

FOR IMMEDIATE RELEASE

BREAKTHROUGH CLINICAL DATA: ORAGLUTIDE DELIVERS SUSTAINED GLUCOSE CONTROL FOR SIX DAYS FROM A SINGLE ORAL CAPSULE — WITH NO REPORTED SIDE EFFECTS

Diabetology Limited presents first-in-human oral capsule, intestinally absorbed GLP-1 RA data at ADA 86th Scientific Sessions,

- *Demonstrating longer duration of action consistent with novel depot effect of 'Oraglutide™' for a low dose, low side effect, once weekly, oral diabetes and obesity therapy; and*
- *Opens the development path to 'Satietyde™', a safe, lower cost, daily microdose therapy to address the growing post-Obesity therapy rebound and maintenance dilemma*

KEY HIGHLIGHTS

- **6-day glucose control:** A single 4 mg oral dose of Oraglutide™ produced a sustained fall in glucose. Measuring 14% at Day 6 (p=.046), the longest duration presented from a single oral GLP-1 dose in a human IVGTT study.
 - **28% increase in insulin secretion:** Relative to placebo, insulin percent AUC increased by 12% on dosing day 0, (p=0.019) and 28% Day 1 (p = 0.025).
 - **Novel intestinal depot effect:** Blood levels of Oraglutide™ were higher on Day 1 than dosing on Day 0, consistent with a lipid associated depot effect in the intestinal wall — a fundamentally new pharmacological finding.
 - **No nausea or side effects observed:** No adverse events were observed across the 8-subject cohort over one week, consistent with the targeted vagal afferent mechanism that avoids peak off target outer circulation exposures.
 - **Dose >6x lower than Rybelsus:** Biopotency at least six-fold greater than Rybelsus (R2) demonstrating Oraglutide™ low dose, long acting potential and opens the door to Satietyde™ microdose maintenance and rebound prevention formulations.
 - **Circulating Blood Levels** sufficient to trigger pancreatic GLP-1 receptors observed to Day 4
 - **Platform patent cover to 2044:** Diabetology's licensed Axxess™ formulations technology is protected by patents and applications extending to 2044.
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Diabetology Limited (Jersey, British Isles) today presented poster 1724-P at the American Diabetes Association's 86th Scientific Sessions, reporting the first human data from **Oraglutide™**, an intestinally absorbed oral semaglutide capsule formulated using the licensed proprietary **Axcess™** delivery technology. The data reveal an unprecedented duration of action following a single low oral dose, with no observed side effects, and provides strong mechanistic evidence for a previously undescribed intestinal lipid depot effect.

"These results represent a genuine paradigm shift in oral GLP-1 therapy," said **Dr Roger New PhD, Chief Scientific Officer of Diabetology Limited Group**. "We are seeing six days of glucose-lowering activity from a single 4 mg dose, at one-sixth the dose of currently approved oral semaglutide and with a completely clean safety profile so far. This data changes what we thought was possible with oral peptide delivery and is applicable to other lipidated GLP1 Peptides."

STUDY DESIGN & RESULTS

The randomised, placebo-controlled study enrolled 8 healthy individuals aged 20–60 years with normal HOMA-IR at Breakthrough T1D Centre of Excellence, Perth, Western Australia (Principal Investigator: Prof Tim Jones). Participants received Diabetology's Axcess™ placebo capsule on Day -2 and Oraglutide capsule formulation (4 mg semaglutide) on Days 0,1,4 and 6 on an empty stomach, with Intravenous Glucose Tolerance Testing (IVGTT) conducted at Days -2, 0, 1, 4 and 6.

Primary efficacy findings:

- Mean difference in percentage glucose AUC between Day 6 and Day -2 (placebo baseline) of 14% was statistically significant ($p = 0.046$), demonstrating continued glucose lowering six days after a single dose.
- Insulin percent AUC secretion relative to placebo, increased by 12% Day 0 ($p=0.02$) and 28% Day 1 ($p = 0.025$),
- No glucose reversion to baseline was observed at Day 6, suggesting the depot effect continues to activate responses well beyond the acute absorption phase.

