Feature

Does pharma R&D need a strategic reset? Adapting to a changing US landscape

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R&D productivity has long challenged research-based pharmaceutical companies, raising concerns about the sustainability of their research-driven business models. These firms have traditionally relied on the U.S. as a stable hub for biomedical innovation, skilled talent, and high-price markets—supporting the biotech-leveraged pharma company (BIPCO) model However, recent geopolitical shifts—especially under the new Trump administration, including FDA budget cuts, reduced U.S. research funding, and pharmaceutical tariffs—are destabilizing this foundation. The once-reliable "safe harbor" is no longer secure. As a result, pharma R&D now faces strategic risks beyond its prior scope. With the weakening of the U.S.-centered innovation model, companies must rethink R&D pipelines, secure key technologies, maintain global clinical networks, and adjust supply chain and tax strategies. The viability of the current R&D model—rooted in U.S. leadership and premium markets—is now uncertain, requiring urgent strategic realignment.

Keywords: Pharma; R&D; R&D model; drug discovery; innovation; biotech; transformation; geopolitics; biomedical talent; budget cuts

FEATURE

Introduction

The industry structure for research-based pharmaceutical companies is characterized by relatively stable elements, such as competitive stability, few new market entrants, generics, and biosimilars as substitution products, limited to moderate bargaining power of suppliers and customers, and, in Porter's terms, a strong regulatory force in the form of high approval barriers and quality standards.[(p1),(p2)] This structure served as a stabilizing anchor, allowing companies to operate in a relatively low-dynamic environment. The main source of change typically derives from complexity in science and breakthroughs in technology, rather than from new competitors or new rules of engagement. The Coronavirus 2019 (COVID-19) pandemic temporarily created unique challenges as a result of geopolitical shifts and nationalist protectionism, while also driving record-high investments in biotech.[(p3)]

This industry structure has also had a 'side effect': low research and development (R&D) productivity, defined as the return-on-investment rate of R&D,[(p4)] which has been the most important challenge for the pharmaceutical industry to date.[(p5)] For instance, in 2021, public and private investors collectively spent US$276 billion on pharmaceutical R&D, an effort increasingly supported over the years by steadily rising public-sector innovation funding.[(p6),(p7)] That same year, the US Food

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and Drug Administration (FDA) approved 50 new drugs.[p8] At the very least, the insufficient R&D output and the related low R&D efficiency have raised questions about the sustainability of the business models of some of the leading pharmaceutical companies.[p9],[p10]

This has led most leading companies to reshape their business model toward greater external innovation, what is now referred to as the biotech-leveraged pharma company (BIPCO) model.[p11] In doing so, leading pharmaceutical companies significantly impact biotech through licensing, venture capital/equity investments, co-development agreements and acquisitions, creating mutual business model support.[p12] In parallel, biotech innovators have increased their share of new drug approvals, particularly in orphan drug niches, benefiting from FDA incentives, such as tax credits and advisory support.

At the same time, the global pharmaceutical industry has profited from a growing and relatively stable US market, in terms of R&D investments, pricing, and global market relevance,[p13],[p14],[p15] supported by a policy environment that promoted basic research, drug discovery, clinical research, and the US biotech industry.[p6],[p16]

Today, the previously stable industry structure is increasingly under pressure, raising the question: what are the most pressing challenges? Ongoing shifts are disrupting the system and putting traditional R&D strategies to the test.

For example: (i) US science agencies canceled over 1000 grants in the first quarter of 2025[p17],[p18],[p19]; (ii) President Donald Trump announced tariffs on pharmaceutical products[p20]; (iii) Harvard University faces a US$2.4 billion cut in grants and enrollment restriction for international students.[p21] This particularly affects Harvard, given that, in 2024, federal grants of US$686 million accounted for most of its research funding and 11% of the total revenue of the university[p21]; (iv) President Trump issued an Executive Order on drug pricing, stating that US patients should be able to access medication at prices comparable to those in other developed nations [Most-Favored-Nation (MFN) status]; currently, prices in the USA are approximately three times higher than in comparable countries[p22]; (v) Members of the Alliance for mRNA Medicines reported that shifting US policies, particularly regarding grants and funding, have had a negative impact on mRNA technology development.[p23] As discussed in the international press, Robert F. Kennedy, Secretary of Health and Human Services (HHS), canceled US$766 million in funding from the Biomedical Advanced Research and Development Authority (BARDA) to Moderna for the development of an mRNA-based bird flu vaccine; and (vi) HHS also announced that it would cancel contracts with the scientific publisher SpringerNature, because of its high access fees and additional charges for open-access publishing [p24]

