The American Diabetes Association Highlights Innovations in New Drug Therapies for Patients with Obesity

Novel Drugs Demonstrate Benefits of Once Weekly Drugs for Weight Loss and Glycemic and Blood Pressure Control

ORLANDO, FL. (JUNE 23, 2024) – Findings from three studies showcase new data on the latest developments in drug therapy innovations to treat obesity including new insights on GLP-1 (Glucagon-like peptide-1) receptor agonists. The data was presented as a late-breaking poster and oral presentations, respectively at the American Diabetes Association® (ADA) 84th Scientific Sessions in Orlando, FL.

The studies are part of a host of research and development driven by interest in new GLP-1 drugs and concerns about obesity. Obesity affects about 125 million people in the United States — 41.9% of adults and 19.7% of children and adolescents. Notably, 90% of people with diabetes also live with overweight or obesity. Weight gain is a major problem for physicians and patients looking to achieve adequate glycemic, blood pressure and lipid control in patients with diabetes.

“Over the past few years, we have seen the substantial impact of new research working to solve the dual health crisis we are facing, obesity and diabetes,” said Dr. Robert Gabbay, chief scientific and medical officer for the ADA. “The studies we are seeing presented at this year’s annual meeting show great promise to fuel new solutions and treatment options for patients across the globe living with type 2 diabetes and obesity.”

Drug Treatment for Obesity Effectively Reduces Body Weight and Blood Pressure

HRS9531 is a dual GLP-1/GIP (glucose-dependent insulinotropic polypeptide) receptor agonist, offering a treatment option for individuals with overweight or obesity, as well as type 2 diabetes. This Phase 2 study evaluated the efficacy and safety of HRS9531 in obese adults without diabetes. The research found HRS9531 effectively reduced body weight, blood pressure, blood glucose, and triglycerides, with a favorable safety profile.

The double-blind, randomized, placebo-controlled Phase 2 trial studied a total of 249 Chinese adults with a body mass index of 28-40 kg/m². Participants were randomized into five groups to receive once-weekly subcutaneous injections of HRS9531 (1.0 mg, 3.0 mg, 4.5 mg, and 6.0 mg) or placebo for 24 weeks. The primary endpoint was the percentage change in body weight at week 24.

Greater weight loss was achieved in individuals receiving HRS9531 compared with those receiving placebo. At the end of the 24-week intervention, participants in 1.0 mg, 3.0 mg, 4.5 mg, and 6.0 mg HRS9531 groups achieved weight reductions of 5.4%, 13.4%, 14.0%, and 16.8% respectively, as compared with 0.1% reduction in the placebo group. Moreover, the proportion of participants achieving ≥5% weight reduction was 52.0%, 88.2%, 92.0%, 91.8%, and 10.2%, respectively. Most adverse events (AEs) were mild or moderate, and the most common AEs were nausea, diarrhea, decreased appetite, and vomiting, occurring primarily during dose escalation. The overall safety and tolerability profile of HRS9531 is consistent with other GLP-1 agonists.

“People living with obesity are at a high risk of developing chronic diseases such as type 2 diabetes and cardiovascular disease. Losing weight significantly reduces the risk of those diseases,” said Xiaoying Li, MD, PhD. Professor and Director, Department of Endocrinology and Metabolism, Zhongshan Hospital Fudan University, China, and senior author. “Since dietary and exercise intervention alone is often not enough, we were pleased to see that this could be a potentially promising treatment for weight management, potentially enhancing their overall health and significantly reducing the societal burden of obesity.”

The authors of the study note a Phase 3 study with HRS9531 in Chinese overweight or obese individuals is already ongoing and multi-regional studies are being planned.

Experimental Medication, Pemvidutide, Reveals 15.6% Average Total Body Weight Loss for Patients with Overweight and Obesity

The Phase 2 MOMENTUM trial evaluated the potential for pemvidutide, Altimmune’s investigational medication, a GLP-1/Glucagon dual receptor agonist, in development for obesity and a liver disease called metabolic-dysfunction associated steatohepatitis (MASH), to help people with overweight and obesity lose weight. The trial revealed promising results - significantly reducing body weight and serum lipids over 48 weeks of treatment. In addition, body composition analysis demonstrated class-leading preservation of lean mass.

This Phase 2, randomized, placebo-controlled trial enrolled 391 subjects with overweight or obesity, but without diabetes, and administered either pemvidutide at three dose levels (1.2, 1.8, 2.4 mg) or a placebo weekly for 48 weeks. Neither the investigators nor the subjects knew what treatment they were receiving.

After 48 weeks, subjects at the highest pemvidutide dose had lost an average of 15.6% of their total body weight, and the treatment appeared to be safe and well-tolerated. Several potential advantages of this approach to weight loss were identified, including a simple dosing regimen and significant decreases in the amount of lipids (such as cholesterol and triglycerides) present in the blood and the liver, which may help reduce the risk of cardiovascular disease. Additionally, results from a body composition sub-study were presented indicating class-leading preservation of lean mass, with only 21.9% attributable to lean mass and 78.1% of weight loss due to fat. Preserving lean mass, which primarily includes muscle, is believed to be critical for maintaining physical function and decreasing the risk of bone fractures.

