Biopharma's New Evidence Era is Holding a Mirror Up to Sub-par Commercialisation Strategy

Evidence has never been more central to commercial success. Payers demand it before reimbursement. HTA bodies are raising the bar with sweeping new frameworks, most significantly the EU's Joint Clinical Assessment process, which launched in January 2025 as a major step toward harmonising clinical evidence requirements across all EU member states.[1] Furthermore, regulators are signalling that the era of selective disclosure is over. An FDA study found that sponsors omitted 85% of the agency's safety and efficacy concerns in public announcements, a transparency gap that has since prompted the FDA to begin publishing complete response letters that companies had historically kept confidential.[2]

Yet, according to McKinsey, only 20% of leading pharmaceutical companies currently develop an integrated evidence generation plan across the full lifecycle of a product, with most leaders still generating evidence in silos rather than for the needs of the wider organisation and its stakeholders.[3] Indeed, the vast majority are still building their evidence base reactively. Commissioning studies after payer rejections, scrambling to answer regulatory questions or plugging gaps that should have been identified years earlier.

In biopharma's new evidence era, this approach to what is a vital element of commercialisation strategy development no longer cuts it. What's needed instead is a fundamental rethink. One in which evidence generation is not a downstream activity delegated to HEOR or medical affairs, but a strategic, cross-functional and proactive discipline. This must be built on the foundations of a clear winning aspiration, confidence in where to play and how to win there, and deliberate prioritisation of the evidence needed to deliver for regulators, patients, payers and providers.

The Case for a Clear Commercial Focus

Ask biopharma companies what problem their asset solves and it's unlikely each team will answer consistently. This poses a key strategic problem and it's where evidence generation can begin to break down, not at the point of study design, but at the point where no one has agreed on what the evidence is for. Without a unifying goal to align strategic focus around, the risk is that every function defaults to its own interpretation of what winning looks like and builds its evidence plan accordingly.

Many cross-functional teams consistently skip the most important strategic questions: what is the specific problem our product solves, for which patients, versus which alternative and as valued by whom? Instead, they move straight into execution. Clinical designs for regulatory approval. HEOR models for a hypothetical payer. Medical builds a KOL narrative. The brand develops positioning around a differentiator that no one has validated externally. Each workstream generates evidence, but none of it connects because it was never anchored to a shared North Star, a clear, interrogated definition of the commercial problem the product exists to solve.

That North Star matters for a reason that goes beyond alignment. A winning aspiration sets the context for the problem a team needs to solve and guides strategic focus across the organisation. However, it doesn't directly produce decisions. What it produces is the guard rails for a menu of options, the choices about where to focus for growth, how to win there and what evidence to invest in, that the cross-functional team can then evaluate together. A constraint at the top of that cascade shapes everything downstream. Teams end up with a narrower set of possibilities than they realise. Often, the most valuable strategic alternatives never appear on the menu because the framing has implicitly excluded them before anyone has had the chance to consider their merit.

This is why narrowing focus to achieve the North Star means doing something that most teams resist: identifying and prioritising the key challenges that stand between the current reality and commercial success and letting those challenges drive evidence priorities. As the competitive landscape evolves, label negotiations may narrow the approved population, and emerging data may shift treatment expectations; teams need to revisit this activity regularly. After all, the problem they are trying to solve can look very different at launch than it did in Phase II.

Imbruvica's story helps illustrate what's at stake when a problem definition shifts and the evidence strategy doesn't move with it. Reconstructing the story from what's available in the public domain, ibrutinib's commercial problem at launch in 2013 appears unambiguous: FCR dominated CLL but was punishing for the elderly majority of patients[4] and del(17p) patients had no durable option at all. Ibrutinib was chemo-free, oral and worked where chemo couldn't.[5] The evidence strategy was tightly aligned to that problem, and it worked until it didn't. When Calquence entered decisively in 2021, the problem had moved. With BTKi now the category default, AstraZeneca didn't argue against chemotherapy; it argued against Imbruvica, positioning acalabrutinib's selectivity against ibrutinib's cardiovascular toxicity signal in a population already prone to cardiac comorbidities.[6] Ibrutinib's own demographic strength had become its vulnerability. Then in 2022, ALPINE showed that BeiGene's zanubrutinib/Brukinsa was superior to ibrutinib on both PFS and cardiac safety.[7] Imbruvica was no longer the safest or the most effective option and J&J and AbbVie revenue paid the price.[8,9]

One read of this scenario is that ibrutinib's launch problem framing had been so successful that it built the category in which it was later commoditised. Once chemo-free BTKi became table stakes, the external landscape had fundamentally changed and without clear context to guide decision-making at each competitive inflexion point, the evidence base was stranded in a problem the market had already solved.

For development teams, the implication is clear. Evidence generation must be anchored to a clearly defined strategic commercial problem, stress-tested for the competitive dynamics that could redraw it and revisited at every major milestone. Establishing that unifying goal and keeping it honest is the foundation on which everything else is built. But it doesn't yet tell you where the real opportunity lies or what it will take to win there. That's where the work continues.