These are some examples that illustrate how the previously stable industry structure is being disrupted. The 'America First' rhetoric of the Trump administration was more than just a campaign slogan: it represented a broader paradigm shift. Protectionist US trade policies, budget pressures, reduced public funding, or National Institute of Health (NIH) grant rejections are challenging longstanding assumptions about the access to basic research knowledge, origin of innovation, availability of talent pool, as well as location and structure of pharmaceutical R&D (Table 1):

FDA budget cuts could negatively impact its capabilities,[p25] particularly its regulatory capacity and scientific excellence, which could trigger a cascade of further consequences, such as: (i) reduced support for drug sponsors throughout the regulatory process; (ii) slower approval of clinical trials; (iii) delays in drug development; and (iv) postponed launches of new drugs. A freeze or decline in funding for US-based research, currently supporting 646 000 researchers through federal grants, would mean unreimbursed work, uncertainty for future research at leading institutions, and blocked early career paths, potentially leading to a brain drain from the USA.[p17],[p24] Funding cuts and tariffs might impact the biomedical job market in the USA directly and indirectly, because institutions such as the NIH, Center for Disease Control and Prevention (CDC), and FDA, as well as top research institutions and universities, will need to adapt to the new financial framework conditions,[p17],[p26] which, in turn, weakens the R&D ecosystem in the USA. Cuts in public research funding could also lead to: (i) a future decline in relevant foundational biomedical knowledge; and (ii) fewer publicly funded early-stage discoveries, both of which could negatively impact the innovative capacity of the pharmaceutical industry. This is particularly concerning given that public research institutions and biotech companies, most of which are spin-offs from universities, contribute significantly to the innovative potential of leading pharmaceutical companies[p11],[p27]; one example is the development of mRNA vaccines during the COVID-19 pandemic.[p28] Although a few biotech innovators, such as Vertex, have become established players,[p29] most other biotech firms have yet to develop sustainable business models. Shifts in institutional funding, advantages for orphan drug development, or changes in FDA support could threaten their future success. Lower drug prices could lead to reduced revenues for biotech and pharmaceutical companies, limiting their capacity to invest in R&D,[p22] potentially negatively impacting the leading role of the USA in biomedical science and breakthrough technologies [p30]

This new reality raises some existential questions for research-based pharma companies: (i) how should the R&D organization be positioned in the future within this dynamically changing environment? (ii) How could a sustainable R&D pipeline be developed if the innovation potential of the US-based R&D ecosystem declines? (iii) How could breakthrough technologies and competencies be secured if access to US-funded research and top-tier US talent becomes uncertain? And (iv) How can the current US-centered clinical trial infrastructure be preserved in the face of rising protectionism?

These emerging questions converge into one key strategic question: can the established business model of leading pharmaceutical companies continue to be viable? That is, a model that relies heavily on value creation driven by the US-based biotech and top research institutions, essentially the innovation potential of the US-based biomedical R&D ecosystem, while its value capture mechanism is rooted in an open, high-price U.S. market.

