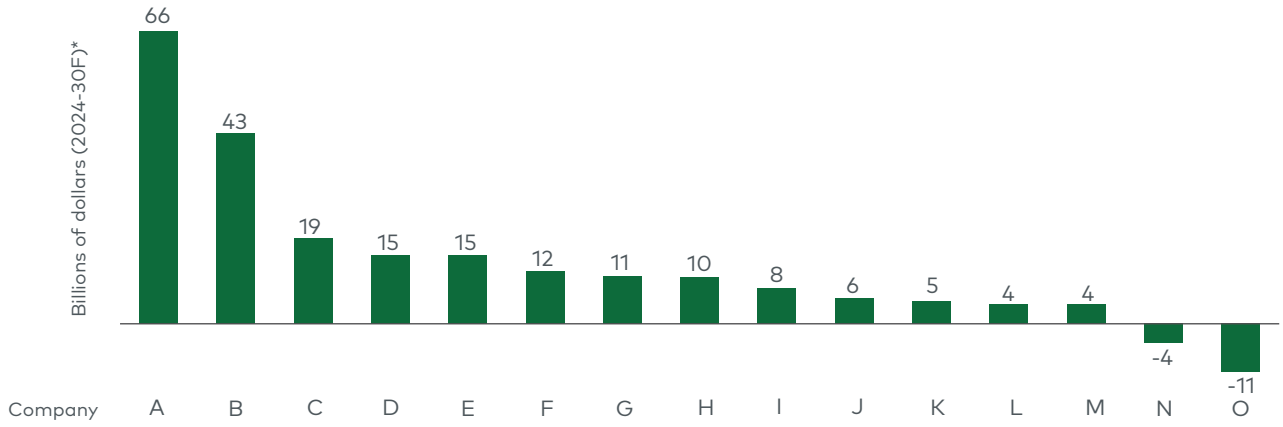
How Pharma Companies Are Driving the Next Wave of Revenue Growth

Introduction

The top 15 biopharma companies account for 75% of total industry revenue, making their future performance a defining factor for the sector at large. Their strategies, investment decisions and execution disproportionately shape the trajectory of innovation and the creation of shareholder value across the entire sector. Despite facing loss of exclusivity (LOE) risks impacting 25%-30% of 2024 revenue, these companies are projected to grow their combined revenue by approximately $200 billion — a 30% increase — by 2030 (see Figure 1).

Figure 1

Top 15 biopharma revenue growth (2024-30F)



*Total revenue includes Rx sales, Alliance/copromotion revenue, and royalty and licensing income, and excludes over-the-counter products
Note: Rx=prescription
Source: FDA; EvaluatePharma

Yet this growth is highly uneven. Nearly 80% of the projected revenue expansion is expected to come from just five companies, highlighting the growing divide between market leaders and the rest of the industry.

As executive teams navigate where and how to invest, a clear understanding of the underlying growth drivers — ranging from asset concentration and the mix of in-line versus pipeline contributions to life cycle potential, therapeutic focus and innovation sourcing — is critical for making informed decisions and sustaining long-term value creation.

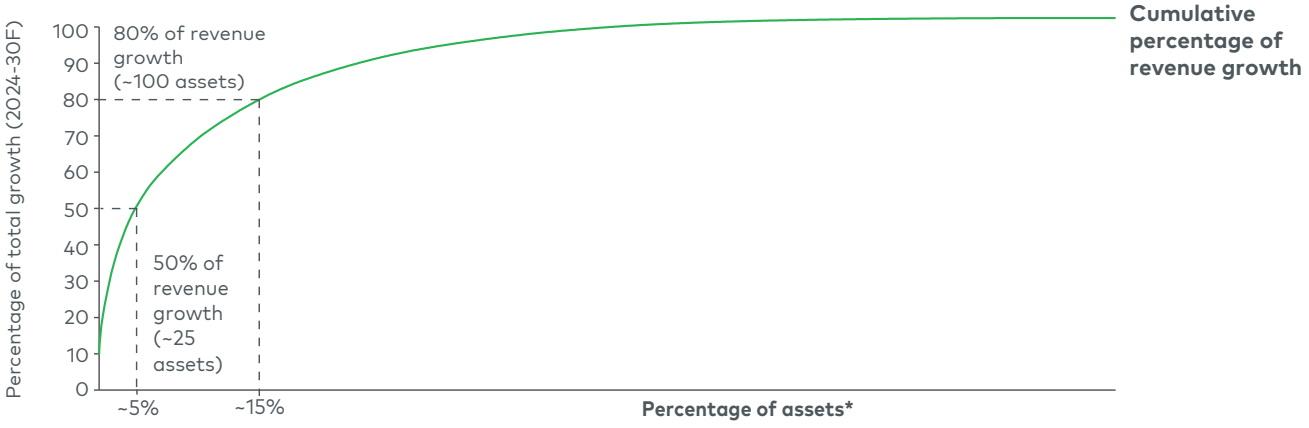
Growth is concentrated — not evenly distributed

Growth through 2030 for the top 15 biopharma companies is driven by around 600 assets, half of which were marketed in 2024 and half of which are expected to be approved between 2025 and 2030.1 Yet revenue growth remains highly concentrated: Just 15% of top-performing assets are expected to drive 80% of the industry's projected growth through 2030. Even excluding glucagon-like peptide-1 agonists (GLP-1s), which account for nearly half of the top 15's projected growth, the pattern holds, with 20% of non-GLP-1 assets generating 80% of the remaining growth (see Figure 2).

Top-performing companies don't just aim for more product approvals; they strategically channel capital and resources into assets with the greatest potential for outsize commercial returns. These high-impact assets tend to scale well beyond their initial launch, often driven by geographic expansion, label extensions or significant differentiation in clinical outcomes. For leadership teams, the imperative is clear: Identify high-conviction opportunities early and commit decisively. Spreading investments too thinly across a broad portfolio may dilute impact and prove less commercially effective.

Figure 2

Concentration of revenue growth among top 15 biopharma assets



*Assets experiencing declining sales or LOE are not included in analysis
Note: LOE=loss of exclusivity

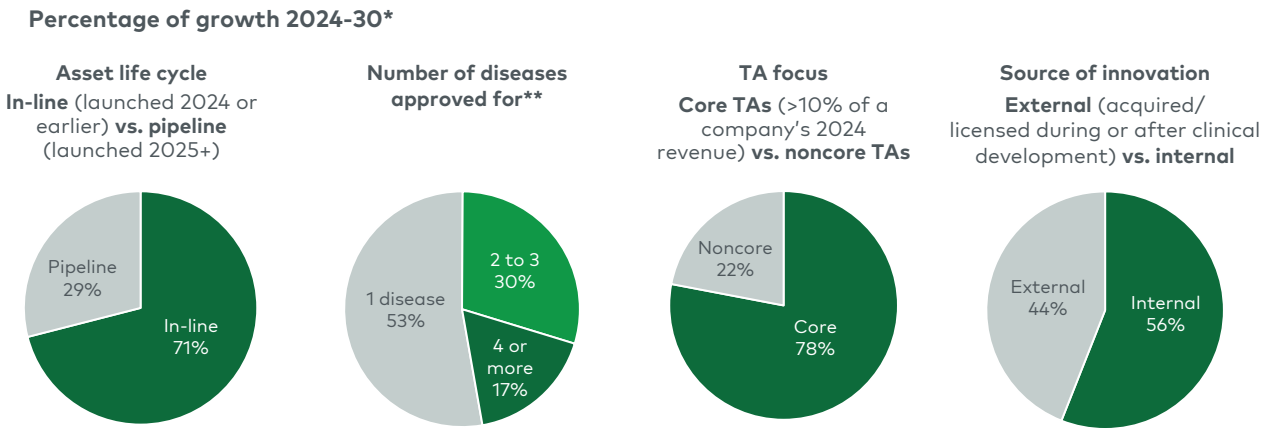
In-line assets are the backbone of growth

Over 70% of projected revenue growth through 2030 will come from in-line assets already on the market as of 2024 (see Figure 3). This places a premium on execution and life cycle management. To fully capture this value, companies must excel in launch performance, optimize market access and expand geographic reach. Sustained growth will depend less on new approvals and more on maximizing the potential of existing assets — ensuring they meet revenue expectations and then exceed them.

Relying exclusively on existing products is not a viable strategy for long-term growth. Even the strongest in-line portfolios will inevitably face pressure from market saturation and LOE. To sustain momentum, companies must complement in-line growth with a consistent cadence of new product launches — not only to offset revenue decline but also to refresh the portfolio, maintain commercial relevance and reinforce investor confidence in the company's innovation engine.

Figure 3

Composition of top 15 biopharma 2024-30F revenue growth



*Does not include collaboration, copromotion or licensing revenue, and excludes assets losing exclusivity or decreasing revenue 2024-30
**Number of diseases per asset based on EvaluatePharma "indication-level" data
Note: TA=therapeutic area
Source: FDA; EvaluatePharma

Multidisease assets drive disproportionate value

"Portfolio-in-a-product" assets — therapies with the potential to address multiple diseases — are emerging as some of the most powerful growth drivers among the top 15 companies. Although they represent only about one-third of the combined portfolio density, these multi-indication assets are expected to account for nearly half of total projected revenue growth. Notably, just 13 such therapies, each spanning four or more indications, are set to deliver nearly 20% of topline expansion through 2030. Their outsize impact is a key differentiator between

higher- and lower-growth players: The top five companies alone anticipate over $100 billion in growth from these assets — more than double the combined contribution expected from the bottom 10.

This underscores a critical strategic consideration. Therapies with the potential to scale across multiple diseases should be prioritized, as they offer not only greater revenue potential but also improved return on R&D and commercial investment.

Core therapeutic areas drive the majority of growth

Nearly 80% of projected revenue growth through 2030 is concentrated in core therapeutic areas — those already accounting for at least 10% of a company's revenue. This trend highlights the strategic advantage of building from a position of strength. By doubling down on familiar territory, companies can leverage established scientific expertise, trusted stakeholder relationships and existing commercial infrastructure to develop evidence strategies that resonate, accelerate launches, optimize access and gain share more efficiently than in less-familiar therapeutic areas.

In an environment defined by growing scientific complexity and mounting commercial pressure, companies that deepen their presence and enhance execution in core areas will be best positioned to drive consistent, capital-efficient growth.

Finding the right balance between external innovation and organic growth

External innovation — through M&A, in-licensing or strategic partnerships — remains a critical engine of growth in biopharma. Projections through 2030 show revenue growth is nearly evenly divided between internally developed assets and those sourced externally during or after clinical development. This balance does not yet reflect future deal activity, which is likely to tilt the mix even further toward external innovation over time.

This dynamic highlights a key strategic imperative: Companies must carefully balance internal R&D with external sourcing to remain competitive. Overdependence on internal pipelines can limit exposure to novel modalities and emerging science, while excessive reliance on external innovation may compress margins, introduce integration challenges and reduce long-term pipeline visibility. Striking the right balance is essential for sustained, capital-efficient growth in an increasingly complex and competitive landscape.

Key implications for pharma executives

Future growth in biopharma will depend on deliberate, insight-driven portfolio choices. The next generation of outperformers will distinguish themselves by reconfiguring their portfolios around a few core strategic principles:

- **Elevate post-launch execution and life cycle management**
  Treat post-launch execution with the same strategic rigor as clinical development. Prioritize indication expansion, global market penetration and long-term value creation to fully realize the potential of in-line assets.
- **Double down on high-impact, scalable assets**
  Focus investment on a select group of high-conviction programs with label expansion potential. Concentrating capital behind these assets can unlock disproportionate returns and build momentum across the portfolio.
- **Leverage strength in core therapeutic areas**
  Deepen presence in therapeutic areas where scientific expertise, stakeholder relationships and commercial infrastructure already exist. Avoid the dilution and complexity that come with overdiversification into unfamiliar domains.
- **Balance internal R&D with external innovation**
  Maintain sourcing agility through a dual-engine model that combines internal research with targeted M&A, licensing and strategic partnerships. This approach ensures access to innovation across modalities and development stages while managing risk and capital efficiency.

Companies that align their commercial, development and investment strategies with these principles will be best positioned to drive sustainable, high-quality growth in an increasingly competitive environment.

For more information, please **contact us**.

Author's note: Almost 50% of forecast revenue growth is attributed to the GLP-1 class. This concentration, however, does not impact the core findings and recommendations in the article.

Note: AI tools were used in the drafting of this article.

Endnote

1The number of assets is not risk-adjusted for likelihood of approval

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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.

