CRA Charles River Associates

Europe's pharmaceutical innovation gap: An assessment of missing and delayed regulatory approvals compared with the US and China (2016–2025) and implications for Germany

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Executive summary

Europe's position as a location for pharmaceutical innovation is weakening in both the number of new regulatory approvals and the timing of approvals. Between 2016 and 2025, a substantial share of novel medicines approved in the United States (US) did not obtain authorisation from the European Medicines Agency (EMA) and therefore are unlikely to reach patients in Germany. At the same time, global 'first approvals' are shifting away from Europe, while China's National Medical Products Administration (NMPA) is becoming a more prominent early approval jurisdiction.

The German Association of Research-Based Pharmaceutical Companies (vfa) commissioned Charles River Associates (CRA) to quantify this widening innovation gap between Europe and comparator markets, particularly the US and China. This innovation gap is defined as the difference between innovative medicines authorised in comparator markets and those authorised in the European Union within a comparable time frame. The analysis focused on regulatory approvals, with particular attention to implications for Germany.

CRA examined novel medicines first approved between 2016 and 2025, drawing on regulatory approvals and (where available) submission and review timing. The dataset focuses on new molecular entities, biologics and advanced therapy medicinal products deemed innovative by relevant agencies; generics, biosimilars and line extensions were excluded.

Key findings

The innovation gap is large and driven mainly by non-submission:

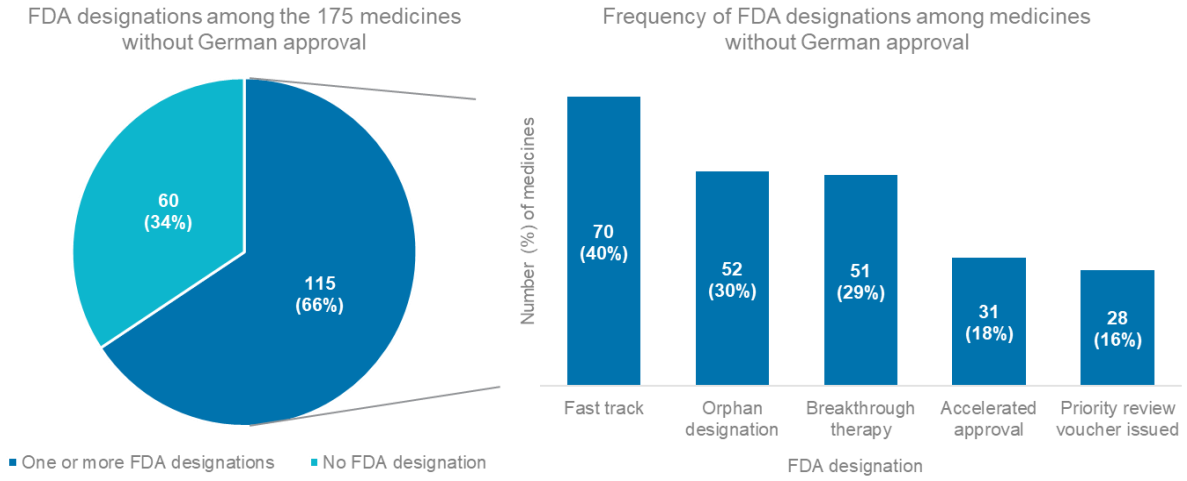
1. **A substantial share of innovations approved in the US are not approved in Germany:** Among 526 medicines approved by the US Food and Drug Administration (FDA) from 2016 to 2025, 175 (33%) lack approval in Germany and 193 (37%) lack EMA approval. Only 333 (63%) received approval from both the FDA and EMA. Germany's national authorisation route adds just 18 medicines (3%) beyond EMA approvals, underscoring that Germany cannot offset a Europe-level regulatory gap through national pathways.

Figure 1: Comparison of US novel medicine approvals to Germany, inclusive of national authorisations (2016–2025)

*An additional 33 medicines with EMA, but not FDA, approval have been omitted from the Germany column to allow comparison against the US as a baseline. Source: CRA (2026)

2. **The missing products are often high-value medicines:** Of the medicines lacking approval in Germany, 66% have at least one FDA designation associated with high therapeutic relevance (e.g. fast track, breakthrough therapy, orphan status, accelerated approval). In addition, 16% received priority review vouchers (including rare paediatric disease vouchers), suggesting that many 'missing' medicines are high-value innovations.

Figure 2: FDA designations for the 175 medicines lacking approval in Germany (2016–2025)



Source: CRA (2026)

3. **Non-submission is the primary driver:** Of FDA-approved medicines without German authorisation, 117 of 175 (67%) were never submitted to the EMA. Only a smaller share reflects pending reviews, withdrawals or negative outcomes. Importantly, where companies intend to seek EMA approval, they typically do so quickly: among products with FDA approval first, 89% that eventually obtain EMA approval do so within two years. This implies that medicines not filed in that window are unlikely to reach German patients.

Global dynamics: Europe is getting fewer 'first approvals' as China rises

Across the US, the European Union and China, 711 novel medicines received a first approval in 2016–2025. The FDA authorised 526 (74%), while the EMA and NMPA each authorised roughly half (366 (51%) and 356 (50%), respectively). The FDA was first to approve in 63% of cases, the NMPA in 24%, and the EMA in 13%.

The sequencing of approvals has shifted: by 2025, the FDA's share of first approvals declined to just 50%, while China's NMPA rose sharply to 36%, and the EMA's share fell to ~6% in 2024 before recovering to ~14% in 2025. NMPA approvals also exceeded 90 in 2025, but many are 'catch-up' approvals: 64% of NMPA approvals (2016–2025) followed a prior FDA/EMA approval, with a median lag of four years.

These data indicate that Europe is increasingly positioned as a follow-on market in global launch sequencing, while China is becoming a more prominent early approval jurisdiction for some products.

Where the gap is most pronounced:

4. **Micro companies are increasingly important but face worse EMA outcomes:** Innovation is shifting toward smaller developers. In 2025, micro companies (global revenue < USD 1 billion) accounted for 52% of novel medicine approvals across the FDA and EMA (up from 38% in 2016), while the share attributed to large companies fell from 41% to 31%. However,

regulatory outcomes diverge sharply by region. For micro-company products, 92% achieved FDA approval, versus 51% achieving EMA authorisation. Micro companies also account for 63% of medicines not submitted to the EMA, indicating a disproportionate role in nonengagement with Europe's regulatory route.

For products approved by both agencies, micro companies experience longer delays: the median FDA to EMA approval lag is 255 days (vs. 163 days for large companies). This is partly due to later EMA filings (median submission gap of 94 days for micro companies vs. 30 days for large ones). Review time also differs: the median EMA submission-to-authorisation time is 488 days for micro-company medicines (vs. 414 for large at EMA and 331 at FDA).

5. **Smaller therapeutic areas show lower EMA approval rates:** Therapeutic areas with fewer than 20 medicines have a markedly lower EMA approval rate (52%) compared with areas with 20-plus medicines (68%). FDA approval rates remain consistently high regardless of medicine count per therapeutic area (93% vs. 95%).
6. **Orphan medicines are approved at similar rates but reach Europe later:** The EMA approved 67% of medicines with FDA orphan designation (118 of 176), broadly similar to non-orphan approvals (62%, 221 of 356). The difference is timing. Orphan medicines reach EMA approval a median of 268 days after FDA approval, versus 154 days for non-orphans. The delay is driven mainly by later EMA submissions (median submission gap of 84 vs. 39 days), not by longer EMA review once filed (review times are 429 vs. 431 days).

Timing: Europe is slower on both submission and review

Across medicines approved by both agencies, EMA assessment (including clock-stops) is slower: the EMA took a median 146 additional days versus the FDA and longer in 80% of cases. Companies also file later in Europe: median submission gap is 49 days, with later EMA submission in 73% of cases (and a mean gap of 114 days, indicating a subset with much longer delays).

Implications and policy reflection

The evidence indicates that Europe's innovation gap is most harmful for micro companies, in therapeutic areas with smaller medicine counts and for some orphan-designated products, combined with longer timelines when Europe is pursued. This constrains what national systems (including Germany) can deliver downstream, as national access pathways cannot compensate for absent or delayed EMA authorisation.

To prevent a widening innovation gap, the findings point to the need for adequate incentives that encourage developers to pursue EMA review for high-value medicines, with particular focus on the segments where non-submission and delay are most pronounced (micro companies, small medicine count per therapeutic area, and FDA orphan products). Options discussed in the report include measures that improve predictability and commercial attractiveness, reduce process burden and enable more streamlined regulatory interactions for high-uncertainty innovations while maintaining standards for quality, safety and efficacy.

Finally, fundamental systemic changes such as a US 'most-favoured-nation' (MFN) drug pricing model are likely to have significant global repercussions. MFN will likely influence approval strategies, launch sequencing and supply security in Europe and Germany, with the potential to further accelerate Europe's decline as an early access market for innovation. Germany and Europe should adapt their framework conditions to strengthen their attractiveness as a location for research and development while ensuring timely access to innovative medicines for patients. This requires a competitive, innovation-friendly and growth-oriented market environment grounded in value-based pricing.

1. Introduction: The innovation gap and why it matters

The German Association of Research-Based Pharmaceutical Companies (vfa) has commissioned Charles River Associates (CRA) to examine the growing innovation gap between the European Union (EU) and other leading markets, notably the United States (US) and China. This analysis builds on previous work by the vfa, including its 2025 publication 'Innovation Gap: Unlocking Potential in European Access to Pharmaceutical Innovations (2015–2024).'[1]

1.1 Background

Timely access to innovative medicines is important for patients, the health care system and wider issues such as competitiveness. There is a broad consensus that health systems that enable the rapid development, approval and uptake of new treatments are better positioned to address unmet medical needs while sustaining a dynamic research and innovation ecosystem.[2] Access to innovation is increasingly intertwined with broader economic and industrial policy objectives.[3] For Europe, this link has become more pronounced as concerns grow that patients experience slower and less consistent access to new medicines compared with other major global markets, with implications for both population health and long-term innovation capacity.[4]

Many studies have linked this pattern to differences in regulatory, reimbursement and market-structure conditions, including the predictability of access pathways.[5] While Europe benefits from centralised regulatory review through the European Medicines Agency (EMA), the timing of regulatory approval remains a key inflection point in the overall access pathway. Regulatory approval refers to the formal authorisation of a medicine by a regulatory authority (e.g. the EMA), confirming its quality, safety and efficacy; availability describes whether an approved medicine has negotiated the pricing and reimbursement process; and access refers to whether patients can receive the medicine through routine use.

More recently, the global comparison has extended beyond Europe and the US. A growing body of academic literature highlights China's rapid progress in pharmaceutical innovation, driven by sustained regulatory reform and expanded investment in clinical development. Accelerated approval pathways, increased clinical trial activity, and closer alignment with international regulatory standards have together reduced historical drug lag and shortened timelines from drug development to marketing authorisation, enabling faster availability of new medicines in China.[6,7] From a European policy perspective, this shift is strategically relevant, as regulatory efficiency has emerged as a core

1 The German Association of Research-Based Pharmaceutical Companies (vfa), "Innovation Gap: Unlocking Potential in European Access to Pharmaceutical Innovations (2015–2024)," May 5, 2025, https://www.vfa.de/de/gesundheit-versorgung/amnog/innovationsrueckstand-eu-usa.

2 Simona Gamba, Laura Magazzini, and Paolo Pertile, "Improving Access to Medicines and Promoting Pharmaceutical Innovation," European Parliamentary Research Service, November 2023, https://www.europarl.europa.eu/RegData/etudes/STUD/2023/753166/EPRS_STU%282023%29753166_EN.pdf.

3 OECD Health Policy Studies, *Pharmaceutical Innovation and Access to Medicines* (Paris: OECD, 2018), https://www.oecd.org/content/dam/oecd/en/publications/reports/2018/11/pharmaceutical-innovation-and-access-to-medicines_g1g98d77/9789264307391-en.pdf.

4 Sanae Akodad, Michael Goldman, and Hilde Stevens, "Early Access Disparities in Innovative Therapies Across the US, EU, China, and Japan," *Frontiers in Medicine* 12 (2025).

5 Nicolas S. Downing, Jenerius A. Aminawung, Nilay D. Shah, Joel B. Braunstein, Harlan M. Krumholz, and Joseph S. Ross, "Regulatory Review of Novel Therapeutics—Comparison of Three Regulatory Agencies," *New England Journal of Medicine* 366, no. 24 (2012): 2284–2293.

