Embargoed until Monday, June 8, 2026, at 1:30 p.m. CT

ACHIEVE Trials Demonstrate Comparative Benefits of Novel, Small-Molecule Oral GLP-1 RA, Expanding Oral Treatment Options for Patient Population in Need of Alternative Solutions

First Head-to-Head Trial Compares Two Oral GLP-1 RAs Effects on Glucose Control and Weight Changes in Type 2 Diabetes

NEW ORLEANS, La. (June 8, 2026) – New data show the benefits of orforglipron, the first oral, small molecule, non-peptide glucagon-like peptide-1 receptor agonist (GLP-1 RA) to successfully complete a phase 3 program, for blood glucose and weight management in individuals living with type 2 diabetes, compared to existing treatment options. Researchers presented this data as symposia at the 2026 Scientific Sessions of the American Diabetes Association® (ADA) in New Orleans. This follows findings from the ACHIEVE-1 trial presented at ADA's Scientific Sessions last year, demonstrating the safety and effectiveness of orforglipron in individuals living with type 2 diabetes.

Recent studies show many people living with type 2 diabetes delay or avoid starting injectable therapies due to fear of needles, inconvenience, or the complexity of managing injections. In fact, in 2024, nearly 3 in 4 adults with diagnosed diabetes were not currently using injectable GLP-1 RA therapies, creating an unmet need for effective oral options.

Orforglipron is an investigational once-daily pill designed to help adults with type 2 diabetes lower blood glucose levels and support weight loss by mimicking GLP-1, a natural hormone involved in regulating appetite and insulin. In the ACHIEVE 2,3, and 5 studies, researchers evaluated the pill compared to dapagliflozin, oral semaglutide, and placebo, respectively.

ACHIEVE-2 Trial Shows Oral Orforglipron Superior to Dapagliflozin Across Glycemic, Weight Loss, and Cardiometabolic Endpoints in Adults with Type 2 Diabetes

The ACHIEVE-2 trial is a phase 3, 40-week, randomized, active-controlled, open-label study, which was conducted at 73 sites across the United States, China, Mexico, Germany, Poland, and Taiwan between January 10, 2024, and September 26, 2025. The study compared the efficacy and safety of orforglipron at 3 mg, 12 mg, and 36 mg doses to dapagliflozin at a 10 mg dose among 962 patients.

As published in *The Lancet*, results showed orforglipron met the primary endpoint of non-inferiority to dapagliflozin for change in A1c from baseline at week 40 and demonstrated superiority across all primary and key secondary endpoints (including triglyceride levels, non-HDL cholesterol, and systolic blood pressure). Treatment with orforglipron resulted in A1C reductions ranging from 1.3% to 1.7%, compared with a 0.8% reduction with dapagliflozin, while up to 80% of participants achieved an A1C level below 7% and up to 69% achieved an A1C level of 6.5% or lower. Orforglipron also produced greater percentage body weight loss, with reductions ranging from 6.3% to 7.3% depending on dose, compared with 3.0% for dapagliflozin.

“Although we know that incretin therapy is more effective than the SGLT2i class in regard to A1C and weight control, we were surprised by the magnitude of the effect in this study,” said Michelle D. Welch, MD, lead author of the study. “As many patients and providers are reluctant to start injectable medications, orforglipron can deliver impactful improvements in blood glucose control and weight goals in a simple daily oral medication. This will hopefully make incretin therapy more accessible to patients living with type 2 diabetes.”

Once-Daily Orforglipron, an Investigational Pill, Helped Lower Blood Glucose and Weight More Than Oral Semaglutide at Doses Approved for Type 2 Diabetes

The ACHIEVE-3 trial is a phase 3, 52-week, randomized, open-label trial evaluating the efficacy and safety of orforglipron compared with oral semaglutide in adults with type 2 diabetes inadequately controlled with oral semaglutide, an often first-line oral medication for patients with type 2 diabetes. Similar to orforglipron, oral semaglutide targets the GLP-1 pathway to help lower blood glucose and support weight loss in adults with type 2 diabetes. However, oral semaglutide must be taken on an empty stomach with a small amount of water and requires patients to wait before eating or drinking. The trial randomized 1,698 participants across the U.S., Argentina, China, Japan, Mexico, and Puerto Rico to receive either 12 mg or 36 mg of oforglipron or 7 mg or 14 mg of oral semaglutide.

After a year of treatment, the daily pill provided greater improvements in glycemic control and weight loss than oral semaglutide at doses approved for type 2 diabetes, but orforglipron was associated with a higher occurrence of gastrointestinal symptoms and a slightly greater increase in heart rate. A1C was reduced by 1.9% vs. 1.5%, and body weight was reduced by 8.2% vs 5.3% with orforglipron 36 mg vs. oral semaglutide 14mg, respectively.

“The findings support orforglipron as a potential new oral GLP-1 RA effective option, when approved, for people living with type 2 diabetes to address key known barriers associated with current injection therapy or administration recommendations,” said Julio Rosenstock, MD, lead author of the study published in *The Lancet.*

Up to 70% of Patients with Type 2 Diabetes Receiving Daily Pill Achieved HbA1c Below 7%

ACHIEVE-5 is a 40-week phase 3 study evaluating the safety and efficacy of orforglipron (3 mg, 12 mg, and 36 mg) in adults with type 2 diabetes taking insulin glargine, with or without other diabetes medications (metformin and/or SGLT-2 inhibitors). Insulin glargine is a long-acting insulin that helps keep blood glucose levels stable throughout the day and night.