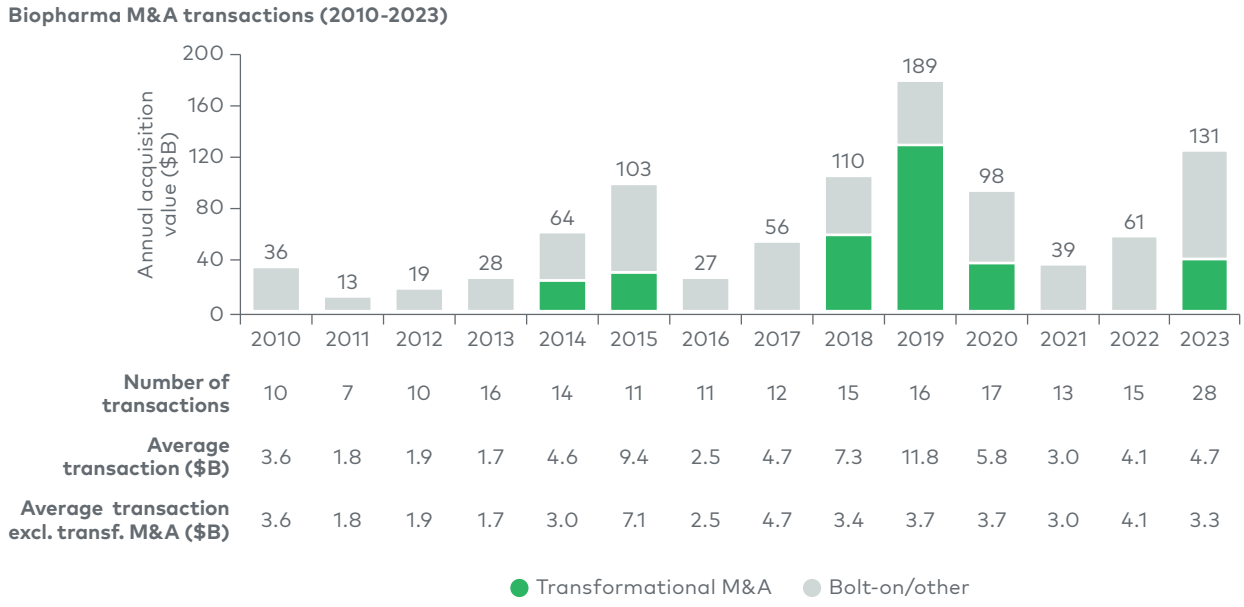
Biopharma consolidation since 2010

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



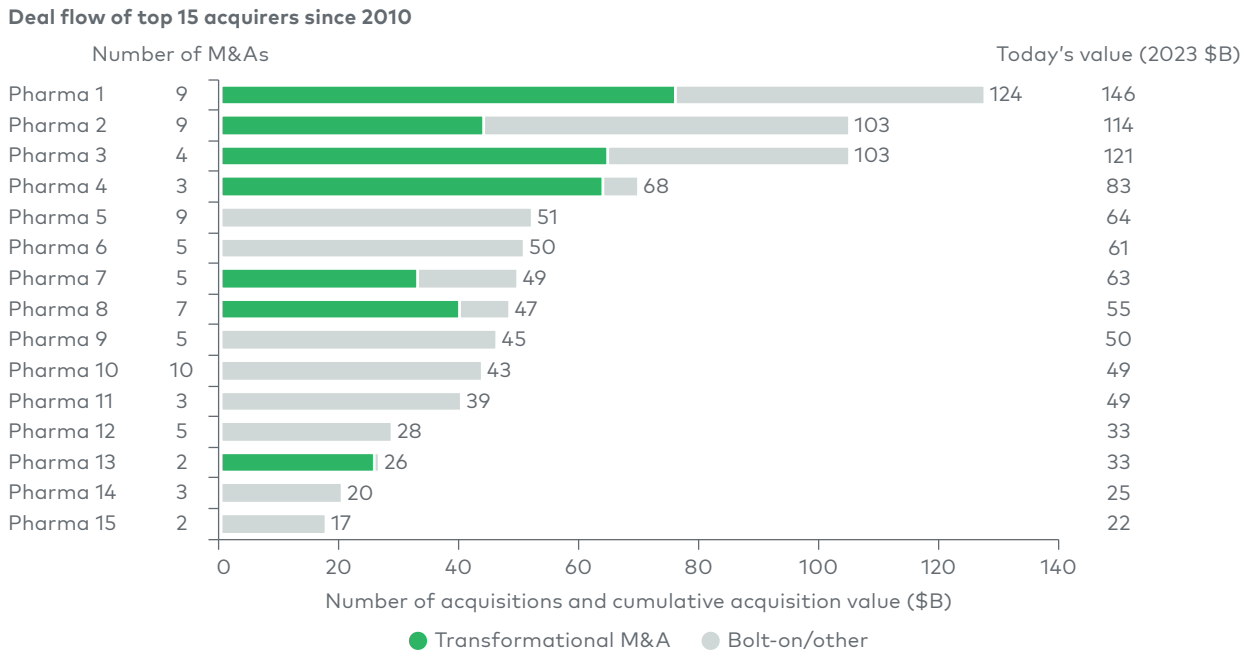
Note: Includes clinical- and commercial-stage public M&A transactions only
Source: L.E.K. research and analysis of Cortellis, company investor materials and SEC filings, S&P Capital IQ

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

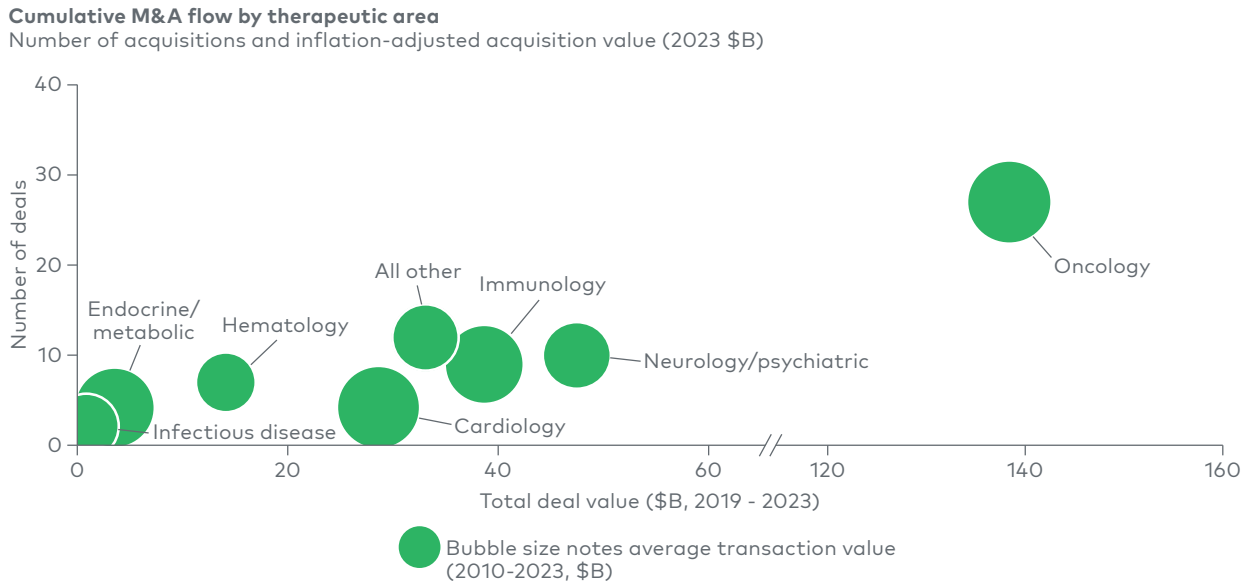
Number of acquisitions and average inflation-adjusted acquisition value (2023 $B)

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.

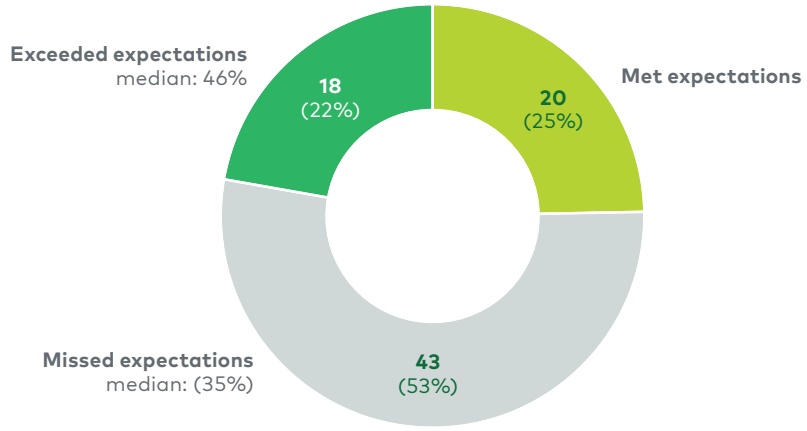
In our analysis of 195 M&A transactions, data for reliable three years post-launch revenue was available for only 81 lead assets. The first insight is that acquirers are proficient at progressing assets through the different phases of clinical development, with their clinical and regulatory

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)

Lead asset revenue performance vs. consensus 3 years after M&A
Number of assets, (percentage of total assets) and median level of revenue performance versus sell-side consensus



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.

EXECUTIVE INSIGHTS

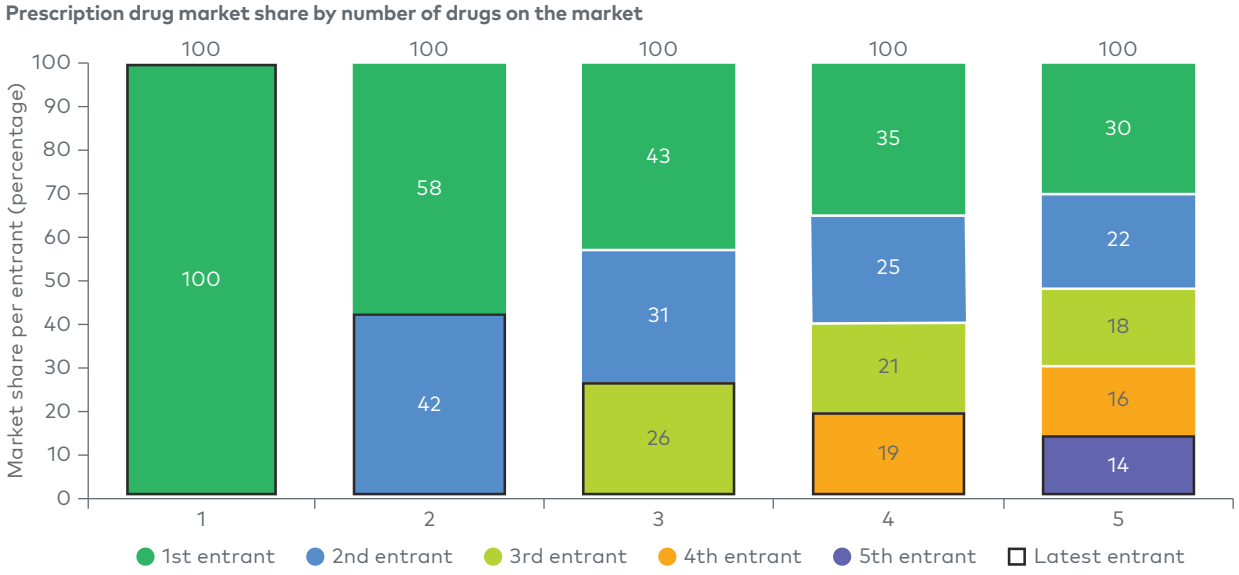
First vs. Best in Class — Simplifying the Equation for Biopharma

Over the past 20 years, there have been a number of attempts to answer the age-old biopharma argument of whether it is better to be first[1] or best in class. The complexity of these analyses has varied from calculating simple averages (e.g., market share by order of entry) to using multivariate equations (i.e., characterizing and weighting the level of differentiation and timing of entry to calculate expected share).[2,3,4] The problem with many of these analyses is that an algorithmic look across a large aggregation of products obscures a key fact: For most products, the outcome is more binary. The idea is analogous to a risk-adjusted revenue forecast — the only certainty is that the risk-adjusted revenue number is unlikely. In reality, revenues will likely be much higher or lower than the risk-adjusted middle ground.

The same shortcoming impacts most order-of-entry-based share projections. While traditional order-of-entry tables are easy- and intuitive-to-use benchmarks, few if any product categories (e.g., classes, markets) approximate the share dynamics that the benchmarks would project. Traditional order-of-entry tables project a steady step-down in share expectations as a product's entry order declines. So, the same product would achieve less share if it were third to market rather than second to market. The tables also predict that the more products there are on the market, the lower the share expectations are for all the products (see Figure 1).

