## Orforglipron: Eli Lilly's Oral GLP-1 Agonist

**Description:** Orforglipron is an oral GLP-1 receptor agonist developed by Eli Lilly for the treatment of type 2 diabetes and weight management. It is a small molecule drug, potentially easier to manufacture than peptide-based GLP-1 drugs.

**Mechanism of Action:** Mimics the GLP-1 hormone, enhancing glucose-dependent insulin secretion, suppressing glucagon release, slowing gastric emptying, and reducing appetite and food intake.

**Clinical Trial Data:**

- **Efficacy:** Demonstrated statistically significant A1C reduction (1.3% to 1.6% from a baseline of 8.0% at 40 weeks) and weight loss (up to 16.0 lbs (7.9%) at the highest dose over 40 weeks). Over 65% of participants on the highest dose achieved an A1C $\leq$ 6.5%.
- **Safety:** Overall safety and tolerability consistent with the GLP-1 class. Common adverse events were mild to moderate gastrointestinal issues (diarrhea, nausea). Discontinuation rates due to adverse events were 6-8% for orforglipron vs. 1% with placebo. No hepatic safety signal was observed.

**Comparison to Other GLP-1 Drugs:**

- Oral administration, unlike many injectable GLP-1s.
- No food and water restrictions, unlike oral semaglutide (Rybelsus).
- Small molecule

**Market Impact:**

- Expected to compete with Rybelsus and gain market share in the diabetes and obesity markets.
- Potential sales projected to reach $11.8 billion in 2030.
- Positive trial results have positively impacted Eli Lilly's stock price.

**Competition:**

- Key competitors: Novo Nordisk (Rybelsus, oral Wegovy in development) and other companies developing GLP-1 drugs include Pfizer, AstraZeneca, Viking Therapeutics and Metsera.

**Approval Status & Availability:**

- Eli Lilly plans to submit orforglipron for weight management approval by the end of 2025 and for type 2 diabetes treatment in 2026.
- First oral small molecule GLP-1 to successfully complete a Phase 3 trial.
- Potential launch for weight management expected by the end of 2025, and for Type 2 diabetes in 2026.
- Eli Lilly anticipates no supply constraints for a worldwide launch.