GELESIS

Health & Wellness

Health and Wellness by Gelesis

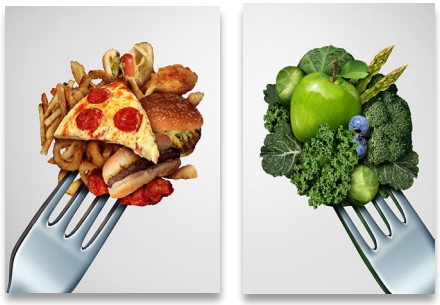
- **Introducing a first of its kind platform for better metabolic, immune, and gut health**
- **Our first product, Plenity, helped more than 200,000 people manage their weight & generated $39.5M of revenue* as an FDA-cleared Rx product**
- **We now plan to multiply our impact by enabling our breakthrough technology to reach the health & wellness market**

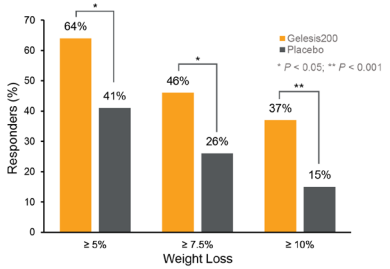
** Cumulative product revenue, net, from Plenity first being made commercially available through December 31, 2022*

GELESIS

GS200 Combats the Negative Effects of Western Diet

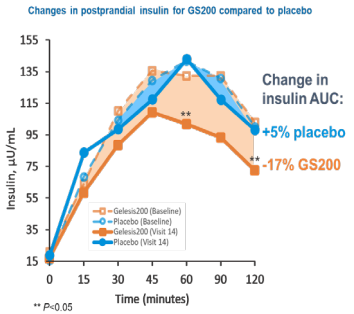
In clinical and/or pre-clinical studies, Gelesis' proprietary hydrogel demonstrated the following potential benefits:





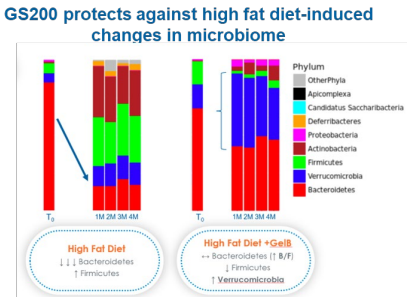
Weight loss in people with pre-diabetes or type 2 diabetes

1



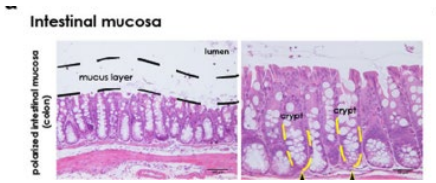
Improve glucose tolerance and insulin sensitivity

2



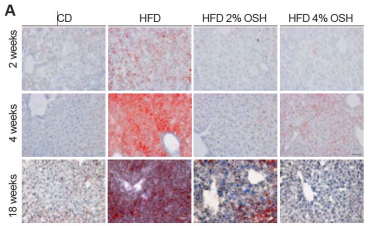
Improve the gut microbiota with beneficial strains

