EXECUTIVE INSIGHTS

In Pursuit of Prevalent Disease: Where the Next Mega-Blockbusters Will Be Built

Biopharma is entering a period during which the scale of its revenue base and the expectations placed on it by investors are fundamentally reshaping where the industry's largest value pools will emerge. L.E.K. Consulting's analysis suggests that the next generation of mega-blockbusters (products with more than $5 billion of peak revenue) will increasingly be found in highly prevalent, chronic diseases rather than in traditional specialty or rare indications.

Three forces underpin this view. First, the world's largest pharmaceutical companies now operate from revenue bases so large that only outsized assets can materially move the needle on growth and shareholder returns.

Second, returns in many specialty markets are under pressure from crowding, pricing scrutiny and constrained life-cycle value, while scientific advances are unlocking credible therapeutic innovation in large historically underserved diseases.

Third, the obesity/GLP-1 market has demonstrated that once-overlooked mass-market conditions can become highly valuable franchises but only when companies pair scientific conviction with new evidence, access and commercial models.

Taken together, these evolving dynamics point to a future landscape where mega-blockbusters will disproportionately emerge from prevalent diseases, and biopharma companies that fail to adapt their portfolios and capabilities accordingly risk structural disadvantage over the next decade.

Why mega-blockbusters are increasingly important

Revenue scale is redefining the growth equation

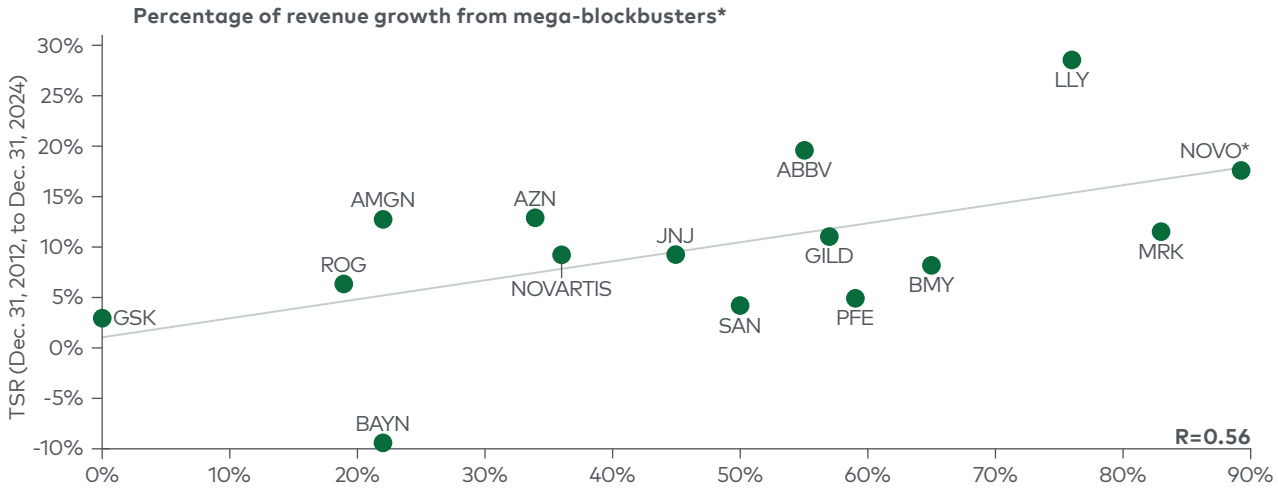
The revenue bases of large pharmaceutical companies have expanded to unprecedented levels. The average top 15 pharma company now generates more than $50 billion in annual revenue. Interestingly, only five pharma companies have reached more than $300 billion in market capitalization and all of them are anchored by at least one mega-blockbuster product (see Figure 1).

Figure 1
Largest pharma by peak market cap and primary anchor product (peak annual sales)

Source: S&P Capital IQ; Evaluate Pharma

As revenue bases grow, so too does the dependence on outsized assets. Our analysis shows a strong positive relationship between the share of revenue growth driven by $5 billion-plus products and long-term total shareholder return. In practical terms, sustaining even mid-single-digit growth increasingly requires multiple assets capable of scaling to $5 billion or $10 billion-plus in annual sales, a threshold that most specialty and rare indications cannot support (see Figure 2).

