

Anti-obesity drug development: Advances, challenges and mitigations to maximize success



A KEY QUESTION

How can sponsors maximize the success of anti-obesity drug development in an increasingly competitive and rapidly evolving landscape?

KEYWORDS

Obesity Drug Development, Clinical Trial Design, Long-term Weight Management, Patient Outcomes, Treatment Persistence

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Navigating the rapidly evolving anti-obesity drug development landscape

Although obesity prevalence continues to increase globally, emerging epidemiological data suggests that overall obesity rates may be reaching a plateau in some high-income countries.¹ However, this apparent stabilization masks important disparities. Obesity prevalence continues to rise among certain ethnic minority populations, socioeconomically disadvantaged groups, children and adolescents and individuals with limited access to healthcare, healthy foods and opportunities for physical activity.² Consequently, the health burden associated with obesity is expected to continue growing, particularly through its impact on cardiovascular disease, Type 2 diabetes, metabolic dysfunction-associated steatotic liver disease or metabolic dysfunction-associated steatohepatitis (MASLD/MASH), chronic kidney disease, sleep apnea, osteoarthritis and certain cancers.

The approval of GLP-1 receptor agonists and dual incretin therapies have fundamentally transformed obesity treatment. Semaglutide and tirzepatide have demonstrated that pharmacological intervention can achieve clinically meaningful and sustained weight loss previously attainable only with bariatric surgery.^{3,4} As a result, obesity is increasingly recognized and treated as a chronic biological disease rather than solely a lifestyle condition.

The success of incretin-based therapies have accelerated investment across the entire obesity development landscape. There are currently hundreds of companies developing anti-obesity therapies, ranging from next-generation incretin combinations to compounds targeting entirely different biological pathways. Multiple late-stage programs are advancing rapidly, including oral GLP-1 agonists, dual agonists and triple agonists designed to deliver greater efficacy while improving the overall patient experience.

Among these, retatrutide, a triple agonist targeting GLP-1, GIP and glucagon receptors, has emerged as one of the most promising next-generation therapies. Recent Phase III studies reported mean weight reductions approaching 30% in some patient populations, together with significant improvements in cardiometabolic risk factors.⁵ Publicly announced timelines suggest regulatory submissions may occur in 2027, potentially further raising the efficacy benchmark for future obesity therapies. Beyond retatrutide, several dual and triple agonists, including survodutide, pemvidutide, mazdutide, efocipegrutide and other emerging multi-agonist programs, are progressing rapidly through clinical development and are expected to intensify competition in the obesity market.

Despite these remarkable advances, substantial unmet needs remain. Real-world evidence consistently demonstrates that a significant proportion of patients discontinue treatment within the first year.⁶ The reasons are multifactorial and include gastrointestinal adverse events, treatment fatigue, challenges associated with chronic injectable therapy, reimbursement restrictions, medication costs, supply limitations and patient expectations that may not align with the realities of long-term obesity management. In addition, most patients experience weight regain following treatment discontinuation, reinforcing the concept that obesity requires lifelong disease management similar to hypertension or diabetes.⁷



Consequently, the next generation of obesity therapies must focus not only on greater weight reduction but also on optimizing long-term treatment persistence and durability of response. Sponsors are increasingly exploring complementary mechanisms of action that can be combined with incretin therapies to enable lower incretin doses, improve tolerability, reduce gastrointestinal side effects and maximize efficacy. These include approaches targeting energy expenditure, mitochondrial metabolism, glucagon signaling, amylin pathways, muscle biology, adipose tissue remodeling and nutrient sensing pathways.

Looking ahead to the next generation of anti-obesity compounds

There is no doubt that a new era in obesity care has begun. Semaglutide, tirzepatide and the emerging generation of dual and triple agonists are establishing new expectations for efficacy, with weight loss approaching or exceeding that achieved with some bariatric procedures.

Weight reduction of 20% - 30% may become increasingly achievable through pharmacological intervention alone.

However, future success in obesity treatment will be measured by more than total body weight loss. Increasing attention is being directed toward the quality of weight loss, including preferential reduction of adipose tissue, preservation of lean body mass and maintenance of physical function.⁸ As obesity-related complications are responsible for the majority of long-term morbidity and mortality, therapies that deliver meaningful improvements in cardiovascular risk factors, metabolic health, liver disease, renal outcomes and overall quality of life, may ultimately be viewed as providing greater value than weight loss alone.⁹

Long-term weight maintenance is emerging as perhaps the most important challenge facing the field. Clinical experience and numerous studies have shown that the biological drivers of obesity persist even after weight loss has been achieved. Continuous treatment strategies, maintenance regimens and combination therapies will therefore play an increasingly important role in sustaining outcomes over time.

The future obesity treatment landscape is likely to evolve toward personalized combination approaches, where incretin-based therapies serve as a foundation complemented by additional mechanisms tailored to individual patient needs. Such combinations may increase efficacy, improve tolerability, preserve lean mass, enhance energy expenditure, address obesity-related comorbidities and ultimately improve long-term adherence.

As the field continues to mature, clinical development programs must adapt accordingly. Future trials will need to evaluate not only weight loss but also body composition, durability of effect, treatment persistence, patient-reported outcomes, cardiovascular benefit and broader measures of metabolic health. The ultimate goal is no longer simply helping patients lose weight, but helping them achieve sustained improvements in health, function and quality of life across the spectrum of obesity-related disease.

Foreseeing these changes and being prepared to proactively address them is the key to seamlessly delivering new options to patients. Fortrea is at the forefront of obesity research, and we are ready to maximize the value of your asset in a rapidly changing environment.

Want to learn more?

Get more information about our obesity capabilities at fortrea.com



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