6 Ruirong Tan et al., "Current Landscape of Innovative Drug Development and Regulatory Support in China," *Signal Transduction and Targeted Therapy* 10, no. 1 (2025): 220.

7 Yang Liu et al., "Evolution of Drug Regulations and Regulatory Innovation for Anticancer Drugs in China," *Acta Pharmaceutica Sinica B* 12, no. 12 (2022): 4365–4377.

component of global competitiveness in life sciences, and developments beyond the US increasingly shape the benchmark against which Europe is assessed. The speed and predictability of EMA marketing authorisation have become increasingly central to debates on Europe's access to innovation and competitiveness in the life sciences.

Systematic analysis of the innovation gap is critical for three reasons. First, it has direct implications for patient access: delays in regulatory authorisation mean that treatments available to patients in comparator markets remain unavailable in Europe, with particularly acute consequences for diseases with high unmet need. Second, understanding the structural drivers of the gap—including differences in submission timing, review duration and regulatory sequencing across therapy areas and company characteristics—is essential to inform evidence-based policy reform. Third, the gap has strategic implications for the competitiveness of Europe's life sciences: persistent delays risk discouraging investment in European clinical development and reinforcing a pattern in which Europe is treated as a secondary, or even tertiary, market in global launch strategies.

To investigate this, the vfa has conducted several studies and examined the innovation gap, which is defined as the difference between innovative medicines authorised in comparator markets and those authorised in the EU within a comparable time frame. Based on the findings from this study, out of the 526 novel medicines approved by the US Food and Drug Administration (FDA) between 2016 and 2025, 175 (33%) lack approval in Germany.[8] This implies a tangible shortfall in treatment options, particularly for medicines with high therapeutic relevance (e.g. breakthrough therapies and orphan drugs). This shows that the EU's regulatory pathway is, on average, slower than that of the FDA: based on our analysis of 333 novel medicines approved by both agencies between 2016 and 2025, where review times incorporate all clock-stop periods, the EMA's regulatory assessment took a median of 146 additional days compared with the FDA, with the EMA taking longer in 80% of cases. This is consistent with, and slightly exceeds, the 120-day clock-stop-inclusive gap estimated in the literature for 2023, suggesting that the EU's speed disadvantage has persisted and may be widening across the broader 2016–2025 period. In addition, our data show a median submission gap of 49 days (1.6 months), with companies filing later with the EMA in 73% of cases—broadly in line with prior estimates—though a mean gap of 114 days (3.7 months) indicates that a meaningful subset of products experience substantially longer delays before EMA submission. However, addressing the innovation gap requires a clearer understanding of regulatory delay, including differences in submission timing, review duration and regulatory sequencing across therapy areas, manufacturer size and company headquarters. This report provides an evidence-based, granular analysis of these drivers.

1.2 Scope and definitions

This report examines the innovation gap in novel medicines across three geographical regions between 2016 and 2025: the US, the EU and China, with a particular focus on implications for Germany. The analysis focuses on regulatory approvals and patterns, comparing approvals by the FDA, the EMA, alongside national approvals in Germany by the Federal Institute for Drugs and Medical Devices (BfArM), and China's National Medical Products Administration (NMPA), to assess the innovation gap between these three geographical regions.

The scope of products includes new molecular entities (NMEs), biologics, and advanced therapy medicinal products (ATMPs) classified as innovative by the FDA's Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research, the EMA, or the NMPA. Generics,

8 In Germany, medicines must obtain either centralised EU marketing authorisation (via the EMA) or a national marketing authorisation (via national, decentralised or mutual recognition procedures).

biosimilars, vaccines, traditional Chinese medicines, blood cord products, diagnostics, reformulations, new strengths, and line extensions are excluded unless they represent a first approval in the region for a new active substance (NAS). Combination products are included only where they contain NASs.

The analysis also explores differences by manufacturer size and therapeutic area. Five overarching case study themes were identified based on predefined hypotheses to illustrate how regulatory delay and non-submission manifest in practice, including limited approvals of ATMPs, China-first regulatory submissions by global companies, delayed European access to China-origin innovations, regulatory challenges faced by micro and small companies, and barriers affecting products with novel mechanisms of action (MoAs). Full details of the quantitative methodology and the sources of data are provided in the appendix.

1.3 Hypotheses regarding Europe's pharmaceutical innovation gap and global launch prioritisation

This report investigates a number of different questions regarding Europe's position in the global pharmaceutical innovation landscape:

- Are fewer new innovative medicines approved in the EU compared with the US and China? Is the difference growing over time?
- Does this vary for particular types of product, and does this tell us whether the pharmaceutical innovation gap is driven by scientific inferiority or structural regulatory and economic barriers that shape company behaviour? Are certain categories of high-innovation products more likely to face delayed approval or deprioritisation within European regulatory pathways?
- Are there differences for products developed by manufacturers based in different regions or of particular size? What does this tell us about whether barriers disproportionately affect smaller companies and non-European companies?

1.4 Structure of the report

The remainder of the report is organised as follows:

- Chapter 2 quantifies the innovation gap by assessing the extent to which innovative medicines fail to achieve regulatory approval in Europe and Germany. It then goes on to examine global first-launch dynamics, analysing which markets receive innovative medicines earliest and exploring the implications of China's emerging role as an increasingly important early launch market.
- Chapter 3 investigates how the innovation gap varies by company characteristics, including company size and headquarters location.
- Chapter 4 analyses differences by medicine characteristics, focusing on which therapeutic areas and product types have the largest innovation gap.
- Chapter 5 presents selected case studies to illustrate how the innovation gap materialises in practice across different contexts.
- Chapter 6 discusses the broader implications for Europe and Germany—including consequences for patient access, investment decisions, and the long-term competitiveness of the life sciences sector—and concludes with policy reflections and considerations for addressing the identified gaps.

2. Quantifying the innovation gap

2.1 How many innovative medicines achieve regulatory approval in Germany?

Of the 526 novel medicines approved by the FDA in 2016–2025, 175 (33%) are not authorised in Germany and 193 (37%) lack EMA approval, indicating a substantial regulatory access gap.

We first look at a sample of products approved in the US, Europe and China between 2016 and 2025. Across these three major markets, 711 novel medicines received their first approval during this period (Table 1). The FDA was the most active regulatory approver, authorising 526 medicines (74%), followed closely by the NMPA and EMA, each approving around half of all medicines (356 and 366, respectively, or 50% and 51%). Only 157 medicines (22%) achieved approval across all three agencies, while 152 (21%) were approved exclusively by the NMPA and were not approved by the FDA and EMA. The scale of China-only approvals likely reflects a combination of factors beyond regulatory access alone, including medicines developed specifically for disease burdens more prevalent in China, domestic innovation with no immediate commercial strategy in the US and EU markets, and differing clinical data requirements that may preclude straightforward EMA or FDA submissions. For this reason, the subsequent analysis focuses on the medicines approved by either the FDA or the EMA, where the drivers of the European regulatory gap are more directly comparable.

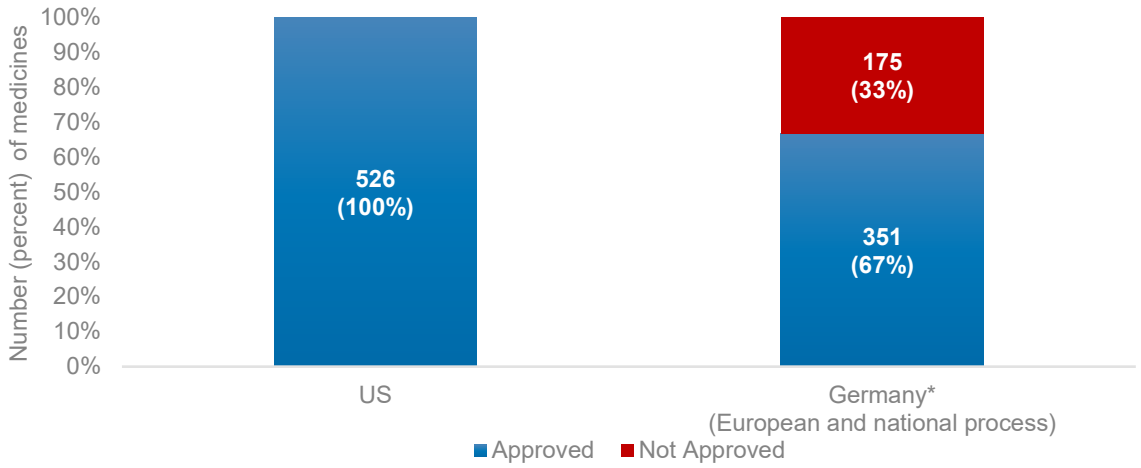
Table 1: Summary of FDA, EMA, and NMPA novel medicine approvals (2016–2025)

	Total novel medicines approved	FDA approved	NMPA approved	EMA approved
All three regulators	157	157	157	157
FDA & EMA only	176	176	-	176
FDA & NMPA only	38	38	38	-
EMA & NMPA only	9	-	9	9
FDA only	155	155	-	-
EMA only	24	-	-	24
NMPA only	152	-	152	-
TOTAL	**711**	**526**	**356**	**366**

A large share of global pharmaceutical innovation has not yet achieved regulatory approval in Europe or Germany and is therefore not accessible to European or German patients. As shown in Figure 3, of the 526 medicines approved by the FDA between 2016 and 2025, 175 (33%) lack approval in Germany, 193 (37%) have not received EMA approval,[9] and 333 (63%) secured approval from both the FDA and EMA. Germany's national authorisation pathway (BfArM) added 18 medicines (3%) beyond EMA approvals. An additional 33 medicines were approved by the EMA without FDA approval (not pictured).

9 Once granted by the European Commission, an EMA-centralised marketing authorisation is legally valid in all EU member states, including Germany.

Figure 3: Comparison of US novel medicine approvals to Germany, inclusive of national authorisations (2016–2025)



*An additional 33 medicines with EMA, but not FDA, approval, have been omitted from the Germany column to allow comparison against the US as a baseline.

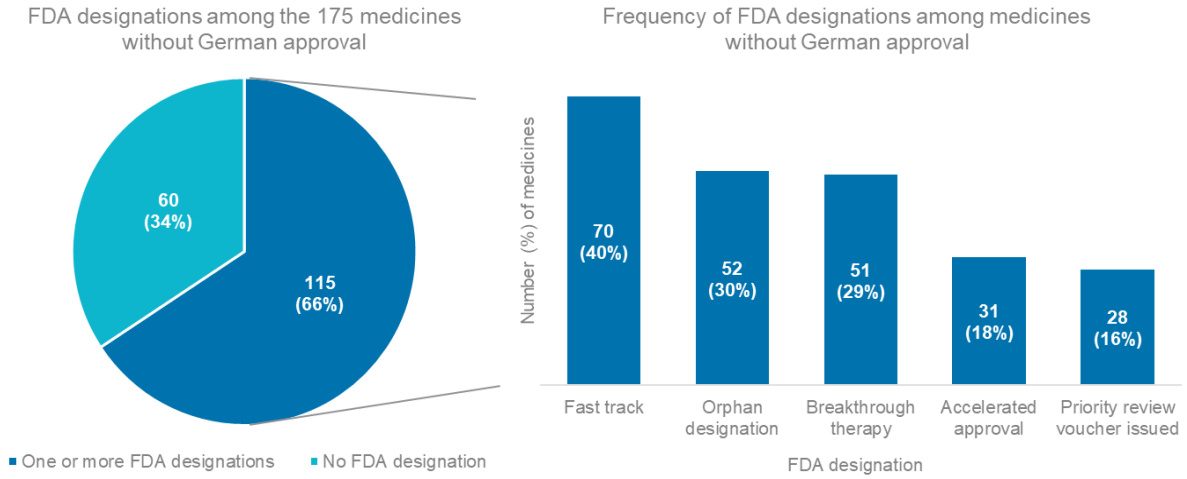
Source: CRA (2026)

Using the definition set out in the introduction, there is an innovation gap of 175 innovative medicines. This gap is particularly concerning because many of the medicines without authorisation in Germany carry FDA designations that signal high potential value. Two-thirds of these medicines have at least one designation, such as fast track, orphan status, breakthrough therapy or accelerated approval (Figure 4).[10,11] Additionally, 28 medicines received priority review vouchers, including 22 for rare paediatric diseases. These indicators suggest that the medicines missing from the German market are not marginal innovations but often address high-need conditions.