Figure 2
Large pharma reliance on mega-blockbusters ($5B+)



*NOVO=Novo Nordisk, among assets whose revenue increased from 2013 to 2024, percentage of growth from assets reaching $5 billion in WW revenue by 2024
Source: S&P Capital IQ

Specialty markets face mounting structural headwinds

Over the past decade, lower-prevalence specialty and rare-disease therapies benefited from favorable pricing dynamics, relatively limited competition and strong payer receptivity to innovation. Today, many of those tailwinds are under pressure. Across oncology, immunology and rare disease, companies now face intensifying competition in crowded categories, growing payer and policy scrutiny, increased patient segmentation, and diminishing life-cycle extension opportunities, particularly in the context of the Inflation Reduction Act, recent most favored nation policy and other pricing pressure.

While specialty markets remain critical engines of innovation, their ability to consistently produce mega-blockbusters is increasingly constrained. As a result, the industry's largest growth opportunities are reconcentrating in diseases with large, chronic and expandable patient populations.

The top-selling drug mix is shifting back toward prevalence

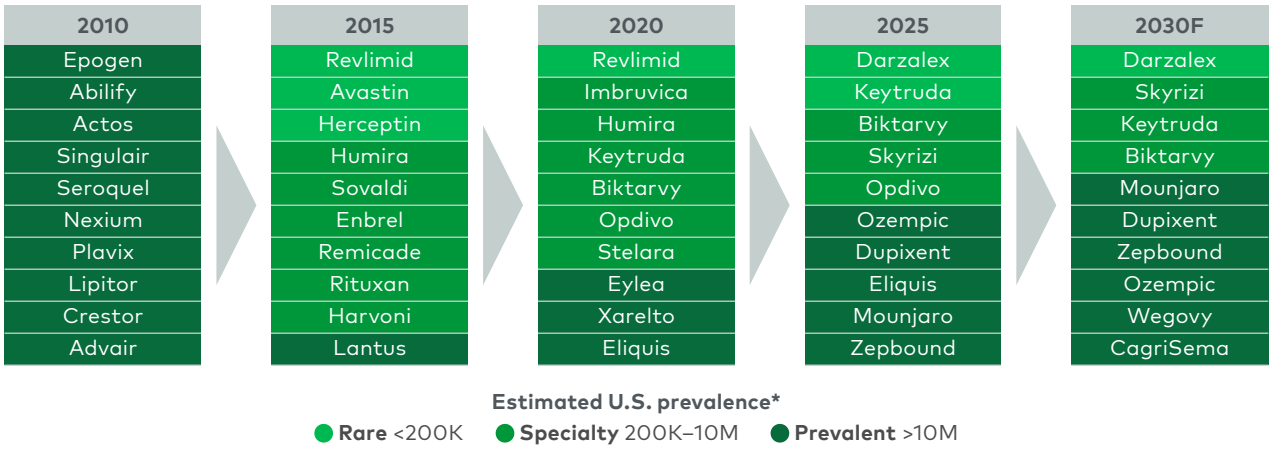
This shift is already visible in the composition of the world's top-selling therapies. After more than a decade in which specialty and lower-prevalence products dominated the blockbuster rankings, the pendulum is swinging back.

As seen in Figure 3, by the mid-2020s and increasingly toward 2030, cardiometabolic agents, dermatology biologics and other mass-market therapies account for a growing share of

the industry's largest products, a trend that is expected to continue as we look at pipeline expectations into the mid-2030s.

The message is not that specialty innovation no longer matters, but that the largest absolute value creation is once again occurring in diseases affecting tens of millions of patients.

Figure 3
Top 10 selling pharmaceutical products, by year



*High-level estimate of total eligible U.S. population across indications; for I&I therapies, counts only advanced therapy-eligible patients; for oncology therapies, estimate of annual incident population for all approved indications
Source: Evaluate Pharma; S&P Capital IQ; CDC; NIH; Sanofi investor materials

Obesity as proof point: How GLP-1s redefined what is possible

Few therapeutic areas illustrate this shift more clearly than obesity.

For decades, obesity was widely viewed as commercially unattractive: Early products suffered from safety and efficacy issues, stigma limited physician adoption and payers resisted reimbursement absent clear outcomes data. These dynamics led many companies to deprioritize the category entirely.

Yet GLP-1–based therapies fundamentally altered the equation. Step-change improvements in efficacy combined with better safety have fueled patient demand and willingness to pay for these products even in the absence of broad reimbursement. In addition, broader health outcomes data has validated hard clinical benefits beyond weight loss, which is beginning to shift the perception of obesity from a lifestyle market into a medically anchored disease, unlocking the payer coverage required for adoption at scale.