Pharmacokinetics — the intestinal depot:

Oraglutide™ (4 mg in Axcess™) produced a peak blood concentration of 2.8 ng/ml (0.68 nmol/L) above background at Day 1. Critically, blood levels were *higher on Day 1 than Day 0*, supporting the hypothesis that lipophilic semaglutide in the Axcess™ formulation forms a depot effect within intestinal tissue, gradually releasing peptide into the systemic and enteric compartments over multiple days. Blood levels remained above 100 pmol/L for 4 day, sufficient to trigger pancreatic GLP-1 receptors.

COMPARISON WITH RYBELSUS

When compared with published Rybelsus data (Overgaard et al., *Clin Pharm*, 2021; 60:1335–1348), Oraglutide™ at 4 mg achieved similar blood concentrations comparable to those of Rybelsus (R1) single dose, when correcting for dose.

Rybelsus (SNAC formulation) achieves absorption primarily in the *stomach*, where GLP-1 receptors function as mechanoreceptors rather than metabolic signal transducers, and has minimal access to the intestinal vagal afferents that are the physiological site of GLP-1 action. Oraglutide™, delivered to the *small intestine*, reaches GLP-1 receptors on vagal afferent neurons projecting into the intestinal lumen and lamina propria — the natural site of action of endogenous GLP-1. Oraglutide's™ dual acting pathway, delivered to the small intestine, reaches both GLP-1 receptors on vagal afferent neurons projecting into the intestinal lumen and lamina propria, the natural site of action of endogenous GLP-1, as well as sustaining sufficient outer circulating blood levels to day 4 to stimulate GLP1 receptors in the pancreas.

MECHANISM: INTESTINAL VAGAL AFFERENTS AND THE AXCESS™ DEPOT EFFECT

The Axcress™ formulation comprises a unique combination of excipients acting as absorption enhancers together with the receptor directed drug and has previously been validated in humans to deliver oral insulin safely and efficaciously (Luzio et al., 2009; New et al., 2022). In the GLP-1 context, the Axcress™ formulation directs a portion of the lipophilic semaglutide molecule into the lipid-processing pathway, which associate with vagal afferents along the intestinal wall, creating the novel longer acting depot-like effect observed here.

This mechanism is fundamentally different from SNAC-based oral GLP1 RA's, which increases peptide absorption principally through the gastric epithelium (stomach) into peripheral blood. As described in Diabetology's published preclinical work (*Frontiers in Endocrinology*, 2025), in the same way as native GLP1, GLP-1 RAs administered via the intestinal route will interact directly with GLP-1 receptors on vagal afferent neurons, which are located in a different part of the brain from the nausea receptors (Huang et al., Nature 632 585-598) avoiding CNS exposure and the associated nausea and adverse events seen with injectable and SNAC-based formulations. Injectable GLP-1 agents, for example liraglutide, semaglutide, tirzepatide, achieve their effects primarily via peripheral blood entry to the hindbrain and hippocampus. These systemic exposures are associated with gastrointestinal effects such as nausea and delayed gastric emptying, and safety signals for pancreatitis and gallbladder events have been reported and remain under investigation.

Diabetology's gut-targeting hypothesis is supported by preclinical intestinal-route work (Diabetology; *Frontiers in Endocrinology*, 2025) suggesting stimulation of vagal afferent GLP-1 receptors in those models, and further clinical confirmation of efficacy in humans is being carried out in a phase 2 diabetes and obesity study to establish that this approach translates into a materially improved tolerability profile.

