GUILHERME ANDRETTA
Director, Therapeutic Strategy
Clinical Scientist
IQVIA

ERICA CAVENEY
VP and Head of Obesity
Center of Excellence
IQVIA

VIVIANE PEREIRA
Senior Director
Therapeutic Strategy Lead
IQVIA

An Inflection Point in Obesity R&D

How clinical trial stakeholders aim to redefine and expand development opportunities.

The World Obesity Federation's Global Obesity Observatory estimates that 1 billion adults will have obesity by 2030, and more than half of the world's population[1] will live with overweight or obesity levels by 2035. As such, there has been tremendous focus and growth in obesity drug development, with Wegovy (semaglutide) and Zepbound (tirzepatide) becoming household names in recent years. In the past five years alone, obesity clinical trials nearly doubled.[2] Furthermore, there has been a 68% increase in obesity treatment trials from 2022, with more than 124 drugs in active development.

This growing pipeline of novel anti-obesity medications is grabbing the attention of the public worldwide, and clinical trial sponsors are geared to further accelerate the drug development momentum in this critical therapeutic space, vying to open opportunities for effective options.

In 2024, the highly dynamic anti-obesity medication market truly took shape. Now, it is important to keep up with the progress and changes, consistently gauging what patient subpopulations need and where obesity R&D is heading to ultimately help make a positive impact on this global health epidemic.

	Diabetes	Cardiovascular	Kidney disease	Knee osteoarthritis	Obstructive sleep apnea	MASH
Semaglutide (Novo Nordisk)	**STEP-10** Reversion to nomoglycaemia	**STEP-HFpEF** Reduction of heart failure symptoms	**FLOW** Reduction in risk of kidney disease worsening, kidney failure and death due to CVD in adults with T2D and chronic kidney disease	**STEP-9** Reduction in knee OA-related pain; functional benefits		**ESSENCE** MASH resolution in adults with moderate to advanced liver fibrosis (stage 2 or 3)
Tirzepatide (Lilly)	**SURMOUNT-1** (104-wk extension) Risk reduction of progression to T2D	**SUMMIT** Risk reduction in HFpEF outcomes; functional benefits	**TREASURE-CKD** Reduction in risk of chronic kidney disease worsening in adults with obesity and T2D or without T2D	**STOP KNEE-OA** Efficacy and safety in individuals with obesity and knee OA	**SURMOUNT-OSA** Reduction in apnea-hypopnea index	**SYNERGY-NASH** MASH resolution, fibrosis improvement
Survodutide (Boehringer Ingelheim)	**SYNCHRONIZE-2** Efficacy and safety in individuals with obesity or overweight who also have T2D	**SYNCHRONIZE-CVOT** Long-term CVD safety; risk of major adverse cardiac events				**LIVERAGE** MASH resolution, fibrosis improvement in adults with moderate or advanced liver fibrosis (stage 2 or 3) **LIVERAGE-Cirrhosis** MASH resolution, fibrosis

Figure 1. R&D for indication expansion continues to move beyond obesity

DEVELOPING TREATMENTS WITH PATIENTS

Among those living with obesity, patient insights gained through surveys and other means indicate they believe they understand their personal needs and challenges better than anyone else. And because patients are more proactive in managing their healthcare preferences, listening to their perspectives in terms of motivators or hinderances to participating in critical clinical research, can offer tremendous value.

Trial sponsors are recognizing that if patients are asked to commit their time—and their healthcare approach—for research, they deserve to be treated as active partners. Though there is no one-size-fits-all approach to trial design for drug development, sponsors, clinical research organizations and study teams can thoughtfully try to understand patient needs earlier in trial planning stages to ensure tailored solutions are integrated into trial design.

From patient insights, discussions with patient advocacy groups and health economics and research, we know that obesity can have a toll on emotional and mental health. Some patients with obesity have said that prior to clinical trial participation, they have already had daily and even lifelong struggles with making healthy lifestyle changes to lose weight, leaving some feeling frustrated. Most often, they are aware of what steps they need to take to improve health outcomes, but barriers to change can be wide ranging, including frustration from previous attempts and failures to manage or lose weight.