10 The FDA-expedited programmes/designations referenced in this report are defined as follows. Fast track designation is a process 'designed to facilitate the development, and expedite the review' of drugs that treat serious conditions and fill an unmet medical need. Breakthrough therapy designation is a process to expedite development and review of drugs intended to treat a serious condition where preliminary clinical evidence indicates the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint. Orphan drug designation ('orphan status') may be granted for a drug/biologic intended to prevent, diagnose or treat a rare disease or condition; the Orphan Drug Act defines a rare disease as one affecting fewer than 200,000 people in the US (with orphan designation providing specified incentives). Accelerated approval regulations allow earlier approval for drugs for serious conditions that fill an unmet medical need based on a surrogate endpoint (or, as amended, a surrogate or intermediate clinical endpoint reasonably likely to predict clinical benefit), with confirmatory studies required post-approval to verify/describe clinical benefit. Available at https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review.

11 FDA-expedited program designations are not mutually exclusive. A single medicine may qualify for and receive more than one designation (e.g. fast track and orphan drug, or breakthrough therapy and accelerated approval), so category counts can overlap.

Figure 4: FDA designations for the 175 medicines lacking approval in Germany (2016–2025)



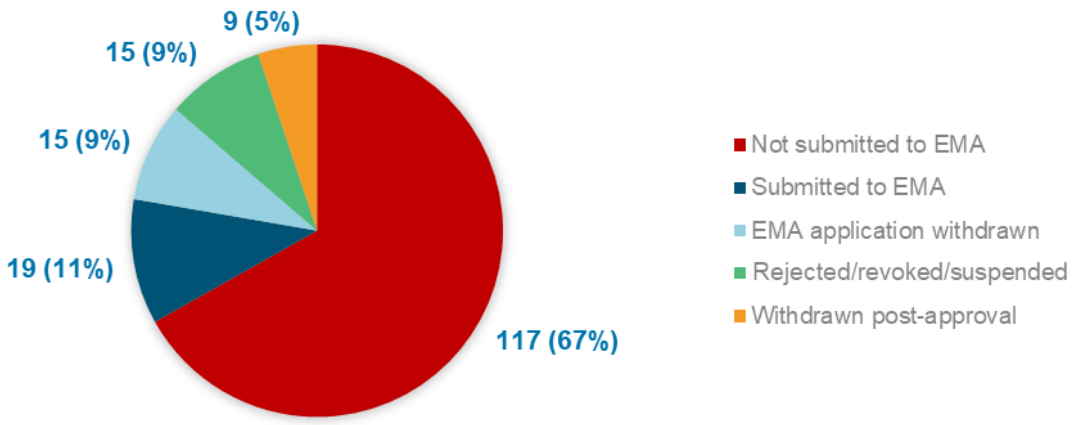
Source: CRA (2026)

2.2 Non-submission is a primary driver of Europe's innovation gap

Most of the innovation gap reflects non-submission, not rejection: two-thirds of FDA-approved medicines missing in Germany were never filed with the EMA, and products not submitted within about two years of FDA approval rarely reach Germany later.

The innovation gap could reflect non-submission or rejection. Sixty-seven percent of FDA-approved medicines without authorisation in Germany (117 of 175) were never submitted to the EMA, indicating that companies are deciding not to apply for regulatory approval (Figure 5). Fourteen of the 117 medicines not yet submitted to the EMA have received orphan designations or paediatric plans. Only 19 medicines were submitted to EMA but are pending review, while smaller numbers were withdrawn post-approval due to 'commercial reasons' (9), rejected or revoked (15) or had their EMA application withdrawn (15).

Figure 5: EMA review actions for the 175 medicines lacking approval in Germany (2016–2025)



Source: CRA (2026)

The evidence suggests that medicines not submitted to the EMA within a few years of FDA approval are unlikely to ever receive authorisation in Germany. Among the 262 medicines approved by the FDA before the EMA, 89% received EMA approval within two years, indicating that companies intending to seek European approval almost always do so within this window. Of the 117 medicines never submitted to the EMA, 69 were approved before 2024, thereby falling outside the typical two-year submission window and unlikely to ever proceed to EMA review. This means that the persistent innovation gap stands at around 108 medicines: 69 were never submitted to the EMA, plus 39 rejected or revoked, commercially withdrawn or withdrawn during review.

This analysis aligns with findings from other studies[12] indicating that pharmaceutical companies may choose not to pursue regulatory approval where expected commercial returns do not justify the cost and effort of submission, consistent with the instances of post-approval withdrawal for stated 'commercial reasons' observed above.

2.3 Shifting geography of first approvals

Europe's share of first approvals has fallen sharply, while China's NMPA has emerged as an early approval jurisdiction, indicating that global launch sequencing is shifting away from Europe even as overall FDA/EMA approval volumes remain broadly stable.

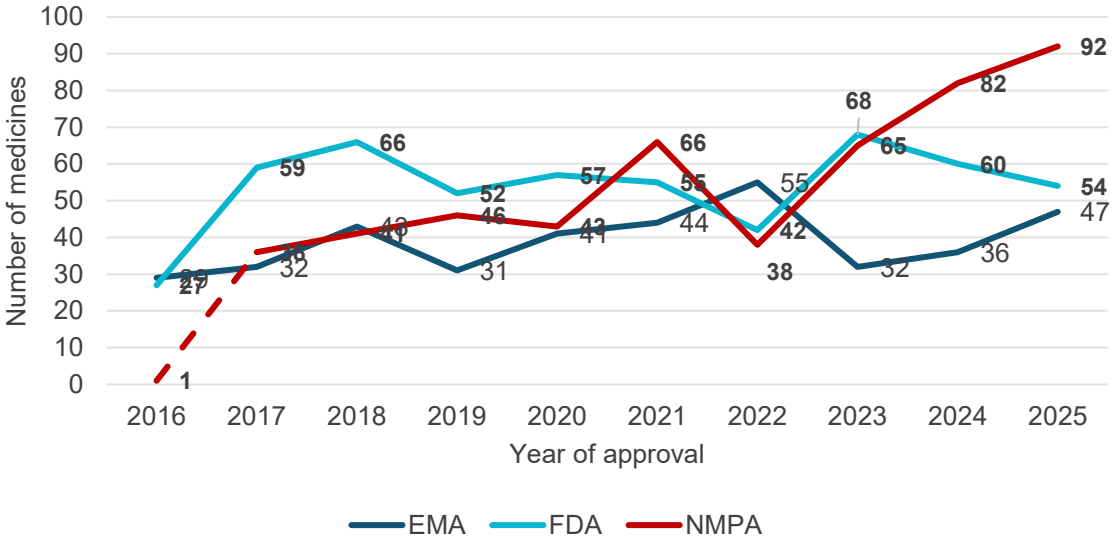
We also examine which regions were the first to approve particular medicines. We find that Europe's share of first regulatory approvals has declined sharply, while China's NMPA has become a more prominent approval authority, both through higher total approvals and a rising share of first approvals. While overall approval volumes across major regulators (mainly FDA and EMA) remain broadly comparable, the sequencing of approvals has changed over time.

In absolute terms, the FDA and EMA each approve roughly 30–70 NMEs and biologics annually. China's NMPA approvals exceeded 90 in 2025, surpassing those of the FDA and EMA (Figure 6). However, annual approval totals need to be understood in context. Of the 510 NMPA approvals between 2016 and 2025, 64% were medicines that had already received FDA or EMA approval in a prior year, with a median lag of 4 years between Western approval and NMPA approval, and 18% of catch-up approvals followed a Western approval by more than 10 years. This catch-up effect was most pronounced in the early years of the dataset, when 88% of NMPA approvals in 2017 and 2018 were medicines already approved in the West, reflecting the processing of a large backlog following China's regulatory reforms. While this share has declined over time, falling to around 52%–60% by 2024–2025, catch-up regulatory approvals still account for the majority of NMPA volume. As a result, absolute approval counts should not be interpreted as a pure proxy for current-year innovation output, and cross-market comparisons of annual approval totals should be treated with caution.[13]

12 European Federation of Pharmaceutical Industries and Associations, "The Root Causes of Unavailability of Innovative Medicines and Delay in Access: Shortening the Wait," May 2025, https://www.efpia.eu/media/er5dshuq/cra-efpia-root-causes-of-unavailability-and-delay-final-2025-report-29-apr-2025-stc.pdf.

13 Shaohong Wang et al., "Trends, Lag and Characteristics of Rare Disease Drug Approval in the USA and China, 1983–2022," *Orphanet Journal of Rare Diseases* 20, no. 1 (2025).

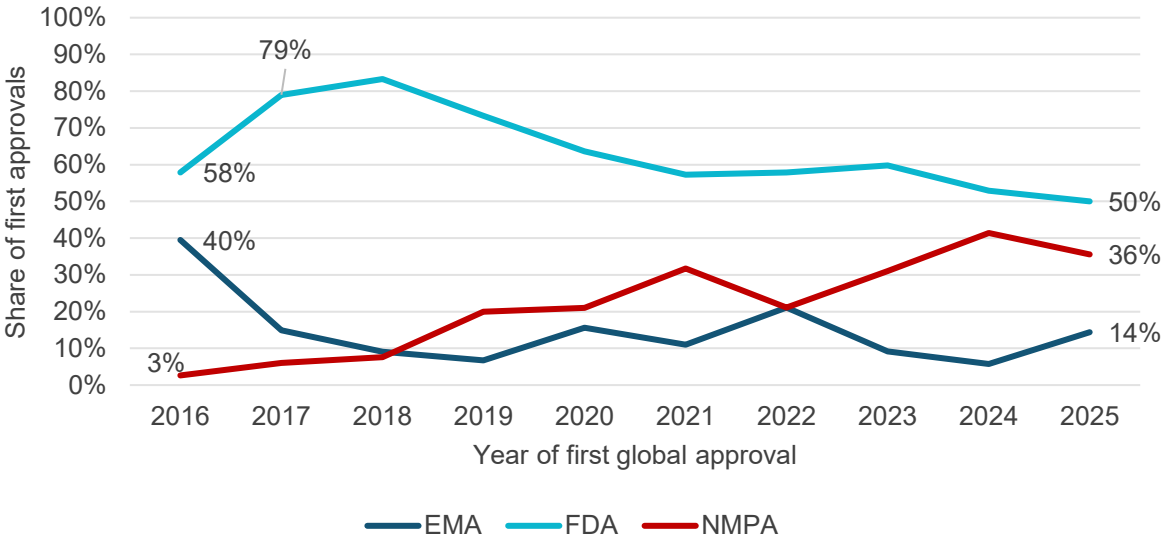
Figure 6: Novel medicines approved per year by the EMA, FDA, or NMPA (2016–2025)



Source: CRA (2026)

As shown in Figure 6, the FDA's share of first approvals declined from approximately 79% to 50% over the period analysed, excluding 2016, which was an outlier year. Despite this decline, the FDA remains the most frequent first-approval authority. In contrast, the EMA's share of first approvals fell from around 15% to 6% in 2024 before recovering to 14% in 2025, indicating a reduced role in initial market entry for innovative medicines.

Figure 7: Share of novel medicines first approved by the EMA, FDA, or NMPA (2016–2025)



Source: CRA (2026)

Over the same period, China's NMPA experienced a substantial increase in both total approvals and first approvals. The NMPA's share of first approvals rose from approximately 6% to 36%, reflecting China's growing role as an early regulatory jurisdiction for innovative products.

Taken together, these trends indicate a shift in first-launch activity away from Europe and towards China, alongside a partial diversification away from exclusive reliance on the US. Europe's declining share of first approvals occurs despite stable overall approval volumes, suggesting that the change reflects launch sequencing decisions rather than a reduction in regulatory output.

2.4 Factors affecting China's rise in first regulatory approvals

Historically anchored by the FDA, global first-approval patterns are now shifting as China's NMPA, following sustained regulatory reforms, emerges more often as an early approval jurisdiction, sometimes even preceding EMA sequencing.

Historically, the FDA has been the predominant first-approval jurisdiction for innovative medicines, reflecting policy choices that reduce regulatory uncertainty and accelerate time to market. These include structured early scientific engagement, multiple expedited approval pathways embedded in statute, and the fact that FDA approval confers immediate national market access.[14,15] Together, these features have positioned the FDA as the anchor regulator for global development programmes and shaped submission sequencing across major markets.

