

Glyscend, Inc.
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Pharmacologic duodenal exclusion: a novel therapy for metabolic diseases

Glyscend Therapeutics is developing first-in-class polymer drugs that uniquely interact with the gut wall to treat metabolic and chronic conditions. The company's lead candidate, GLY-200, is advancing into phase 2 clinical studies for the treatment of type 2 diabetes.

The gastrointestinal (GI) tract is a major player in metabolic regulation due to its role in modulating hormonal signaling between the gut, liver, and brain. Roux-en-Y gastric bypass (RYGB), a form of metabolic surgery, establishes duodenal exclusion by diverting intestinal contents away from the upper GI tract. This intervention—commonly referred to as bariatric surgery in the context of obesity—results in an immediate and substantial improvement in markers of abnormal metabolism, including blood glucose levels, even prior to dramatic weight loss. However, bariatric surgery, or any invasive intervention, carries with it the risk of significant complications.

To circumvent these drawbacks and address issues of reduced accessibility and affordability, Glyscend Therapeutics, a clinical-stage biopharmaceutical company, is pioneering a new generation of orally administered polymer therapies known as mucin-complexing polymers (MCPs) that safely and temporarily elicit duodenal exclusion. MCPs are non-absorbed and naturally eliminated through the GI tract. "At Glyscend, our goal is to leverage the remarkable disease-modifying effects of metabolic surgery with a convenient, non-invasive, oral therapy," said Ashish Nimgaonkar, President and CEO of Glyscend. "Utilizing our proprietary MCP platform, we aim to recreate the effects of metabolic surgery in a safe and accessible way, particularly with a consideration toward chronic use."

Pharmacologic duodenal exclusion therapy

Mucin is the main component of mucus that lines the gut epithelium. It acts as a selective barrier to nutrient absorption and signal transmission to the rest of the body. Based on technology from Johns Hopkins University, Glyscend's MCPs are designed to crosslink native GI tract mucin in a pH-dependent manner, enhancing the natural mucus barrier in the duodenum (Fig. 1). This enhanced barrier results in a pharmacologic 'duodenal exclusion' that may non-invasively and safely reproduce many of the beneficial effects of metabolic surgery in patients suffering from a variety of metabolic disorders, including type 2 diabetes (T2D), while avoiding the complications associated with invasive surgeries and procedures.

Addressing a growing T2D challenge

T2D is a disease characterized by complex metabolic dysregulation resulting in high morbidity, mortality, and treatment costs, affecting approximately 500 million people worldwide. The current standard of

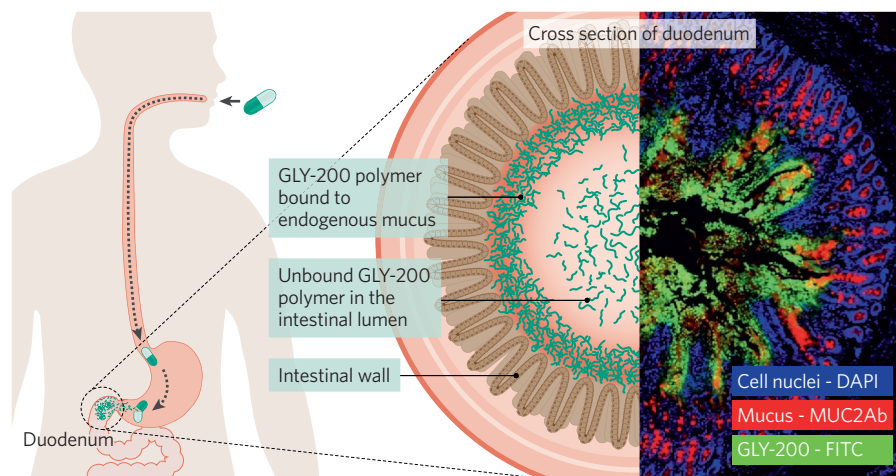


Fig. 1 | Novel mucin-complexing polymers for the treatment of type 2 diabetes. Glyscend's drug candidate, GLY-200, is taken orally via capsule (left). The natural pH change in the upper small intestine causes it to complex with endogenous mucus to create a temporary intestinal coating. A representative histology image of this coating is shown two hours after dosing in a rat model (right).

care escalates therapeutic interventions from lifestyle alterations to oral drugs, injected medications, insulin, and, in a select few, metabolic surgery. Despite these therapeutic options, close to half of T2D patients continue to exhibit uncontrolled diabetes. Moreover, with the exception of metabolic surgery, none of these therapies are disease modifying, and progressing from simple early interventions to more advanced treatments often results in reduced accessibility and/or increased risk for undesired side effects.

Of all interventions, metabolic surgery has been shown to have the most immediate and profound effects on improving blood glucose, cellular response to insulin, and body weight reduction, and on reducing long-term micro- and macrovascular complications related to T2D. Glyscend's lead candidate, GLY-200, is optimized for controlling glycemia in patients with T2D to treat and potentially slow or even halt disease progression. Preclinical studies have demonstrated profound improvements in post-prandial glucose, insulin resistance, and weight loss, without safety signals in multiple animal models of T2D. The GLY-200 program has recently completed a successful phase 1 safety and tolerability clinical trial and is advancing to phase 2 efficacy trials in T2D patients with top-line data expected in early 2023.

"The inclusion of metabolic surgery in the treatment algorithm for T2D in 2017 brought a renewed sense of hope for diabetes patients worldwide," said

Nimgaonkar. "At Glyscend, we continue to work on making this promise accessible to all through a safe and affordable alternative that harnesses the immense therapeutic potential of polymer technologies for treating metabolic diseases."

Unlocking the potential of polymer drugs in GI tract

Initially focused on treating metabolic diseases such as T2D and obesity with its MCP platform, Glyscend is expanding its pipeline to include programs that address topical GI as well as systemic, inflammatory, and autoimmune conditions. The company is also investigating its technology to unlock novel GI luminal targets with polymer-drug conjugates and to enhance bioavailability of oral peptide therapies. With one program in the clinic, and several other programs in pre-investigational new drug (IND) application and preclinical stages, Glyscend seeks to continue expanding the potential of its unique polymer technology through co-development partnerships.

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