SATIETYDE™: A NEW APPROACH TO POST GLP-1 MAINTENANCE

The extended duration of action demonstrated by Oraglutide's™ intestinal depot effect opens a new therapeutic opportunity: Satietyde™, Diabetology's planned low-cost, long-acting microdose Oral GLP-1 RA rebound and maintenance formulation designed to address the growing clinical dilemma of post-therapy maintenance and weight rebound.

Post-GLP-1 rebound is now one of the most pressing unmet needs in obesity medicine. Recent meta-analyses confirm:

- Pooled mean weight regain of 5.63 kg (95% CI: 3.52–7.73) within months of discontinuing GLP-1 therapy, with approximately 50–60% of lost weight regained within one year (Tzang et al., eClinicalMedicine, 2025).
- When weight is regained after GLP-1 discontinuation, *recovery is almost exclusively fat* — while muscle is not restored at the same rate, potentially creating sarcopenic obesity with a significantly worse fat-to-lean body mass ratio than before treatment began (Cureus, 2026,doi:10.7759/cureus.468578).
- Over half of patients discontinue GLP-1 therapy within 24 months (Penn Medicine, 2026), and those who stop-and-restart may face progressively diminished drug efficacy as the muscle:fat ratio deteriorates.

Satietyde™, enabled by the long-acting Axxess™ intestinal depot, would provide a **low-dose, lower-cost, oral maintenance option** — targeting the vagal afferent satiety pathway at a fraction of the dose required by conventional GLP-1 therapies. By intervening at the point patients drop below therapeutic GLP-1 receptor stimulation, Satietyde™ could prevent the disproportionate fat-to-muscle rebound and its associated cardiometabolic harms, making weight management genuinely sustainable for the long term.

"The rebound problem is creating a new chronic disease burden," said Dr New. "Patients who were successfully treated with GLP-1 therapy and then stopped — for cost, achieving target weight, or side effects— potentially end up with worse body composition than before treatment. Satietyde™ is designed to fill this gap with an affordable, safe, orally taken maintenance option that leverages the safe intestinal vagal afferent pathway."

FURTHER DEVELOPMENT PLANS

- Phase 2 clinical trials are underway in obese patients with and without type 2 diabetes.
- Large animal studies corroborate the human data.
- The Axxess™ platform is applicable to a range of peptides and peptide combinations, enabling future combination GLP-1 RA products.
- Patent protection for the Axxess™ technology extends to 2044, with recent improvements providing IP cover beyond that date.

ABOUT ORAGLUTIDE AND AXCESS™

Oraglutide is Diabetology Limited's oral capsule, small intestine directed formulation of semaglutide (and other lipidated GLP1's and combinations) using the licensed proprietary Axxess™ oral peptide delivery technology. Axxess™ was originally conceived by co-founders in 2003 and uses 3 key pharmacopeial or food grade excipients to direct lipophilic peptides preferentially into the chylomicron pathway, enhancing delivery to intestinal vagal afferent GLP-1 receptors. The formulation has been previously validated in a 25,000 dose human clinical studies for oral insulin delivery (Luzio et al., 2009 and New et al DOM 2022).

ABOUT DIABETOLOGY LIMITED

Diabetology Limited is a Jersey-based biopharmaceutical company focused on the development of novel oral peptide therapies for diabetes and obesity. The co-lead projects are Oraglutide™ in Phase 2 and Capsulin™ oral insulin preparing for T2D phase 3 following a peer reviewed and published positive phase 2b with a 25,000 dose, safe usage over 3 months. The company's licensed Axxcess™ platform enables intestinal delivery of GLP-1 receptor agonists and other peptides, exploiting the gut–brain vagal afferent axis as the primary site of therapeutic action.

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Poster 1724-P: "Long Duration of an Oral Semaglutide Administered via the Intestine in Healthy Humans" was presented at the American Diabetes Association 86th Scientific Sessions, New Orleans, LA, 5–8 June 2026. This press release is embargoed until the ADA scientific embargo is lifted on Friday 5 June 2026 at the time stipulated by the ADA.