3



Reverse gut damage and restore gut barrier function

4



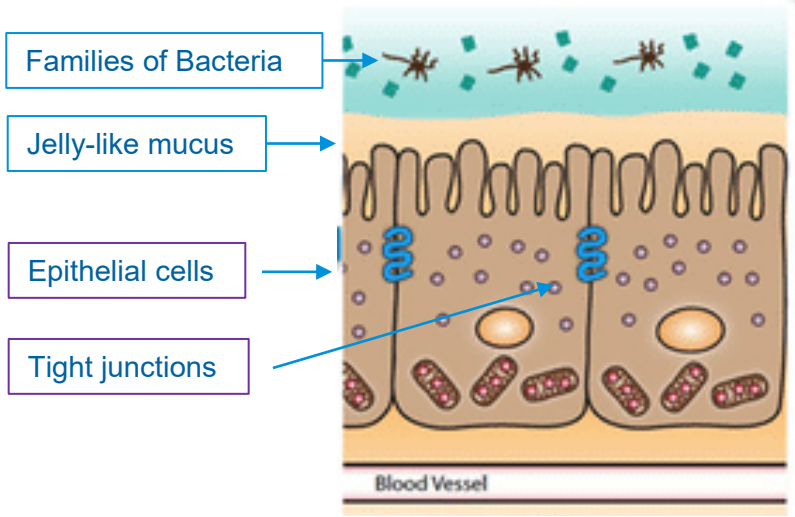
Prevent fat accumulation in the liver

5

GELESIS

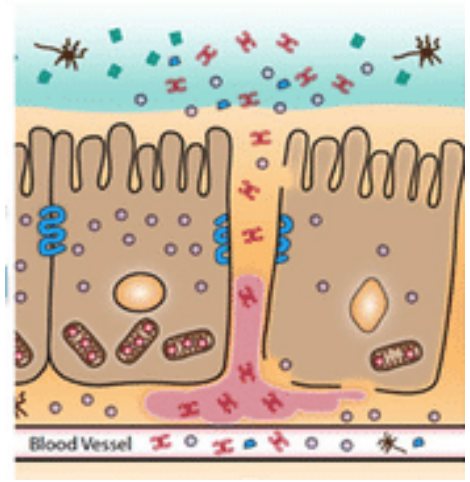
Western Diet Leads to Compromised Gut Barrier Function

Majority of Individuals with Prediabetes or Type 2 Diabetes have Impaired Gut Permeability



Healthy Gut Barrier

GI barrier intact, thick mucosal lining, well functioning tight junctions and normal microbiome



"Leaky Gut"

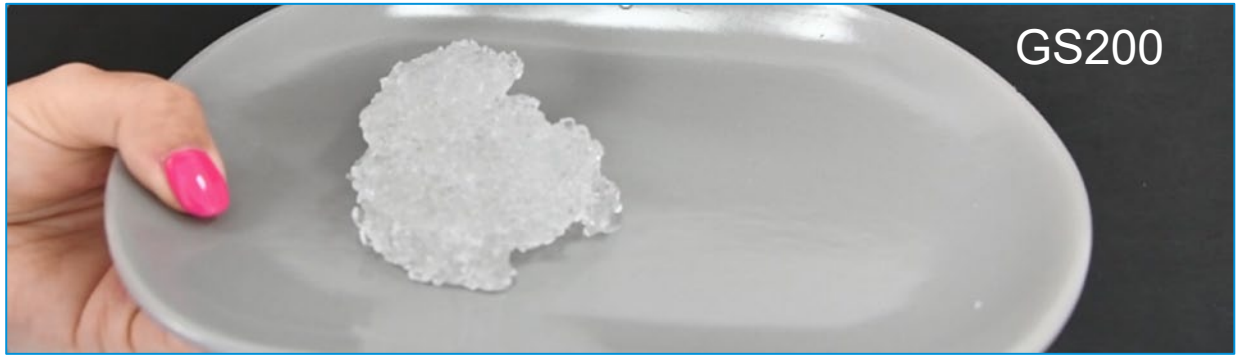
Compromised intestinal barrier, bacteria crossing into circulation, **development of chronic inflammation and metabolic diseases**

Adapted from Merra et al. Nutrients. 2021.
Ghanim H, et al. Presented at Obesity Week 2020, November 2-6 Poster #234

GELESIS

The Only Superabsorbent Hydrogel Made from Foods/GRAS Building Blocks

Emulating the Properties of Ingested Raw Vegetables



GS200 hydrogel particles form a large volume of non-aggregating gel pieces, with a size, composition & firmness similar to ingested raw vegetables, within minutes in the stomach

As shown in the photos, only 2.1g (0.8oz) of GS200 particles would create about ½ pound of gel pieces similar in size, composition and elasticity (firmness) as ½ pound of cucumber without any caloric value