In reality, this is not the case. Order of entry is incredibly important when products are undifferentiated, but aggregate benchmarks underestimate the effect. In fact, in classes where later entrants are not perceived to be differentiated, the first-in-class product often retains more than a 60% share, with later entrants generally capturing less than

Figure 1
Traditional order-of-entry benchmark

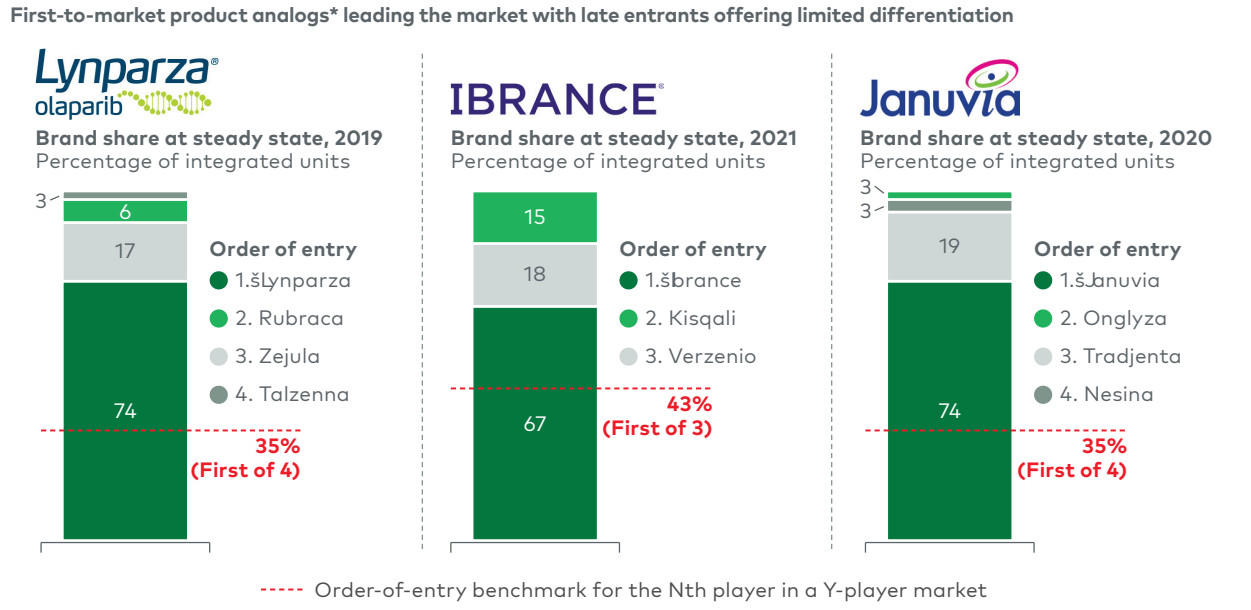


Source: Adapted from International GK Associates, Journal of Pharmaceutical and Healthcare Marketing (2008)

20% and often less than 10% of the class share. Several product classes demonstrate this dynamic, but it can be seen clearly when looking at the poly (ADP-ribose) polymerase inhibitors, the cyclin-dependent kinase 4 and 6 inhibitors, and the dipeptidyl peptidase-4 inhibitors. In each of these classes, traditional order-of-entry tables would have projected that the first-in-class asset would retain considerably less share and, conversely, that later entrants would capture a much larger share of the market than they did in reality (see Figure 2).

Conversely, when a product is truly differentiated, order of entry plays a far lesser role. This phenomenon has been demonstrated across a wide range of disease areas, where a best-in-class product enters the market years after the first-in-class product and still captures majority market share. It is also consistent with L.E.K. Consulting's prior analysis of the makings of a blockbuster, which showed that differentiation was the single greatest predictor of blockbuster revenue outside of company size.[5] Tagrisso, Eliquis, Firazyr and Fasenra are among countless examples of molecules that exceeded order-of-entry benchmark expectations through significant differentiation (see Figure 3). While significant differentiation is most frequently based on efficacy (e.g., Tagrisso), it can also be achieved through other dimensions, such as safety (Eliquis), route of administration (Firazyr) and dose frequency (Fasenra). Such products are often underestimated by analysts with order-of-entry benchmarks.

Figure 2
First-to-market products can maintain market leadership if follow-on entrants offer only modest differentiation

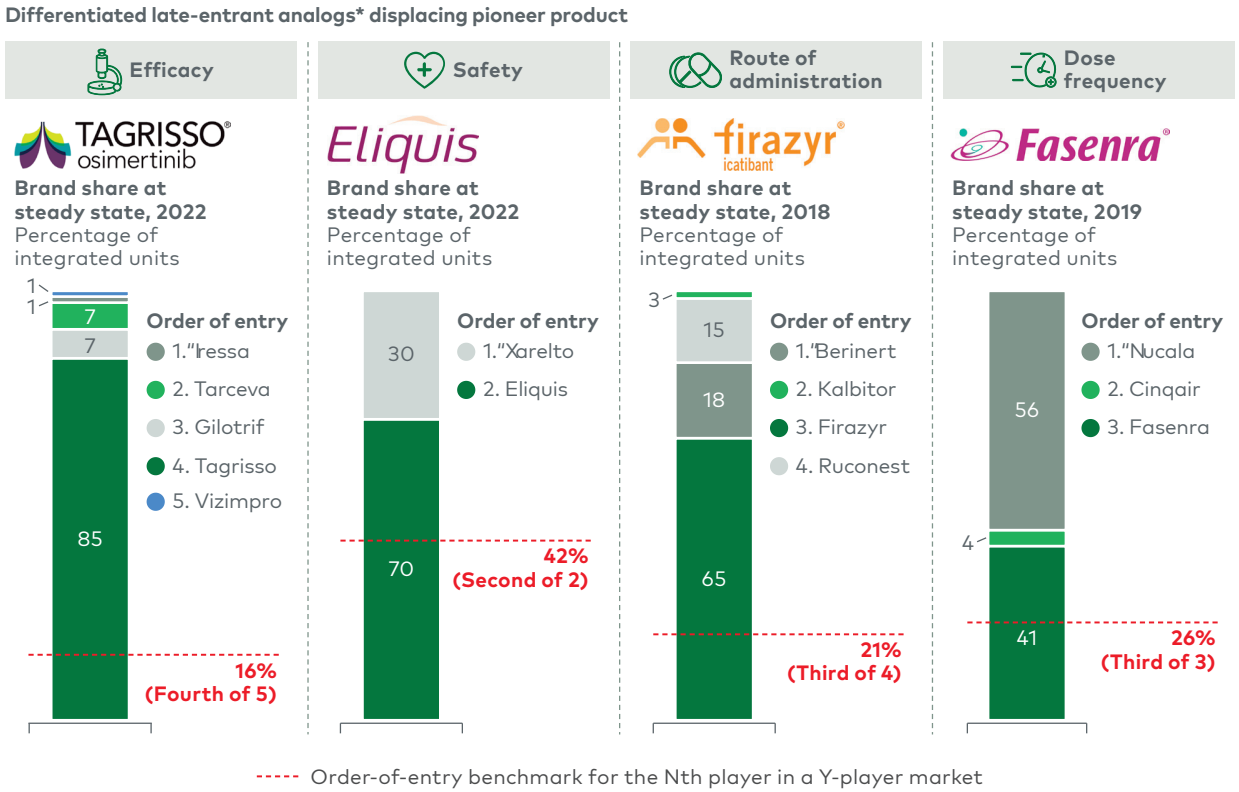


*Integrated units from Symphony prescription data were adjusted based on formulations, dosing volumes and dosing frequency to reflect the actual annual patient volume
Source: Bloomberg Symphony; Food and Drug Administration (FDA) labels; Datamonitor; Cowen (October 2022, March 2023); GK Associates

Applying this more binary approach to estimating share seems simple until one tries to define "differentiation." There are several confounding factors when looking to define differentiation, such as evolving market access dynamics, biomarker strategies, commercial model innovation and even legislation/public policy. Still, one of the most important and avoidable factors is lacking a transparent and objective assessment of what differentiation means within a specific disease area, patient population and competitive landscape. For example:

- In one tumor type, a physician may find a few months' improvement in overall survival to be highly differentiating; in another tumor type, greater improvement may be required.
- In a slowly progressing disease with safe and efficacious options delivered via monthly infusion, a twice-yearly infusion with similar efficacy may be highly differentiating, whereas in a rapidly progressing disease requiring frequent monitoring, extended dosing may be less differentiating.
- Reducing gastrointestinal (GI) adverse events may be highly differentiating for an oral product that must be taken daily for a chronic disease, while that same reduction in GI adverse events may not move the needle for a product that is taken for a short period of time to address a life-threatening disease.

Figure 3
Product differentiation can overcome order-of-entry dynamics to achieve impactful market share



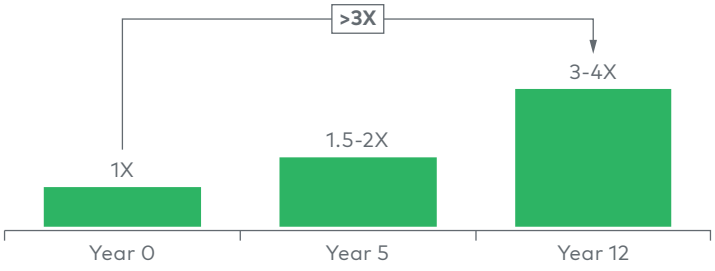
*Integrated units from Symphony prescription data were adjusted based on formulations, dosing volumes and dosing frequency to reflect the actual annual patient volume
Source: Bloomberg Symphony; FDA labels; Datamonitor; Cowen (October 2022, March 2023); GK Associates

Furthermore, new entrants will need to consider market expansion, which is not captured by order-of-entry benchmarks. In addition to capturing share from the existing standard of care, new market entrants, especially differentiated ones, often attract broader adoption for the class. This is exemplified by many autoimmune diseases, such as psoriasis. New advanced therapies (i.e., biologics, novel orals) have grown the number of patients on such therapies, more than tripling the advanced therapy penetration rate over the past decade (see Figure 4).

Given the cost of drug development and commercialization, it is critical to understand both whether a product is truly differentiated and whether the market is likely to expand in order to accurately gauge its commercial potential. Errors could have immense consequences, such as striving for a value proposition that does not resonate with key stakeholders, or deprioritizing an asset that would have been differentiated and missing out on a potential blockbuster. Over 60% of all innovative branded products approved between 2004 and 2018 failed to reach $250 million in U.S. revenues.[6] Most of these

Figure 4
New entrants, especially differentiated ones, can expand the market

Advanced therapy-treated psoriasis patients (US)
Indexed to Year 0



Unique MOAs	2 (TNF, IL-12/23)	4 (+PDE4, IL-17)	6 (+IL-23, TYK2)
Endpoint evolution	PASI 75 (primary)	PASI 75 (primary) PASI 90 (secondary)	PASI 90 (primary) PASI 100 (secondary)
Safety	No black box (decreasing number of label warnings/precautions)		
ROA/dosing	Q12W SC	Oral	

Note: MOA=mechanism of action; PASI=Psoriasis Area and Severity Index (e.g., PASI 75 is a 75% or greater reduction in PASI scores from baseline); ROA=route of administration
Source: L.E.K. analysis and directional triangulation of EvaluatePharma, Symphony, Cowen reports and claims data

products underperformed expectations, often because a team did not understand which endpoints were most important or what performance thresholds were required across these endpoints, or was not realistic about the probability of achieving such thresholds.

The Inflation Reduction Act,[7,8,9] which may incentivize companies to accelerate development given a potentially shorter drug life span, could further exacerbate companies' inability to accurately gauge their products' market potential. However, striving for faster development pathways should not come at the expense of understanding the target product profile required for commercial success. Still, many organizations are using outdated approaches to assess both internal and external product opportunities.

So, what's the solution? With hundreds of millions of dollars hanging in the balance, how should investment and attention be focused on the winners?

- **Have a clear target product profile** with both R&D and commercial input. Make sure it is based on performance thresholds across key endpoints that will enable share capture and that the R&D team feels are achievable.
- **Focus on differentiation that addresses an unmet need**, not just numerical advantages. It is critical to understand which endpoints are valued and what performance is impactful if achieved. This can only be done through open and objective discussions with physicians, payers and patients.

- **Do not rely on mechanistic rationale** as the differentiator. While a difference in binding affinity could create promise of differentiation, commercial uptake will follow only if that mechanistic advantage drives better clinical performance on endpoints that physicians feel are important.
- **Be honest about the probability of achieving the target product profile** once performance thresholds have been defined. Often teams rely on traditional probability-of-success benchmarks, which typically reflect the probability of approval but not necessarily the probability of achieving a commercially successful product profile.
- **Learn from analogs** to sense-check assumptions. For instance, looking at analogs with L.E.K.'s proprietary Launch Monitor tool would highlight that a 40% share estimate for a late-to-market product with only minor advantages in side effects physicians are not worried about should raise red flags.

If you would like to discuss these findings further, please contact lifesciences@lek.com.

We would like to thank David Knoff, Grace Mizuno and Jiayang Chen for their contributions to this piece.

Endnotes

[1]Lek.com, "First-in-Class Products for Biotech." https://www.lek.com/insights/hea/us/sc/first-class-products-biotech

[2]Nature.com, "What matters most in commercial success: first-in-class or best-in-class?" https://www.nature.com/articles/nrd4035

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EXECUTIVE INSIGHTS

Preparing for Innovation: A Maturity Framework for Artificial Intelligence in Life Sciences

Key takeaways

1. L.E.K. Consulting has developed an artificial intelligence (AI) maturity framework that can be deployed across use cases to assess the fit of AI, data availability, the strength of existing capabilities, the market environment and the extent of impact demonstrated
2. L.E.K. applies this framework to use cases within drug discovery — namely drug repurposing, drug target identification, small molecule drug design and antibody drug design — to assess the level of AI maturity
3. While some use cases (e.g. repurposing drug candidates) are more mature and have started demonstrating impact, barriers such as data availability are still being overcome in other use cases.
4. Advancements in technology, such as generative AI, are expected to lower barriers and accelerate the adoption of AI in life sciences.