Against this policy backdrop, the increasing prominence of China as an early approval jurisdiction warrants closer examination. It is challenging to establish the causal link between trends in regulatory approval and the policy environments, but China's growing role as an early approval jurisdiction is consistent with a decade of regulatory reforms designed to reduce historic 'drug lag' and increase alignment with international standards. In 2015, the State Council issued the 'Opinions on Reforming the Review and Approval System for Drugs and Medical Devices' (Guo Fa [2015] No. 44), explicitly aiming to improve review efficiency and resolve the backlog of drug applications.[16] China further advanced international harmonisation by joining the International Council for Harmonisation (ICH) as a regulatory member in 2017.[17] Subsequent reforms supported faster and more globally integrated development, including issuance of technical guidance to accept overseas clinical trial data (2018) and institutional restructuring that consolidated regulatory functions under the NMPA (2018).[18,19] The 2019 revised Drug Administration Law formalised key modern regulatory features, including a nationwide marketing authorisation holder system.[20] Together, these changes are widely cited as drivers of China's increased regulatory throughput and its more prominent position in global submission sequencing.[21]

Recent approval patterns indicate an increasing role for China's NMPA in the global regulatory landscape for innovative medicines. A majority of medicines receiving first approval from the NMPA are developed by companies headquartered in Asia, reflecting both the geographic distribution of

14 Beatrice Brown et al., "Trends in the Quality of Evidence Supporting FDA Drug Approvals: Results from a Literature Review," *Journal of Health Politics, Policy and Law* 47, no. 6 (2022): 649–672.

15 Linda J. B. Jeng and Jeffrey Siegel, "Surrogate Endpoints in Regulatory Decision-Making," *Clinical and Translational Science* 18, no. 12 (2025).

16 Ruilin Song, Guowei Sang, Meiyu Geng, and Hualiang Jiang, "China's Reform of the Regulatory System for Medical Products and Its Impact," *National Science Review* 6, no. 1 (2019).

17 ICH, "ICH Assembly, Montreal, Canada, May/June 2017," June 19, 2017, https://www.ich.org/pressrelease/ich-assembly-montreal-canada-mayjune-2017.

18 Weifang Tang et al., "Evolving Drug Regulatory Landscape in China: A Clinical Pharmacology Perspective," *Clinical and Translational Science* 14, no. 4 (2021): 1222–1230.

19 Xuan Ye, Qingli Wang, and Haixue Wang, "New Era of Drug Innovation in China," *Acta Pharmaceutica Sinica B* 9, no. 5 (2019): 1084–1085.

20 National Medical Products Administration, "Drug Administration Law of the People's Republic of China," last updated September 26, 2019, https://english.nmpa.gov.cn/2019-09/26/c_773012.htm.

21 Yilong Yan et al., "New Drug Approvals in China: An International Comparative Analysis, 2019–2023," *Drug Design, Development and Therapy* (2025): 2629–2639.

developers and the growing alignment between regional innovation activity and Chinese regulatory pathways.

A notable share of NMPA-first medicines—approximately 89%—have not received subsequent approval from either the FDA or EMA. This pattern suggests that, for many of these products, regulatory approval has been pursued selectively rather than as part of a global launch strategy spanning all major markets. Possible contributing factors include differences in target populations, development strategies, regulatory requirements or commercial priorities, though these cannot be inferred directly from approval data alone.

The data also show instances in which non-Chinese companies submit to the NMPA earlier than to the EMA. This sequencing indicates that China is, in some cases, incorporated earlier into global development and approval plans than Europe. While the approval data do not allow conclusions about the motivations behind these decisions, the observed sequencing is consistent with the NMPA being regarded as a viable pathway for early regulatory approval.

Overall, the evidence documents a shift in global launch patterns in which China more frequently appears as an early or initial approval jurisdiction for certain innovative medicines. This reflects a change in how global developers sequence regulatory submissions across major markets, with China occupying a more prominent position than in earlier periods.

3. The impact of company characteristics on the innovation gap

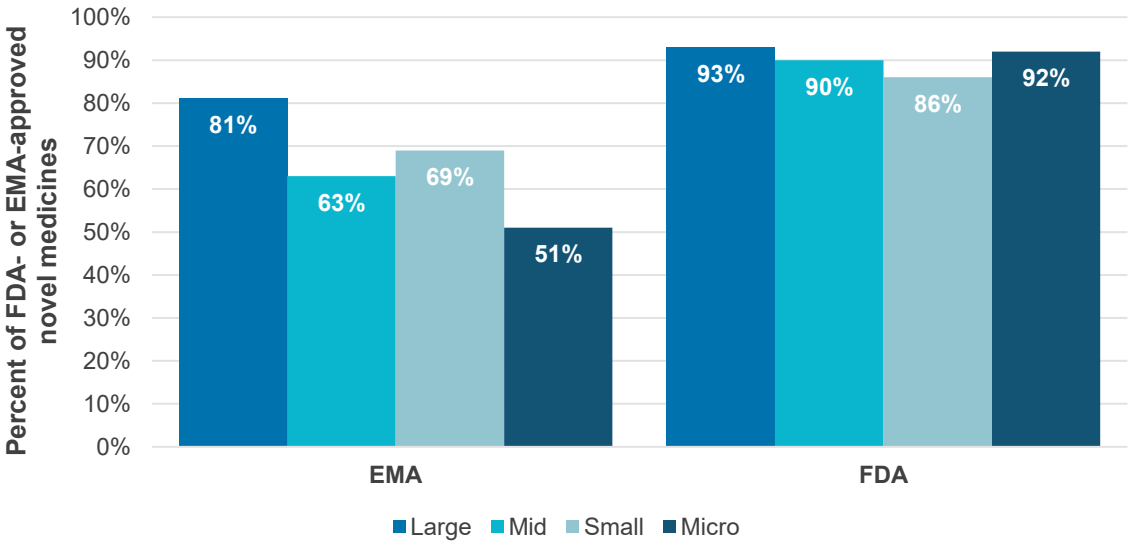
3.1 Differences in regulatory outcomes for micro companies

Micro companies now account for a large and growing share of pharmaceutical innovation but experience lower approval rates, longer delays and extended review timelines in Europe compared with the US.

Micro companies, defined as firms with annual global revenues below USD 1 billion, account for a growing share of pharmaceutical innovation. In 2025, they were responsible for 52% of all novel medicines approved across the FDA and the EMA, an increase from 38% in 2016. Over the same period, the share of approvals attributed to large companies declined from 41% to 31%, indicating a structural shift in the composition of innovators.[22]

However, the data reveal a markedly greater disparity in EMA approval rates among micro companies relative to their larger counterparts. While 92% of novel medicines originating from micro companies received FDA approval, only 51% achieved EMA authorisation, a differential of 41 percentage points that substantially exceeds the equivalent gap observed for larger companies (Figure 8Figure 9). Another way to view this is that micro companies account for 63% of medicines that are not submitted to the EMA, suggesting a higher likelihood of nonengagement with the European regulatory process.

Figure 8: FDA and EMA approval rates by company size (2016–2025)



Source: CRA (2026)

For medicines approved by both regulators, micro companies also face longer delays between US and European approval. The median time from FDA approval to EMA approval for micro-company products is 255 days, compared with 163 days for large companies. Part of this gap is explained by

22 Attribution is based on the company recorded as the sponsor/applicant at the time of regulatory approval (FDA/EMA). This approach may overstate the role of 'micro companies' because it does not fully capture (i) subsequent acquisitions of the originating firm or asset, (ii) late-stage licensing, co-development or joint marketing arrangements, or (iii) situations where commercial rights are transferred to a larger company after approval.

later EMA submissions: micro companies have a median submission gap of 94 days between their FDA and EMA filings, compared with just 30 days for large companies, indicating that smaller firms take considerably longer to initiate their European regulatory submissions after US filing.

Looking across all medicines approved by each agency, the authorisation process itself also takes longer for micro companies in Europe: the median time from submission to authorisation for micro-company medicines is 488 days at the EMA, compared with 331 days at the FDA and 414 days for large companies at the EMA, indicating that micro companies face a longer review process both relative to the FDA and relative to larger firms within the same European regulatory framework.

Taken together, these findings indicate that micro companies are more likely to experience lower approval rates, longer delays before initiating EMA submissions, and extended review timelines in the EMA regulatory process. These differences arise despite the increasing role of micro companies in generating pharmaceutical innovation and highlight variation in regulatory outcomes by firm size.

These findings are consistent with published academic evidence indicating that smaller and first-time sponsors face greater regulatory challenges in Europe than in the US. Comparative studies of FDA and EMA decision-making show that differences in approval outcomes and review timelines are most pronounced for products developed under conditions of higher clinical uncertainty and limited regulatory precedent, which are disproportionately represented among smaller and first-time sponsors.[23,24] The FDA's broader use of expedited review pathways and greater acceptance of surrogate endpoints has been shown to support higher approval success for smaller innovators.[25]

3.2 Declining EMA approvals for medicines developed by European-headquartered companies

Medicines developed by European-headquartered companies remain more likely to receive EMA approval than those developed elsewhere, but their share of EMA-approved innovation is declining, and Europe is increasingly not the first approval destination.

The share of EMA approvals differs by company headquarters location. Among the 559 medicines approved by the FDA (526) or EMA (an additional 33) between 2016 and 2025, European-headquartered companies had the highest share of their medicines receiving EMA approval at 71%, compared with 63% for North American-headquartered companies, 61% for companies based in the Asia-Pacific region and 42% for companies headquartered in the Middle East and North Africa.

However, the share of total EMA-approved medicines developed by European-headquartered companies has declined over time, falling from 81% in 2016 to 67% in 2024, equivalent to an average reduction of approximately 2 percentage points per year. This trend suggests a gradual decrease in the relative contribution of European-headquartered firms to the pool of EMA-approved innovative medicines.

First-approval sequencing further highlights differences in regulatory prioritisation. Among medicines developed by European-headquartered companies, only 30% received first approval from the EMA, while 68% were first approved by the FDA. By comparison, only 10% of medicines developed by

23 Mwango Kashoki et al., "A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014–2016: Concordance, Discordance, and Why," *Clinical Pharmacology & Therapeutics* 107, no. 1 (2020): 195–202; Kesselheim, Wang, Franklin, and Darrow, "Trends in Utilization of FDA Expedited Drug Development and Approval Programs."

24 Roberta Joppi, Vittorio Bertele, Tommaso Vannini, Silvio Garattini, and Rita Banzi, "Food and Drug Administration vs. European Medicines Agency: Review Times and Clinical Evidence on Novel Drugs at the Time of Approval," *British Journal of Clinical Pharmacology* 86, no. 1 (2020): 170–174.

25 Kesselheim et al., "Trends in Utilization of FDA Expedited Drug Development and Approval Programs."

North American-headquartered companies were first approved by the EMA, indicating that US developers are less likely to prioritise Europe for initial regulatory approval, while European-headquartered companies are more likely to prioritise EMA submission.

These results should be interpreted with caution, as company size and headquarters location are closely related. Approximately 65% of micro companies are headquartered in the US, suggesting that some of the observed differences in approval outcomes and sequencing may reflect the underlying distribution of firm size across regions rather than headquarters location alone.

Overall, the findings show that while European-headquartered companies continue to have higher EMA approval rates than non-European firms, their share of EMA-approved medicines is declining, and Europe is not the first-approval jurisdiction even for 7 in 10 medicines developed by European-headquartered companies.