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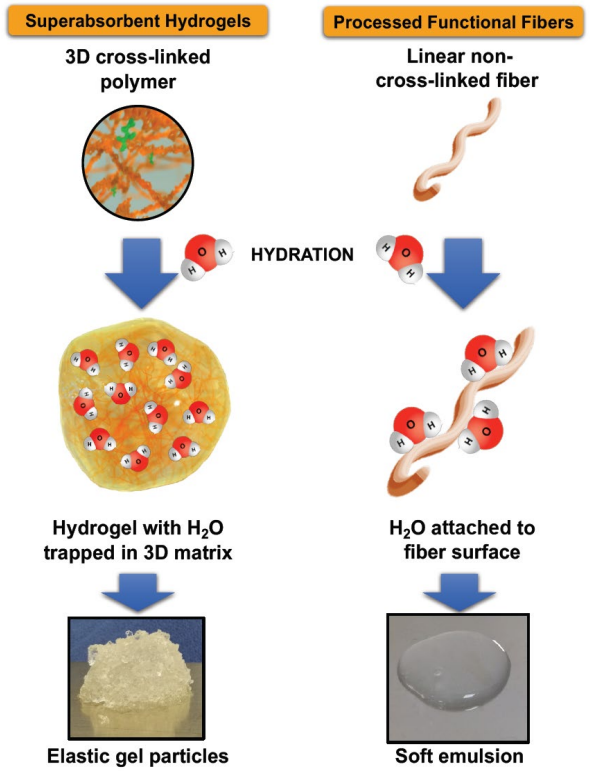
GS200 Structure Creates Faster & Orders of Magnitude Higher Elasticity than Fibers, Similar to Raw Vegetables

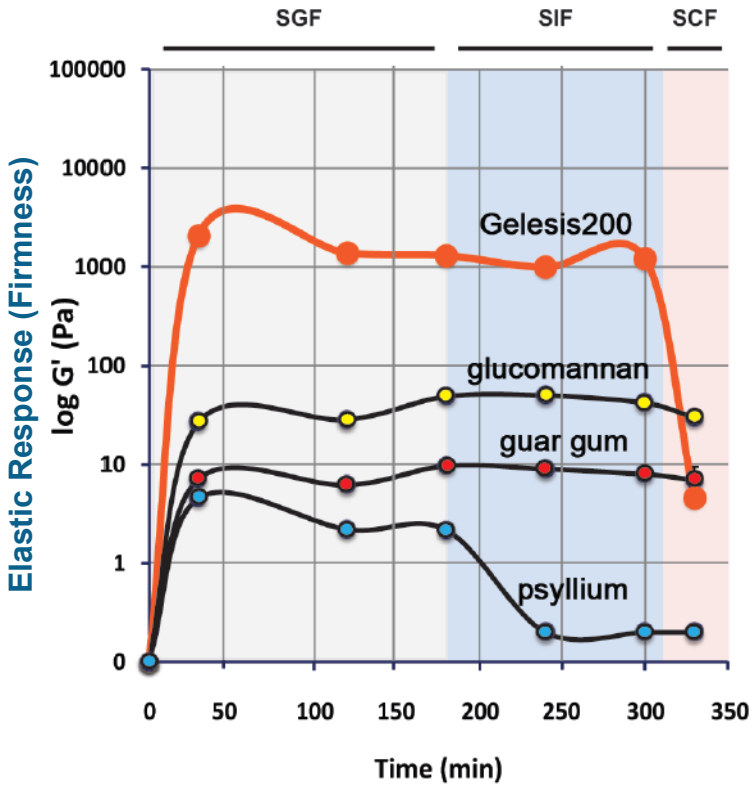
Presented at the American Diabetes Association & published in Nature Scientific Reports

GS200's Unique Structure Creates Superior Elastic Response
(Satiety Enhancement Property)