Key action points arising from the changing industry structure

Regardless of the fact that pharma executives are seeking ways to respond

TABLE 1

US domestic policy shifts and their potential impact on pharmaceutical R&D

Policy measure	Potential effects	Potential impact on pharma R&D	Refs
FDA budget cuts	Reduced FDA regulatory support for drug sponsors Reduced excellence in regulatory science and innovationSlowdown in the assessment and approval of clinical trials	Delays in the development and approval of drug candidates and new medications, reducing the effective patent-protected commercialization time	(p25)
Reduced public research funding (e.g., NIH, universities)	Reduction in number of publicly funded early-stage discoveries/start-ups Blocked early careers Brain-drain as scientific talent relocates to better-funded and more stable regions, such as EU and China	Decline in relevant foundational biomedical knowledge in US R&D ecosystem Reduced knowledge spillover from US universities to biotech and pharmaceutical companies Reduced biomedical talent pool Fewer biotech spin-offs from US universitiesDecline in pharmaceutical innovation potential, given that public research institutions have crucial role in driving industry R&D	(p18), (p19), (p21)
Enrollment restrictions for international students	Less international talent/students in US academic system	Reduced biomedical talent pool	(p21)
Challenged private sector R&D incentives, such as tax credits and grants	Startups and smaller biotech firms rely on these incentives to operate effectively with limited financial resources	Some parts of innovative biotech could break away from value creation chain of large pharma	(p23)
Tariffs on pharma products	Increasing costs for labware and scientific/experimental instruments	In combination with reduced funding, higher costs lead to diminished innovation potential of public research institutions Potentially negative impact on US biomedical job market	(p20)
Comparable pricing schemes (MFN status)	Reduced revenues of biotech firms and pharma companies	Limited capacity of biotech and pharma to reinvest in R&D and therapies Reduced innovative capacity of US R&D ecosystem	(p22)

diplomatically to changes such as the threatened reduction in drug prices in the USA and to adjust decisions accordingly, changes in the industry structure make it necessary to thoughtfully address four strategic domains[(p31),(p32)]: (i) R&D model; (ii) innovation sourcing; (iii) regulatory compliance; and (iv) organizational flexibility.

First, the R&D model of leading pharma companies is more fragile than previously recognized, particularly due to its reliance on innovation and technology from US-based biotech and NIH funding,[(p11),(p27)] and clinical trial networks in the USA.[(p33)] Thus, companies must assess the resilience of their R&D units not only in face of the R&D productivity challenge, but also by realigning and restructuring their R&D ecosystem in the face of geopolitical dynamics. It is essential to understand the potential impact of US institutional budget cuts and FDA slowdowns on academic and research institutions, other industry players, such as biotech, funding sources, and collaborations networks.

At the same time, pharmaceutical companies must evaluate whether a centralized or diversified R&D model, such as a US-centered hub versus transition to a more globally distributed R&D network, offers greater long-term sustainability in terms of efficiency and effectiveness. It also raises questions about the potential to strengthen strategic partnerships with research clusters in Europe, Asia, and emerging markets.

Second, in terms of innovation sourcing, pharmaceutical executives must address fundamental questions, most notably, determining the optimal balance between internal and external innovation. This also involves assessing the extent to which their R&D output depends on US-based biotech companies, which, in turn, often rely on US academic institutions and NIH-funded research, and strengthening of internal innovation capabilities, particularly in high-risk areas, such as cell and gene therapy.

For instance, it is worth questioning how an increasingly external innovation sourcing can be continued under a protectionist US policy: (i) will the focus shift back to internal R&D? (ii) Can external innovation be sourced from other (non-USA) regions? Or (iii) will companies focus solely on the USA as the future geography of innovation?

In this context, and as recently reported in the press, AstraZeneca is considering listing the company on a US stock exchange and potentially relocating its headquarters to the USA. In our view, this could, on the one hand, reflect a strategic response to postpandemic austerity measures in the European Union (EU) and the UK (such as price cuts and rebates), but may also represent a direct reaction to recent industry structure changes. Which of these interpretations is ultimately correct is debatable; however, it clearly signals that companies are fundamentally reassessing how to position themselves for the future in a rapidly evolving industry landscape.

Third, within the strategic domain of regulatory compliance, regulatory agility is emerging as a key competitive advantage in the current volatile policy landscape. To navigate this complexity, pharmaceutical companies need to build dynamic capabilities in policy monitoring and governmental affairs, enabling them to stay ahead of geopolitical and regulatory changes rather than merely reacting to them. Furthermore, they need to develop flexible regulatory strategies that can adapt to slower FDA processes or diverging international standards. These strategies should also enable adjustments of commercial fore-

casts to account for extended regulatory lead times and their implications for project portfolio valuations, time-to-market analysis and future revenue streams.

Finally, in the context of organizational flexibility, many of the emerging changes and potential threats are too critical to the value creation of a company to be managed solely at the operational level. The strategic realignment and organizational flexibility require active engagement from executives. Strategic plans must fully account for geopolitical and policy-related risks, and R&D organizations, similar to a breathing organism that inhales and exhales flexibly as needed, based on a stable internal R&D organization, must be ready to either proactively shift R&D activities abroad or respond effectively to mandates for re- or near shoring. In this context, one could envision a continuation, and even intensification, of a recent trend, in which leading pharmaceutical companies increasingly outsource late-stage development activities to external clinical research organizations (CROs). At the same time, they focus their internal knowledge, skills, and competencies on research to early development (RED), operating as a 'breathing organization'. This approach allows them to flexibly and cost-efficiently acquire the resource-intensive late-stage activities required for regulatory approval from external partners, thereby enhancing overall R&D efficiency.

