



Designing for uncertainty, value, and investor scrutiny: What MFN means for early-stage biotech

A new kind of question in biotech

For years, early-stage biotech companies have operated with a relatively clear value logic: strong science, a meaningful unmet need, and a compelling clinical profile would translate into a credible commercial opportunity. That foundation, while still essential, is no longer sufficient.

The emergence of Most Favored Nation (MFN) pricing dynamics signals a deeper structural shift in how pharmaceutical value is assessed. Instead of a system anchored primarily in US pricing, we are moving toward a world in which prices, and therefore value, are increasingly interconnected across geographies.

The immediate challenge this creates is uncertainty around long-term asset value, and the growing expectation that companies can explain and defend that value under multiple possible futures.

A new question is taking center stage in investor conversations:

What does MFN mean for your asset's value, and how resilient is that value across plausible future scenarios?



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The answer to this question differs depending on where a company's value is geographically anchored. While US pricing has historically been the primary driver of global value, not all biotech companies (particularly those headquartered outside the US) optimize around the same assumptions. Understanding those differences is one of the more strategic tasks today.

From pricing pressure to valuation uncertainty

It is tempting to think of MFN as a pricing issue, but for early-stage companies, it functions primarily as a valuation challenge.

MFN introduces several layers of uncertainty simultaneously. There is the possibility of US price compression, but also the less straightforward question of how ex-US markets will respond - whether through price increases, tighter access

controls, or both. In parallel, global price referencing mechanisms may amplify spillover effects across markets.

On top of this sits ongoing policy volatility, including uncertainty around scope, implementation timelines, and what might happen beyond the current policy horizon.

All these factors together shift how investors think. Rather than accepting a single peak sales estimate, they increasingly evaluate assets through a range of scenarios. The conversation moves away from "what is the value?" toward "how stable is the value under different assumptions?"

In this sense, MFN acts as a multiplier of uncertainty. It does not simply reduce value: it makes it more contingent, more debatable, and more dependent on the quality of a company's strategic thinking.



Why time horizon matters more than ever

One of the most important (and often underappreciated) implications of MFN is that it forces companies to think across multiple time horizons. The years leading up to 2029 may be characterized by partial implementation and evolving rules. The period beyond 2029 could bring expansion, modification, or even replacement of the current framework, although some form of international reference pricing in the US will likely persist.

This creates several plausible futures. MFN could expand and become more restrictive. It could soften or narrow in scope. Or it could disappear altogether while leaving behind broader reforms that still reshape pricing dynamics.

Value, in other words, can no longer be tied to a single assumed environment at launch. Instead, companies are implicitly being asked to demonstrate resilience and show that their assets can retain value across different policy regimes.

The relevance of these scenarios differs by company archetype. Biotechs with a strong US commercial focus may be more directly exposed to pricing compression, while companies anchored in Europe or Asia may face more indirect (but still material) effects through reference pricing, access dynamics, and partnering structures.

The changing investor lens

These structural shifts are already visible in how investors and potential partners frame their questions. The central issue is no longer just the size of the opportunity, but the credibility and resilience of that opportunity under scrutiny.

Increasingly, investors are pressure-testing assets through a more granular and scenario-driven lens. Rather than accepting headline assumptions, they are asking more specific, and often more demanding, questions such as:

- What happens to your valuation under moderate and severe MFN scenarios?
- Where is your value geographically anchored and how does launch sequencing affect future US pricing flexibility under MFN?
- Which countries matter most for reference-price spillover?
- What is your ex-US launch logic, and what are you willing to delay or trade off?
- What evidence package supports payer and HTA value, not just regulatory approval?
- Which indication and partner strategy best protects long-term pricing power?

Investors want to understand how value changes under different MFN scenarios, where that value is generated, and whether the company has a realistic view of how global access will play out.

Importantly, evaluation frameworks vary depending on the company's starting point. US-based biotechs are often assessed on their ability to protect US pricing power, whereas ex-US companies may be evaluated more on their ability to optimize regional access, sequence global expansion, and structure partnerships effectively.

Companies that are unable to engage with these questions in a structured and credible way risk being discounted - not only for the perceived risk, but also for the lack of preparedness.

Rethinking how value is built

As MFN reshapes the landscape, it also changes how value must be constructed during development. Pricing strategy can no longer be treated as a late-stage consideration. It becomes an integral part of early decision-making, with real trade-offs that need to be understood and managed.

For some companies, this may involve prioritizing US pricing protection, potentially delaying or

sequencing ex-US launches carefully to avoid negative reference price spillover. For others, particularly those headquartered outside the US, the emphasis may shift toward securing strong positioning in HTA-driven markets first, even if this implies a different global price corridor.

These differences reflect fundamentally different strategic archetypes rather than right-or-wrong choices.