Exploring Different Routes to Win

Defining the problem that you're solving is necessary. But it doesn't answer the next question: where are you going to focus for growth and how are you going to win there? These are the strategic choices that determine whether an evidence base can do the job it's being built for.

Winning in a given space depends on two things. The behaviour change that you need to compel (from clinicians, payers, patients or all three) and the belief that will drive that behaviour change. Different patient segments, care settings and competitive contexts will each demand a different answer to both questions. That's why exploring different routes to win isn't an optional exercise in creative strategy development, but a mechanism by which teams discover which evidence will actually matter.

Incidentally, most biopharma teams believe that they've made these choices deliberately. In practice, the choices are often made implicitly. They're embedded in the commercial framing adopted early in development, long before anyone has mapped the full landscape of where real value lies. Indeed, the most consequential strategic decisions are frequently the ones teams didn't realise they were making.

The Imbruvica example illustrates this point. When Calquence reframed the problem from chemo being too toxic to first-generation BTKi being too toxic, ibrutinib's team faced a genuine strategic options question of where to focus for growth and how to win in a market that had shifted under them. From an outsider's perspective, two routes were visible if the landscape had been explored with fresh eyes. The first was population selectivity, walking away from the frailest and most elderly patients where cardiovascular risk was highest and defending a more defined position in the patients where ibrutinib's benefit-risk profile remained most compelling. The second was clinical partnership, working proactively with cardiologists to develop and evidence cardiovascular side-effect mitigation strategies, turning a perceived liability into a managed and documented risk. Either route represented a genuine path to continued relevance and neither required starting from scratch. Yet both required asking 'what would have to be true for this option to succeed?' early enough.

Incidentally, this question is one of the most valuable tools a cross-functional team can apply to a menu of strategic options. It forces assumptions into the open, surfaces the drivers and barriers attached to each route, and reduces a long list of possibilities to the options that deserve serious investment. It also means that when a team does commit to a direction, they've already anticipated the conditions that will determine whether it works.

Getting to that quality of strategic options demands analytical rigour, but it also requires deliberately tapping into the skills and perspectives of people across the organisation. By this, I mean functions that don't always sit at the strategy table but carry intelligence that can reshape the landscape when surfaced. It requires a framework that enables informed decision-making rather than defaulting to the loudest voice or the most familiar precedent. It requires cultivating the kind of innovative thinking that questions not just where teams have played before, but where the untapped or underserved value lives.

Biogen's Aduhelm is perhaps the most publicly documented example of what's at stake when this exploration is absent. When the FDA approved aducanumab in June 2021[10] as the first disease-modifying Alzheimer's therapy in nearly two decades,[11] Biogen's apparent winning aspiration was to deliver a category-defining franchise. We can assume the strategic problem, as framed, was how to reach the market before donanemab and lecanemab arrived. That framing made certain choices feel obvious: a broad label across all early Alzheimer's patients, premium pricing consistent with a category-defining asset and patient advocacy as the primary demand-generation mechanism.

However, what this framing suppressed was equally consequential. A narrow biomarker-defined sub-population felt like under-claiming the aspiration. Payer engagement during evidence design felt premature. A third confirmatory trial to resolve the conflicting EMERGE and ENGAGE clinical trial results[12] felt like a delay the timeline couldn't absorb. We can conclude that none of these options surfaced naturally because the strategic problem had been defined by timing rather than credibility. This matters because a problem framed around speed produces a very different menu of options than one framed around multi-stakeholder evidence robustness.

The consequences in this case were total. Ten out of eleven FDA advisory committee members voted against recommending approval.[13] Major medical institutions, including the Cleveland Clinic and Mount Sinai, announced they would not prescribe it.[14] The Institute for Clinical and Economic Review concluded that the drug would only be cost-effective at 85–95% below its list price.[15] In January 2022, CMS restricted reimbursement to patients enrolled in qualifying clinical trials,[16] effectively closing the commercial market. Biogen discontinued Aduhelm in January 2024,[17] an asset framed as franchise-defining, withdrawn within three years of approval, having generated minimal revenue and caused lasting reputational damage that complicated the launch environment for lecanemab, a better-evidenced asset in the same category.

The Aduhelm story is unusual only in its visibility. The pattern it illustrates (a winning aspiration potentially sized to a commercial opportunity the evidence base could not credibly support across regulators, clinicians and payers simultaneously) is not. Most teams don't fail this publicly, but the dynamic exists nonetheless in launches that underperform without ever surfacing the upstream framing that made underperformance almost inevitable.

So then, knowing where to focus for growth and how to win there isn't a market access question settled at launch. It's a strategic question that must be answered, and with a genuine exploration of the full option space, before evidence priorities are set.

Building an Integrated Evidence Base

The third foundation of a proactive evidence strategy is the deliberate identification of gaps and needs to build your strongest evidence base, one designed for every stakeholder who will determine commercial success, at every decision point that matters.