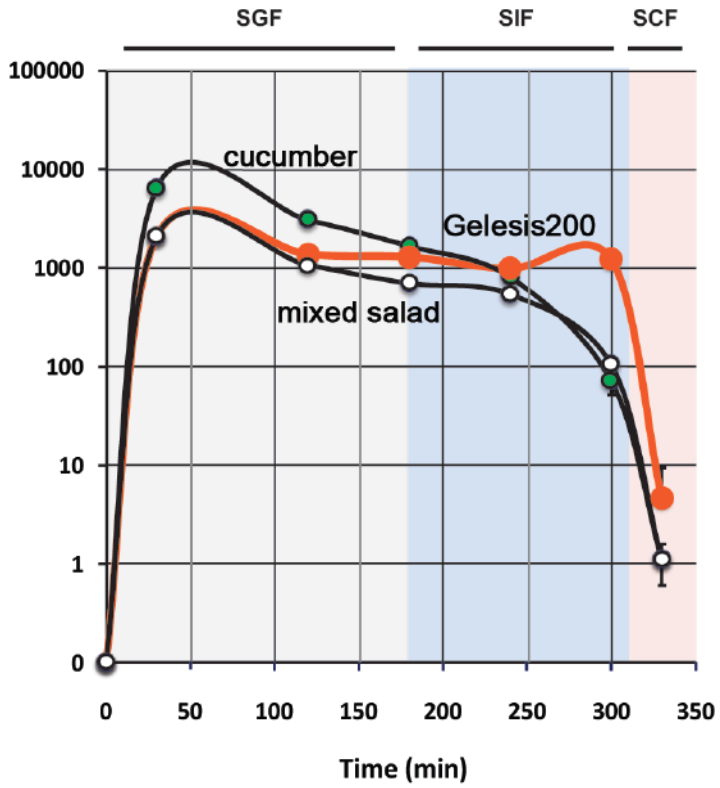


Comparing the Elastic Response (Firmness) of GS200 to Fibers & Raw Vegetables in Simulated Digestion Process:
Simulated Gastric Fluids **(SGF),** Small Intestinal Fluids **(SIF)** & Colonic Fluids **(SCF)**

GS200 vs. Fibers



GS200 vs. Vegetables



Demitri C, et al. Presented at American Diabetes Association Scientific Sessions 2017.

Madaghiele M, et al. Nature Scientific Reports. 2021;11(1):21394. doi: 10.1038/s41598-021-00884-5.

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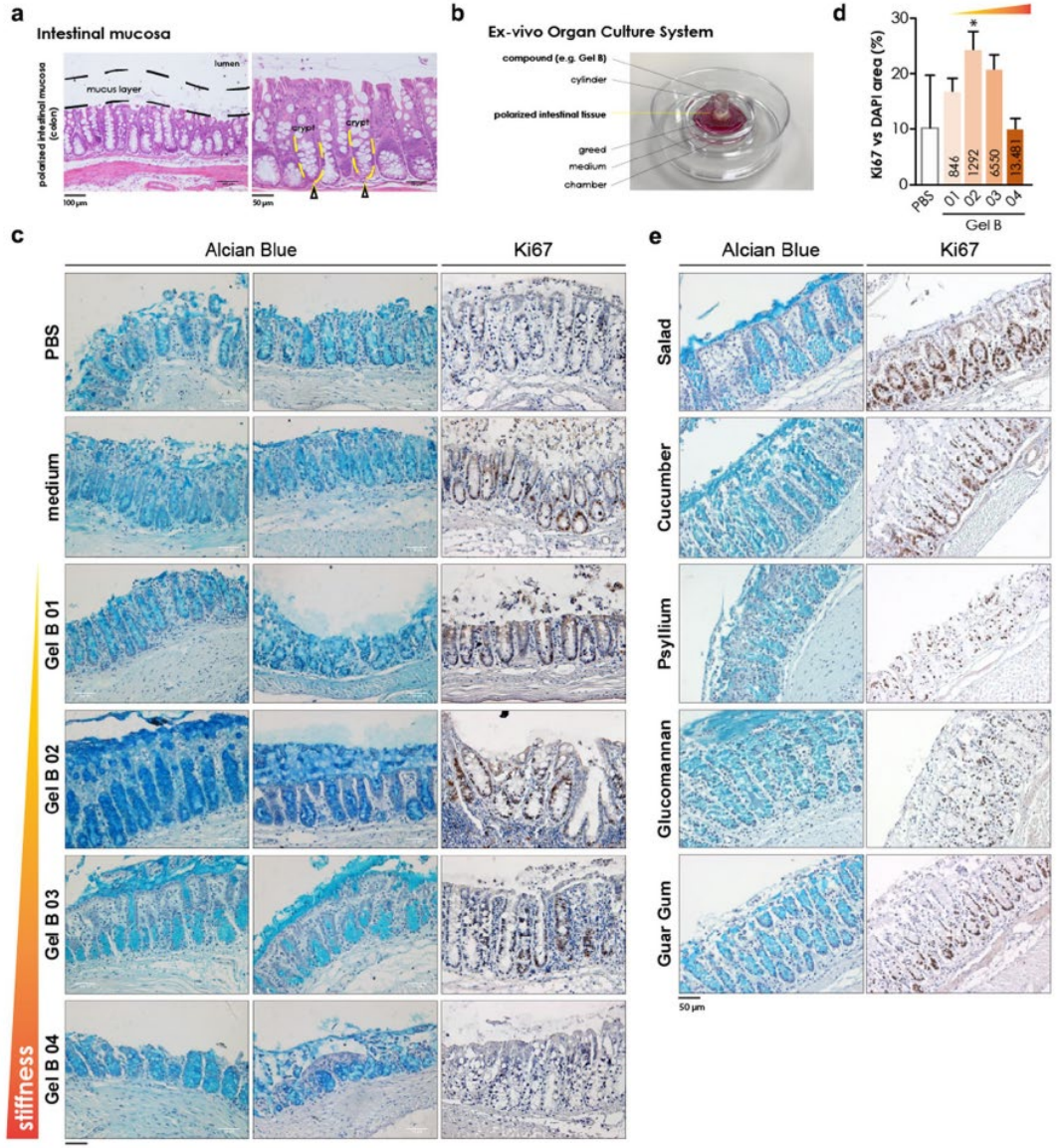
GS200's Positive Effects on the Gut Tissue Health

