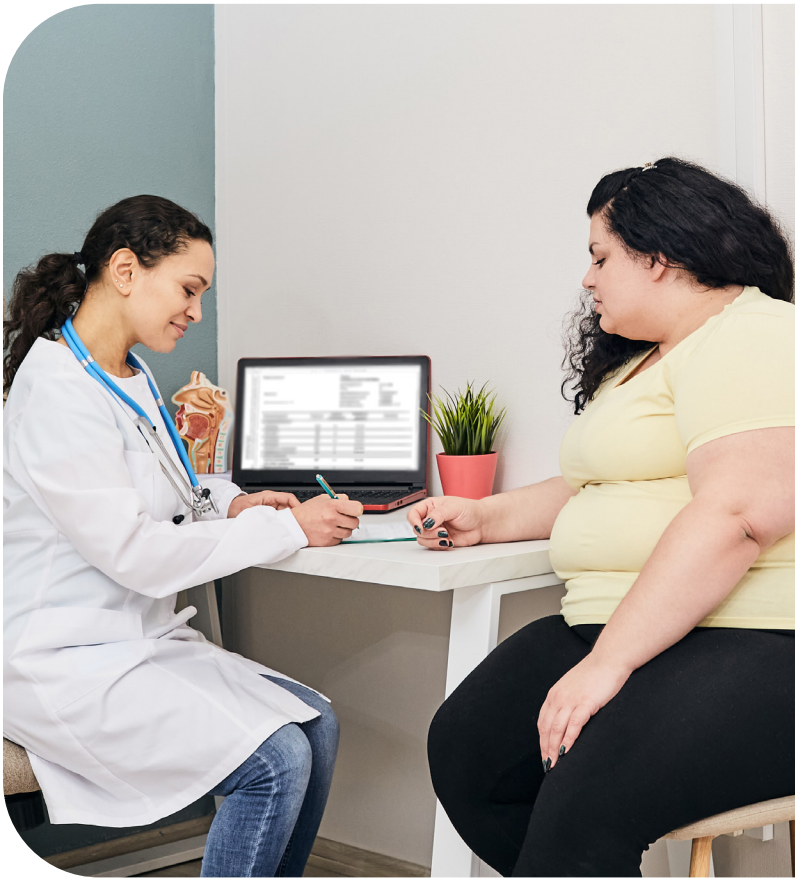
Beyond Weight Loss: The Future of Obesity Treatment

Obesity treatments are at a critical inflection point. What began as breakthrough therapies for weight management has evolved into a comprehensive approach targeting multiple co-morbidities simultaneously. This transformation signals the beginning of a new era where GLP-1 receptor agonists and potentially other incretins become backbone therapies across diverse therapeutic areas, helping manage some of the world's most serious and challenging conditions.



Why cardiometabolic leads the way

The most compelling opportunities for indication expansion lie within cardiometabolic disease, where GLP-1 receptor agonists address both consequences of obesity: fat mass-based complications and metabolic dysfunction.

Cardiovascular disease remains the world's biggest killer. The SELECT trial, which enrolled more than 17,000 patients to evaluate cardiovascular outcomes in people with obesity but without diabetes demonstrated a 20 percent reduction in major cardiovascular events among those treated with semaglutide. This landmark study was the first to prove that agents targeting obesity can deliver clinically meaningful outcomes beyond weight loss — in this case, cardiovascular risk.[1]

The therapeutic mechanisms that drive weight loss also address the underlying pathophysiology of related cardiometabolic conditions. Chronic kidney disease, metabolic dysfunction-associated steatohepatitis (MASH, formerly known as NASH), and metabolic syndrome share common pathways with obesity, creating

opportunities for synchronized therapeutic approaches that address multiple conditions simultaneously.

This is what makes cardiometabolic expansion so compelling from a development perspective. You're not chasing entirely new mechanisms or hoping for serendipitous effects. You're following a clear biological rationale in which reducing obesity helps address the organ damage that excess weight causes.

