

A novel oral MOA in the treatment for type 2 diabetes with obesity

AJN003 - Transient luminal coating and protection of the proximal gut: Delivering powerful metabolic effects by shifting nutrient sensing distally

Experienced and successful team

AltrixBio team brings deep expertise in metabolic drug development and first in class trailblazing



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Chief Medical Officer



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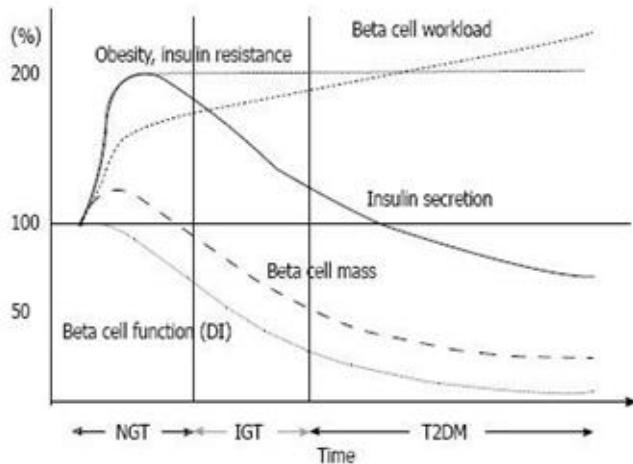


Dylan Benningfield, MA
Senior Scientist

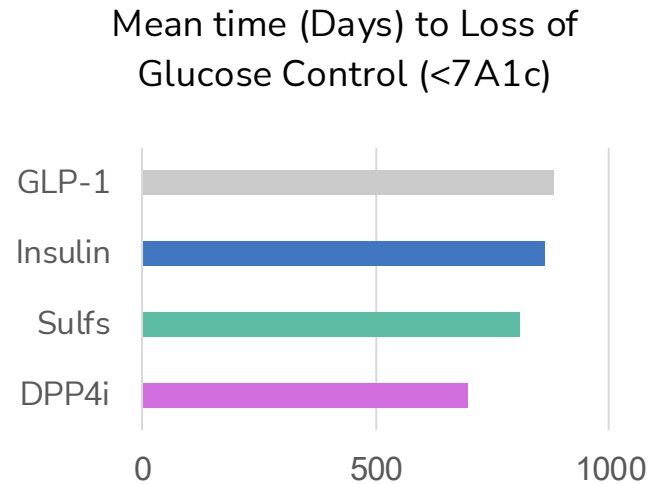


In this \$50B+ market, there is a need for a new type 2 diabetes therapy that is well tolerated, delivers weight loss, & complements SOC

Diabetes is progressive



Therapies fail over time

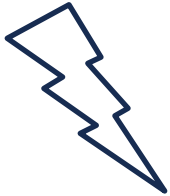


Unmet need

- Majority of patients still do not reach A1C goals
- Most people require multiple diabetes therapies...and still are not in control.
- Many diabetes therapies...
 - are not well tolerated (metformin, GLP)
 - cause weight gain and hypoglycemia (Insulin, Sulfs)
 - Require injections and titration

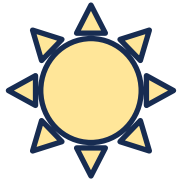
Novel MOA leveraging the emerging metabolic role of the gut to treat diabetes