Artificial intelligence has emerged as a transformative force in the life sciences industry, with a remarkable capacity to process extensive datasets, identify patterns and make predictions. AI is increasingly being used to accelerate drug discovery, optimise clinical trials and enhance patient care. These advancements hold promises from reshaping innovation and designing of life-saving therapies to shaping life sciences companies' strategic decision-making.

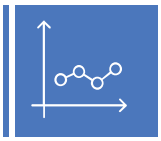
In this *Executive Insights*, we describe a framework for assessing the maturity of AI capabilities and utilisation across different use cases within drug discovery.

Framework to measure AI maturity

L.E.K. has devised a comprehensive framework to gauge the development and deployment stages of AI solutions, enabling organisations to gain precise insights into the readiness and potential of AI initiatives. Our framework considers five critical dimensions (see Figure 1) used to evaluate AI maturity (see Figure 2).

Right problem

Determines the suitability and advantages of AI solutions over traditional approaches



Right data

Evaluates current data availability, accessibility and quality

Right capabilities

Examines the available tools, platforms and expertise required for effective execution

Right market configuration

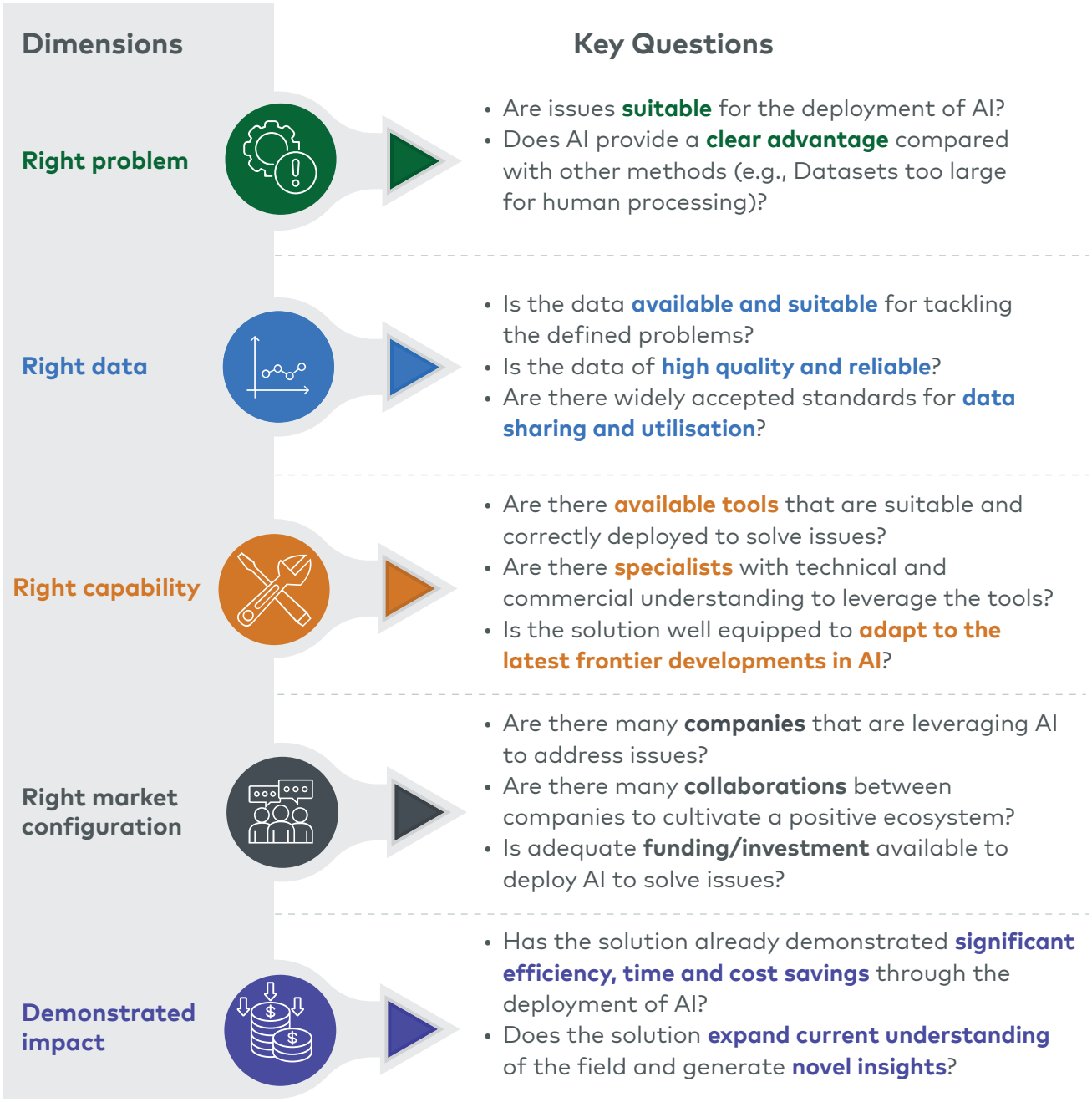
Considers the number of active players and the extent of collaboration interest from pharmacuetical companies

Demonstrated impact

Evaluates AI's ability to generate novel insights and identifies tangible successes achieved thus far

Figure 1

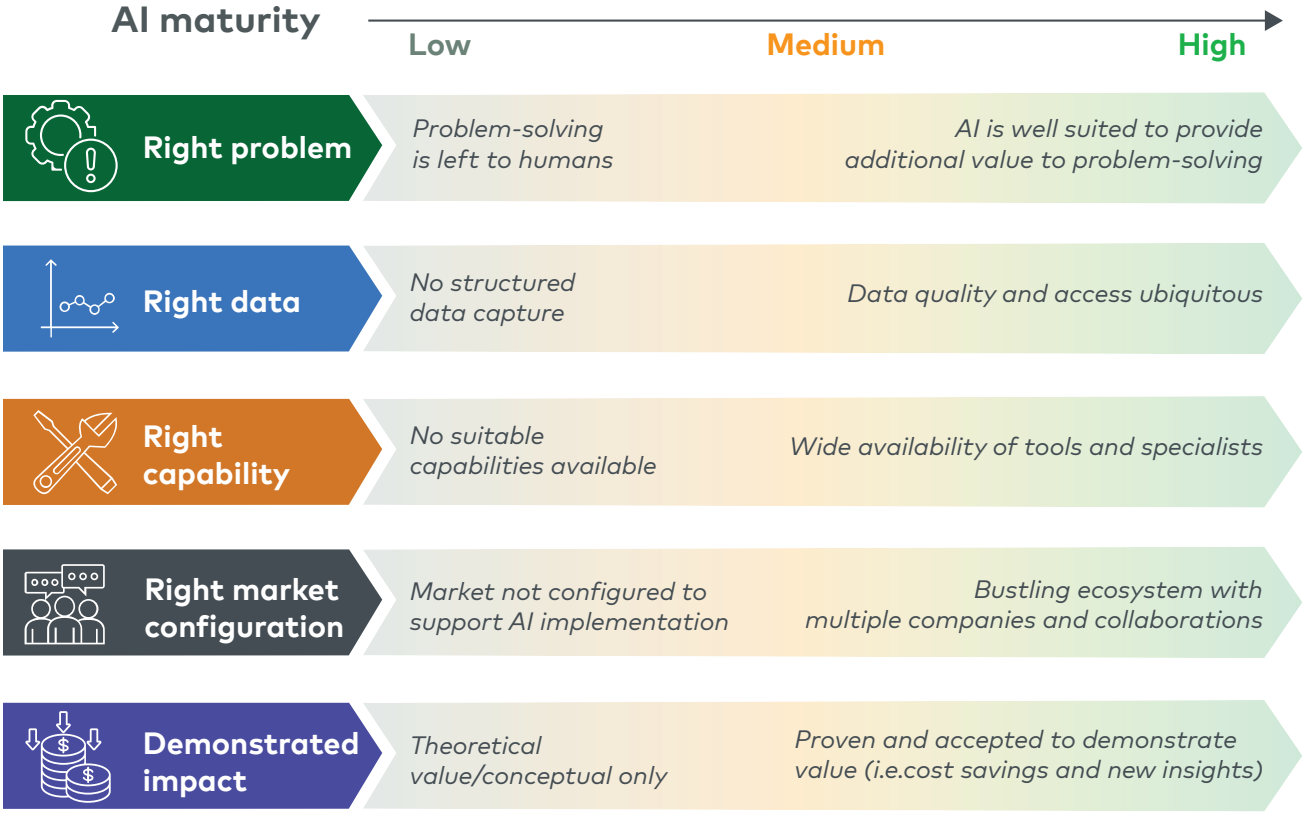
The AI use case framework



Note: the AI (artificial intelligence) maturity framework presented in other L.E.K. publications was adapted to Life Sciences use cases.
Source: L.E.K. research and analysis

Figure 2

Different levels of AI maturity and ranges



Note: AI=artificial intelligence
Source: L.E.K. research and analysis

Assessment of AI in drug discovery use cases

Four AI use cases in drug discovery have been considered to illustrate the use of the framework in assessing AI maturity (see Figure 3).

Figure 3

Four use cases for AI in drug discovery in the life sciences

	Repurposing existing drug candidates	Drug target identification	Small molecule drug design	Antibody drug design
Description	Identification of existing molecules that can bind a given target to be used in other indications	Identification of druggable targets and biomarkers	Identification and optimisation of new **small molecule** candidate medicines	Identification and optimisation of new **antibody** candidate medicines
Example companies	• Atomwise • BenevolentAI • HealX • BioXcel Therapeutics	• Insitro • Insilico Medicine • Exscientia • BPGbio • e-therapeutics	• Recursion • Valo • Nuritas • Iktos • Deepcure	• BigHat Biosciences • MAbSilico • iBio • Antiverse

Note: AI=artificial intelligence
Source: L.E.K. research and analysis

1. Repurposing existing drug candidates

The use of AI in drug discovery so far is perhaps best demonstrated in drug repurposing, where AI can rapidly identify alternative indications for existing molecules. Over 250 companies are currently working on repurposing drugs through AI, with COVID-19 having provided a unique opportunity to apply this quick and flexible approach to drug discovery.

Baricitinib, a Janus kinase inhibitor for rheumatoid arthritis, was identified as a potential treatment for COVID-19 by BenevolentAI using their knowledge graph platform. It received emergency use authorization from the U.S. FDA in 2020 for treatment of COVID-19 in hospitalised patients followed by full approval in 2022, based on the results of four randomised clinical trials.

Most compounds identified by AI repurposing approaches are still under evaluation in clinical trials. The outlook is positive: data availability and quality are expected to improve as data becomes more diverse and accessible. That should fuel efforts in this space.

2. Drug target identification

AI techniques can rapidly build molecular disease models and much more efficiently identify druggable targets and biomarkers than traditional methods. An enormous volume of biomedical data is available, although the integration of multiple unstructured datasets is challenging. AI can be employed to extract and analyse findings from unstructured datasets, such as journal articles and omics databases as well as imaging and real-world patient data. Knowledge graphs are used to identify novel connections between entities, although the capabilities of these approaches are limited by the quality of standardisation and labelling of underlying datasets.

Initial programs using AI in drug target identification have moved through discovery and preclinical development, and at least 20 drugs with novel disease-target associations identified by AI are progressing through phase 1 and 2 studies. As companies expand datasets and feed findings back into AI algorithms, increasing numbers of drugs with novel disease-target associations — or entirely novel targets — are expected to emerge.

3. Small molecule drug design

Using available chemical structure data, AI can simulate complex chemical properties or enable the design of drug structures significantly faster and more accurately than traditional methods. Within this use case, companies can use AI to screen existing chemical libraries or to generate novel chemical designs. The availability and usability of underlying datasets remain key challenges in this use case, with training sets being comparatively small compared with the full chemical space of billions of compounds. In addition, data availability varies across different target classes, with kinases and G protein-coupled receptors being the most well characterised, which limits generalisable models and the novelty of resulting drug candidates.

Individual AI-driven tools are already an integral part of the drug design process for small molecules, with larger predictive solutions undergoing iterative development. Small molecules designed using AI are significantly more common than antibodies designed using AI at this point. Clinical programs from companies such as Exscientia and Insilico Medicine are part of the first wave of AI-designed small molecule drugs undergoing phase 2 trials, the results of which are likely to begin to illustrate the maturity and future potential of this use case.

4. Antibody drug design

Antibody design is a growing use case for AI through both optimisation of existing structures and de novo candidate design. To date, few AI-designed antibodies have reached the clinic, and the more complex nature of these molecules poses distinct challenges compared with small molecule drug design — such as with the computational capabilities required to run larger models. AI models for antibody design are also limited by the availability of datasets for antibody sequences and antibody-antigen pairs. In addition, with a large proportion of training data being derived from the same libraries used for traditional antibody design approaches, many of the traditional challenges, such as balancing specificity and affinity, persist.