Beyond cardiometabolic: Exploring new frontiers

But the story doesn't end with cardiometabolic disease. Expansion into areas like Central Nervous System (CNS) disorders presents different opportunities and challenges. Alzheimer's disease represents a particularly intriguing frontier where emerging real-world evidence suggests protective effects that may be distinct from weight loss mechanisms. The evoke and evoke+ trials are investigating 14-mg oral semaglutide versus placebo in early-stage symptomatic Alzheimer's disease and will provide critical insights into this potential indication.[2]

A recent study published in *Nature*, with a sample size of 2 million veterans provided by the U.S. Veterans Administration, showed that those who were diabetic and on GLP-1 receptor agonists (n=215,970) had evidence of risk reduction across 175 health outcomes, including substance use disorders and various neurological conditions.[3] This massive retrospective analysis reveals the breadth of potential therapeutic applications, though it also highlights the challenge of understanding which benefits stem from weight loss versus other mechanisms of action.

Of course, proving these effects clinically is a necessary next step.

The evidence generation challenge

Collecting evidence required for indication expansion presents formidable challenges across three key areas: study size, duration, and population representation. The scale varies dramatically by therapeutic area and the endpoints selected for measurement.

Alzheimer's studies, for instance, involve different complexities than cardiovascular studies. Rather than waiting for discrete events, researchers follow patients through disease progression to determine whether interventions slow deterioration over time. Duration becomes the critical factor, requiring studies of several years to detect meaningful differences in cognitive decline.

Real-world data analysis should inform trial design by identifying appropriate patient cohorts. Virtual trial methodologies can improve patient retention by reducing clinic visit burden, while careful selection of trial centers can optimize recruitment and retention rates across diverse therapeutic areas.

The bottom line is that these studies require large sample sizes, extended durations and rigorous methodological design, and therefore, substantial investment.

The next wave of innovation

The diversity of the obesity treatment pipeline, with more than 60 mechanisms of action in development, signals that current GLP-1 dominance represents just the beginning of therapeutic innovation.[4] Next-generation approaches include dual- and triple-hormone receptor agonists, novel CNS targets, and mechanisms that may demonstrate distinct therapeutic profiles across various indications.

Muscle-sparing therapies, for example, represent a critical emerging innovation. Current treatments carry risk for muscle mass loss along with fat loss, and as patients achieve substantial weight loss, maintaining lean muscle mass becomes essential for long-term metabolic health.[5] Next-generation approaches, such as bimagrumab from Eli Lilly (in combination with semaglutide), enobosarm from Veru, and HU6 from Rivus, may offer superior body composition outcomes alongside weight loss.

Precision medicine opportunities are becoming increasingly apparent as companies develop approaches to match specific medications to patient phenotypes.

Genetic markers, metabolic profiling and biomarker analysis may enable personalized treatment selection that optimizes outcomes, not just for weight loss but for specific comorbidities like cardiovascular disease, kidney dysfunction, or CNS conditions.

Combination therapy strategies recognize that comprehensive health benefits may require multiple targeted interventions. Rather than seeking single agents to address all aspects of disease, leading companies are exploring rational combinations that synergistically target complementary pathways across therapeutic areas.

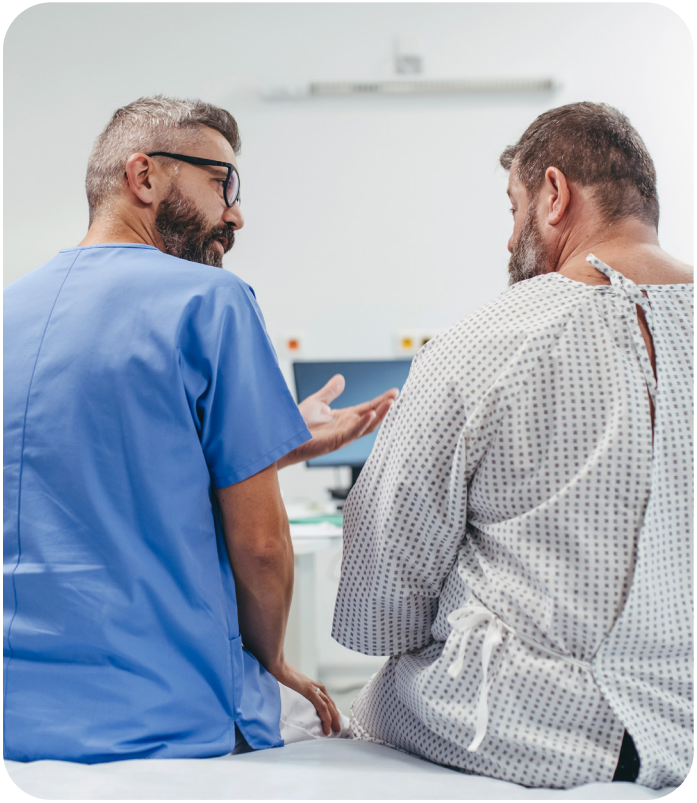
What companies must do now

Success in multi-indication development requires fundamental shifts in commercial strategy, evidence generation, and market positioning.