Better to invest in strategic resilience now than losing competitiveness later

If additional price reductions, reportedly up to 80%, were to occur in the US market, this could have catastrophic effects on most of the leading pharmaceutical companies, because they generate most of the revenue in the USA.[p34] Although there are also perspectives and approaches, particularly regarding high-priced anti-cancer drugs, that could reconcile high R&D costs with affordability and profitability,[p35] it is recommended that companies invest in strategic resilience.

What is required now is a dynamic R&D strategy that is grounded in an open R&D model, built on flexible innovation sourcing, and driven by regulatory agility and organizational flexibility. To this end, companies are advised to: (i) acknowledge the complexity of the current situation and seek a deep understanding of the change drivers; (ii) develop forward-looking strategic R&D positions that, for example, anticipate the potential implications of MFN price transparency on international product launches, and assess how this might affect RED priorities as well as the future strategic importance of non-US markets; (iii) adapt the R&D business model to reflect industry dynamics, align with the new reality, and potentially enable greater diversification; and (iv) understand the opportunity costs of inaction, and the implication for long-term competitiveness.

In detail, this means that geopolitical dynamics, domestic fiscal policies, and evolving regulatory landscapes are no longer isolated forces: they are closely interconnected and have a significant impact on pharmaceutical R&D. Thus, R&D policy is no longer merely operational: it has become a critical strategic risk. Companies must develop holistic, scenario-based, and flexible/agile ('breathing') strategies to navigate disruption effectively. These scenarios should go beyond theoretical planning and address actionable priorities, such as investment decisions, resource allocation, partnerships, and comprehensive risk management.

Strategic resilience in R&D includes: (i) building a core R&D organization capable of independently addressing emerging technological breakthroughs; (ii) forming strategic partnerships with academic institutions outside the USA; (iii) if not already in place, expanding R&D operations in the EU and Asia-Pacific regions; and (iv) investing in digital infrastructure to support a 'breathing' R&D organization, for example, through decentralized and flexible clinical trials. These actions will strengthen the capability and innovation base of R&D organizations while reducing reliance on a single geography or R&D ecosystem.

Finally, inaction or the inability to adapt to the new norm will come at a high cost. Regulatory setbacks, disrupted trials, and supply chain breakdowns not only cause delays, as already witnessed during the COVID-19 pandemic, but also lead to reduced competitive advantage, shorter commercialization time, potential revenue losses, and diminished investor trust. Therefore, it makes sense to invest in strategic resilience, before a potential next wave of policy disruption leaves companies unable to act.

Concluding remarks

In summary, there are increasingly evident signs that a new political and economic era is unfolding, both in the USA and globally. This fundamental shift demands that pharmaceutical companies reassess their strategic dependencies/direction, question longstanding assumptions, and embrace transformative change. This is not about improving R&D productivity, which remain a big challenge, or refining existing R&D strategies. It calls for a profound rethinking of how value is created and captured through R&D on a global scale. The decisions made today will determine the ability of companies to gain a competitive edge in the highly dynamic environment of tomorrow, ultimately leading to stronger economic performance. Organizations that have sufficient dynamic capabilities to proactively adapt to change and excellent absorptive capacity to search for innovation and translate new knowledge into commercial value will be best positioned to thrive during this period of transformation. These companies will not only navigate these dynamic times effectively, but also grow faster and emerge as the next generation of global leaders in drug discovery and development.

CRediT authorship contribution statement

Sebastian Kwisda: Writing – review & editing, Writing – original draft, Conceptualization. **Malte Kremer:** Writing – review & editing, Writing – original draft. **Niels Sievertsen:** Writing – review & editing, Writing – original draft. **Oliver Gassmann:** Writing – review & editing, Writing – original draft. **Dominik Hartl:** Writing – review & editing, Writing – original draft. **Alexander Schuhmacher:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Investigation, Conceptualization.

Data availability

No data was used for the research described in the article.

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