The ecosystem of researchers and companies focused on AI for antibody drug design is growing, with a flurry of announcements from large pharma companies over the past year disclosing innovative internal capabilities or collaborations with start-ups or big tech. Most recently, more than US$1 billion was secured by Xaira Therapeutics, which plans to initially focus on de novo antibodies, having employed researchers with experience designing leading diffusion models for protein and antibody design alongside genomics and proteomics groups. Continued collaborations between AI platforms and pharma companies, as well as an increase in standardised and open source data, are expected to grow the maturity of this use case.

Outlook: Maturity of AI across use cases

AI maturity in life sciences is a diverse landscape and varies across use cases (see Figure 4). While applications like repurposing existing drug candidates and target identification have made significant strides, others like antibody drug design are still in the relatively early stages.

Figure 4

AI maturity across highlighted drug discovery use cases

	Repurposing existing drug candidates	Drug target identification	Small molecule drug design	Antibody drug design
Right problem	High	High	High	High
Right data	Medium	Medium	Medium	Low
Right capability	High	Medium	Medium	Low
Right market configuration	High	High	High	Medium
Demonstrated impact	High	Medium	Medium	Low

Note: AI=artificial intelligence
Source: L.E.K. research and analysis

Generative AI is one of the most significant developments in recent years for AI in life sciences. The ability to autonomously generate novel molecular structures and other complex data could accelerate innovation and cost savings above traditional predictive AI systems. In June 2023, Insilico's small molecule drug (INS018_055) for idiopathic pulmonary fibrosis became the first drug discovered and designed completely by generative AI to enter a phase 2 clinical trial. Insilico completed preclinical development at only c.10% of the typical cost and in less than half the time required for traditional method

Despite challenges in data availability and algorithm optimisation, innovation and collaborative efforts will continue to drive further enhancement. As these advancements take root and AI integrates further into the life sciences ecosystem, we anticipate a substantial shift in AI maturity, unlocking new possibilities in problem-solving capabilities and deliverable impact across a wide range of use cases.

How L.E.K. Consulting can help

With AI increasingly being used to accelerate drug discovery, optimise clinical trials and enhance patient care, L.E.K.'s AI maturity framework helps to gauge the development and deployment stages of AI solutions, enabling organisations to gain insights into the readiness and potential of their AI initiatives. More broadly, L.E.K. can support AI companies with business model choices, BD/M&A, valuation, organisation design and scale-up and key strategic choices.

To find out more and for a further discussion, please contact the partners below.

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EXECUTIVE INSIGHTS

Oncology BD&L: Winning in an Increasingly Competitive Environment

Key takeaways

1. Oncology leads biopharma business development and licensing (BD&L), accounting for about 50% of global deal volume. Growing oncology pipelines provide a rich set of BD&L targets, with emerging biopharma now accounting for 60% of all oncology trials.
2. Since 2020, large pharmas have shifted to later-stage dealmaking to secure near-term, de-risked revenues in response to upcoming patent cliffs and the impact of the US Inflation Reduction Act.
3. BD&L is crucial for accessing innovation, with antibody drug conjugates (ADCs) and multispecifics now representing 35% of early-stage transactions, up from 10% in 2019. BD&L is often more viable than in-house origination of these modalities.
4. China has become a significant source of oncology innovation, contributing around 30% of all oncology licensing deals in 2023 as its R&D increasingly focuses on novel mechanisms.

Introduction

Oncology is the single largest therapeutic area for global pharmaceutical sales, accounting for c.18% of all prescription drug sales in 2023 – a substantial increase from c.13% in 2018. This growth, exceeding 10% p.a. over the past five years, has been driven largely by innovative drug launches and expanding treatment accessibility. High unmet patient needs and substantial commercial potential continue to attract a breadth of biopharma

organisations. Companies outside the top 10 oncology players now generate c.45% of all oncology revenues, up from c.30% five years ago, with small and mid-sized biopharmas carving out niches in specific tumours or treatment modalities.

Oncology thrives on innovation given the degree of unmet needs across tumour types. As a result, it dominates the global drug development pipeline, representing c.40% of all assets in clinical development. Biopharma companies of all sizes compete for the most innovative assets at all stages of drug development. Regardless of their internal capabilities, leaders in oncology rely on external innovation to supplement their internal R&D or as a sole source of pipeline assets.

In our recent *Executive Insights* focused on biopharma M&A deals, we observed that oncology represents the most significant area of M&A dealmaking. Oncology also dominates biopharma business development and licensing (BD&L), accounting for c.50% of global deal volume. Growing oncology pipelines provide a rich set of BD&L targets, with emerging biopharma now spearheading c.60% of all oncology trials, compared with 33% a decade ago. Reduced public market valuations mean many biotechs require BD&L proceeds to lengthen their cash runways in order to invest in further groundbreaking innovation.

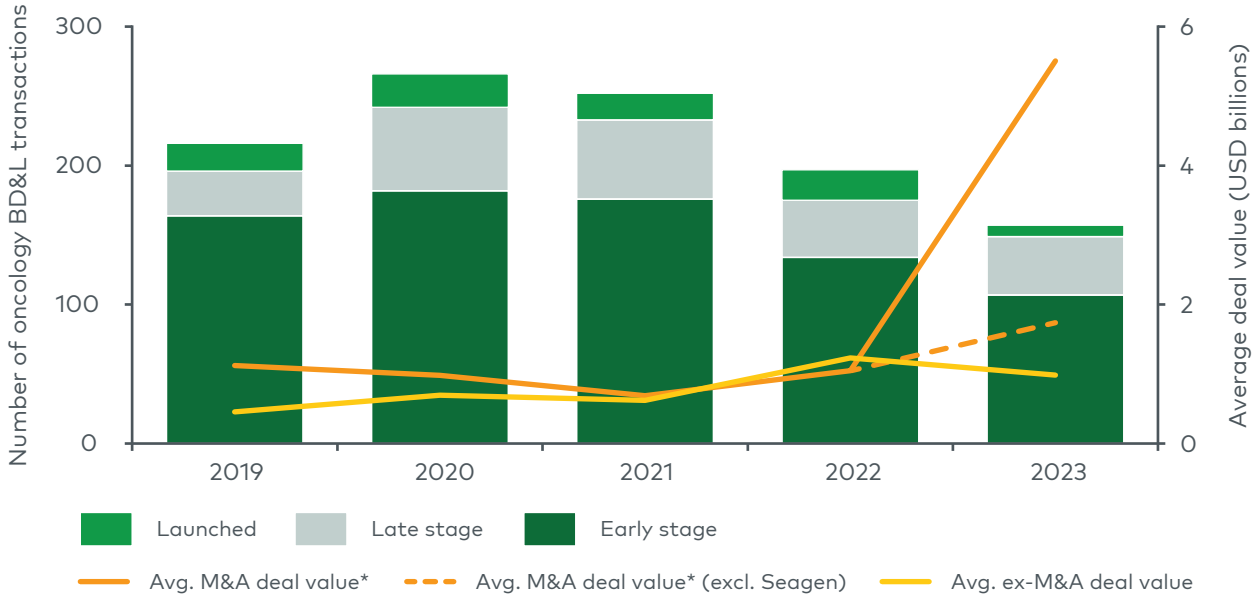
In this *Executive Insights*, we review the past five years of BD&L dealmaking in oncology and outline what it takes for small to large biopharma organisations to win in this increasingly competitive space. We have considered all global oncology deals between 2019 and 2023, including M&A, licensing, collaborations and co-promotions, and excluded deals for non-pharmaceutical products (e.g. companion diagnostics, manufacturing agreements).

A shift towards late-stage dealmaking

Oncology BD&L transactions peaked in 2020, coinciding with the highest levels of broader biotech funding, deals and initial public offerings. While the total number of BD&L transactions has decreased since 2020, larger transactions have remained resilient, particularly those of late-stage and launched assets. The average oncology M&A deal value in 2023 was higher than any of the previous four years, and 1.8x the 2019-22 average more than trebling between 2021 and 2023, even when the contribution of Pfizer's $43bn acquisition of Seagen is excluded from the analysis (see Figure 1).

Figure 1

Trends in deal volume/value (2019-23)



Notes: *Total deal value at signing, excludes deals with undisclosed values
Source: L.E.K. research and analysis of Cortellis, company investor materials and press releases

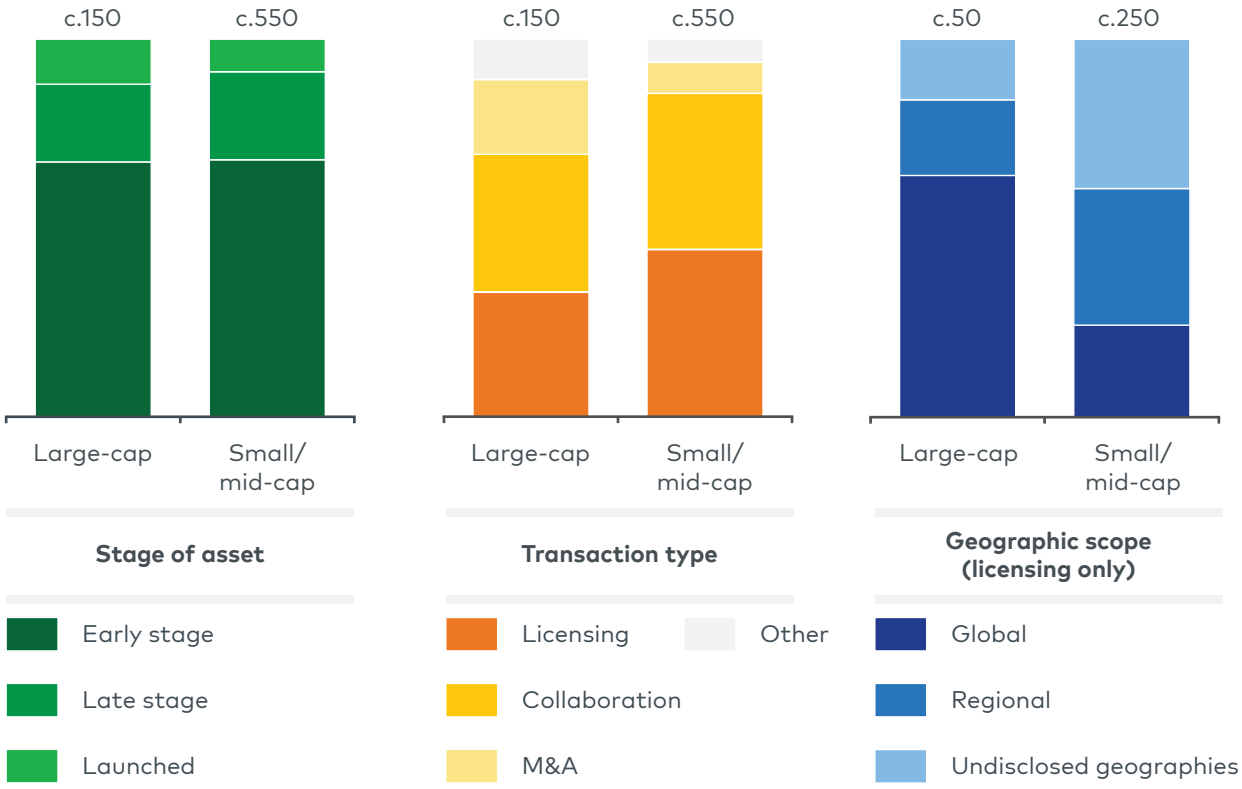
The shift to higher-value, later-stage deals highlights the preference for biopharmas to secure nearer-term revenues with higher certainty. This reflects the requirement to compensate for headwinds to inline portfolios, including impending patent cliffs and the Inflation Reduction Act in the US.

Competition for attractive oncology assets is intense across all development stages, but particularly for late-stage opportunities. The proportion of oncology deals executed by small/mid-cap buyers reached a peak of >80% in 2021. Big pharma has increased its share of deal volume in recent years, with these buyers accounting for c.35% of all transactions since 2021. Compared to their smaller peers, large-cap pharmas have a greater affinity for transacting already-launched assets, typically via M&A, with their deep cash reserves allowing them to pay the premium for de-risked assets (see Figure 2).

While deal premiums today are higher than they were a decade ago across therapeutic areas, nowhere is this more apparent than in oncology, with four whole-company acquisitions fetching premiums in excess of 200% in the past five years (2019-23). Given their financial firepower, large-cap companies opt for M&A transactions twice as frequently as small/mid-cap buyers, who opt for licensing deals in 45% of transactions. Licensing deals permit smaller buyers to transact at a regional level aligned with their existing footprint, deals for which large-cap pharmas typically have less interest.