Additionally, trial participation itself may bring about concerns about anti-obesity medication side effects and impact on daily life. Patient feedback also shows that, in some cases, they believe providers don't take their concerns about weight management and related diseases seriously.

For stronger patient recruitment and retention in obesity trials, it is critical to keep the patient sensitivities and experiences above in mind as trials are designed.

TRIAL AND TREATMENT SUPPORT

Creating tailored communications that help tell specific patient populations what to expect in the process is an integral step to consider in design stages for obesity trials. From initial outreach, site teams will need to touch on the unique concerns that may come about during the trial. This includes clearly outlining and discussing points in detail, such as:

- How the patient's obesity can ultimately lead to debilitating comorbidities that go well beyond feelings of discomfort with physical appearance, for example.
- The day-to-day impact of trial participation, including site visits, to gauge what levels of support may be needed to keep patients engaged and compliant with treatment.
- Managing expectations for how much weight may be lost during the trial and if the treatment does not work as hoped. This is especially important since GLP-1s have become popular points of discussion and participants can have preconceived ideas of these treatments' effectiveness and/or inaccurate information as they begin the trial.

- Being clear from the screening process onward that the value for patients extends beyond the investigational treatment itself, such as engaging lifestyle coaches, regular monitoring of underlying conditions, etc.
- Monitoring potential adverse effects of obesity treatment, such as gastrointestinal issues, and treating these in a manner that is in line with the protocol.
- Concerns regarding access to treatment once the trial is completed. Talking through potential next steps and options.

Given the underlying emotional aspects for individuals on their weight management journeys, end-to-end personalized support can be a determining factor in strong patient engagement and overall trial success. In many cases, this may mean going beyond treatment administration to ensure participants are adhering to their broader weight loss plans. Sponsors can consider integrating supplemental support in trials, such as regular counseling on food and activity habits and emotional state, dietitian referrals, personalized fitness plans or trainer support, etc.

ADJUSTING OBESITY TRIAL DESIGN

Because patient retention in obesity trials may be influenced by the amount of weight lost, trial sponsors are recognizing the impact of trial design on this factor too. For example, let's look at two Phase III studies[3] (SURMOUNT-3 and SURMOUNT-4) examining Eli Lilly and Company's Zepbound in adults with obesity.

In these studies, design included two periods for evaluation:

- In SURMOUNT-3, participants started with a 12-week lifestyle intervention period, which involved a low-calorie diet, physical activity and weekly counseling sessions. This period led to participants achieving a 6.9% mean weight loss. So, prior to going into the 72-week double-blind treatment period with placebo arm, participants experienced weight loss and had a monitored lifestyle plan to help them stay engaged in the trial.
- In SURMOUNT-4, participants first received tirzepatide for the initial 36-week open label lead-in period, resulting in a 21.1% mean weight loss before transitioning into the randomized 52-week double-blind treatment period. Providing the medication to all participants in the initial 36-week period may have resolved concerns about being placed in the placebo arm from the start as patients may have experienced common adverse events associated with the treatment.

RETHINKING OBESITY

Alongside designing trials with patients' needs in mind, as we see expanded investment and focus on novel anti-obesity treatments, the industry is coming to an inflection point. Rethinking how to prevent and treat obesity as a global health issue will call for a larger drawing board and mapping out a multi-pronged approach. To transform the treatment paradigm, there are multiple aspects of obesity R&D that require a deeper dive.

CROSS-THERAPEUTIC VALUE

Data show that 75% of U.S. patients who are overweight (body mass index greater than or equal to 25 kg/m2)[4] have one or more weight-related co-morbidities.

Also, in February 2025, findings from a Phase II, double-blind, randomized clinical trial published in Journal of the American Medical Association Psychiatry[5] showed participants receiving semaglutide reduced weekly alcohol craving relative to placebo and "some drinking outcomes," which the authors said justifies further evaluations of GLP-1s for alcohol use disorder through larger clinical trials.

When exploring the potential for pipeline pathways, real-world evidence is becoming more important for understanding implications of obesity treatments while also considering the heterogeneity in patient populations (e.g., multiple comorbidities) and varying degrees of adherence and behaviors around treatment switching.