Inspiration

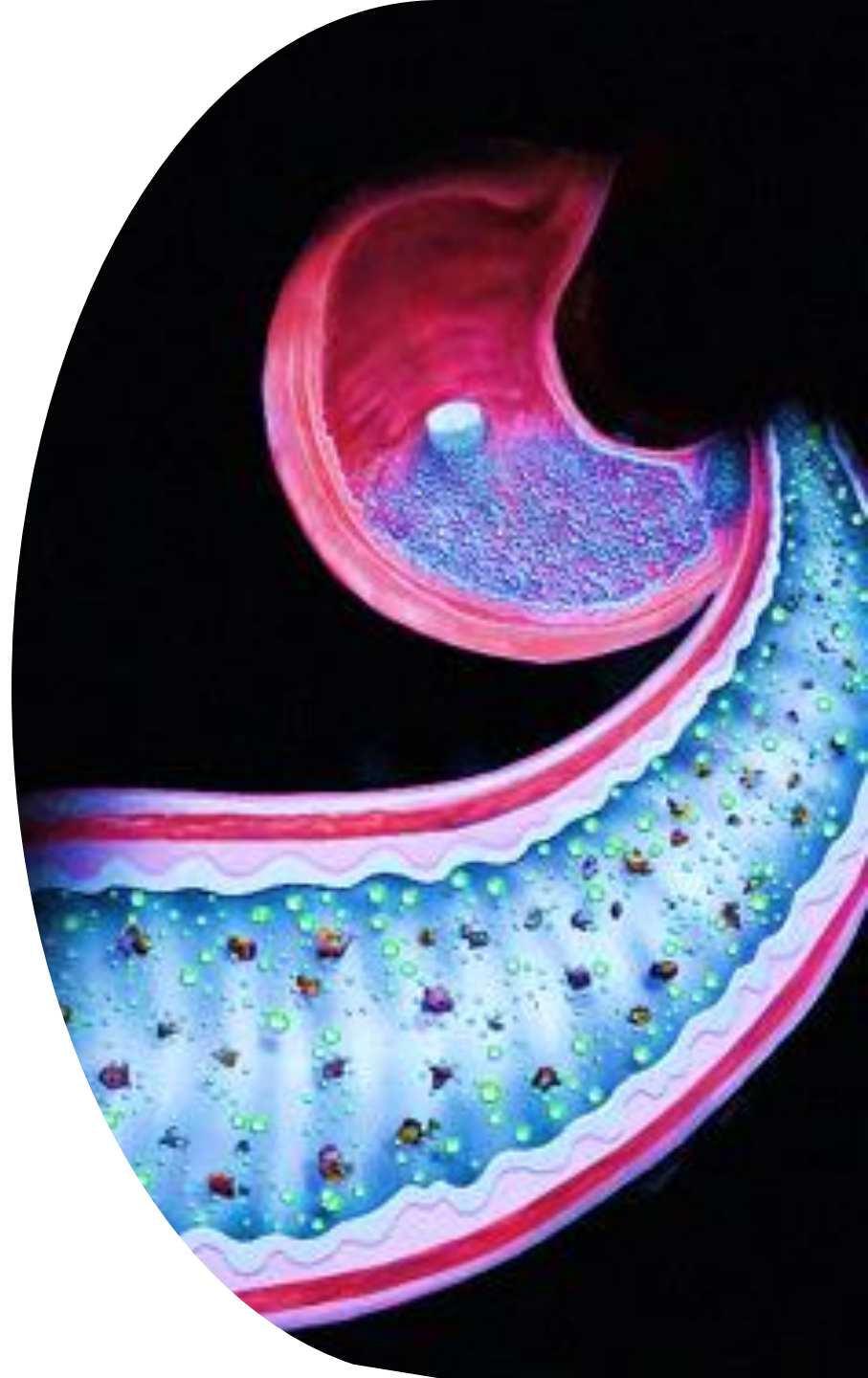


The upper intestine is a **critical metabolic signaling pathway through nutrient sensing - that maladapts to westernized diet exposure**. The immediate postoperative effects of bariatric surgery demonstrate its metabolic importance.

Innovation



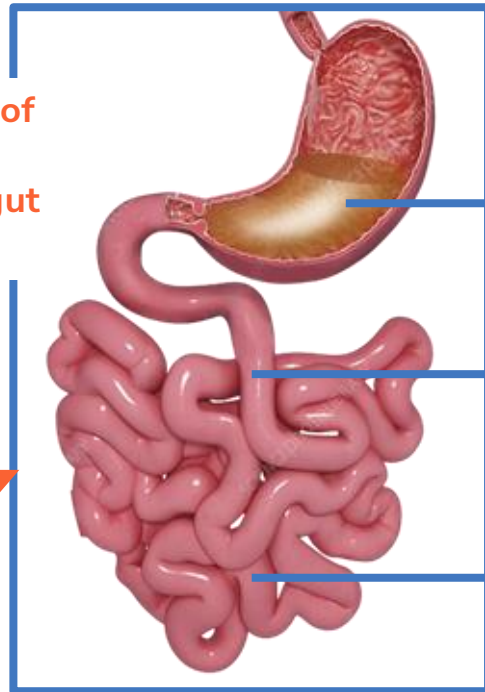
Treating the luminal surface of the upper intestine with a transient protective barrier allows correction of maladaptive changes while shifting nutrient sensing distally, enabling **durable metabolic improvement**.