4. The impact of the type of medicine on the innovation gap

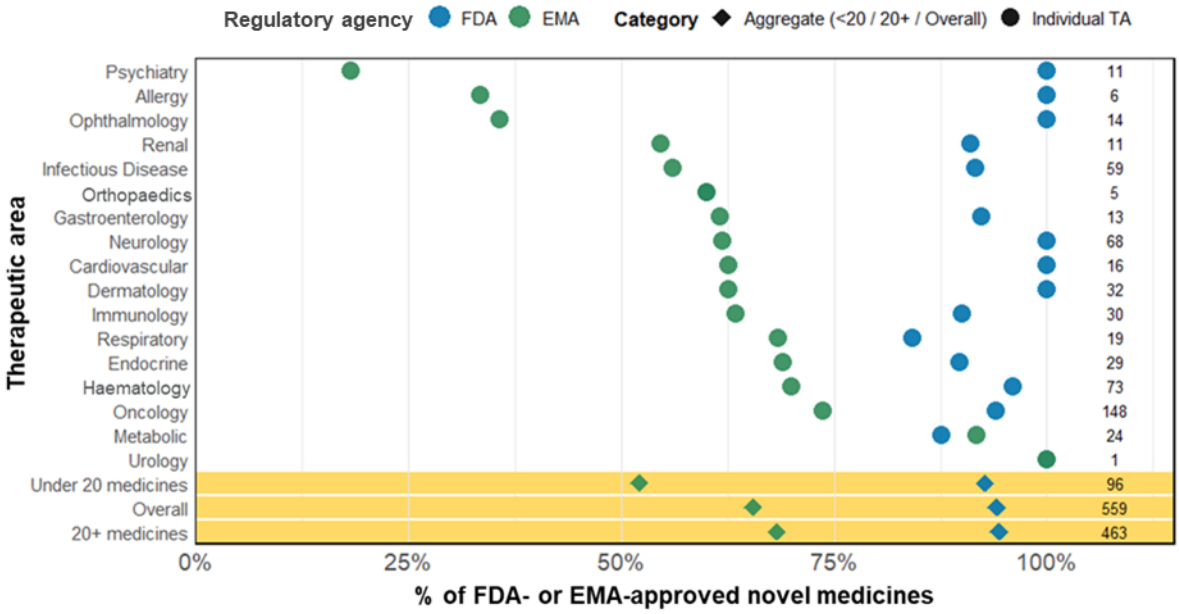
4.1 Uneven regulatory approval performance across therapeutic areas

Regulatory approval of innovative medicines varies across therapeutic areas in Europe, with lower approval rates and longer timelines concentrated in therapeutic areas with fewer medicines.

Approval rates (the percentage of products in our sample approved by the relevant regulator) differ across therapeutic areas. There are several ways to examine this.

One approach is to examine the number of products within each therapeutic area. Therapeutic areas with fewer than 20 medicines show lower EMA approval shares: 52% compared with 68% in areas with 20 or more medicines, a gap of 16 percentage points. By contrast, FDA approval shares remain consistently high regardless of the number of medicines in a therapeutic area (93% vs. 95%), indicating that approval outcomes vary more by medicine count in the European context (Figure 9). Therapeutic areas with fewer than 20 medicines accounted for a total of 96 medicines. In descending order of the number of new medicines, these areas were cardiovascular, gastroenterology, ophthalmology, psychiatry, renal, allergy, orthopaedics and urology.

Figure 9: EMA vs. FDA approval rate by therapeutic area among FDA- or EMA-approved medicines (2016–2025)



Source: CRA (2026)

Differences are also evident in approval timing. Oncology and neurology show the longest median delays between FDA and EMA approval, at 274 and 276 days, respectively, compared with a median delay of 187 days across all therapeutic areas. These areas also have lower shares of first approval by the EMA (10% and 12%, respectively), compared with 17% across all therapeutic areas. Importantly, recent comparative evidence in oncology indicates that the EU–US gap reflects longer time in review at the EMA in addition to submission sequencing: for antineoplastic new drug applications with final decisions in 2018–2022, median time from submission to approval was 424

days at the EMA versus 216 days at the FDA, and 19% of oncology new drug applications submitted to the EMA were rejected or withdrawn.[26]

Across multiple disease areas where most products receive FDA priority review—including oncology, haematology, respiratory, infectious disease and metabolic conditions—median EMA review timelines exceed those of the FDA by approximately 150–250 days. This pattern is consistent with EMA-wide process data showing that clock-stops are a major driver of elapsed time. In 2023, the average clock-stop for initial MAAs (198 days) was comparable to the agency's average active assessment time (204 days), and 42% of applicants requested extended clock-stops because data were not mature at submission.[27] These dynamics are particularly pronounced in highly specialised therapies: a 2025 analysis of ATMPs reports a median clock-stop duration of 164 days and long overall timelines, with substantial variation by product type.[28]

Across therapeutic areas, the observed differences in access are primarily driven by medicines that are not approved by the EMA rather than by post-approval restrictions or limitations on indications. This indicates that disparities arise mainly at the point of regulatory approval, consistent with EMA–FDA comparison studies showing that when both agencies approve a medicine, indications are often similar (e.g. 79% in a 2014–2016 cohort), while residual divergence is more often about approval versus non-approval in specific cases than routine label narrowing.[29]

EU institutions and the EMA have acknowledged the need to address procedural complexity and review timelines through the ongoing comprehensive reform of EU pharmaceutical legislation. A political agreement reached in December 2025 aims to simplify regulatory procedures, improve internal efficiency and reduce administrative burden, including through common electronic submission formats and regulatory sandboxes for innovative therapies, while maintaining safety standards.[30]

Taken together, the evidence indicates that therapeutic areas with fewer medicines and greater clinical uncertainty are associated with fewer approvals and longer regulatory timelines in Europe, with clock-stops and the resolution of evidentiary questions playing an important role in the observed delays. Comparative analyses show that, relative to the FDA, longer EMA review timelines and fewer approved medicines contribute materially to these disparities, particularly in areas characterised by clinical uncertainty and reliance on expedited development pathways.[31,32] International comparisons further suggest that this pattern is not unique to the EU–US context: recent reforms at China's NMPA have been explicitly designed to accelerate approvals in priority disease areas, contributing to faster review timelines and earlier patient access in oncology and rare diseases.[33] Collectively, the literature

26 Allan Cramer, Freja K. H. Sørup, Hanne R. Christensen, Tonny S. Petersen, and Kristian Karstoft, "Cancer Drug Applications to the EMA and the FDA: A Comparison of New Drugs and Extension of Indication in Terms of Approval Decisions and Time in Review," *British Journal of Clinical Pharmacology* 91, no. 5 (2025): 1431–1438.

27 EMA, "Improving Efficiency of Approval Process for New Medicines in the EU," October 2, 2024, https://www.ema.europa.eu/en/news/improving-efficiency-approval-process-new-medicines-eu.

28 Simonita Alaburde, Justinas Ivaska, Greta Kaspute, and Tatjana Ivaskiene, "Impact of Regulatory Measures on the Approval Timelines of Advanced Therapy Medicinal Products by the European Medicines Agency," *Frontiers in Medicine* 12 (2025).

29 Kashoki et al., "A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014–2016."

30 European Parliament, "Deal on Comprehensive Reform of EU Pharmaceutical Legislation," December 11, 2025, https://www.europarl.europa.eu/news/en/press-room/20251209IPR32110/deal-on-comprehensive-reform-of-eu-pharmaceutical-legislation.

31 Joppi et al., "Food and Drug Administration vs. European Medicines Agency."

32 Ariadna Tibau et al., "Factors in Time to Full Approval or Withdrawal for Anticancer Medicines Granted Accelerated Approval by the FDA," *JAMA Network Open* 8, no. 3 (2025): e252026–e252026.

33 Qi Li et al., "Regulatory and Clinical Outcomes of Priority-Reviewed Innovative Cancer Drugs in China Between 2015 and 2024: An Observational Study," *BMC Cancer* 25, no. 1 (2025): 1175.

indicates that differences in regulatory design and use of expedited pathways play a central role in shaping uneven access to innovation across therapeutic areas.

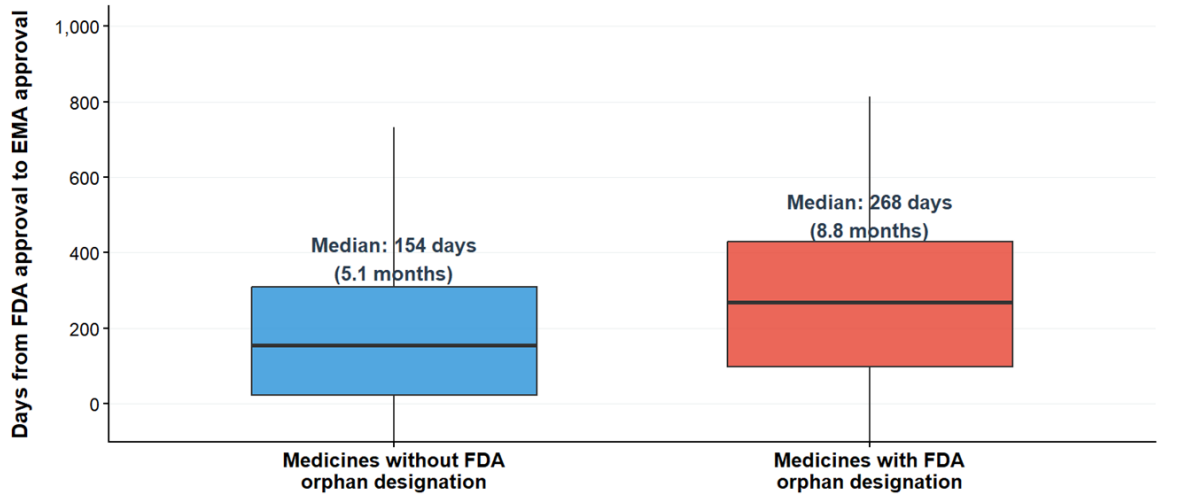
4.2 Orphan medicines have longer approval delays

Orphan medicines reach EMA approval substantially later than non-orphan medicines and are less likely to be first approved in Europe despite similar overall approval rates.

Between 2016 and 2025, the EMA approved approximately 67% of medicines that had previously received orphan designation from the FDA, corresponding to 118 of 176 orphan medicines. Over the same period, the EMA also approved 62% of non-orphan medicines (221 of 356), indicating broadly similar approval rates once products are submitted and assessed.

Despite comparable approval probabilities, orphan medicines experience substantially longer delays to EMA approval following FDA approval. The median time to EMA approval for medicines with an FDA orphan designation is 268 days after FDA approval, compared with 154 days for non-orphan medicines, a difference of approximately 3.7 months (Figure 10). This suggests that timing, rather than approval likelihood, is the primary source of divergence between orphan and non-orphan products in Europe.

Figure 10: EMA and FDA approval delays by FDA orphan designation



Box shows interquartile range (25th–75th percentile); horizontal line indicates median.
Medicines with FDA orphan designation (n = 114): median = 268 days (IQR: 97–429). Medicines without FDA orphan designation (n = 215): median = 154 days (IQR: 23–310).
Difference in medians: 114 days (3.8 months). Despite similar EMA approval rates (67% for orphan vs 62% for non-orphan),
Orphan medicines experience substantially longer delays to EMA approval following FDA approval.

Source: CRA (2026)

Differences are also evident in first-approval sequencing. Only 11% of medicines with an FDA orphan designation were first approved by the EMA, compared with 28% of non-orphan medicines. This indicates that orphan products are less likely to prioritise Europe as an initial approval jurisdiction and more frequently enter the European market after approval elsewhere.

The delay gap is driven primarily by later EMA submissions rather than longer review times: the median submission gap between FDA and EMA filing is 84 days for orphan medicines, compared with 39 days for non-orphan medicines, while EMA review times from submission to authorisation are virtually identical across both groups (429 days vs. 431 days). Notably, the FDA reviews orphan medicines considerably faster than non-orphan medicines (244 days vs. 334 days), likely reflecting the effect of priority review and other expedited designations, a differential that is absent at the EMA.

Taken together, the longer delay to European approval for orphan medicines appears to reflect companies filing later with the EMA and less frequently seeking European approval first, suggesting that strategic sequencing decisions are the primary driver of delayed European access for this group of medicines. This analysis is consistent with literature findings showing that orphan medicines are associated with higher evidentiary complexity, smaller and less mature clinical datasets, and greater uncertainty at the time of submission, all of which tend to prolong regulatory review in Europe despite broadly comparable approval probabilities once assessed.[34,35]

34 Joppi et al., "Food and Drug Administration vs. European Medicines Agency."

35 Rick A. Vreman et al., "Decision Making Under Uncertainty: Comparing Regulatory and Health Technology Assessment Reviews of Medicines in the United States and Europe," *Clinical Pharmacology & Therapeutics* 108, no. 2 (2020): 350–357.

5. Case studies: How the innovation gap manifests in practice

5.1 ATMPs

ATMPs are less likely to seek approval in Europe (EMA) versus the US (FDA) due to limited commercial viability.

Evidence from recent ATMP experience indicates that limited availability in Europe is frequently driven by non-submission, non-launch or post-authorisation withdrawal rather than failure to obtain marketing authorisation, supporting this hypothesis. Several ATMPs that received European approval were subsequently withdrawn for commercial reasons (Box 1). These cases illustrate that regulatory approval alone has not been sufficient to ensure sustained market presence for ATMPs in Europe.

