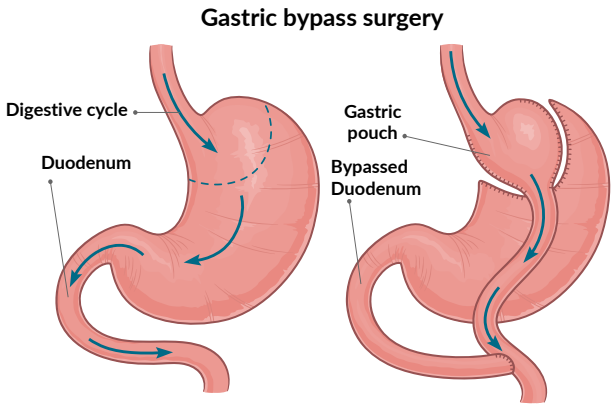
Type 2 Diabetes – A Global Crisis[1,2]

The global diabetes health crisis is one of the world's largest unmet clinical needs. Type 2 Diabetes (T2D), a chronic condition where the body cannot metabolize glucose adequately, affects 420 million people worldwide and is expected to grow to 520 million by 2030.

Left untreated, **T2D sufferers are at higher risk for experiencing heart disease and stroke, high blood pressure, blindness, and many other serious conditions**. Diabetes poses significant medical, social, and fiscal burdens on society with worldwide direct costs estimated at $760 billion in 2019 growing to $825 billion by 2030. Spending in the U.S. alone represents approximately 40% of the total. Agil's solution represents a $10B to $20B market potential.

Conventional Treatment[3,4]

Currently available treatment options focus on managing T2D through lifestyle modifications (diet, exercise), and a range of oral and injectable glucose-lowering medications. Although a combination of these options can be effective for many patients, there remains a group of T2D patients who do not achieve optimal glycemic control. Poor adherence to treatment protocols due to the complexity of medication, dosing, safety and tolerability have been major drivers for failure with this group, and it is important to remember that **none of these options can cure T2D but only serve to manage the condition**.



Gastric Bypass Surgery[5]

Gastric bypass surgery, originally developed for weight loss reduction, has emerged as a unique treatment option demonstrating significant glycemic control benefits extending beyond medication, and lifestyle changes. In a large majority of patients (>70%), improvement and even the elimination of T2D occurs almost immediately. Although this is **a significant improvement over conventional treatments**, gastric bypass is not a viable alternative due to procedure cost, morbidity, mortality, and patient recovery.

Endoscopic Treatment

The positive glycemic regulation seen after gastric bypass surgery has led researchers to focus on the duodenum for disease-modifying treatments (see insert to the right). One such endoscopic treatment targets the duodenum whereby the inner lining is burned away (resurfaced) using a hot balloon (heat-based ablation). By resurfacing the duodenum's inner lining, glucose control mechanisms can be restored. **This technique is safe, less invasive, and more cost-effective than surgery**. While the hot balloon procedure has elicited positive glycemic improvement, **the technique is difficult to perform** (requiring multiple steps under fluoroscopy), extensive investment in capital equipment, and has limits on efficacy (allowing only one treatment per patient).

The Duodenum and Type 2 Diabetes

The duodenum plays a key role in obesity, insulin resistance and subsequent development of T2D. The body regulates glucose via insulin, a hormone produced in the pancreas, but it is the duodenum (via metabolic signaling) that controls insulin action and thereby insulin resistance.

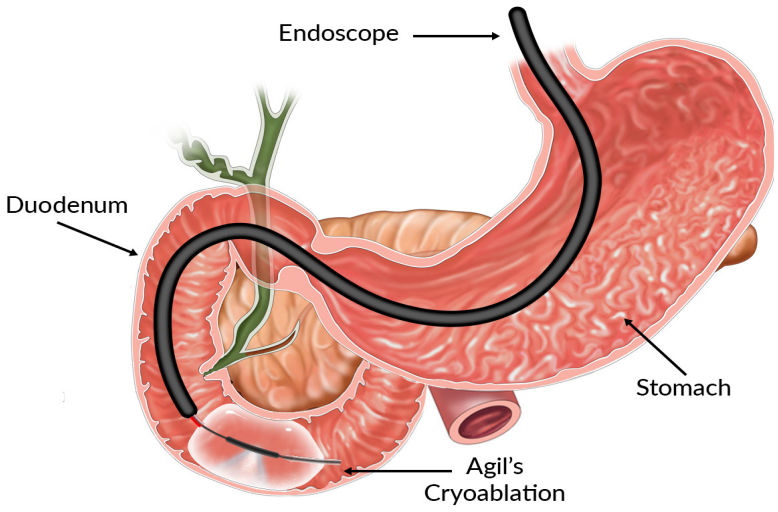
A critical insight of the importance of the duodenum was the immediate improvement or elimination of T2D in post-operative gastric bypass surgery patients.