Transient protective GI coating shifts nutrient sensing distally enabling gut healing and producing a powerful metabolic reset

Reducing nutrient exposure in the upper small intestine (stomach, duodenum & jejunum) will heal local maladaptive changes and shift nutrient sensing distally - driving a **metabolic reset**:

Distal shift of nutrient sensing at gut surface



Gastric Effect: Reduction in hunger stimulating hormones ghrelin and leptin

Duo-jejunal Effects: Increased insulin sensitization
Increased bile acids and downstream metabolic benefits

Jejunal-Ileal Effect: Augmented GLP1 and GIP incretin response

These lead to **improved glycemia, weight loss**, and other cardiometabolic improvement**

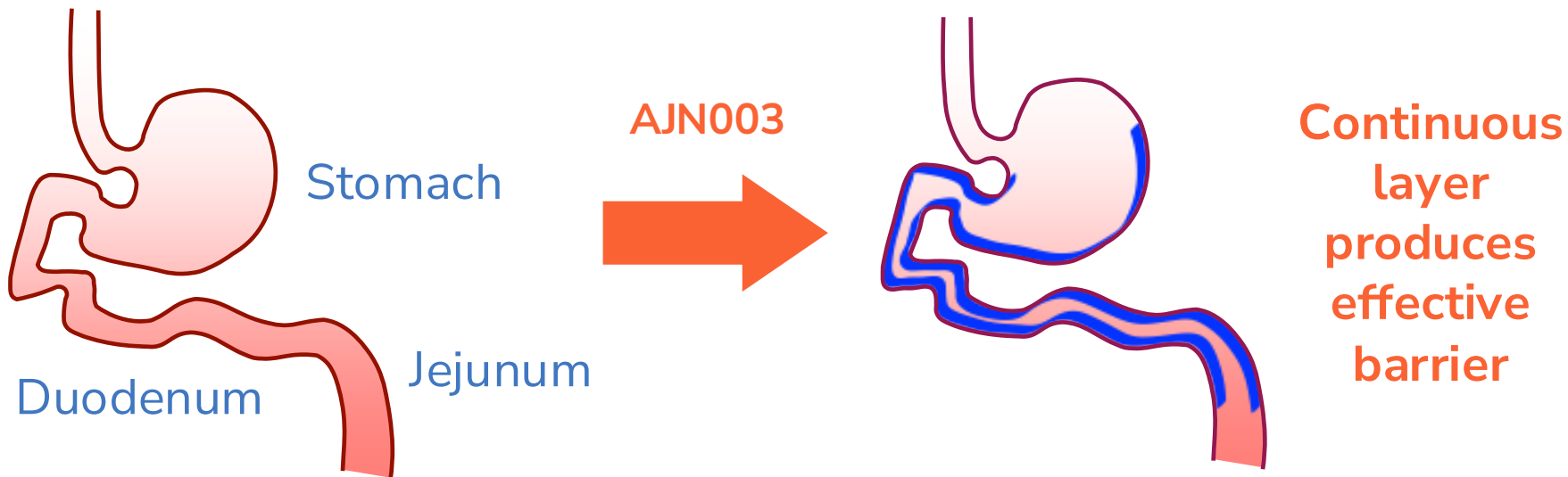
* Shifting nutrient sensing distally does not necessarily imply reduced nutrient absorption or malabsorption.

** Demonstrated in preclinical models and clinically with the immediate diabetes remission and medication reduction after bariatric surgeries

A protective barrier in the stomach and proximal intestine (duodenum and jejunum)

Sucralfate, an oral, non-systemic small molecule with a **strong safety record over 40 years** has been bioengineered to transiently coat and protect the upper intestine.

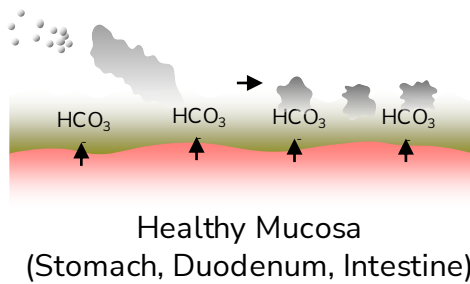
Issued core composition of matter patents and an expedited pathway to market (a successful pre-IND FDA meeting) enable de-risked development.