Results, as published in *JAMA*, showed the once-daily pill significantly improved glycemic control and body weight without increasing hypoglycemia risk in participants with type 2 diabetes inadequately controlled by insulin glargine. Among 546 randomized participants (median age 61 years, 52.9% male), the mean A1C was 8.5%, and BMI was 30.8. Up to about 70% of participants receiving orforglipron achieved A1C below 7% (a common target for blood glucose control), compared with about 25% on placebo. Nearly half achieved at least 5% body weight reduction at the higher doses. The mean A1C change was -1.58%, -1.88%, and -1.82% with orforglipron 3mg, 12mg, and 36 mg, respectively, versus -0.79% with placebo. All key secondary outcomes, including mean percent body weight change, demonstrated statistically significant differences in favor of orforglipron compared with placebo.

“ACHIEVE-5 results are encouraging because they suggest a once-daily oral GLP-1 option like orforglipron could help improve blood glucose control for people with type 2 diabetes who are already managing complex treatment routines, including basal insulin,” said Professor Francesco Giorgino, MD, PhD, lead author of the study. “For many patients, basal insulin alone is not enough to maintain glycemic control, and an oral GLP-1 therapy could offer a simpler alternative to intensifying insulin treatment while giving healthcare professionals greater flexibility in managing care.”

The authors note longer term data will be needed to determine how these findings will translate into broader clinical practice. Additionally, the ACHIEVE-4 trial and a dedicated cardiovascular outcomes trial are currently assessing cardiovascular safety.

Research presentation details:

Orforglipron Compared with Dapagliflozin in Type 2 Diabetes: Results from ACHIEVE-2

- Michelle D. Welch, MD
- Symposium: From Pen to Pill: Achieving a Paradigm Shift in Type 2 Diabetes—The Orforglipron 'ACHIEVE' Clinical Trial Program
- Monday, June 8 from 1:30-1:50 p.m. CT
- Ernest N. Morial Convention Center, Great Hall A (Level 1)

Also presented as an oral presentation: Orforglipron vs. Dapagliflozin in Type 2 Diabetes Inadequately Controlled with Metformin

- Michelle D. Welch, MD
- Oral presentations: Novel Approaches to Glucose Control (with the ADA president’s select abstract presentation)
- Sunday, June 7 from 3:30-3:45 p.m. CT
- Ernest N. Morial Convention Center, Great Hall B (Level 1)

Orforglipron Compared with Oral Semaglutide in Type 2 Diabetes: Results from ACHIEVE-3

- Julio Rosenstock, MD
- Symposium: From Pen to Pill: Achieving a Paradigm Shift in Type 2 Diabetes—The Orforglipron 'ACHIEVE' Clinical Trial Program
- Monday, June 8 from 1:50-2:10 p.m. CT
- Ernest N. Morial Convention Center, Great Hall A (Level 1)

Orforglipron Compared with Placebo as an Add-On to Titrated Insulin Glargine: Results from ACHIEVE-5

- Francesco Giorgino, MD, PhD
- Symposium: From Pen to Pill: Achieving a Paradigm Shift in Type 2 Diabetes—The Orforglipron 'ACHIEVE' Clinical Trial Program
- Monday, June 8 from 2:10-2:30 p.m. CT
- Ernest N. Morial Convention Center, Great Hall A (Level 1)

Also presented as an oral presentation: ADA Presidents' Select Abstract: Efficacy and Safety of Orforglipron vs. Placebo Added to Titrated Insulin Glargine in Adults with Long-Standing Type 2 Diabetes: ACHIEVE-5

- Francesco Giorgino, MD, PhD
- Oral presentations: Novel Approaches to Glucose Control (with the ADA president's select abstract presentation)
- Sunday, June 7 from 3:15-3:30 p.m. CT
- Ernest N. Morial Convention Center, Great Hall B (Level 1)

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About American Diabetes Association's 2026 Scientific Sessions

The ADA's 2026 Scientific Sessions, the world's largest scientific meeting focused on diabetes research, prevention, and care, will be held in New Orleans, LA, from June 5-8. Thousands of leading physicians, scientists, and healthcare 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 #ADASciSessions.

About American Diabetes Association

The American Diabetes Association (ADA) is the nation's leading voluntary health organization fighting to end diabetes and helping people thrive. This year, the ADA celebrates 85 years of driving discovery and research to prevent, manage, treat, and ultimately cure diabetes—and we're not stopping. There are over 155 million

Americans living with diabetes or prediabetes. Through advocacy, program development, and education, we're fighting for them all. To learn more or to get involved, visit us at diabetes.org or call 1-800-DIABETES (800-342-2383). Join us in the fight on Facebook (American Diabetes Association), Spanish Facebook (Asociación Americana de la Diabetes), LinkedIn (American Diabetes Association), and Instagram (@AmDiabetesAssn). To learn more about how we are advocating for everyone affected by diabetes, visit us on X (@AmDiabetesAssn). (@AmDiabetesAssn). To learn more about how we are advocating for everyone affected by diabetes, visit us on X (@AmDiabetesAssn).