As the collection of data insights expands, obesity drug developers will gain opportunities to better examine the broader potential of their assets and what may be key market differentiators for the long-term.

VARYING REGIONAL POLICY ON OBESITY

According to the World Health Organization,[6] currently, more people are obese than underweight in every region of the world except Southeast Asia.What was once thought of as a health issue in developed, higher-income countries, obesity is now most prevalent in middle-income countries worldwide, making it a global public health priority. As the global obesity R&D industry looks ahead, it is important for trial sponsors, regulators and other stakeholders to closely monitor how obesity is defined and viewed in various regions, its impact and the related growth of drug development efforts beyond the U.S. and parts of Europe. It will be key to continue diving deeper into questions, such as "What approaches will help better evaluate and treat obesity in different types of patient segments and cultures worldwide?"

- The current FDA draft guidance[7] for developing drugs and biological products for weight reduction, updated from the 2007 version, establishes standards for clinical trials, including trial sizes and representation of varying populations and endpoints. It also notes less stringent recommendations for pediatric trials.
- The Lancet Diabetes & Endocrinology Commission's recommendation on definition and diagnostic criteria of clinical obesity[8] focuses on the difference between pre-obesity as

a risk factor compared to clinical obesity as a standalone disease, defined by the functional impact on organs. This guidance also proposes looking beyond BMI alone to diagnose obesity.

Clinical development of new anti-obesity treatments in the U.S. may be more costly and operationally challenging, with more complexities in entrance criteria that can impact patient recruitment efforts in an already competitive marketplace.

MORE TO COME AND QUICKLY IN A HIGHLY DYNAMIC MARKET

As we go further in 2025, we are certain the obesity R&D landscape will rapidly evolve. Building on last year's progress, we will see updates regarding newly approved treatment options, expanding indications and further evaluations of treatments in combination for various patient subpopulations.

Given the R&D industry's excitement about the innovation of anti-obesity treatments, in 2025 and onward, there will be much food for thought for clinical trial sponsors, regulators, CROs and the broader healthcare ecosystem regarding treatment innovation and related access. Whether long-term patient engagement and related follow-up, adequate supply, pathways for medication cost and coverage or the potential to develop oral anti-obesity medications, there is no shortage of variables that will need to be considered as anti-obesity drug development maintains its hold on the attention of many worldwide. In the U.S., two important pieces were published in January 2025 that indicate how stakeholders are looking to update or shift how obesity is defined and evaluated: **CP**

References

1. *https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/iqvia-institute-obesity-summary.pdf*
2. *https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2024-activity-productivity-and-enablers*
3. *https://investor.lilly.com/news-releases/news-release-details/tirzepatide-demonstrated-significant-and-superior-weight-loss*
4. *https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight*
5. *https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2829811*
6. *https://www.who.int/health-topics/obesity#tab=tab_1*
7. *https://www.fda.gov/media/71252/download*
8. *https://doi.org/10.1016/S2213-8587(24)00316-4*

GUILHERME ANDRETTA has more than 15 years of experience in the pharmaceutical industry, primarily in clinical trial strategy and operations and medical affairs and marketing. His areas of therapeutic expertise include diabetes, cardiovascular, rare diseases, immunology and hematology.

Board Certified in Endocrinology, Diabetes, and Metabolism and Internal Medicine, DR. CAVENEY leads IQVIA's Obesity, Cardiovascular, Endocrine, Renal and Reproductive Health Centers of Excellence, consisting of physicians, scientists and senior operational experts experienced in diabetes drug development strategy and implementation.

VIVIANE PEREIRA has 25 years of experience in the pharmaceutical industry, working across various areas in clinical research, including monitoring, operational delivery and regional and global project oversight. Areas of expertise include Cardiovascular, Endocrine & Metabolism, Nephrology, Solid Organ Transplant (Kidney), Respiratory and Muscular-skeletal. Viviane holds a PharmD in Pharmacy and Biochemistry from the University of São Paulo, Brazil and an MBA in Strategic & Economic Project Management from Fundação Getúlio Vargas, São Paulo, Brazil.