CT image of rodent GI tract: opacity indicates AJN003 coating in stomach and foregut

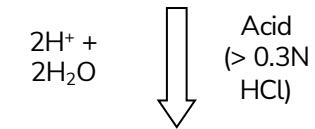
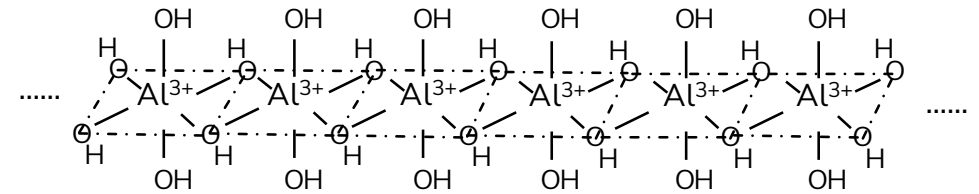
AJN003 is specifically bioengineered to create a protective coating that shifts nutrient absorption: sucralfate adheres only to diseased tissue (erosions, ulcers)

Forms stiff aggregates in low pH, adhering only to ulcerated tissue

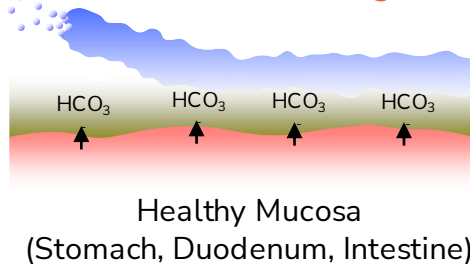


sucralfate
No metabolic effects

High MW PAC

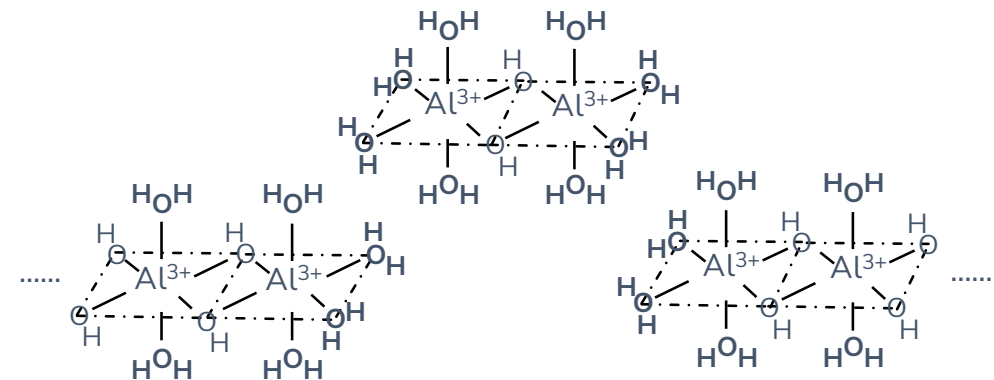


Forms low viscosity paste, pH-independent, creating a continuous coating



AJN003

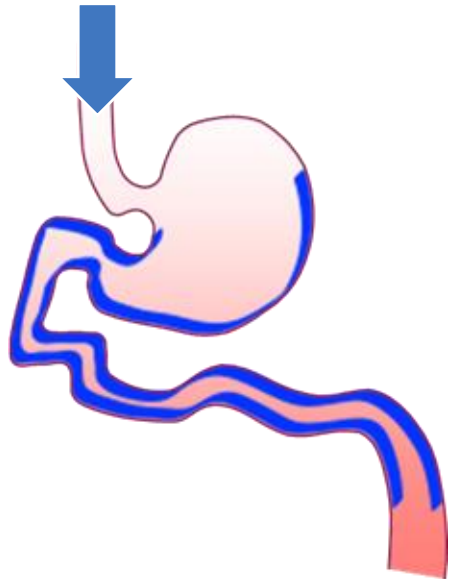
Improved glycemia, weight loss, & other cardiometabolic improvements