Published in Nature Scientific Reports

In an Ex Vivo Organ Culture (EVOC) system which measures mucus integrity and tissue proliferation, GS200 (GelB 02) had superior effects compared to fibers, similar to raw vegetables that have similar level of elasticity (firmness) and composition (cellulose and water)



Madaghiele M, et al. Nature Scientific Reports. 2021;11(1):21394. doi: 10.1038/s41598-021-00884-5.

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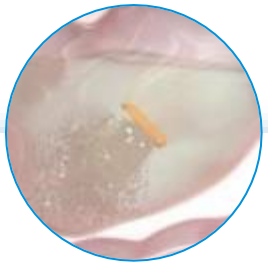
GS200 Transition Through the GI System

Not Absorbed, Not Habit Forming & Designed to Change the Composition and Elasticity of Ingested Meals Without Any Additional Calories

Administered as capsules with water before meals or incorporated in foods such as food bars

1



Hydrate rapidly in the stomach to create small individual non-aggregating gel pieces

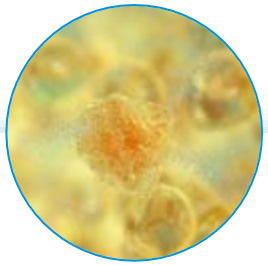
2

Gel pieces mix homogenously with the meal increase its volume & reduce its caloric density*

3

This increases the elastic response (firmness) of the ingested food both in the stomach and the small intestine

4



Not absorbed. Eliminated through the natural digestive process after partial degradation in the large intestine