Figure 2

Oncology BD&L transactions, by company size (2019-23)



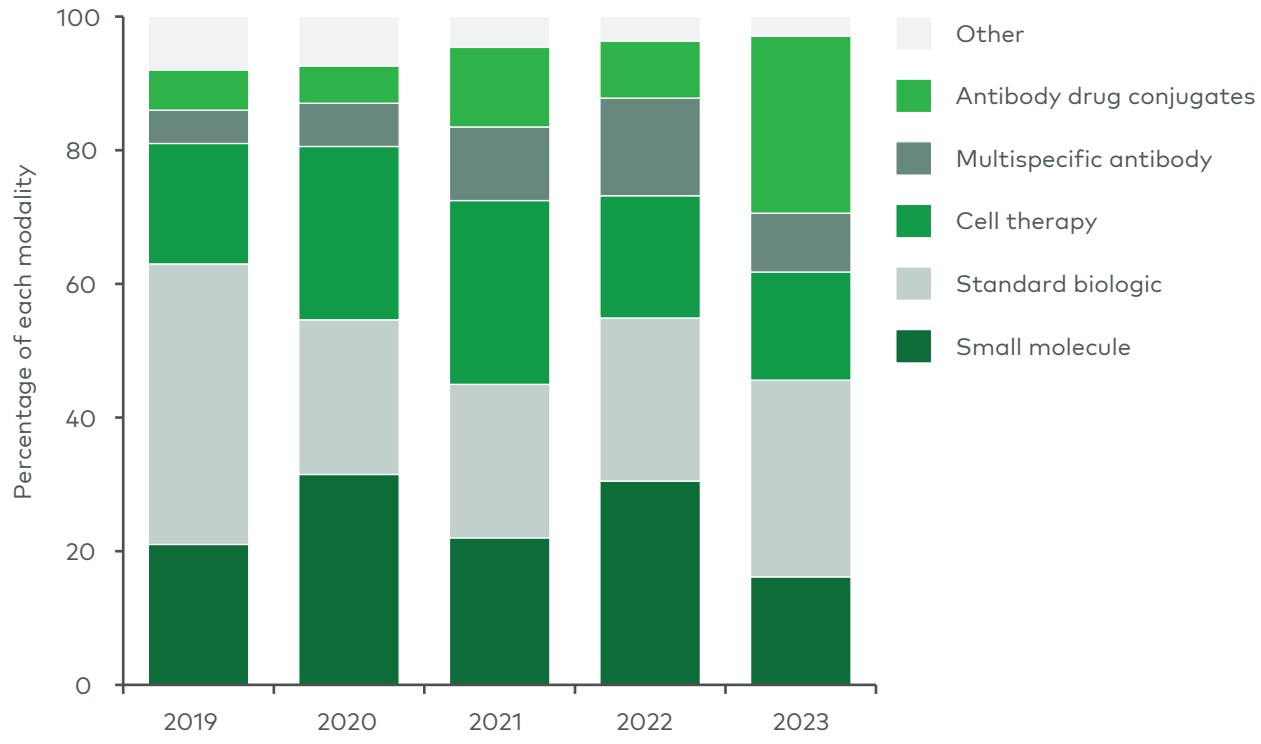
Source: L.E.K. research and analysis of Cortellis, company investor materials and press releases

The rise of ADCs and multispecifics

BD&L has become an increasingly important strategy for both large and small/mid-cap pharmas to access innovation, particularly in novel modalities where biotech companies have been at the forefront of discovery efforts. ADCs and multispecific antibodies now represent 35% of all early-stage transactions, up from only 10% in 2019 (see Figure 3). For these modalities, BD&L is often a more viable strategy than development of in-house capabilities, given the need for validated technology platforms and highly specialised expertise. Conversely, cell therapies, which represented c.25% of deals as recently as 2021, have seen a recent decline in deal share. This shift reflects growing recognition of the challenges in development, access and commercialisation of these therapies.

Figure 3

Early-stage BD&L deals, by type of modality (2019-23)



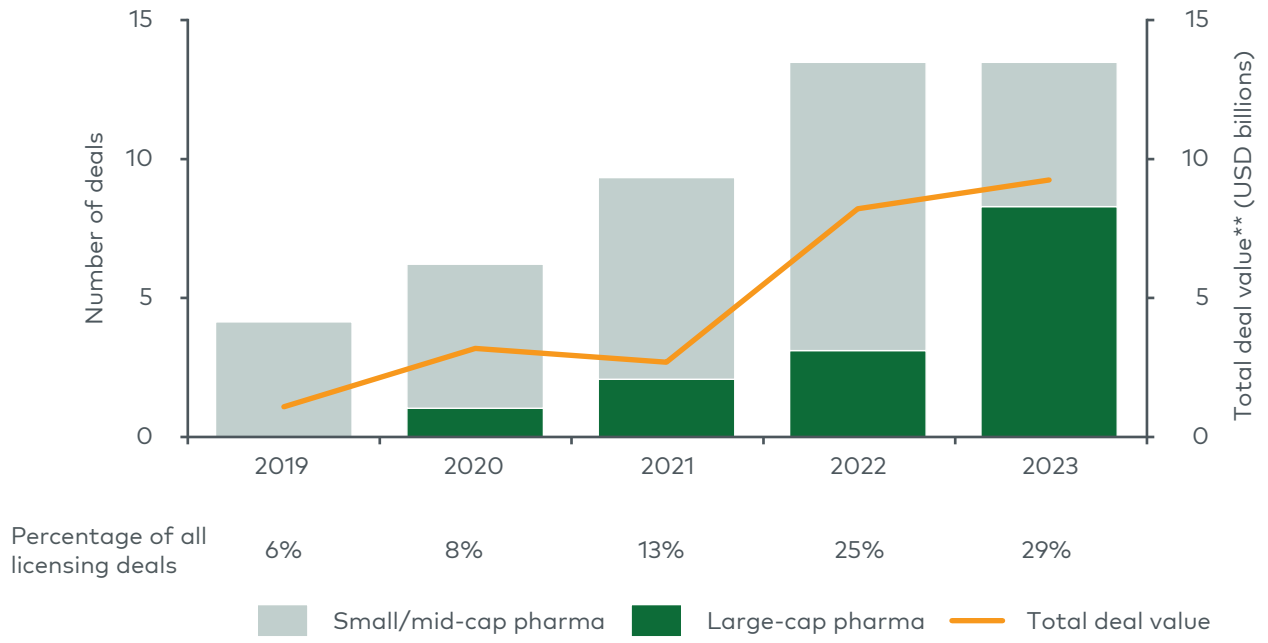
Source: L.E.K. research and analysis of Cortellis, company investor materials and press releases

China as a growing source of innovation

China has emerged as an important source of oncology innovation over the past five years, with Chinese-headquartered companies the source of c.30% of all oncology licensing deals in 2023 (see Figure 4). China has attracted both large and small/mid-cap licensees as domestic R&D increasingly focuses on novel mechanisms and modalities. Oncology has been at the leading edge of this surge in innovation, with clinical trial starts in China for ADCs and bispecific antibodies growing at compound annual growth rates of c.70% and 125%, respectively. As global biopharma accumulates experience of Chinese-led innovation, large biopharma companies have shown increased interest, culminating in a more than tenfold increase in total deal value since 2019.

Figure 4

Oncology licensing deals originating from China, by company size* (2019-23)



*Including Chinese licensors and excluding Chinese licensees; **including only disclosed deal values
Source: L.E.K. research and analysis of Cortellis, company investor materials and press releases

Conclusions and implications

The oncology transaction landscape is becoming increasingly competitive, characterised by fewer but more expensive deals commanding higher premiums. Innovation sources are evolving, increasingly coming from novel modalities and geographies. Successful execution in this rapidly evolving environment requires well-structured scouting and screening processes. Teams wishing to transact in oncology must consistently monitor the landscape and upcoming events of companies of interest. They should be ready to move quickly after key readouts to appraise the asset and approach the company with an up-to-date, attractive offer.

Success in this context demands that all biopharmas adopt robust, well-structured diligence processes to ensure they can offer their most competitive, yet still affordable, deal terms. For small/mid-cap pharmas that cannot compete with the deep pockets of large pharmas for global deals, strategic focus is crucial. This requires careful determination of specific assets, deal types and geographical areas where they can offer competitive terms. This may involve focusing on specific tumour types or call points for licensing deals in select geographies.

Anne Dhulesia and Sean Dyson are Partners in our European Life Sciences practice. They support oncology players on a number of key strategic topics: BD support (screening and opportunity evaluation), portfolio planning, R&D strategy, and commercial strategy including launch preparation. For more information or for a discussion, please reach out to the team below.

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EXECUTIVE INSIGHTS

From Niche to Widespread Use: The Turning Point for Radiotherapeutics

Key takeaways

1. Radiopharmaceuticals have the potential to transition to mainstream use, driven by their dual role in diagnostics and therapy, especially in oncology.
2. Recent commercial success with beta-emitting treatments like Lutathera and Pluvicto signal strong growth, while a rich overall pipeline increasingly diversifies towards emerging alpha-emitting isotopes and novel ligand targets.
3. Biopharma companies interested in radiotherapeutics need to carefully assess investment in the right innovation areas – potentially via M&A – alongside a subsequent build of a broader radiotherapeutics presence.
4. To support a successful launch, biopharma must consider commercial capability build-out and decide whether to in-house or outsource often complex supply chain and manufacturing.

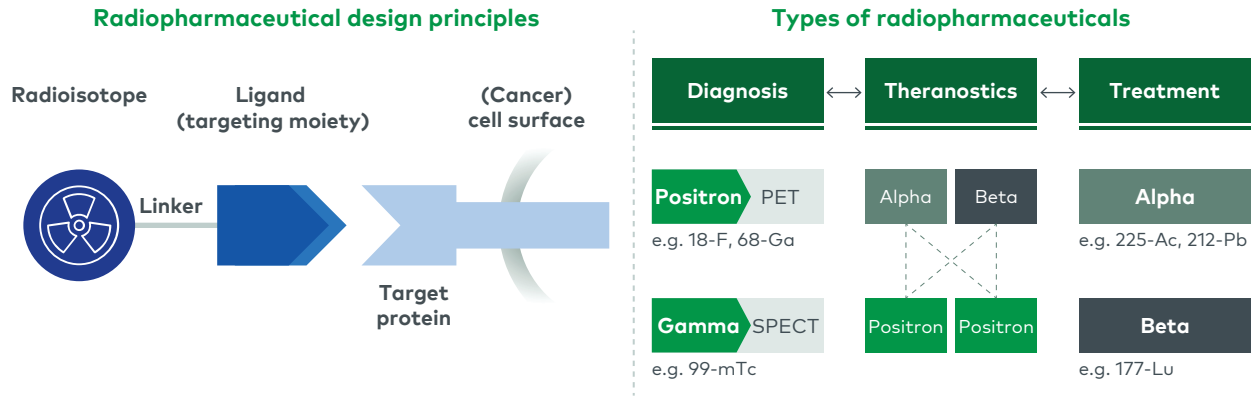
Radiopharmaceuticals are seeing increased use across diagnosis and treatment

Radiopharmaceuticals are a rapidly advancing class of compounds used for diagnosis and treatment in oncology and other therapeutic areas. Their dual capabilities in imaging and therapy have attracted substantial pipeline development and recent M&A interest. As companies seek to capitalise on precision medicine, radiopharmaceuticals have the potential to move to widespread use.

Radiopharmaceutical compounds rely on the combination of a radioactive isotope and a linked ligand (targeting moiety) which helps direct the isotope to specific cells within the body that express the marker of interest (see Figure 1).

Figure 1

Radiopharmaceutical design principles and types of radiopharmaceuticals



Note: PET=positron emission tomography, SPECT=single photon emission computed tomography
Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

In diagnostics, isotopes must emit rays that can travel out of the patient to be imaged and that have a half-life suitable for decay within hours following imaging. PET (positron emission tomography) and SPECT (single photon emission computed tomography) are leading techniques. PET uses positron-emitting isotopes like 18-F, providing high-resolution, 3D images essential for early diagnosis and monitoring of progression. SPECT, employing gamma-emitting isotopes like 99-mTc, offers an accessible yet lower-resolution alternative. The higher resolution offered through PET is commonly used for functional imaging of cancer and brain disorders, while more widely available and cost-effective SPECT sees use in cardiac imaging.