Low MW PAC

Chronic dosing of AJN003 suppresses stomach-derived appetite-stimulating hormones

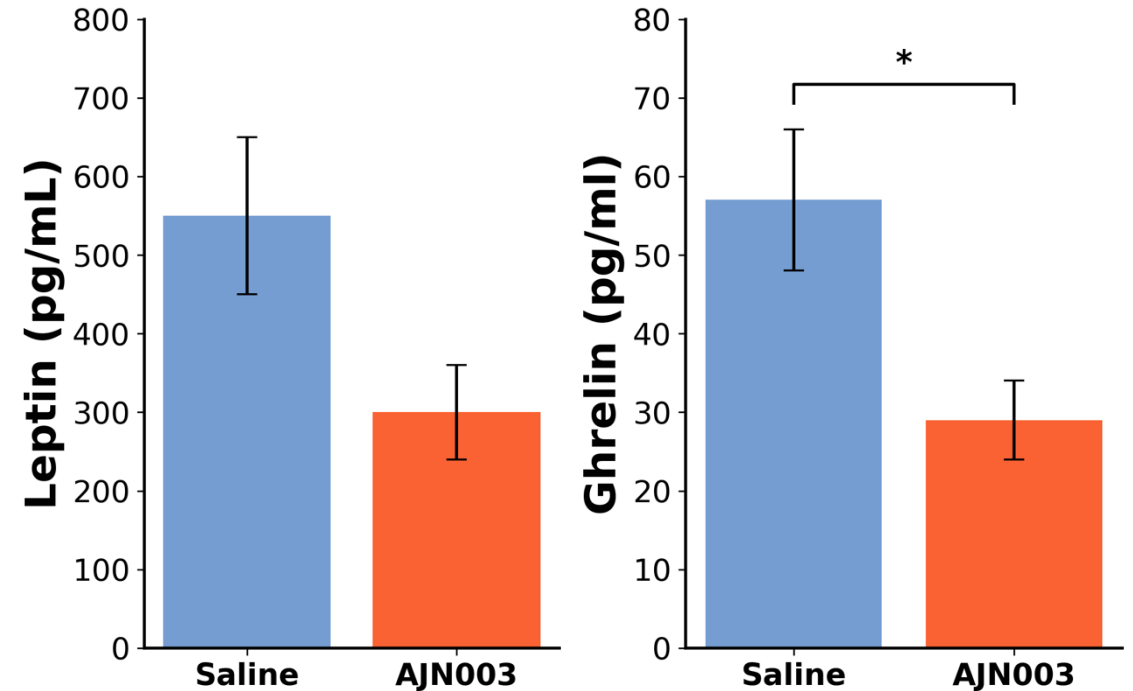
AJN003
daily dosing



Gastric Effect



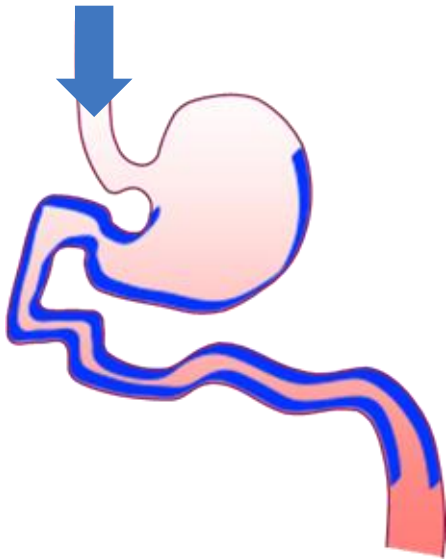
Suppression of appetite
stimulating hormones



Fasting hormone levels at 35 days in DIO model

Chronic dosing of AJN003 increases gut-derived incretin hormones and improves insulin sensitivity