“Obesity and its associated comorbidities represent a major and growing health challenge. A variety of therapeutic approaches will be required to meet the specific needs of each patient to effectively manage their weight and address other obesity-related conditions they may have,” said Louis J. Aronne, MD, FACP, DABOM, Weill Cornell Medicine, New York City, NY, and primary investigator. “These findings demonstrated that the use of pemvidutide may have important effects on the quality of weight loss and cardiometabolic-associated comorbidities of obesity. Furthermore, as the focus shifts to long-term weight management, the preservation of lean mass will be critical for patient care.”

The authors of this study are preparing for larger Phase 3 registrational trials intended to demonstrate the safety and clinical benefit of pemvidutide for weight management. In addition, because obesity can lead to the accumulation of excess liver fat and MASH, they are also studying pemvidutide in patients with this condition.

Retatrutide Improves Ability of Insulin to Lower Blood Sugar for People Living with Type 2 Diabetes

Biomarker analyses may help in the understanding of diseases and identifying specific therapeutic targets. A new study evaluated biomarkers to observe how treatment with retatrutide affects pancreatic beta cells that make insulin as well as biomarkers associated with the body’s ability to respond to insulin to lower blood sugar. In this study, exploratory biomarker research within phase 2 clinical trials was examined to further understand on the molecular level how retatrutide may work and further help explain primary results.

The research found treatment with retatrutide increased markers of well-functioning insulin-producing beta cells (HOMA2-B) and the ability of insulin to lower blood sugar

(adiponectin). The results also demonstrated how retatrutide decreased markers of stress on insulin-producing cells, as assessed by measuring immature insulin (proinsulin) and reduction in a marker of insulin resistance (HOMA2-IR).

“This study matters because many people living with type 2 diabetes are taking multiple diabetes medications to try to reach blood sugar targets, and new medications that have the potential to help simplify treatment regimens are needed,” said Melissa K. Thomas, MD, PhD, Vice President, Diabetes and Metabolic Research, Lilly Research Laboratories, Indianapolis, IN, and one of the investigators conducting the study. “We are encouraged to see that people living with either obesity or with type 2 diabetes in our clinical studies had lowered blood sugar and had improved responses to insulin.”

Several Phase 3 clinical trials are underway studying retatrutide in people living with type 2 diabetes or obesity without type 2 diabetes including the TRIUMPH and TRANSCEND Phase 3 trials.

Research presentation details:

Dr. Zeng will present the findings at the following late-breaking poster session:

- Late-Breaking Posters:
  Efficacy and Safety of HRS9531, a Novel Dual GLP-1/GIP Receptor Agonist, in Obese Adults—A Phase 2 Trial
- Presented on Saturday, June 22, 2024 at 12:30 PM EDT

Dr. Aronne will present the findings at the following presentation session:

- Oral Presentations - Weighing Opportunities of Incretin-Based Therapy in Obesity
  Pemvidutide, a GLP-1/Glucagon Dual Receptor Agonist, in Subjects with Overweight or Obesity—A 48-Week, Placebo-Controlled, Phase 2 (MOMENTUM) Trial
- Presented on Sunday, June 23, 2024 at 1:45 PM EDT

Dr. Thomas will present the findings at the following oral presentation session:

- Oral Presentations - Weighing Opportunities of Incretin-Based Therapy in Obesity
  Retatrutide, an Agonist of GIP, GLP-1, and Glucagon Receptors, Improves Markers of Pancreatic Beta-Cell Function and Insulin Sensitivity
- Presented on Sunday, June 23, 2024 at 2:45 PM EDT

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About the ADA's Scientific Sessions

The ADA's 84th Scientific Sessions, the world's largest scientific meeting focused on diabetes research, prevention, and care, will be held in Orlando, FL on June 21-24. More than 11,000 leading physicians, scientists, and health care professionals from around the world are expected to convene both in person and virtually to unveil cutting-edge research, treatment recommendations, and advances toward a cure for diabetes. Attendees will receive exclusive access to thousands of original research presentations and take part in provocative and engaging exchanges with leading diabetes experts. Join the Scientific Sessions conversation on social media using #ADAScientificSessions.

About the American Diabetes Association

The American Diabetes Association (ADA) is the nation's leading voluntary health organization fighting to bend the curve on the diabetes epidemic and help people living with diabetes thrive. For 83 years, the ADA has driven discovery and research to treat, manage, and prevent diabetes while working relentlessly for a cure. Through advocacy, program development, and education we aim to improve the quality of life for the over 136 million Americans living with diabetes or prediabetes. Diabetes has brought us together. What we do next will make us Connected for Life®. To learn more or to get involved, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383). Join the fight with us on Facebook (American Diabetes Association), Spanish Facebook (Asociación Americana de la Diabetes), LinkedIn (American Diabetes Association), Twitter (@AmDiabetesAssn), and Instagram (@AmDiabetesAssn).