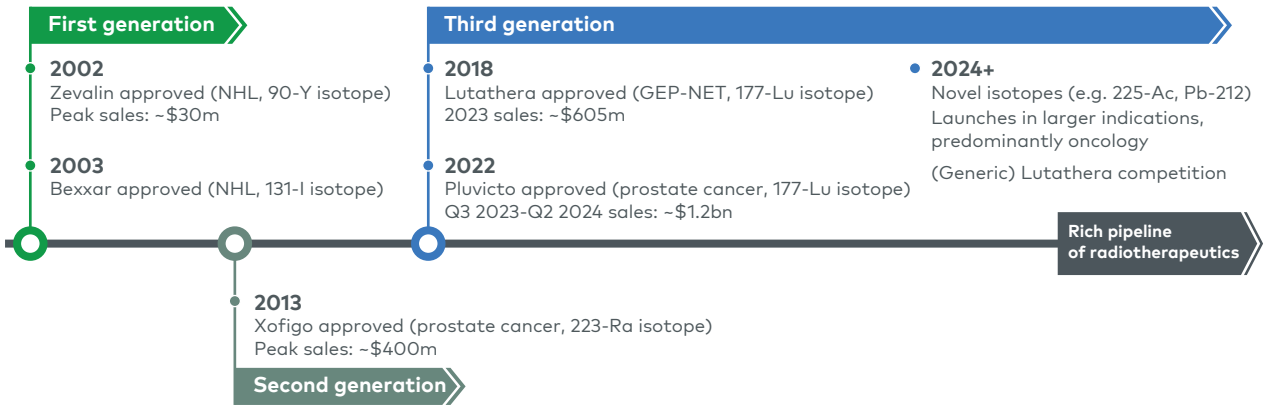
In therapeutics, direct delivery to tumour cells minimises damage to healthy tissue throughout the body. Damage to surrounding tissue is minimised by the short tissue penetration of the alpha and beta particles. This contrasts with radiosensitisers, which are non-radioactive agents that aim to make tumours more susceptible to external radiation therapy (e.g. NBTXR3, AGuIX). Treatment with radiopharmaceuticals can be achieved through alpha- and beta-emitting isotopes. Alpha-emitters (e.g. 225-Ac) deliver highly localised radiation and are ideal for targeting small clusters of cancer cells but are an emerging and less proven treatment option. Conversely, beta-emitters (e.g. 177-Lu) penetrate tissue further with lower energy, treating larger or more diffuse tumours, and are more established.

Radiotherapeutics have historically faced an uphill battle (see Figure 2). First-generation approvals faced substantial commercial challenges. Zevalin (2002, 90-Y isotope) and Bexxar (2003, 131-I isotope), launched in non-Hodgkin lymphoma, relied on isotopes with a relatively short half-life of around 2.7 days and central manufacturing sites posing geographical barriers on addressable patient populations. Physician preference for Rituxan further limited market penetration.

Xofigo (2013, 223-Ra) was the first alpha-emitter to enter the market in 2013. While it addressed many of the first-generation limitations, it has never lived up to its commercial promise of $1.5bn peak sales despite its perceived high efficacy and targeting specificity in late-stage prostate cancer – instead peaking at around $400m.[1] The asset suffered from safety concerns in combination with J&J's Zytiga and the emergence of novel non-radiotherapy options.

Figure 2

Resurgence following initial hurdles



Note: NHL=non-Hodgkin lymphoma, GEP-NET=gastroenteropancreatic neuroendocrine tumour
Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

From initial hurdles to resurgence in radiotherapeutics development

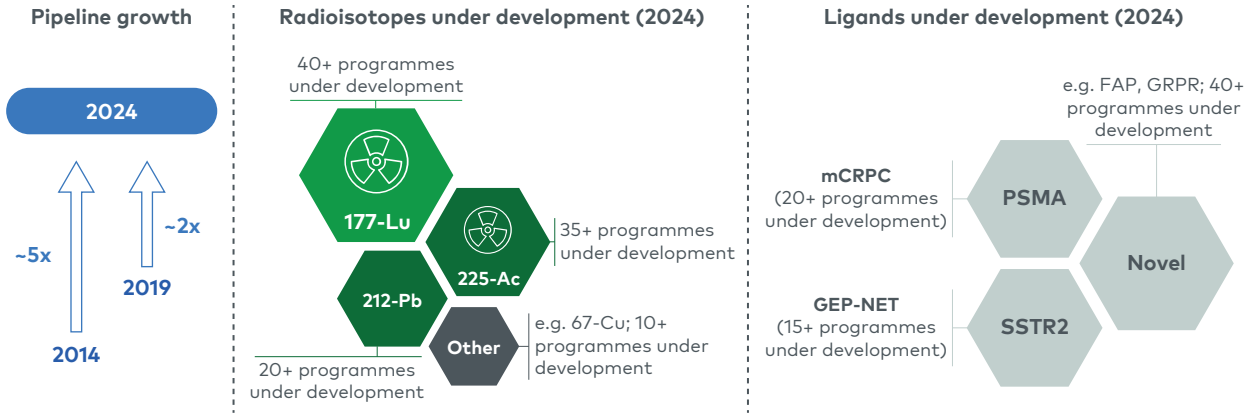
Clear commercial successes have been achieved more recently with beta-emitting 177-Lu compounds, predominantly through Novartis in mCRPC (Pluvicto, 2022) and GEP-NET (Lutathera, 2018). Pluvicto reached $345m in Q2 2024 sales,[2] with analysts expecting blockbuster status reaching close to $2bn by 2026F,[3] particularly as temporary supply constraints observed in 2022 and 2023 have been resolved with the opening of a fourth manufacturing site in Indianapolis, Indiana, in early 2024.

The recent clinical and commercial validation and the upcoming loss of exclusivity of Lutathera have spurred further sector interest. The therapeutics pipeline is particularly healthy, with over 100 programmes in development as of September 2024 (see Figure 3); the pipeline has

doubled over the past five years. Focus remains largely on oncology indications, contrary to diagnostics – where cardiology and neurology are key additional therapeutic areas.

Figure 3

Rich pipeline increasingly diversifying towards novel isotopes and targets



Note: mCRPC=metastatic castration-resistant prostate cancer, GEP-NET=gastroenteropancreatic neuroendocrine tumour, FAP=fibroblast activation protein, GRPR=gastrin-releasing peptide receptor, PSMA=prostate specific membrane antigen, SSTR2=somatostatin receptor 2
Source: L.E.K. research and analysis of company investor materials, press releases and industry reports

For beta-therapies, 177-Lu sees large late-stage activity, partially driven by the development of generic alternatives to Lutathera; multiple entrants submitted applications for approval in H1 2024. Copper-67 (67-Cu) provides a lesser-proven alternative isotope that mostly sees activity in early-stage Phase I/II development combined with de-risked ligands trialled with 177-Lu assets (e.g. PSMA, SSTR).

For alpha therapies, discussion around the optimal isotope is continuing. Despite Xofigo's first 223-Ra launch, research activity had gravitated towards 225-Ac with pipeline assets positioned as the next wave behind 177-Lu. Interest is driven by its roughly 10-day half-life and relatively manageable ability to be linked to targeting moieties. 212-Pb is, however, increasing in popularity among investigators, where a substantially shorter half-life of around 10 hours opens the possibility for optimising a dosing schedule through administration of a lower number of larger doses (fractionation) as well as balancing of adverse exposure to healthy tissue while achieving a therapeutic effect.

The industry is expanding its interest beyond PSMA and SSTR targeting ligands with the emergence of novel targets for other predominantly oncology indications. In particular, FAP (fibroblast activation protein) has seen early-stage development activity due to its theranostic potential across tumour types.

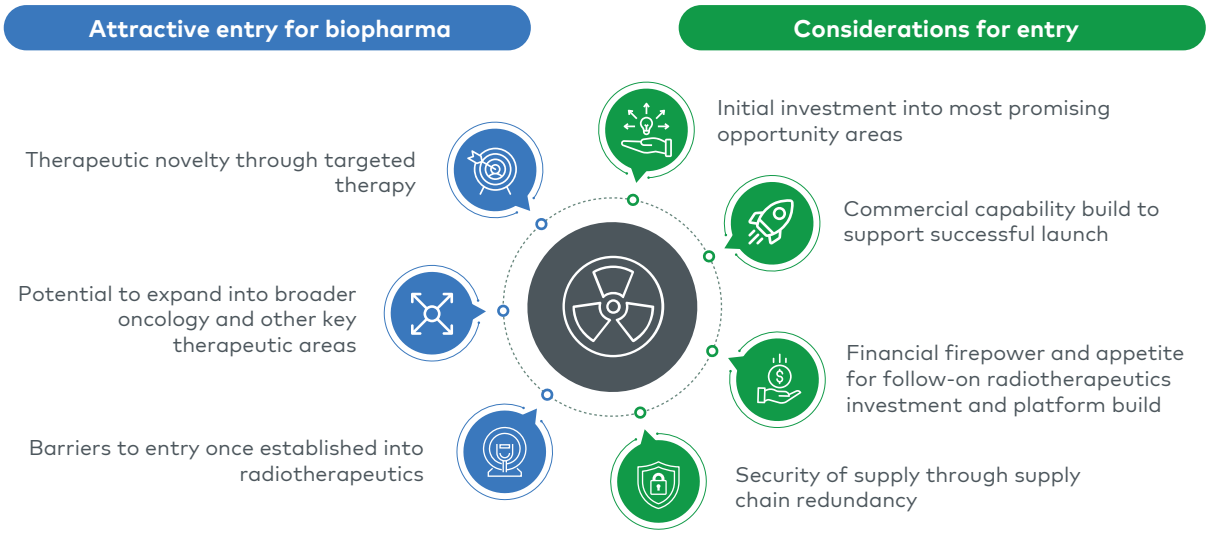
Key considerations for biopharma assessing potential entry into radiotherapeutics

As the radiopharmaceuticals sector is experiencing unprecedented interest, biopharma will need to consider key elements to succeed (see Figure 4). Initial investment in the right innovation areas – by isotope, ligand, therapeutic indication – should be carefully assessed, in addition to follow-on investment to build a broader radiotherapeutics platform. To support a successful launch, consideration must be given to commercial capability build-out, as well as decision-making regarding whether to in-house or outsource manufacturing, which itself can be quite complex. Notably, the shorter half-life of some of these radioisotopes (i.e. those that are measured in hours) will require different manufacturing and supply chain infrastructure that could significantly impact operations and financials.

M&A offers biopharma an accelerated path into radiotherapeutics and has been a preferred route in recent years for big pharma. Novartis, AstraZeneca, Bristol Myers Squibb and Eli Lilly were responsible for four of six key radiotherapeutics acquisitions announced since February 2023, with a total deal value equalling $8.6bn. Other big pharma companies, such as Sanofi, are increasing exposure to radiotherapeutics through agreements with early-stage private companies.[4]

Figure 4

Considerations for biopharma entry into radiotherapeutics



Source: L.E.K. research and analysis

M&A substrate continues to grow, as pipeline growth has been underpinned by a rising number of biotechs dedicating R&D investment. We have tracked over 70 companies with an active pipeline portfolio of radiotherapy assets. Around two-thirds are privately held, with a geographical split roughly equal between North America, Europe and Asia-Pacific.

Public small-/mid-cap companies have some cash runway, with median cash on hand at around $20m and median enterprise value at roughly $125m. Public funding surged in 2020 and 2021 due to several IPOs (e.g. Clarity Pharmaceuticals) and has since continued at a more moderate pace, with RayzeBio's IPO in 2023 as a notable exception. Similarly, private companies have typically seen a median $40m-$50m Series A or B investment as recently as the last two or three years. In 2023, radiopharmaceutical companies raised close to $1bn in private funding. These earlier-stage companies are typically driving research in novel ligands beyond PSMA and SSTR.

Selection of the right M&A target for established pharma needs to consider both the clinical and commercial potential of the portfolio as well as the target's supply chain and manufacturing capabilities. Securing redundancy in supply chains is apparent from partnership activity, with four supply partnerships between isotope suppliers and biopharma announced from January to April 2024 alone.

Biopharma will need to decide between in-house versus outsourced manufacturing. Manufacturing and supply chain improvements are likely to remain a topic of discussion and a key area of investment focus. Consideration of isotope half-lives and diverging manufacturing routes (e.g. through generators or particle accelerators) – which provide trade-offs between capital investment, ease of set-up, footprint and expertise required to run – will continue to be an area of diligence.

Conclusion

Ongoing innovation and strategic acquisitions underscore the sector's vitality and promising trajectory, representing a key turning point for radiotherapeutics to transition to more mainstream treatment.

To explore how L.E.K. can help you navigate the opportunities and challenges in radiotherapeutics, please reach out to our team. We can offer strategic guidance to set you up for success in this rapidly evolving space.

Endnotes

[1]Emanuele Ostuni and Martin R G Taylor (2023), "Commercial and business aspects of alpha radioligand therapeutics." Frontiers in Medicine, https://pmc.ncbi.nlm.nih.gov/articles/PMC9932801/#B43

[2]Novartis (2024), "Condensed Interim Financial Report – Supplementary Data." https://www.novartis.com/sites/novartiscom/files/2024-07-interim-financial-report-en.pdf

[3]Fierce Pharma (2023), "Novartis halts Pluvicto new patient starts, struggles with radiotherapy's supply amid manufacturing expansion." https://www.fiercepharma.com/manufacturing/novartis-halts-pluvicto-new-patient-starts-struggles-radiotherapy-supply-amid

[4]Sanofi (2024), "Communiqué de presse : Accord de licence entre Sanofi, RadioMedix et Orano Med pour le développement d'une nouvelle génération de radiothérapies internes vectorisées contre les cancers rares." https://www.sanofi.com/fr/media-room/communiques-de-presse/2024/2024-09-12-05-00-00-2944919; Sanofi (2024), "Communiqué de presse : Sanofi et Orano Med unissent leurs forces pour développer des radiothérapies internes vectorisées de nouvelle generation." https://www.sanofi.com/fr/media-room/communiques-de-presse/2024/2024-10-17-05-30-00-2964590

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EXECUTIVE INSIGHTS

Cash Preservation in the Biopharmaceutical Industry: Navigating Uncertainty

Setbacks happen. A clinical trial that does not hit, a Food and Drug Administration complete response letter, a delayed manufacturing scale-up or a disappointing first product launch — all are examples of events that often require additional funding in order for an emerging biopharmaceutical company to move forward.