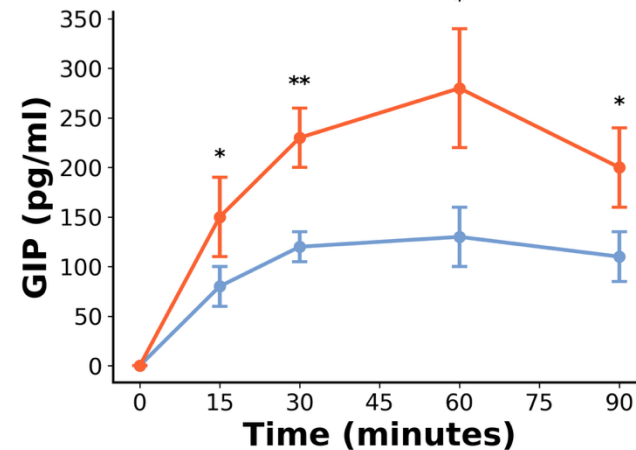
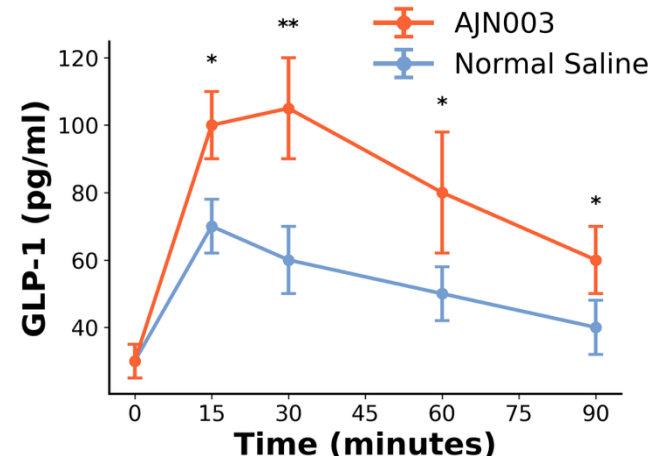
AJN003
daily dosing



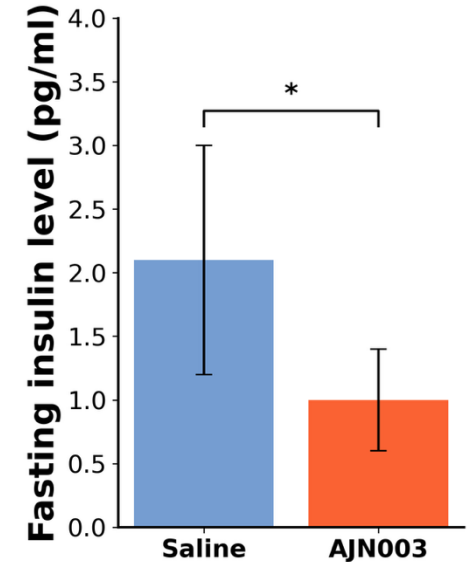
Duo-jejunal Effect



Increases in Incretin Hormone Levels



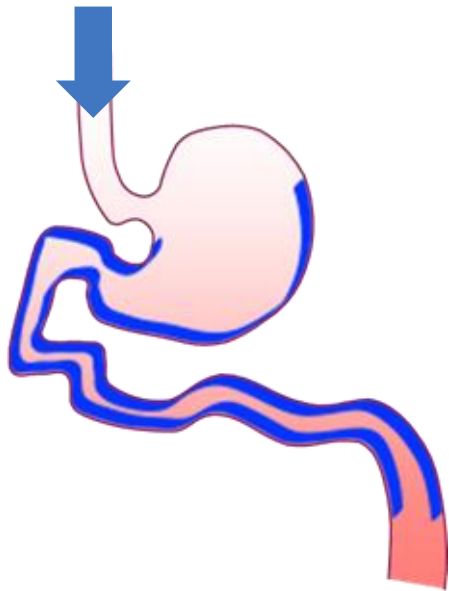
Insulin Sensitization



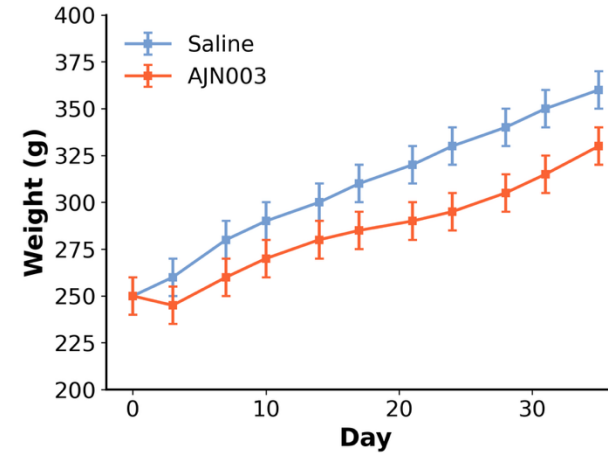
OGTT at 35 days in DIO model

Chronic dosing of AJN003 leads to improved metabolic state and weight loss in rodent DIO model