Many teams don't approach evidence this way. They prioritise evidence needs to support regulatory approval, then build outward reactively. For instance, adding payer endpoints after an HTA request, commissioning quality-of-life instruments after a reimbursement rejection and designing real-world evidence programmes after a launch that's underperforming. By the time the gaps become visible, the trials that could have closed them are already complete.

The alternative is to select evidence that strengthens the strategy rather than merely defends it. This means investing in evidence to benefit various stakeholders simultaneously, so that the same data foundation serves clinician, payer and patient narratives without contradiction.

The SGLT2 inhibitor case study provides a clear example of what integrated evidence options that meet customer needs and boost competitiveness look like in practice. When EMPA-REG OUTCOME published in 2015, showing empagliflozin reduced cardiovascular death by 38% and heart failure hospitalisation by 35% in patients with type 2 diabetes and established cardiovascular disease,[18] the finding was unexpected. The trial had been mandated by the FDA as a post-marketing safety study, designed to rule out harm rather than demonstrate benefit.[19] The cardiovascular signal was, in part, serendipitous.[20]

What distinguished the outcome from a good luck/happy accident story was what AstraZeneca and Boehringer Ingelheim did next. Rather than filing for a cardiovascular benefit label update and returning to diabetes-class competition, the sponsors reorganised around a new strategic problem: how to build an evidence base that would earn cross-speciality adoption across diabetology, cardiology and nephrology, in audiences that hadn't been the original target for these molecules. That reframing changed everything about what evidence was needed and where.

DAPA-HF tested dapagliflozin in patients with heart failure with reduced ejection fraction, regardless of diabetes status, and showed that the benefits extended beyond glycaemic control.[21] DAPA-CKD later broadened the evidence base into chronic kidney disease,[22] while DELIVER and the EMPEROR programme further strengthened the class evidence across both reduced and preserved ejection fraction.[23,24,25] In DAPA-HF, health status was also assessed using the Kansas City Cardiomyopathy Questionnaire as a prespecified endpoint, allowing the trial to capture patient-reported benefit alongside clinical outcomes.[26]

The result was an evidence spine that held across every scrutiny it faced. NICE recommended empagliflozin and dapagliflozin for heart failure.[27] Speciality guidelines across cardiology, nephrology and endocrinology followed.[28] The class became standard of care across multiple domains in a way few drug classes ever achieve. Jardiance and Farxiga each generated multi-billion-dollar revenues, with growth trajectories that are continuing long after the typical post-launch peak.

The parallel with Aduhelm is telling, albeit running in the opposite direction. Where Biogen's upstream framing (sized to a commercial opportunity the evidence base could not credibly support) made parallel and ultimately irreconcilable stakeholder narratives structurally inevitable, the SGLT2 sponsors' reframing

made an integrated evidence spine structurally natural. The difference wasn't execution at launch. It was the strategic problem each set of sponsors chose to solve, and the evidence gaps and needs that each set of sponsors chose to prioritise as a result.

This is the principle that should govern how teams approach the proof stage of evidence generation. The process should begin by exploring what evidence will serve the full range of stakeholders who need convincing. Teams should also consider how that evidence will be built so that those audiences hear the same coherent story, rather than competing versions of it. This is important because integrated value stories are made possible by the framing decisions and evidence prioritisation choices made months or years before any value narrative is written.

A New Approach for a New Evidence Era

Evidence fails not because teams lack rigour, resource or intent, but because the foundations on which it is built are rarely examined with the same discipline as the evidence itself. Without a clearly defined and shared commercial problem, evidence defaults to functional habit. Without rigorous exploration of where to play and how to win there, the option space closes before the best choices are ever visible. Without deliberate prioritisation of gaps and needs across every stakeholder audience, the integrated evidence base that payers, regulators, patients and clinicians demand cannot be built.

Ultimately, the integrated value story problem can't be solved at the eleventh hour. By the time launch teams are reconciling payer, clinician and patient narratives, the upstream framing has already determined whether reconciliation is possible. The question that biopharma leaders should be asking is not how to integrate narratives at launch, but is the winning aspiration sized to what the evidence can credibly support? If not, then they must consider whether they are willing to either resize the aspiration or invest in the evidence to support it.

That these questions remain unspoken in many organisations is reflected in a telling data point: confidence in cross-functional readiness was cited as the single biggest launch planning concern by pharma leaders at last year's Pharma Launch Excellence Summit.[29] Cross-functional misalignment at launch is the downstream consequence of foundations that were never shared. It's the result of teams that never agreed on the problem, never explored the full landscape together and never mapped the evidence gaps that would matter most to the audiences they needed to convince.

Biopharma's new evidence era, with its harmonised HTA requirements, its FDA transparency demands and its payer scrutiny of every efficacy claim, is not creating new strategic problems. The mirror it holds up reflects something that was always true: evidence generation is not a downstream activity but a vital component of effective commercialisation strategy development.

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