Box 1: Examples of ATMPs that were subsequently withdrawn for commercial reasons

- Bluebird Bio requested the withdrawal of EU marketing authorisations for elivaldogene autotemcel (**Skysona**) and betibeglogene autotemcel (**Zynteglo**) in 2021–2022 after discontinuing commercialisation in Europe.[36,37]
- Earlier products such as ChondroCelect, MACI, sipuleucel-T (**Provenge**) and alipogene tiparvovec (**Glybera**) were similarly withdrawn or not renewed following limited uptake, high per-patient costs or unsustainable commercial returns.[38,39,40,41,42]

In parallel, some ATMPs approved in the US have not been approved or launched in Europe. For example, nadofaragene firadenovec (Adstiladrin), approved by the FDA in 2022, has not received EMA approval.[43] Between 2016 and 2025, the US authorised 33 cell and gene therapies, whereas Europe authorised only 24 ATMPs during the same period (3 of which withdrew authorisation and 1 for which authorisation expired), reflecting slower approval and limited commercial incentives.[44]

The observed patterns are closely linked to structural features of the European policy environment that affect commercial viability. ATMP developers face complex and inconsistent regulatory and manufacturing requirements, including limited ATMP-specific guidance, fragmented implementation of genetically modified organism (GMO) legislation, burdensome import and release testing, shortages

36 EMA, "Skysona," last updated April 4, 2022, https://www.ema.europa.eu/en/medicines/human/EPAR/skysona.
37 EMA, "Zynteglo," last updated November 30, 2022, https://www.ema.europa.eu/en/medicines/human/EPAR/zynteglo.
38 EMA, "ChondroCelect," last updated January 12, 2017, https://www.ema.europa.eu/en/medicines/human/EPAR/chondrocelect.
39 EMA, "MACI," last updated July 5, 2018, https://www.ema.europa.eu/en/medicines/human/referrals/maci.
40 EMA, "MACI: Expiry of the Marketing Authorisation in the European Union," July 2, 2018, https://www.ema.europa.eu/en/documents/public-statement/public-statement-maci-expiry-marketing-authorisation-european-union_en.pdf.
41 EMA, "Provenge," last updated May 19, 2015, https://www.ema.europa.eu/en/medicines/human/EPAR/provenge.
42 EMA, "Glybera," last updated October 30, 2017, https://www.ema.europa.eu/en/medicines/human/EPAR/glybera.
43 FDA, "Adstiladrin," last updated October 10, 2025, https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/adstiladrin.
44 CRA analysis. Products for which authorization was withdrawn include Beqvez, Skysona and Zynteglo. MACI's EMA marketing authorisation was suspended and then expired.

of specialised manufacturing staff, and barriers to cross-border movement of cells and patients.[45] These factors increase costs and extend development timelines, particularly for smaller developers that dominate the ATMP pipeline.

Inflexibilities with health technology assessment (HTA) requirements further contribute to uncertainty. ATMPs often rely on small or single-arm trials and generate long-term durability evidence only after launch, yet European HTA frameworks continue to prioritise large randomised controlled trials (RCTs) and long-term durability data. Analyses indicate that 90% of existing ATMPs would not meet strict evidence expectations under proposed EU Joint Clinical Assessment due to the strict RCT expectations.[46] Fragmented national HTA processes and duplicated evidence requirements across member states further weaken predictability and increase administrative burden.

Finally, existing payment and funding models are not designed for high-value, one-time therapies.[47] High upfront costs, combined with uncertainty around long-term outcomes and limited flexibility in reimbursement mechanisms, reduce the commercial attractiveness of European launch and uptake. While several member states have implemented managed entry agreements, these are often short term and constrained by annual budget silos that limit cost-spreading over time. By contrast, the US has experimented with a broader range of financing approaches for high-cost gene and cell therapies, including outcomes-based contracts and multiyear instalment models designed to align long-term value with near-term affordability.[48] Although challenges remain in both markets, the comparatively greater flexibility in US payment models may influence launch sequencing and investment decisions for ATMP developers.

Taken together, the evidence examined in this case study supports the hypothesis that ATMPs are less likely to seek or sustain approval in Europe than in the US, not primarily because of scientific or regulatory failure but because of commercial viability considerations shaped by Europe's regulatory, access, and payment environment.

5.2 China-first approvals by global companies

Some companies with headquarters outside China are receiving an NMPA approval before EMA approval due to the prioritisation of the NMPA submission.

Recent approval patterns provide evidence that China is increasingly positioned as an early or parallel launch market, including for companies without a Chinese headquarters (Box 2). These cases suggest that, for some globally developed medicines, China is being prioritised ahead of Europe in regulatory sequencing.

45 EUCOPE, "EUCOPE White Paper on ATMP Manufacturing," November 2025, https://www.eucope.org/wp-content/uploads/2025/11/eucope-white-paper-atmp-manufacturing.pdf.

46 Alliance for Regenerative Medicine, "Proposed Joint Clinical Assessment Methodology Would Have Rejected Nearly 90% of the ATMPs Currently Authorized in the EU," June 20, 2023, https://alliancerm.org/wp-content/uploads/2023/06/ARM-PR-June-20-2023.pdf.

47 EUCOPE, "Advanced Therapies Medicinal Products: New Payment & Funding Approaches," 2021, https://www.eucope.org/wp-content/uploads/2022/03/eucope-ipm-paper-2021.pdf.

48 Institute for Clinical and Economic Review and NEWDIGS at Tufts Medical Center, "Managing the Challenges of Paying for Gene Therapy: Strategies for Market Action and Policy Reform," April 23, 2024, https://icer.org/wp-content/uploads/2024/04/Managing-the-Challenges-of-Paying-for-Gene-Therapy-_-ICER-NEWDIGS-White-Paper-2024_final.pdf.

Box 2: Examples of companies with headquarters outside China receiving NMPA approval before EMA approval

- Naxitamab (**Danyelza**), developed by Y-mAbs Therapeutics, Inc. (US), was approved by the FDA in 2020 and subsequently by the NMPA in 2022 but has not yet received EMA marketing authorisation despite holding orphan drug designation in the EU.[49,50,51]
- Similarly, deutetrabenazine (**Austedo**), developed by Teva (Israel), received FDA approval in 2017 and NMPA approval in 2020 and only just received EMA approval in January 2026.[52,53,54]

More recent examples reinforce this pattern. Efbemalenograstim alfa (Ryznueita), developed by Evive Biotechnology (a Singapore-based micro-company), received NMPA approval in May 2023, followed by FDA approval later that year and EMA approval only in 2024.[55,56,57] While not all products follow the same sequence, these cases demonstrate that NMPA approval can precede EMA approval even for companies with headquarters outside China, indicating a shift in how global regulatory strategies are structured.

This change in sequencing is closely linked to reforms implemented by the NMPA over the past decade, which have materially altered the relative attractiveness of China as an important regulatory market. These reforms include the introduction of priority review pathways, acceptance of foreign clinical trial data, significant reductions in investigational new drug review timelines, and China's accession to the International Council for Harmonisation (ICH).[58,59,60,61] Together, these changes have reduced submission and approval timelines and increased regulatory predictability, enabling earlier market entry.

For global developers, particularly those with limited resources or products targeting high-unmet-need indications, these reforms can make China a strategically attractive market to prioritise alongside or

49 FDA, "FDA Grants Accelerated Approval to Naxitamab for High-Risk Neuroblastoma in Bone or Bone Marrow," November 27, 2020, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-naxitamab-high-risk-neuroblastoma-bone-or-bone-marrow.

50 Y-mAbs Therapeutics, Inc., "Y-mAbs' DANYELZA® (naxitamab-gqgk) for the Treatment of High-Risk Neuroblastoma Approved in China," December 8, 2022, https://ir.ymabs.com/news-releases/news-release-details/y-mabs-danyelzar-naxitamab-gqgk-treatment-high-risk.

51 EMA, "EU/3/18/2094: Orphan Designation for Treatment of Neuroblastoma," accessed January 6, 2026, https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu-3-18-2094.

52 Sara LaJeunesse, "FDA Approves Deutetrabenazine (AUSTEDO™) to Treat Chorea," *HD Insights* 17 (2017), https://huntingtonstudygroup.org/hd-insights/holisticly-embrace-extensible-benefits-before-value/.

53 Teva, "China Approves AUSTEDO® For Treating Chorea Associated with Huntington's Disease and Tardive Dyskinesia in Adults," May 18, 2020, https://www.tevapharm.com/news-and-media/latest-news/china-approves-austedo-for-treating-chorea-associated-with-huntingtons-disease-and-tardive-dyskinesia-i/.

54 EMA, "Austedo," last updated January 23, 2026, https://www.ema.europa.eu/en/medicines/human/EPAR/austedo.

55 FirstWord Pharma, "Ryzneuta Approved for Use in China," May 10, 2023, https://firstwordpharma.com/story/5738103.

56 FDA, "Drug Trials Snapshots: RYZNEUTA," last updated March 15, 2024, https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots-ryzneuta.

57 EMA, "Ryzneuta," September 3, 2025, https://www.ema.europa.eu/en/medicines/human/EPAR/ryzneuta.

58 Xingyue Zhu and Jinsui Zhang, "Regulatory Efforts to Address the Access Gap for Foreign New Drugs in China: The Priority Review Program and Related Policies," *Global Health Research and Policy* 10, no. 1 (2025): 7.

59 Mengjuan Jiang, Jingjing Huang, Su Wang, Yulu Fan, and Yuwen Chen, "Can the Accepting Foreign Clinical Data Policy Improve Innovation Investment of Pharmaceutical Firms? Empirical Evidence from China," *Frontiers in Public Health* 13 (2025).

60 Angus Liu, "China Proposes Shorter Clinical Trial Reviews in Efforts to Accelerate Drug Development," Fierce Biotech, June 16, 2025, https://www.fiercebiotech.com/biotech/accelerate-drug-development-china-proposes-shorten-clinical-trial-review-time.

61 Xin Du, Zhong Zhao, Xiaoqian Sun, Yongbing Zhang, Yi Zhang, and Xingzian Luo, "Challenges for Chinese Innovative Cancer Drugs in Going Global: Insights from Multiregional Clinical Trials," *The Lancet Oncology* 26, no. 10 (2025), e558–e569.

even ahead of Europe. Taken together, the evidence examined in this section is consistent with the hypothesis that some companies headquartered outside China are obtaining NMPA approval before EMA approval as a result of strategic submission prioritisation.

5.3 Delayed access to Chinese innovation in Europe

Innovative medicines developed and first approved in China are either not approved by the EMA or are approved with significant delays and limitations.

Recent approval patterns indicate that China has become a leading source of innovative medicines, with a growing number of new drugs first approved by the NMPA. Over the 2019–2023 period, the NMPA authorised 256 new medicines, surpassing the US (243) and the EU (191), reflecting the scale and maturity of its innovation ecosystem.[62] A subset of these China-origin medicines reach European patients only after prolonged delays and, in some cases, under narrower indications. These cases are consistent with a pattern of delayed European access to China-origin innovation (Box 3).

Box 3: Examples of innovative medicines developed and first approved in China being approved by the EMA with a significant delay

- Sugemalimab (**Cejemly**) of Cstone Pharmaceuticals (China)—an anti–PD-L1 antibody for the treatment of non-small cell lung cancer—was approved by the NMPA in December 2021 but did not receive EMA approval until July 2024.[63,64]
- Tislelizumab (**Tevimbra**) of Tileilizhu Dankang Zhusheye (China) was first approved in China for the treatment of relapsed or refractory classical Hodgkin's lymphoma in 2019 and authorised by the EMA only in September 2023 (and the FDA in March 2024).
- Tislelizumab is now indicated for multiple indications.[65,66,67] Serplulimab (**Hetronifly**) of Shanghai Henlius Biotech, Inc. (China)—an anti–PD-1 antibody for the treatment of adult patients with advanced unresectable or metastatic microsatellite instability-high (MSI-H) solid tumours—received NMPA approval in 2022, with EMA authorisation following in February 2025.[68,69]

Differences in regulatory timelines and use of expedited pathways help explain these outcomes. Comparative analyses show that the FDA generally completes marketing authorisation reviews more quickly than the EMA. For example, median review time for cancer drugs was ~216 days at the FDA versus ~424 days at the EMA, highlighting faster regulatory processing in the US.[70] The NMPA has increasingly relied on priority review and accelerated pathways to shorten approval timelines; priority-reviewed products complete assessment in 263.5 days compared with 352 days for standard

62 Yan et al., "New Drug Approvals in China."

63 PR Newswire, "Cstone Announced New Drug Approval of Cejemly® (sugemalimab) in China to Potentially Reshape the Landscape of Immuno-Oncology Therapy in Lung Cancer," December 21, 2021, https://www.prnewswire.com/news-releases/cstone-announced-new-drug-approval-of-cejemly-sugemalimab-in-china-to-potentially-reshape-the-landscape-of-immuno-oncology-therapy-in-lung-cancer-301448778.html.