The exact mechanisms for T2D remission with surgery is still under study. It has been shown that surgery increases gastrointestinal hormone secretion. Additionally, surgery may alter or increase signals that improve glucose homeostasis. Finally, surgery may enhance delivery of nutrients to the distal intestine rather than the duodenum.

The information contained is for confidential use of the intended recipient(s).

A Next Generation Approach

Agil Therapeutics' endoscopic solution represents the future of treating T2D by achieving the benefits of gastric bypass at a fraction of the cost (outpatient vs. major surgery) resulting in improved procedural simplicity, decreased recovery times, improved safety, fewer complications, and less patient discomfort.



Agil's cryoablation is elegant and simple to perform, with improved economics, and has the potential to improve efficacy compared to the hot balloon procedure. This allows the physician to use direct visualization via high-definition endoscopy without the need for fluoroscopy. Following placement of a catheter in the duodenum, cryogenic fluid flows down the catheter to a probe at the tip of the catheter which contacts the duodenum. A sprayer inside the probe allows for highly targeted freezing and treatment. The physician can then easily reposition the probe for further treatments.

Treatment	Efficacy	Cost-Effective	Simplicity	Safety
Agil's Cryoablation	**Potential for improved efficacy with capability to treat more tissue**	**High**	**High**	**High**
Hot Balloon	Eliminated the need for insulin in 9 of 16 patients at 18 months[6]	Moderate	Low	High
Gastric Bypass Surgery	T2D remisson occured in >70% of patients[7]	Low	Low	Low
Medical Therapy	Glycemic goals achieved by less than 50% of patients[8]	Moderate	Moderate	High

A Proven Team and Strategy

Agil Therapeutics was founded by seasoned medtech entrepreneurs with over 30 years combined experience using cryogenics to treat various medical conditions. In addition to prior experience at established medtech companies like Guidant, Agil's team was part of four successful startups, including founding C2 Therapeutics which developed an endoscopic cryoablation system to treat esophageal cancer resulting in a successful exit.

Agil employs a fast-follower business strategy similar to the one utilized at C2 Therapeutics, which led to its sale, following $22M in funding, growing the company from 2 to 50 employees, and completing over 12 clinical trials. The C2 product was launched in the US and Europe in 2015.

Investment Opportunity

Incorporated May 2021, Agil Therapeutics has secured initial financing, built the core R&D team, developed a working cryoablation system, and completed initial preclinical studies.

Agil is raising $1.0M under a convertible note and expects to close in Q2 2022. Series A financing will be raised in Q4 2022 upon completion of key milestones. Additional information on the technology, clinical and regulatory strategy, and the investment opportunity can be provided. Please contact Peter Garcia-Meza at **415-828-8280** or **peter@agiltx.com**.

[1]IDF DIABETES ATLAS, 9th edition 2019, International Diabetes Federation, https://www.idf.org/.
[2]Market projections on file at Agil Therapeutics.
[3] García-Pérez LE, et al. Adherence to therapies in patients with type 2 diabetes. Diabetes Ther. 2013 Dec;4(2):175-94.
[4] https://type2diabetes.com/infographic/management-burnout
[5]Mingrone G, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366(17):1577–1585.
[6]van Baar ACG, et al., Duodenal mucosal resurfacing combined with glucagon-like peptide-1 receptor agonism to discontinue insulin in type 2 diabetes: a feasibility study. Gastrointest Endosc. 2021 Jul.
[7]Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366(17):1577–1585.
[8]García-Pérez LE, et al. Adherence to therapies in patients with type 2 diabetes. Diabetes Ther. 2013 Dec;4(2):175-94.