At the same time, the importance of evidence is expanding beyond regulatory approval. Demonstrating clinical efficacy is necessary, but not sufficient. Success in many markets will depend on comparative effectiveness, real-world relevance and data, and the ability to show economic value.

Ex-US markets, meanwhile, are moving from the periphery to the center of strategic thinking. They are no longer simply incremental sources of revenue, they play an active role in anchoring global pricing, shaping access dynamics, and influencing investor perceptions of value.

How MFN impacts ex-US biotechs differently

While MFN is a US-driven policy, its implications are global – and not all biotech companies are affected in the same way.

Ex-US biotechs often have a different center of gravity for value creation. Rather than relying primarily on US pricing, they may build value through earlier commercialization in Europe or Asia, combined with strategic partnerships for US market entry.

Their exposure to MFN is also typically more indirect. Instead of facing immediate US price compression, they are more likely to be affected through global reference pricing mechanisms, changes in access conditions, and shifts in partner expectations. Critically, however, launching first in one of the MFN-reference markets may effectively establish an implicit benchmark for future US

pricing. While ex-US companies are unlikely to achieve traditional US price premiums, an early ex-US launch can nonetheless constrain future US pricing flexibility by creating externally visible reference points before the US value story is fully established.

This significantly increases the importance of determining the US pricing potential and market opportunity early in development, because once pricing is anchored in a reference market, there may be limited opportunity to reset expectations later. Reduced US price premiums could narrow global price differentials further, altering both the relative competitiveness of assets and the strategic sequencing of launches.

Strategic trade-offs may also differ. Where US-based companies may prioritize protecting US price levels, ex-US companies may focus on optimizing access, sequencing launches to align with HTA requirements, or leveraging regional strengths in negotiations with partners.

These differences do not eliminate risk, but they change where risk sits and how it must be managed. As a result, investors are increasingly attentive to how a company's geographic starting point shapes its exposure and strategic choices.

Where value will hold, and where it may erode

As healthcare systems respond to pricing pressure, it is unlikely that overall spending will increase dramatically. Instead, spending will become more selective.

Assets that demonstrate clear and meaningful value (such as those addressing high unmet need or delivering strong clinical outcomes) are more likely to retain pricing power and access across markets.

Conversely, assets with limited or only incremental differentiation may face greater challenges. This does not mean that such therapies are no longer

viable, but that their success will depend more heavily on strategic choices, including geographic focus, positioning, and partnering models.

Integrating pricing and access earlier in development

One of the clearest consequences of MFN is the acceleration of the “shift left.” Pricing and access considerations are becoming integral to strategic planning during clinical development, as early as Phase II.

This makes it critical to develop a robust view of US pricing potential before establishing prices in ex-US reference markets, because launch sequencing decisions may permanently influence future pricing corridors under MFN-linked frameworks.

In this environment, companies are increasingly expected to:

- Design clinical trials that generate evidence relevant for HTA and payer decision-making
- Define early views on target list and net price corridors under different MFN scenarios
- Make deliberate choices on indication sequencing and label strategy
- Clarify ex-US launch sequencing and associated trade-offs
- Assess partnering strategies in light of global pricing implications

Clinical efficacy remains necessary, but investors and partners are increasingly treating commercial and pricing preparedness as an equal requirement.

Preparing for a more demanding environment

In this context, preparation becomes critical. One of the most effective steps an early-stage biotech can take is to move from a single-point valuation to a scenario-based framework.



Companies should be prepared to describe a range of outcomes under different MFN assumptions, and to explain how those outcomes vary depending on geographic exposure and strategic choices.

A practical way to structure this thinking is through the “MFN Value Resilience Framework,” built around three dimensions:

- Value at risk: Where is the asset most exposed (e.g., US pricing, ex-US reference spillover, access constraints)?
- Value protection levers: What actions can preserve value (e.g., evidence generation, launch timing, pricing governance)?
- Value realization choices: How will value ultimately be captured (e.g., geographic prioritization, partnering model)?

Importantly, the relative importance of each dimension may differ depending on whether a company is US- or ex-US-based.

A higher bar, but also a clearer path

MFN may evolve in form, but the broader direction of travel is clear: global pricing is becoming more interconnected, investor scrutiny is increasing, and expectations around early strategic thinking are rising.

For early-stage biotech companies, this does not diminish the importance of science. Breakthrough innovation remains the foundation of value. But translating that innovation into investable and partnerable assets now requires a broader skill set - one that integrates scientific excellence with a clear, credible approach to pricing, access, and global value.

The companies best positioned to succeed in an MFN environment will be those that recognize not only the risks, but also the strategic choices created by a more interconnected global pricing landscape, and act on them early.



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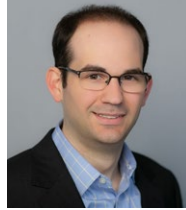
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