Driving Successful Obesity Drug Development with GLP-1 Agonists

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Obesity is a global health issue, affecting 12.5% of the population in 2022, according to WHO. The prevalence has doubled in adults and quadrupled in adolescents since 1990 [1].

Obesity is an important health concern and is associated with health impacts including premature death from associated diseases such as cardiovascular complications, diabetes, cancers, neurological disorders, chronic respiratory diseases, and digestive disorders [2]. Effective management is increasingly important, and current interventions include diet and exercise, behavioral therapy, surgical intervention, and biopharmaceutical medications.

The promise of GLP-1 Agonists

While appetite suppressants and lipase inhibitors are used to treat obesity, GLP-1 Receptor Agonists (GLP-1RAs) have proven most effective. Originally developed for type 2 diabetes (T2D), GLP-1RAs enhance insulin secretion, suppress glucagon, and slow gastric emptying, aiding in appetite regulation.

In 2005, Exenatide was the first GLP-1 agonist approved for the treatment of T2D. Nine years later, the link between GLP-1 and reduced food intake resulted in the development and approval of the first GLP-1RA for obesity (Liraglutide). Since then, many clinical trials have proven that GLP-1RAs are currently the most effective and tolerable anti-obesity medications.

With the FDA approval of semaglutide, it is perceived as the beginning of a new era in anti-obesity medication for weight management, with weight loss efficacy approaching efficacy levels achieved with bariatric surgery [3].

Some GLP-1RAs have been found to be agonists of another metabolic hormones besides GLP-1, such as the glucose-dependent insulinotropic polypeptide (GIP) receptor. Several pharmaceutical companies are pursuing active clinical development of dual GLP-1/GIP agonists, and combination treatments, following the successful approval of Tirzepatide for T2D.

Measuring the effectiveness of anti-obesity medications

The primary endpoint in obesity trials is often weight change, with secondary endpoints including waist circumference, BMI, and blood chemistry (blood glucose, HbA1c and lipid profiles). Patient experience data are increasingly vital for regulatory approval, product differentiation, labeling, and pricing and reimbursement discussions.

To date, Signant Health has supported over 30 obesity clinical trials evaluating GLP-1 RAs, several of which have led to pivotal regulatory approvals. In total, these studies collecting patient experience data in the form of electronic Patient-Reported Outcomes (ePRO), have involved over 50,000 patients, with the largest study in over 17,000 patients across 35 countries studies for an almost five-year study duration.

Our ePRO solutions have supported secondary endpoints and health technology assessments (HTAs) with a variety of measures, including health-related quality of life assessments (HRQoL; e.g., SF-36, Impact of Weight on Quality of Life-Lite- IWQoL-Lite, and EQ-5D-5L) and others targeting food craving (e.g., Control of Eating Questionnaire (CoEQ)), mental health (e.g., Columbia-Suicide Severity Rating Scale (C-SSRS), and Patient Health Questionnaire-9 (PHQ-9), and overall health perception (such as the Patient Global Impression of Severity/Change (PGIS/C).

More generally, PROs are becoming crucial endpoints in clinical trials and prospective studies of obesity treatments [4]. Domains that can be measured by patient-reported outcomes that are important in the assessment of anti-obesity medications include:

- Physical health/symptoms
- Self-esteem
- Mental health
- Social health
- Appetite and eating behavior
- Body image

In the past decade, HRQoL measures are increasingly being adopted as endpoints in weight loss and obesity studies, including incorporation in medication labeling of GLP-1 RAs. The most widely used and well-validated generic measures of patient-reported health status are EuroQol 5-Dimension 5-Level (EQ-5D-5L) and the Short-Form 36 version 2 (SF-36 v2). A commonly used, obesity-specific measure is the Impact of Weight on Quality of Life for Clinical Trials (IWQoL-Lite CT).

The EQ-5D-5L is also one of the most common health-state measures used to support health economic evaluations such as cost-utility analyses. One study in semaglutide evaluating cardiovascular outcomes in 17,604 patients reported significant improvements compared to placebo in the two summary measures of the EQ-5D-5L (index score and VAS score), over a period of 5 years [5].

Driving patient engagement and high-quality outcomes data

Many phase II-IV clinical trials of anti-obesity medications (AOMs) involve large groups of patients, studied for long treatment periods, and across many countries globally. With this operational complexity, at Signant, we understand how to drive successful obesity ePRO studies:

- **SOLUTION**: Our leading eCOA solution provides comprehensive functionality that can fit the requirements of any study protocol.
- **SCIENCE**: Our 50+ clinicians and COA scientists provide the scientific credibility and expertise to generate high quality, reliable evidence
- **SCALE**: We have the architectural and operational capacity and global reach to support large obesity clinical trials across the world – we currently host over 600 active ePRO trials.
- **SERVICE**: Signant brings experienced project teams with mature operational processes, full 24/7 patient- and site-support, hardware logistics, and license/scale management services so that everything is covered.

Our ePRO application isn't only a data collection tool, but provides value to the patient to help improve retention and engagement throughout each clinical trial. Our app can provide access to study and disease information at any time during the study; an active up-to-date visit schedule reminding patients of upcoming visits and how to prepare for them; and built-in video visit capability for remote consultations and follow up.

As experts in optimizing clinical trials to simplify participation for patients and sites, we thoughtfully incorporate decentralized elements such as telemedicine, and remote sample collection, to reduce the need to attend clinic and drive engagement and retention during lengthy follow up periods.

Because Signant Health is the evidence generation company, sponsors and CROs rely on us to generate high quality, reliable data that drives trial endpoints. We are proud to have already supported the successful approvals of GLP-1RAs around the world, and beyond obesity have an outstanding track record of supporting 28% of novel drug approvals in the US and EU since 2016.

Reach out to Signant Health experts to discuss how we can support your protocol.

Authors

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Bill Byrom, PhD serves as Vice President of product intelligence and positioning at Signant Health, where he also serves as a principal ePRO scientist. He has worked in the Pharmaceutical industry for 30 years and is the author of over 70 publications and two industry textbooks on electronic patient-reported outcomes (ePRO). His recent scientific work includes the use of wearable technology and bring- your-own-device (BYOD) eCOA in clinical trials. Bill recently served as Vice Director of the C-PATH ePRO Consortium, and is an active member of the DIA Study Endpoints Community where he leads a cross-disciplinary group on the use of endpoints derived from wearable devices to support labeling claims and regulatory decision making. Bill provides independent eClinical commentary via LinkedIn and Twitter (@billbyrom).

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