64 EMA, "Cejemly," last updated February 18, 2026, https://www.ema.europa.eu/en/medicines/human/EPAR/cejemly.

65 Arnold Lee and Susan J. Keam, "Tislelizumab: First Approval," *Drugs* 80 no. 6 (2020): 617–624.

66 EMA, "Tevimbra," last updated January 26, 2026, https://www.ema.europa.eu/en/medicines/human/EPAR/tevimbra.

67 Janice Reichert, "TEVIMBRA (Tislelizumab-jsgr) Granted First FDA Approval for Esophageal Squamous Cell Carcinoma," Antibody Society, March 18, 2024, https://www.antibodysociety.org/antibody-therapeutic/tevimbra-tislelizumab-jsgr-granted-first-fda-approval-for-esophageal-squamous-cell-carcinoma/.

68 Arnold Lee, "Serplulimab: First Approval," *Drugs* 82, no. 10 (2022): 1137–1141.

69 EMA, "Hetronifly," last updated January 12, 2026, https://www.ema.europa.eu/en/medicines/human/EPAR/hetronifly .

70 Cramer et al., "Cancer Drug Applications to the EMA and the FDA."

reviews.[71] By contrast, the EMA makes more limited use of expedited procedures and typically requires longer review periods.[72]

Taken together, the evidence examined in this section is consistent with the hypothesis that innovative medicines developed and first approved in China face delayed and more limited access in Europe. These delays do not appear to be driven solely by scientific quality but rather by differences in regulatory timelines, use of accelerated pathways and evidentiary expectations. As China's role as a source of pharmaceutical innovation continues to expand, such dynamics risk widening Europe's innovation gap and delaying patient access to globally developed therapies.

5.4 Micro and small company regulatory challenges

Micro and small companies are forgoing EMA submission due to regulatory and access barriers, even for high-value medicines.

Recent examples indicate that several high-value medicines developed by micro and small companies have obtained FDA approval but have not been submitted to or approved by the EMA (Box 4). These cases suggest that the absence of EMA approval is not necessarily driven by a lack of clinical value but by strategic decisions regarding whether to engage with the European regulatory system.

Box 4: Examples from micro and small companies forgoing EMA submission

- Ensartinib (**Ensacove**)—co-developed by Betta Pharmaceuticals (China) and Xcovery Holdings (a US-based micro company, which is a subsidiary company of Betta Pharmaceuticals)—received FDA approval in December 2024 for ALK-positive non-small cell lung cancer but has not been approved in Europe.[73]
- Similarly, Cosibelimab-ipdl (**Unloxcyt**), of Checkpoint Therapeutics, Inc. (a US-based micro company), which was later acquired by Sun Pharma (US), was approved by the FDA in December 2024 for adults with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) but has not received EMA approval.[74]

Evidence from stakeholder analyses indicates that EMA regulatory requirements impose a disproportionate administrative and operational burden on micro and small enterprises (SMEs). Smaller companies consistently report that the volume, complexity and resource intensity of EU regulatory procedures—including documentation requirements, procedural steps and compliance obligations—are difficult to manage with limited staff and financial capacity. This burden is often cited

71 Li et al., "Regulatory and Clinical Outcomes of Priority-Reviewed Innovative Cancer Drugs in China Between 2015 and 2024."

72 CRA analysis.

73 Angus Liu, "Playing Catch-Up with Pfizer and Roche, China-Made ALK Drug Clears FDA in Lung Cancer," Fierce Pharma, December 19, 2024, https://www.fiercepharma.com/pharma/playing-catch-pfizer-and-roche-china-made-alk-drug-clears-fda-lung-cancer.

74 FDA, "FDA Approves Cosibelimab-lpdl for Metastatic or Locally Advanced Cutaneous Squamous Cell Carcinoma," last updated December 13, 2024, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-cosibelimab-ipdl-metastatic-or-locally-advanced-cutaneous-squamous-cell-carcinoma.

as more challenging than the underlying scientific or technical requirements, indicating that regulatory process design itself can act as a deterrent to EMA engagement.[75]

In addition, awareness and uptake of existing EMA support mechanisms for SMEs appear limited. Surveys suggest that while many small companies are broadly aware that the EMA offers SME support, knowledge of specific pathways and tools—such as PRIME, ATMP certification or tailored scientific advice—remains low, with only 15% aware of PRIME support, 11% aware of ATMP certification and just 7% aware of the EMA's Policy 0070 on clinical data publication.[76] As a result, smaller developers may not fully benefit from mechanisms intended to reduce regulatory burden or accelerate development, further weakening the incentive to pursue EMA submission.

Regulatory challenges are compounded by Europe's fragmented post-approval environment. Beyond central authorisation, micro and small companies face the additional challenge of navigating heterogeneous HTA and pricing and reimbursement processes across member states. Unlike larger firms, smaller developers often lack the commercial infrastructure, local affiliates and financial resilience needed to manage multiple parallel negotiations. This challenge is particularly acute for companies headquartered outside Europe, which may have no established European market-access presence.[77,78]

Taken together, the evidence examined in this section supports the hypothesis that micro and small companies are more likely to forgo EMA submission, even for high-value medicines, due to regulatory and access barriers rather than scientific limitations. These dynamics contribute to Europe's innovation gap by disproportionately excluding early-stage and resource-constrained innovators, reducing the diversity of innovation reaching European patients and weakening Europe's attractiveness as a launch market for emerging companies.

5.5 Products with new MoAs

Products with new MoAs are facing regulatory delays/challenges, resulting in fewer novel products with new MoAs being approved in Europe (EMA).

Several high-profile examples illustrate divergent regulatory outcomes for medicines with new MoAs. Differences in evidentiary thresholds can lead to earlier availability in the US but delayed or absent access in Europe for therapies targeting rare or high-unmet-need conditions (Box 5).

75 Nicole Brooks, "How Successful Are the EMA's Pharmaceutical SME Initiatives?," Somerville Development Partners, February 22, 2024, https://somerville-partners.com/how-successful-are-the-emas-sme-initiatives/.

76 Brooks, "How Successful Are the EMA's Pharmaceutical SME Initiatives?"

77 Gamba, Magazzini, and Pertile, "Improving Access to Medicines and Promoting Pharmaceutical Innovation."

78 Hogan Lovells, "Market Access in Europe: Navigating Pricing & Reimbursement Pathways," August 2025, https://www.hoganlovells.com/-/media/hogan-lovells/pdf/2025-pdfs/market-access_reimbursment-and-pricing-in-europe_august-2025.pdf.

Box 5: Examples of products with new MoAs facing regulatory delays and challenges

- Istradefylline (**Nourianz**; EU application: **Nouryant**), of Kyowa Kirin, for Parkinson's disease 'OFF' episodes, was approved by the FDA in August 2019 as an adjunct to levodopa/carbidopa.[79] In contrast, the EMA refused marketing authorisation (confirmed after reexamination in November 2021), concluding that efficacy was not established because results across eight trials were inconsistent, there was no clear dose–response, and no effect was seen in studies conducted in the EU.[80]
- Emapalumab (**Gamifant**), of Swedish Orphan Biovitrum (**Sobi**), for primary haemophagocytic lymphohistiocytosis (pHLH), was approved by the FDA on 20 November 2018 in a high-unmet-need setting.[81] By contrast, the EMA refused marketing authorisation (confirmed after reexamination in November 2020), finding the evidence insufficient to conclude effectiveness because the main dataset was small, included concomitant therapies and variable symptoms over time (making attribution difficult), and raised challenges in fully characterising safety and concerns about data reliability.[82]

These examples reflect broader differences in regulatory flexibility for medicines with novel MoAs. Evidence indicates that the FDA is more likely to accept surrogate endpoints, conditional data and iterative evidence generation for first-in-class products, particularly where there is a significant unmet medical need. By contrast, the EMA applies a more cautious approach, placing greater emphasis on demonstration of clinical benefit and robust safety data at the time of approval. While this approach aims to reduce uncertainty, it can result in longer review timelines, refusals or approvals limited to narrower patient populations.[83]

Differences in the use of expedited regulatory pathways further contribute to this dynamic. Comparative analyses show that the FDA relies on accelerated or expedited approval programmes substantially more frequently than the EMA, particularly for oncology and other innovative therapies: the FDA used expedited approval programmes for 69% of new drugs approved since 2016, compared with just 6% for the EMA (defined as only accelerated approval, not PRIME or conditional approvals).[84] A comparative study of regulatory pathways for new anticancer drugs found that the FDA used one or more expedited regulatory approval programmes for 89% of the new anticancer drugs, whereas the EMA used them for only 43%.[85] The EMA's more limited use of pathways designed to accommodate evidentiary uncertainty may constrain its ability to support first-in-class

79 Kyowa Kirin Co., Ltd., "Kyowa Kirin Announces FDA Approval of NOURIANZ™ (istradefylline) for Use in Parkinson's Disease," August 28, 2019 https://www.kyowakirin.com/media_center/news_releases/2019/e20190828_01.html.

80 EMA, "Nouryant (istradefylline): Refusal of the Marketing Authorisation," last updated January 19, 2022, https://www.ema.europa.eu/en/medicines/human/EPAR/nouryant.

81 FDA, "FDA Approves emapalumab for Hemophagocytic Lymphohistiocytosis," November 20, 2018, https://www.fda.gov/drugs/fda-approves-emapalumab-hemophagocytic-lymphohistiocytosis.

82 EMA, "Gamifant (emapalumab): Refusal of the Marketing Authorisation," last updated March 23, 2021, https://www.ema.europa.eu/en/medicines/human/EPAR/gamifant.

83 Blake Forman, "First-in-Class Drugs Offered Greater Regulatory Flexibility in the US vs. Europe," Technology Networks Drug Discovery, April 2, 2025, https://www.technologynetworks.com/drug-discovery/news/first-in-class-drugs-offered-greater-regulatory-flexibility-in-the-us-vs-europe-398029.

84 CRA analysis.

85 Fabiany da Costa Gonçalves, Ebru Demirci, and Alex Zwiers, "A Detailed Analysis of Expedited Regulatory Review Time of Marketing Authorization Applications for New Anticancer Drugs in the US and EU," *Clinical and Translational Science* 15, no. 8 (2022): 1959–1967.

products. While surrogate endpoints and nontraditional trial designs are accepted, these are primarily applied within conditional marketing authorisation.[86]

Taken together, the evidence examined in this section is consistent with the hypothesis that products with new MoAs face greater regulatory challenges and delays in Europe. These challenges contribute to fewer and later EMA approvals of truly novel therapies, reinforcing the innovation gap and delaying European patient access to medicines at the forefront of scientific development.

86 Rohini Sharma, Anamika Gulati, and Kanwaljit Chopra, "Era of Surrogate Endpoints and Accelerated Approvals: A Comprehensive Review on Applicability, Uncertainties, and Challenges from Regulatory, Payer, and Patient Perspectives," *European Journal of Clinical Pharmacology* 81, no. 5 (2025): 605–623.

6. Implications and conclusions

6.1 Implications for Europe and Germany

The findings of this report point to a widening innovation gap with implications that extend well beyond regulatory timelines. Patterns observed across product types, company characteristics and regulatory sequencing suggest systemic effects on patient access, Europe's innovation ecosystem and Europe's strategic position in global life sciences.

Patient access

Across the analyses presented in this report, a consistent finding is the persistence of a structural innovation gap between Europe and comparator markets. Quantitative analysis shows that a substantial share of innovative medicines authorised elsewhere are either not submitted to the EMA or do not progress through the European regulatory pathway. Even where submissions occur, EMA approvals frequently involve longer review timelines or reexamination.

Case studies reinforce these patterns, illustrating how ATMPs, orphan medicines, China-origin innovations and products with novel MoAs are disproportionately affected by regulatory delay, intensified review processes or non-approval in Europe. These outcomes reflect broader differences in regulatory sequencing, predictability and evidentiary expectations that shape company decisions on where and when to seek approval and increasingly position Europe as a secondary or follow-on market for innovative medicines.