Pharmaceutical companies must help healthcare systems prepare for indication expansion that moves these therapies into the practices of cardiologists, nephrologists, hepatologists, neurologists, and other specialists beyond endocrinology. Each specialty requires tailored medical education and support programs to demonstrate therapeutic value within their specific clinical contexts.

Investment requirements are substantial but necessary for companies seeking long-term market position. The scale of clinical trials, study duration and evidence generation costs will be formidable, but companies that successfully navigate these challenges will establish these agents as backbone therapies across multiple disease areas.

Real-world evidence platforms must simultaneously capture outcomes across therapeutic areas. This requires sophisticated data collection systems that track cardiovascular events, kidney function, liver health, cognitive parameters, and other endpoints over extended periods. Companies need integrated approaches that demonstrate multisystem benefits rather than isolated disease-specific effects.



The path forward

The evolution from obesity medications to comprehensive multi-indication therapies represents one of the most significant opportunities in pharmaceutical development. While cardiometabolic applications provide the clearest pathway, due to shared disease mechanisms, the potential extends far beyond traditional metabolic conditions.

Success requires sophisticated evidence generation across diverse therapeutic areas, multistakeholder engagement strategies and substantial investments to demonstrate value across patient populations. Companies that build comprehensive development capabilities and invest in the necessary evidence to prove benefits beyond weight loss will be best positioned to succeed in this transformed treatment landscape.

Read part II of the series, **Tracking the evolution: Data-driven insights in the maturing obesity treatment landscape**.

Read part I of the series, **Achieving launch excellence in the evolving obesity market**.

About the authors

SARAH RICKWOOD
Vice President,
EMEA Thought Leadership, IQVIA

Rickwood has 30 years' experience as a consultant to the pharmaceutical industry. She has wide experience on international pharmaceutical industry issues, working with most of the world's leading pharmaceutical companies on issues in the U.S., Europe, Japan, and leading emerging markets, and is vice president, European Thought Leadership at IQVIA, a team she has run for 15 years. She also heads up IQVIA EMEA's Obesity Initiative. Rickwood holds a degree in biochemistry from Oxford University.

NATALIE HARB
Vice President, Global Launch Excellence, Global Commercial Solutions, IQVIA

Natalie Harb is vice president of global consulting & launch excellence within IQVIA's Global Commercial Solutions Business. She is responsible for leading the global consulting segment and for driving IQVIA's Global Launch Excellence program. She is a strong advocate for harnessing the power of data-driven strategies amplified by AI and cutting-edge technology. By seamlessly integrating these elements into an organization's ecosystem, she believes organizations can unlock transformative growth, drive informed decision-making, and foster a culture of innovation. Over the past 25 years, she has worked with some of the world's most successful brands across both the pharma and CPG industries in Europe, the Americas and Southeast Asia.

References

1. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med. 2023 Nov 11.
2. Cummings JL, Atri A, Feldman HH, Hansson O, Sano M, Knop FK, Johannsen P, León T, Scheltens P. evoke and evoke+: Design of two large-scale, double-blind, placebo-controlled, phase 3 studies evaluating efficacy, safety, and tolerability of semaglutide in early-stage symptomatic Alzheimer's disease. Alz Res Therapy. 2025 Jan 8.
3. Xie Y, Choi T, Al-Aly Z. Mapping the effectiveness and risks of GLP-1 receptor agonists. Nat Med. 2025 Jan 20.
4. Gores M, Rickwood S. Outlook for obesity in 2025: More than a transition year. IQVIA Blog. 2025 Jan 7.
5. Gores M. Beyond weight loss: Preserving muscle during pharmacotherapy of obesity. IQVIA Blog. 2025 Jul 3.

This article was originally published in PharmaLive.