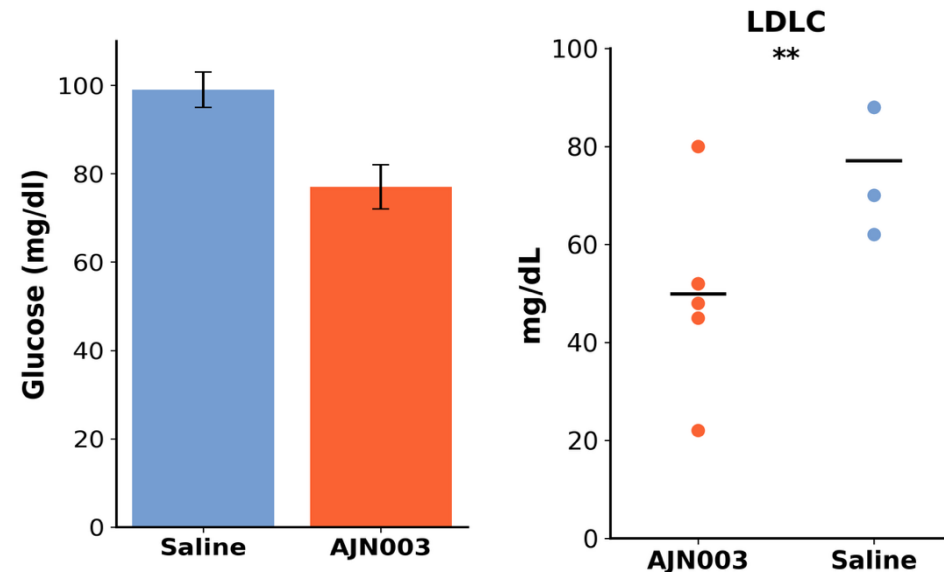
AJN003 daily dosing



Cardio-Metabolic Effect



20%
attenuation of
weight gain



Lowering of
fasting glucose
and LDL-
cholesterol

Limitations of current incretin(GLP-1/GIP) Rx



Side effects



Injectable



Challenging dose titration



Long-term A1C durability (marker of diabetes control)



Cost & coverage



Persistence problem: 50% of GLP-1 patients discontinue within 1 year.¹

T2DM paradigm unlikely to change despite expansion on new treatment options in obesity



Tx paradigm continue as stacking market for new agents with different MOAs vs switching to maximize A1C lowering efficacy



Switching between GI endocrine hormone agonists/antagonist unlikely to significantly impact durability







Goal will be to continue to maximize beta cell function to delay insulin initiation



New metabolic agents focusing on obesity over T2D



Target product profile enables AJN003 use early or later in the treatment continuum, complementing other therapies

				
Patient type	After metformin and/or SGLT2s; not yet ready for injections or incretins (GLPs)	Cannot tolerate current therapy	Combination therapy or before needing to switch to insulin	Maintenance of A1C & weight

Breakthrough approach in T2DM



New MOA in treatment of T2DM with weight loss benefits and preclinical proof established