For Germany, which has historically benefited from efficient post-authorisation processes, the upstream innovation gap increasingly constrains national-level strengths. Where products are not submitted to the EMA, or where regulatory approval is delayed, national procedures cannot offset earlier differences in European regulatory timing and scope.

Innovation ecosystem

The evidence also points to structural consequences for Europe's innovation ecosystem. Across multiple chapters, the report documents how companies adjust regulatory sequencing and market prioritisation in response to predictability, speed and downstream access conditions. Global companies increasingly prioritise the US and, in some cases, China for early approval, while micro and small companies are more likely to forgo EMA submission altogether due to regulatory and access barriers.

These dynamics disproportionately affect early-stage innovators, first-in-class products and advanced therapies, which are inherently associated with higher uncertainty and resource constraints. Where regulatory frameworks, HTA requirements and payment models are less adaptable to such uncertainty, Europe becomes a less attractive environment for high-risk, high-reward innovation. Over time, this can reduce clinical trial activity, delay technology transfer and shift manufacturing and investment away from Europe.

For Germany, this raises concerns about the sustainability of its role as a hub for pharmaceutical development and life sciences investment if upstream European barriers continue to shape global development strategies.

Strategic positioning

The findings from this report suggest a broader shift in Europe's strategic position within the global innovation landscape. Evidence from first-launch dynamics and China-first approvals indicates that Europe is increasingly positioned as a secondary or follow-on market rather than a destination for

early regulatory approval and launch. Products with new MoAs, advanced therapies and China-origin innovations frequently reach Europe later and under more restrictive conditions than in other major markets.

This shift has strategic consequences. As regulatory leadership and early adoption move elsewhere, Europe risks losing influence over global development standards, trial design and evidence generation for emerging technologies. The cumulative effect of delayed approvals, cautious use of expedited pathways, and fragmented post-authorisation access risks creating a self-reinforcing cycle in which Europe's reduced attractiveness further widens the innovation gap.

For both Europe and Germany, addressing these implications is therefore not solely about accelerating individual approvals. It requires a more systemic response that improves regulatory flexibility, aligns evidence expectations with innovation realities, reduces fragmentation in access pathways, and restores confidence that Europe is a viable and attractive market for innovative medicines at the forefront of scientific progress.

6.2 Conclusion and policy reflection

This report finds clear evidence of an emerging innovation gap between Europe and other major pharmaceutical markets. Across advanced therapies, medicines with novel MoAs, China-origin innovations and products developed by micro and small companies, Europe increasingly experiences delayed approvals and non-submission compared with the US and, in some cases, China. These patterns are driven less by regulatory rejection than by strategic decisions from developers responding to regulatory speed, flexibility and downstream access conditions. The result is delayed or foregone patient access to high-value medicines, particularly in areas of high unmet need.

From a policy perspective, the findings suggest that closing the innovation gap will require a more systemic approach. Regulatory frameworks and evidence expectations influence whether developers prioritise EMA review, particularly for innovative products with higher uncertainty. Adequate market and regulatory incentives are needed to encourage developers to pursue European regulatory review for innovative medicines and to prevent a widening innovation gap. These incentives should be targeted at areas where the data suggest the greatest risk of reduced European engagement: micro companies, smaller therapeutic areas, and orphan medicines. This should include streamlined regulatory pathways and greater flexibility in evidence requirements where appropriate. Europe risks becoming a follow-on market for pharmaceutical innovation. Addressing these challenges is central not only to improving patient access but also to safeguarding Europe's long-term competitiveness and leadership in the life sciences industry.

Taken together, these findings also highlight that major policy shifts such as a US 'most-favoured-nation' (MFN) drug pricing model are not confined to domestic US politics. Given the scale of the US market, MFN could become a powerful international reference point, shaping global pricing and commercial strategy decisions with direct knock-on effects on launch sequencing, regulatory filing strategies and ultimately supply security in Europe and Germany. In that sense, MFN could amplify a trend already observed in the data: Europe is increasingly at risk of losing ground as an early access market for pharmaceutical innovation.

Against this backdrop, Germany and Europe need to align their framework conditions so that patients can benefit from medical progress in a timely manner and so that Europe does not further erode its attractiveness as a region for development, regulatory approval and product launch. A key element of such a strategy is to build on Germany's strengths in a targeted manner and to reestablish a framework that is open to innovation.

7. Appendix

7.1 Data collection methodology

7.1.1 Overview

The analysis aimed to provide a comprehensive view of the innovation gap across major global markets by examining regulatory approval patterns, company characteristics and therapeutic areas.

The study period covered January 1, 2016, to December 31, 2025. Regulatory data were sourced from official agency websites and NAVLIN, supplemented by secondary sources for China:

- For the US, data were drawn from Drugs, Center for Drug Evaluation and Research (CDER) annual new molecular entity (NME) lists, and Center for Biologics Evaluation and Research (CBER) reports.
- For Europe, European Public Assessment Reports (EPARs) were used to capture submission and authorization dates for centrally authorised products, while German approval dates were applied for products approved through national procedures.
- For China, data came from the National Medical Products Administration's (NMPA) Center for Drug Evaluation (CDE) annual reports, academic sources, and grey literature, with limitations addressed by triangulating multiple sources. Systematic data availability improved after the China Food and Drug Administration (CFDA) transitioned to the National Medical Products Administration (NMPA) in 2018.

The scope of products included NMEs, biologics, and advanced therapy medicinal products (ATMPs) classified as innovative drugs by CDER or CBER, the European Medicines Agency (EMA), or the NMPA. Generics, biosimilars, vaccines, traditional Chinese medicines (TCMs), reformulations, new strengths and line extensions were excluded unless they represented a first approval in the region for a new active substance (NAS). Combination products were included only if they contained an NAS, and products later withdrawn due to safety or toxicity concerns were removed to avoid overstating sustained access.

7.1.2 Regulatory data

The dataset was compiled from regulators' public databases and documents, supplemented where needed with NAVLIN, academic publications, and grey literature.

For the FDA (US), annual novel drug approvals were compiled from Drugs@FDA, CDER's annual novel drug approval lists (new drug application/biologics license application NMEs), and CBER's yearly biological product approvals. Vaccines, nontherapeutic agents and cord blood stem cell products were excluded. For FDA products, we also extracted regulatory designations (e.g. orphan status, breakthrough therapy, fast track, accelerated approval) and key dates. Where available, submission dates were supplemented using BioMedTracker to support analysis of review timing.

For the EMA (EU), centrally authorised products were identified using EPARs and EMA reporting on NASs. NASs recommended for marketing authorisation were identified from EMA annual reports (2016–2025), excluding vaccines and withdrawn products. From EMA sources, we extracted both regulatory designations (e.g. orphan designation, conditional approval, PRIME, accelerated assessment) and submission dates. Submission dates were taken from the first EPAR version (Section 1.1, 'Submission of the dossier'), excluding renewals and variations. If a submission date was not available, it was recorded as 'Not found' with a brief justification. All dates were standardised to DD/MM/YYYY.

To avoid misclassifying European access when a product was not centrally authorised, medicines approved by the FDA but not approved by the EMA were checked for authorisation via Germany's national procedure, using the German national regulator's (Federal Institute for Drugs and Medical Devices, BfArM) public records. Where a national approval was confirmed, the German approval date was recorded as the European approval proxy.

For the NMPA (China), products were included if classified by the NMPA as innovative: chemical Class 1, innovative chemical Class 5.1, biologic Class 1 and biologic Class 3.1. Vaccines and TCMs were excluded. Because reporting completeness improved after the CFDA-to-NMPA transition, earlier-year gaps were addressed by triangulating NMPA/CDE annual reports with academic sources and grey literature, resolving discrepancies by prioritising primary regulator documentation where available.

Across regions, data limitations were addressed through triangulation across multiple sources, consistent definitions and standardised formatting of dates and regulatory attributes. This produced a harmonised dataset suitable for comparing approval outcomes, timing (where submission dates were available) and use of expedited pathways across the FDA, EMA and NMPA.

7.1.3 Manufacturer size

Manufacturer size was classified using annual global revenue reported in manufacturers' investor relations communications for 2016–2025, aggregated first using Argon AI, an AI-powered operating system designed specifically for the pharmaceutical secondary research, and manually verified for each year. Company size categories are revenue based and adapted from commonly used industry segmentation frameworks—notably IQVIA's definitions by global prescription sales (large > USD 10 billion; mid USD 5–10 billion; small USD 0.5–5 billion) and its 'emerging biopharma' threshold (≤ USD 0.5 billion sales and/or < USD 200 million annual R&D spend)—with cutoffs adjusted to four bands (large ≥ USD 15 billion; mid USD 5–15 billion; small USD 1–5 billion; micro < USD 1 billion) to reflect the scale of global pharma and capture early-stage, often narrow-pipeline innovators.[87] Revenue was selected as the size metric because it is objective, widely reported and closely correlated with organisational scale (including R&D capacity, geographic footprint and portfolio breadth), making it well suited for comparing innovation and strategy across firms. This choice is also consistent with evidence linking pharmaceutical innovation output to market size: Dubois et al. (2014) find a positive elasticity of innovation (measured by new chemical entities) with respect to revenues in the pharmaceutical industry.[88]

All revenue data were drawn from publicly available annual reports and verified industry rankings, and were standardised to the most recent fiscal year reported in USD. Companies were assigned to the category corresponding to their revenue in that year; movements across thresholds over time were noted but not modelled explicitly in the classification. Each product was assigned to a size bucket based on the marketing authorisation holder for the first-approving regulator at the time of approval. Therapeutic areas were mapped to primary Anatomical Therapeutic Chemical categories based on the main indication. For multi-indication products, the first approved indication per FDA or EMA was used. Categories reflect the FDA spectrum of diseases by therapeutic area and included allergy, autoimmune and immunology, cardiovascular, dermatology, endocrine, gastroenterology,

87 IQVIA, "Global Trends in R&D 2024: Activity, Productivity, and Enablers," February 22, 2024, https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2024-activity-productivity-and-enablers.

88 Pierre Dubois, Oliver de Mouzon, Fiona Scott-Morton, and Paul Seabright, "Market Size and Pharmaceutical Innovation," *RAND Journal of Economics* 46, no. 4 (2015): 844–871.

haematology, infectious disease, metabolic, neurology, oncology, ophthalmology, orthopaedics, psychiatry, renal and respiratory.

7.1.4 Resulting dataset

For each medicine, data captured included the international nonproprietary name, therapeutic area, ATMP status, submission and marketing authorisation dates, manufacturer size classification and regulatory outcomes such as orphan status, conditional approval, PRIME or breakthrough therapy designation, and accelerated assessment or fast track status.

7.2 Analysis

All data processing and statistical analysis were conducted in R (version 4.4.3). The underlying dataset is available from the authors upon request.

Approval rates were calculated as the share of medicines in the total pool of novel medicines first approved between 2016 and 2025 that received authorisation from each agency. This differs from a submission-based success rate (approvals divided by total submissions), which could not be calculated comprehensively due to incomplete EMA submission data across all products in scope. Key metrics used to assess the innovation gap included approval rates across the FDA, EMA, and NMPA; regulatory time delays between submission and approval for the FDA and EMA; and the share of novel medicines by company size and therapeutic area, together with associated approval rates and timeline metrics.

Regulatory timelines were assessed using three metrics. Regulatory review time was defined as the number of days from filing to marketing authorisation. The submission gap was defined as the difference in days between a product's FDA and EMA filing dates, with positive values indicating later EMA submission. The approval lag was defined as the number of days between FDA and EMA approval dates for the same product. NMPA review times were excluded, as submission dates are not publicly available in China. Company size analysis for NMPA approvals was similarly omitted due to limited revenue data availability for micro and small firms operating primarily in China.

Catch-up analysis for NMPA approvals classified each NMPA-approved medicine as either a catch-up approval, where the FDA or EMA had approved the same medicine in a prior calendar year, or a new approval where no prior Western approval existed. The lag was calculated in years between first Western approval and NMPA approval.

Trend estimates are derived from ordinary least squares regression on annual data from 2016 to 2024, expressed as average percentage point changes per year. Data from 2025 are included in aggregate counts but excluded from trend analyses due to potentially incomplete approval records at the time of analysis.

About Charles River Associates

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