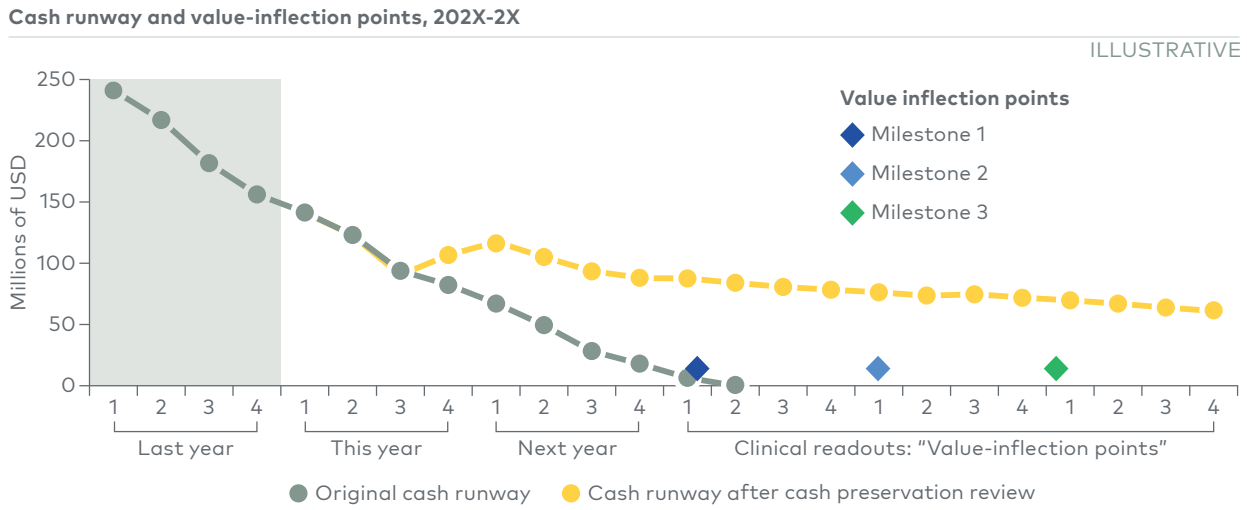
When funding is easily available and interest rates are low, as witnessed during 2020 and 2021, companies can bounce back from the negative news flow following asset setbacks. But in today's capital environment, such setbacks can be detrimental to the viability of biopharma companies, as access to capital is severely constrained. These conditions have resulted in layoffs at approximately 200 biopharma companies from January 2022 to May 2023, many of which are currently trading at a negative enterprise value.

Given these market conditions, biopharma executives need enough capital to reach the next value-inflection point and transform their progress into improved valuations. In this edition of *Executive Insights*, L.E.K. Consulting outlines how biopharma companies can extend their cash reserve to ensure operations past value-inflection points (see Figure 1).

Seeking financing options

Capital-constrained companies should explore a diverse range of options to fund their portfolios. These include traditional financial cash management options (e.g., optimize accounts payables/receivables and engage with debt stakeholders regarding payment terms and schedules) as well as sources of capital such as at-the-market (ATM) financing, private

Figure 1
Impact of cash preservation review — extension of cash runway



Source: L.E.K. research and analysis

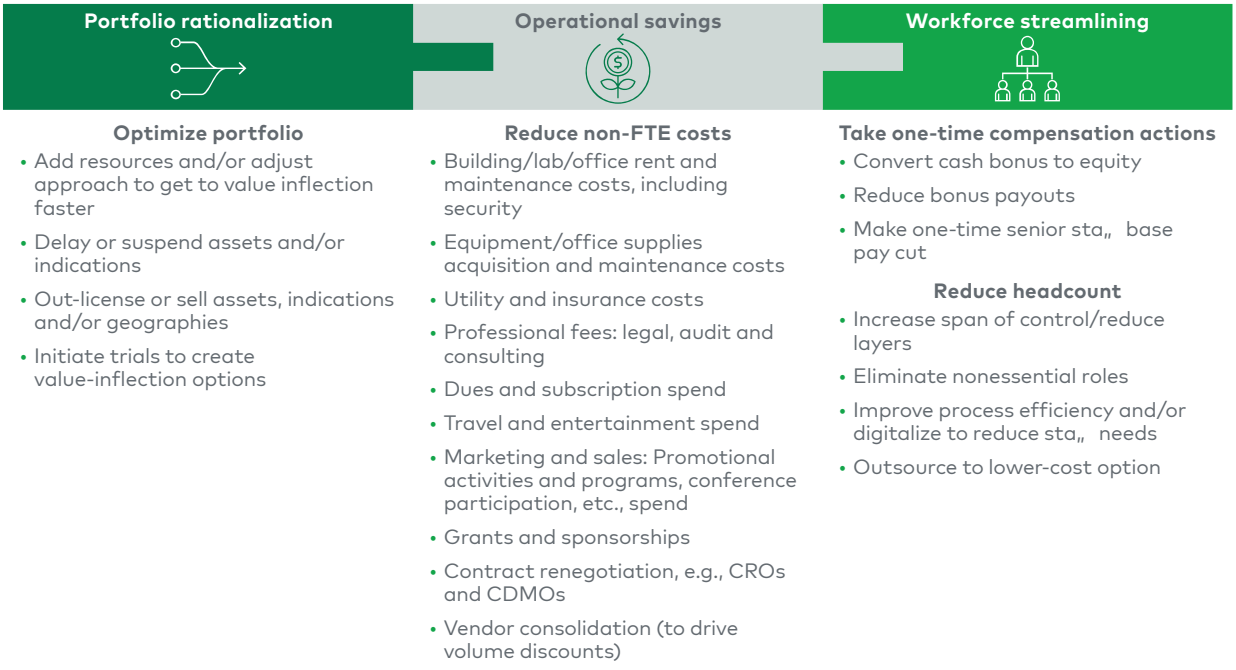
investment in public equities (PIPEs), debt financing, synthetic royalty monetization or mergers with cash-rich shell companies.

There are pros and cons to these different options, which should be carefully considered. For instance, ATM financing and PIPEs can provide faster, more flexible and opportunistic options to generate equity financing; however, depending on company and market conditions, they run the risk of diluting existing shareholders. Royalty monetization or mergers with cash-rich shell companies can provide non-dilutive capital but can take more time to execute and may relinquish potential upside. Ultimately, exploring these avenues in parallel with cash preservation options increases the likelihood that biopharma companies can avoid cash shortfalls and effectively navigate unforeseen challenges.

Implementing cash preservation

Without access to sufficient capital, biopharma executives need to migrate toward cash preservation options. The first step in this process is to determine the number of months of cash runway the company has under different portfolio scenarios, by understanding how long the cash on hand can cover the expected burn rate of the portfolio. Drawing on our experience supporting biopharma companies that "right size," L.E.K. has identified three main categories of cash preservation strategies: portfolio rationalization, operational savings and workforce streamlining — whether one-time compensation actions or headcount reductions (see Figure 2).

Figure 2
Three cash preservation categories to consider



Note: FTE=full-time equivalent; CROs=contract research organizations; CDMOs=contract development and manufacturing organizations; ATM=at-the-market financing; PIPE=private investment in public equity; MoE=merger of equals
Source: L.E.K. research and analysis

Portfolio rationalization

To make "no regret" portfolio choices, the management team — in consultation with the company's board — should confirm its corporate vision and strategy as a foundation for making portfolio decisions. At the same time, alignment on portfolio choices is an iterative process that needs to balance direct R&D investment decisions with concurrent operational savings and organizational restructuring initiatives. With this context in mind, biopharma executives can consider four alternative investment options for each program/asset in their portfolio:

1. Accelerate asset development timeline and value-inflection points
2. Delay development of an asset or indication(s)
3. Partner on an asset or a group of assets
4. Divest and/or terminate an asset or indication(s)

Delaying, partnering or divesting an asset can help free up cash but does so at the expense of reducing long-term portfolio value. As a result, before pulling these levers, biopharma

companies should first identify opportunities to accelerate the development timeline and near-term milestones for their lead asset. Examples of such accelerated clinical development strategies include:

- Negotiating a surrogate endpoint for an indication that significantly reduces the length and complexity of its clinical development program
- Exploring breakthrough designations with the regulatory agencies to shorten both the development and review periods for an asset's development
- Designing adaptive trials to speed dose optimization, adjust sample sizes and use interim analyses to rapidly assess safety and efficacy

In more financially distressed situations, biopharma companies may have to break up their portfolio by out-licensing or divesting assets in exchange for upfront cash and near-term milestones. These moves, though painful, help refocus investment on more advanced and attractive assets, preserving cash and enabling the company to survive in case of future clinical delays or setbacks.

Operational savings

Operational savings target non-full-time equivalent (FTE) cost reduction and should focus on investments that will not impact revenue-generating activities (e.g., core supply chain and commercial activities) or clinical development activities. Cost categories to consider include, for instance, office space, overhead, sales and marketing, and travel and entertainment, among others.

Operational savings need to happen across functions and subfunctions, with a focus on identifying quick wins. When prioritizing these quick wins, executives need to consider the timing of the impact of these cost reductions. Some expense line items such as travel and entertainment can be reduced immediately, while others such as a reduction in office space to save on leasing costs may require several months to realize.

Workforce streamlining

Outsourcing mix is an important lever for streamlining costs related to FTEs. By strategically identifying which functions can be effectively and economically outsourced, biopharma companies can preserve cash without compromising essential operations. There are no one-size-fits-all solutions, but often functions such as manufacturing and supply chain, clinical operations, information technology, human resources, and legal can be outsourced to access cost savings, specialized expertise and streamlined processes. These outsourcing initiatives

enable biopharma companies to optimize their resource allocation around the most valuable internal activities while preserving valuable talent and expertise.

Beyond outsourcing more actively, biopharma companies may have to consider reducing the scale of their organization to preserve cash in order to reach the next value-inflection point. In doing so, executives need to take a systematic approach to evaluate how many FTEs to reduce and determine where FTE reductions should come from. To determine the number of FTEs by function to include in a reduction in force (RIF), biopharma companies need to combine external benchmarking to provide insights on required FTE ranges with a bottom-up, iterative internal organization assessment. Using these different inputs, leadership can set RIF targets by function and communicate final targets to each functional head, with an eye on preserving the talent pool and maintaining company morale through the restructuring. Once it has been verified that budget targets are met and the company can still deliver on its revised portfolio investment strategy with planned FTE reductions, implementation planning should begin.

Implementing cash preservation initiatives

The final and most challenging step of a cash preservation effort is implementing cost reductions with the least amount of disruption to ongoing operations. It is key to preserve the link between the enterprise strategy and the forthcoming cost-reduction actions to avoid too much disruption in the equity narrative of the company and investor expectations.

Successful execution requires elements of traditional change management to maintain company performance. To ensure alignment and timely execution of cost-reduction actions, instituting a project management team is a critical step. This team should be composed of cross-functional individuals who can accelerate implementation and drive ownership of the following activities:

- **Deliver direct and consistent messaging:** Clearly define the desired end state and share objectives broadly with consistent messaging and anticipation of questions
- **Identify interdependencies:** Different cash preservation options/initiatives can impact each other. For example, too-steep headcount reductions could impact the ability to move a pivotal trial forward or delay a tech transfer. The project management team needs to identify these linkages before selecting the recommended initiatives
- **Follow a detailed plan:** Leverage preprepared material to minimize communication hiccups
- **Prioritize talent planning:** Identify talent at risk, and review retention options

- **Establish implementation metrics:** Organize function efforts to align with key value drivers and establish key tracking metrics as well as key functional interdependencies
- **Identify and mitigate key risks:** Work to mitigate risks to the organization's image or potential cultural risk from an RIF, e.g., resentment if there is a perceived different impact by function or geography

As implementation begins, a detailed tracker should be maintained to ensure effective execution and facilitate providing progress updates to leadership.

The way forward

In these uncertain times it is critical for biopharma executives to consider the following questions:

- How much cash is needed to reach near-term inflection points?
- What are the financing options to extend the cash runway of the company?
- Are there portfolio rationalization options that save cash while preserving value?
- Which operational savings and workforce streamlining options could be considered?
- How does the company execute and track progress on these cash preservation initiatives?

We hope that the recommendations outlined in this *Executive Insights* will enable biopharma leaders to address the questions above (and others) in order to adopt the right strategy to build a bridge to less-dilutive future equity offerings after reaching transformative clinical milestones.

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