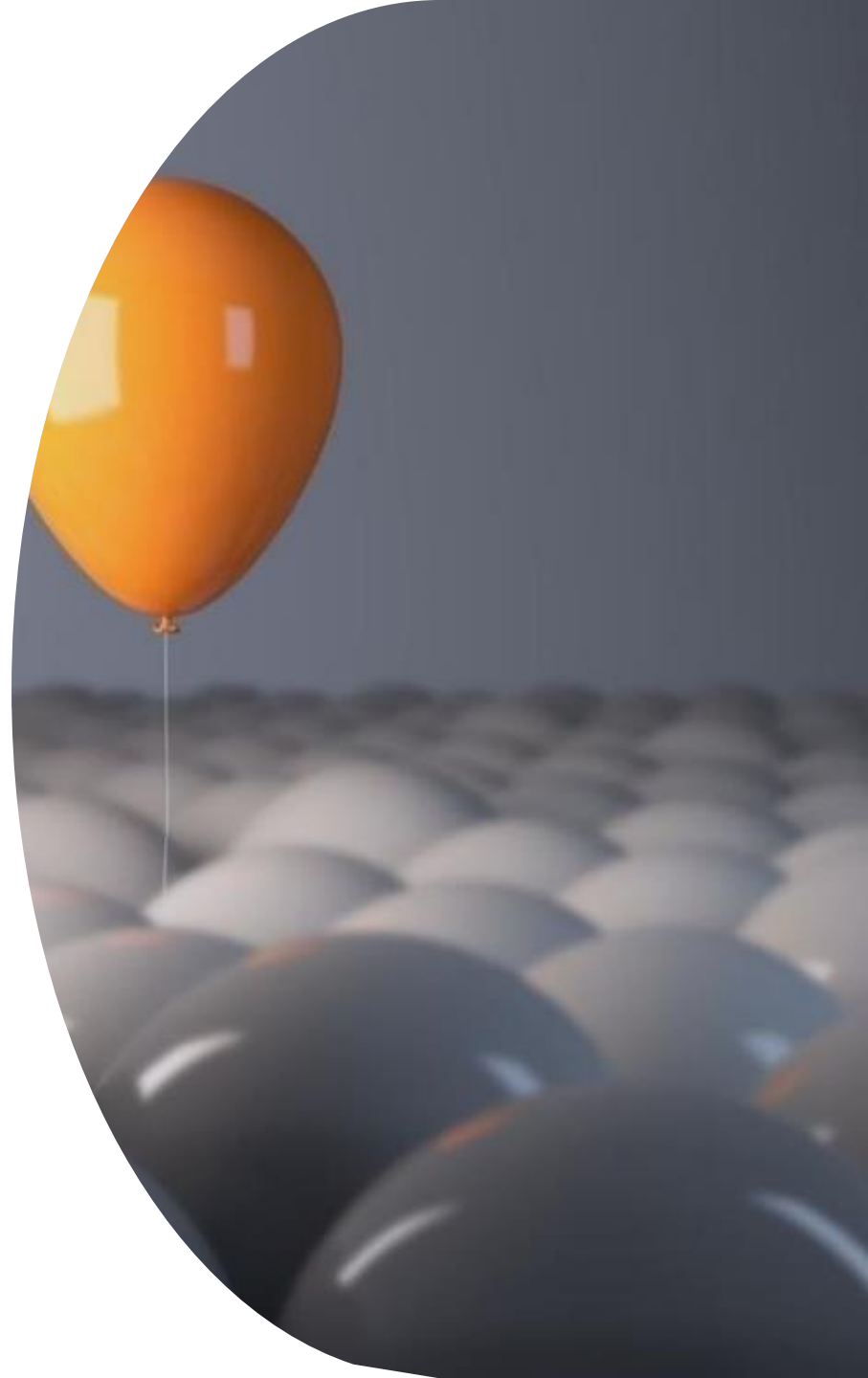
Oral daily dosing expected to be well-tolerated with no titration



Potential for strong durability



Composition of matter patent issued with expedited regulatory pathway (505B2)





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For questions, comments and inquiries

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AltrixBio Board combines passion and expertise



Nancy Briefs, MBA

Co-Founder & Executive Chair of the Board

- Drives strategy for the launch and commercialization of life sciences companies.
- Raised over \$500M in equity + IPO
- 6 venture-backed companies
1 IPO, 3 exits, 1 failed in clinic, 1 commercialized
- 9 boards, 4 exits



Jeff Karp, BEng, PhD.

Co-Founder & Chief Science Advisor

- Prolific inventor and entrepreneur who has raised \$400M+ in the course of founding 7 companies
- Distinguished Chair in Clinical Anesthesiology Perioperative & Pain Medicine, Brigham & Women's Hospital
- Harvard-MIT Division of Health Sciences & Technology (Harvard Medical School, Harvard Stem Cell Institute, MIT Broad Institute)



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Co-Founder & Chief Clinical Advisor

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- Co-Director, Center for Weight Management and Wellness
- Minimally Invasive & Bariatric Surgeon
- Harvard Medical School



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- Former CEO of the Joslin Diabetes Center
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