
CLINICAL INSIGHTS

Weight Loss Medications: What's Coming Next?

Medications like Ozempic, Wegovy, and Mounjaro have taken the world by storm because of their effects on weight loss and opened eyes to the new possibilities that weight loss medications can bring. Before these new medications arose, weight loss research seemed to stall, with prior therapies seeing approximately a 6-19 pound weight loss over the course of a year when added to diet and exercise.¹ However, with the development of new glucagon-like peptide-1 (GLP-1) receptor agonists like semaglutide (branded as Wegovy for weight loss; Ozempic for diabetes) averaging a 22-27 pound weight loss in a year and beyond¹, drug companies have a rejuvenated interest for developing weight loss medications, with several new candidates likely coming on the market in the coming years.

Taking their lead from the success of the GLP-1 receptor agonist family, several new medications under investigation continue to utilize this mechanism and build upon it by affecting other gastric hormones (incretin hormones) that may further enhance weight loss. One such example that will likely be the next approved weight loss medication is tirzepatide (currently available as brand name Mounjaro for diabetes), which combines the effect of GLP-1 receptor agonists along with activating another incretin hormone pathway, glucose-dependent insulinotropic polypeptide (GIP), allowing for enhanced weight loss benefits up to 15% body weight loss (34.4 pounds) in a year and a half.² Additional incretin-active drugs under investigation that we may see in the coming years include ecnoglutide, mazdutide, retatrutide, orfoglipron, and CagriSema, which not only provide additional weight loss options, but also oral tablet forms rather than injectable only, as the current options are.

Many New Drugs are Building on the Success Mechanisms of GLP-1s

A novel medication early in studies is ARD-101, which continues with the incretin hormone trend but also adds a unique mechanism of targeting extraoral bitter taste receptors

(TAS2R). This product seems to not only provide benefits in both weight loss and appetite suppression, but also inflammation. The researchers are beginning studies to look at ARD-101 for both metabolic and inflammatory conditions.³

Rather than supplement incretin hormones, APH-012 is under investigation as a more “natural” option to help re-regulate the body’s own incretin hormone response. It consists of a glucose (sugar) formulation taken before meals that is designed to break down at specific and strategic parts of a person’s digestion to help re-regulate and optimize when each incretin hormone response occurs after eating.⁴

One concern that has arisen from incretin hormone weight loss medications like Wegovy is that weight loss is not coming from fatty tissue only, but also from loss of muscle mass. While the long-term impact of this is unknown, it does raise concerns as muscle is important for enhancing weight loss through burning through fatty tissue, as well as general need for mobility and safety of preventing falls and bone fractures. Bimagrumab is a novel medication under investigation that is a monoclonal antibody (essentially a synthetic protein that matches a biological protein) that has been found to increase muscle growth while simultaneously lowering body fat.⁵ Bimagrumab is being tested both by itself as well as with semaglutide (Wegovy) to determine best weight loss results while maintaining muscle mass.

Another drug taking a unique approach is RES-010, which is instead focusing its mechanism on RNA (i.e., “recipes” that cells use to make different proteins throughout the body). The investigators have identified a target of miR-22 that is involved with regulation of metabolism, and found that with controlling miR-22, they may be able to control multiple factors around metabolism.⁶

These are only a handful of several of the new weight loss medications that we may see come to market over the next few years. With so many new agents becoming available, the questions of why it matters and what to do with all these options remain—however, having options is ideal for patients so that treatment can be tailored and targeted for each individual’s needs. These options now allow adjustments for safety, considerations for concomitant health conditions, management of side effects and tolerability, as well as preference for administration.

Impacts to Obesity Management

With 42% of Americans considered obese (BMI greater than 30), these medications will continue to play a larger role in obesity management. However, it is crucial to recognize that medication alone cannot provide a complete solution. The integration of nutrition and

physical activity counseling is imperative for optimal health outcomes. Many people suffering from obesity require education to adopt healthier behaviors. This lifestyle counseling will ensure that once a healthy weight is achieved, it can be maintained without having to take medication for life.

References:

1. Clinical Resource, Weight Loss Products. Pharmacist's Letter/Prescriber's Letter. August 2021. [370802]
2. Lilly. Lilly's Tirzepatide Achieved up to 15.7% Weight Loss in Adults with Obesity or Overweight and Type 2 Diabetes in SURMOUNT-2. Investor.lilly.com. Published April 27, 2023. Accessed May 12, 2023. <https://investor.lilly.com/news-releases/news-release-details/lillys-tirzepatide-achieved-157-weight-loss-adults-obesity-or-overweight-and-type-2-diabetes-in-surmount-2>
3. Aardvark Therapeutics, Inc. Aardvark Therapeutics, Inc., Announces the Initiation of Enrollment for Three Phase 2 Clinical Trials of Oral ARD-101. Prnewswire.com. Published February 2, 2022. Accessed May 12, 2023. <https://www.prnewswire.com/news-releases/aardvark-therapeutics-inc-announces-the-initiation-of-enrollment-for-three-phase-2-clinical-trials-of-oral-ard-101-301473522.html>
4. Aphaia Pharma. First Patient in Phase 2 Study of APH-012. AphaiaPharma.org. Published October 27, 2022. Accessed May 12, 2023. <https://aphaiapharma.com/news/first-patient-in-phase-2-study/>
5. Heymsfield SB, Coleman LA, Miller R, et al. Effect of Bimagrumab vs Placebo on Body Fat Mass Among Adults With Type 2 Diabetes and Obesity: A Phase 2 Randomized Clinical Trial. JAMA Netw Open. 2021;4(1):e2033457. doi:10.1001/jamanetworkopen.2020.33457
6. Vitale, Gina. Resalis Takes Aim at 'Master Regulator of Metabolism'. Cen.acs.org. Published February 22, 2023. Accessed May 30, 2023. <https://cen.acs.org/biological-chemistry/rna/Resalis-takes-aim-master-regulator/101/web/2023/02>