Beyond redefining obesity's commercial potential, GLP-1s have accelerated the build-out of direct-to-patient and cash-pay infrastructure that can support opportunities across future high-prevalence disease opportunities. Telehealth initiation, digital patient acquisition and

membership-based care models have streamlined an end-to-end "self-service" healthcare platform and normalized consumers paying directly for high-value therapies when coverage is limited. This end-to-end consumer-focused platform has created a commercialization backbone that future high-prevalence products can plug into rather than building it themselves.

The companies that emerged as leaders, notably Novo Nordisk and Eli Lilly, did not succeed overnight. Their advantage was built on decades of investment in incretin science, willingness to fund long and expensive outcomes trials at risk, early commitment to manufacturing scale, and the development of consumer-centric commercial models that complemented traditional physician engagement.

While there is also a fair bit of serendipity involved, both companies were committed to investing at risk once certain clinical performance thresholds were met, despite some of the remaining pricing, access and distribution challenges.

Obesity demonstrates that prevalent diseases can produce large franchises with transformative value, but only when pharma companies fundamentally reexamine their ability to enter nontraditional spaces that may not be thought of as diseases today (e.g., aging or menopause) and rethink how they discover, develop and commercialize therapies for mass markets.

Where the next mega-blockbusters may emerge

Not every prevalent disease will become the "next obesity." However, our analysis highlights a set of therapeutic domains that share several defining characteristics: large chronic populations, meaningful residual unmet need, emerging scientific validation, growing consumer engagement and potential to reduce total cost of care.

Five domains stand out:

1. **Cardiometabolic disease** (e.g., obesity, type 2 diabetes, MASH, hypertension) combines massive scale with increasing biological tractability and clear links to outcomes and healthcare costs.
2. **Neuropsychiatric conditions** (e.g., depression, anxiety, substance use disorders, sleep disorders) represent enormous unmet need, with advances in neuroscience and digital tools beginning to unlock new approaches.
3. **Consumer-oriented health, wellness and aesthetics** (e.g., hair loss, skin health, hormonal optimization) benefit from large patient populations, strong willingness to pay and digital channels, even where payer coverage is limited.
4. **Women's health** (e.g., menopause, PCOS, endometriosis) reflects decades of underinvestment, rising advocacy and growing employer and societal focus.

5. **Diseases of aging** (e.g., mild cognitive impairment, sarcopenia, sensory decline) address expanding populations with high motivation for preventive and quality-of-life interventions.

Each domain presents distinct scientific, access and commercial barriers — but collectively they represent highly plausible sources of future mega-blockbusters.

What it takes to win in prevalent disease

Success in prevalent disease markets requires capabilities that differ meaningfully from those used to win in rare disease and specialty care.

From an R&D perspective, companies must be willing to invest earlier and at greater scale, often funding large long-duration trials and outcomes studies before payer pathways are fully defined. Evidence strategies must anchor value to hard clinical and economic outcomes, not just symptom improvement. Pharma companies must also be willing to consider nontraditional markets that straddle the boundaries of aesthetics, health and wellness, and medical need, but where unmet need and patient willingness to pay are high.

Commercially, mass-market diseases demand consumer-grade engagement models. Seamless end-to-end pathways that leverage new channels, digital acquisition, telehealth platforms, new payment models and simplified distribution will be needed to complement and, in some cases, precede traditional physician-led prescribing. Pricing and access strategies must be designed for sensitivity and scale, often blending reimbursed, employer-based and cash-pay pathways.

Finally, operations and supply chains must be built — from the outset — with scale in mind. In prevalent disease categories, supply constraints can rapidly become the gating factor that determines leadership.

Strategic implications for biopharma leaders

For leadership teams planning the next decade of growth, some potential implications include:

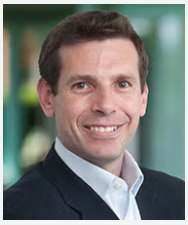
- **Rebalancing portfolios toward large, chronic diseases** where scientific momentum and unmet need can support multibillion-dollar franchises
- **Opening the aperture for investment** to include nontraditional areas (e.g., aging) where unmet need and willingness to pay is high
- **Building consumer-centric commercial capabilities** alongside traditional medical and sales infrastructure
- **Anchoring evidence strategies to outcomes and cost of care**, anticipating payer expectations early
- **Preparing manufacturing and supply chains for mass adoption**, not niche uptake

- **Defining clear trigger points** that justify disproportionate investment as scientific and commercial risk are retired

The next wave of mega-blockbusters will not emerge by accident. They will be built by organizations willing to rethink long-held assumptions about where value can be created, to balance risk-reward trade-offs and to invest accordingly.

Contact us to find out more.

About the Authors



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