5

*caloric density = number of calories in a given mass of food

Rolls BJ. Physiol Behav. 2009;97(5):609-615. doi:10.1016/j.physbeh.2009.03.011

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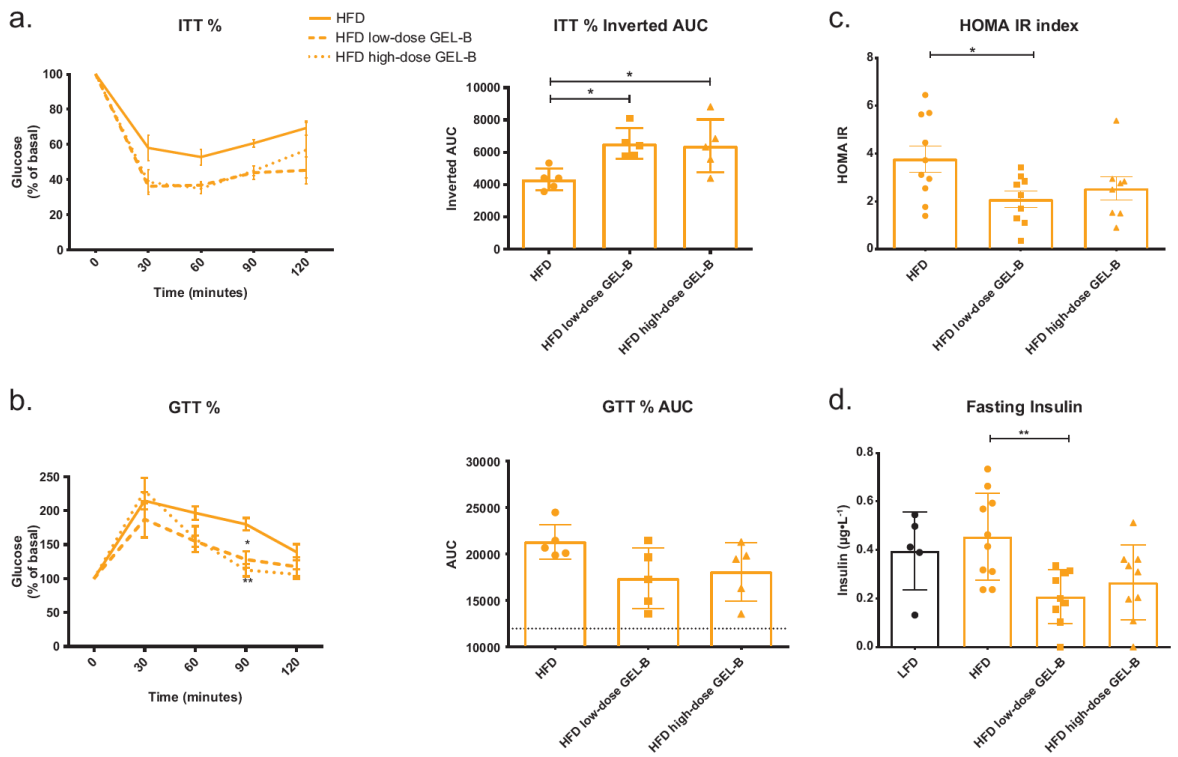
GS200 Pre-Clinical Data Highlights

In Pre-Clinical Studies GS200 Demonstrated Multiple Therapeutic Benefits (1/2)

Published in the Journal of Hepatology

GS200 prevents obesity and insulin resistance in mice on high fat diet

Figure 3. Gel-B prevented insulin-resistance development



Insulin Tolerance test (ITT), Glucose Tolerance test (GTT), HOMA IR, and Glucagon-like peptide 1 (GLP-1).
a. Intra-peritoneal ITT and respective inverted area under the curve (AUC); **b.** Intra-peritoneal GTT and respective AUC. Both tests were performed after 17 weeks of feeding following 4 hours of morning fasting; **c.** HOMA IR values; **d.** Serum insulin levels measured after morning fasting, outliers were calculated with Graphpad Prism outlier calculator software and removed from the analysis (*P <0.05, **P <0.01, one-way ANOVA, Bonferroni's multiple comparisons test).

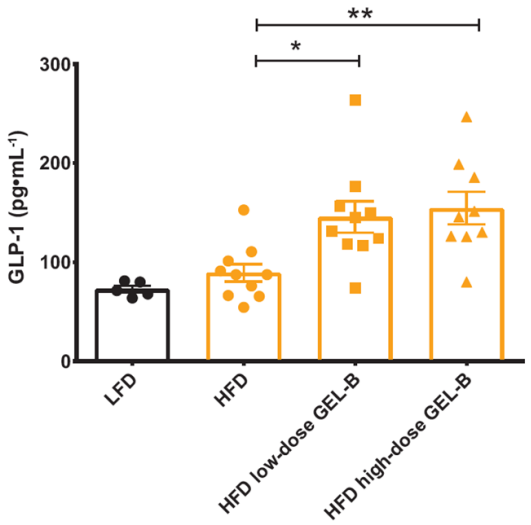
Silvestri, A. et al. 2019. Journal of Hepatology 70:e157-158.

In Pre-Clinical Studies GS200 Demonstrated Multiple Therapeutic Benefits (2/2)

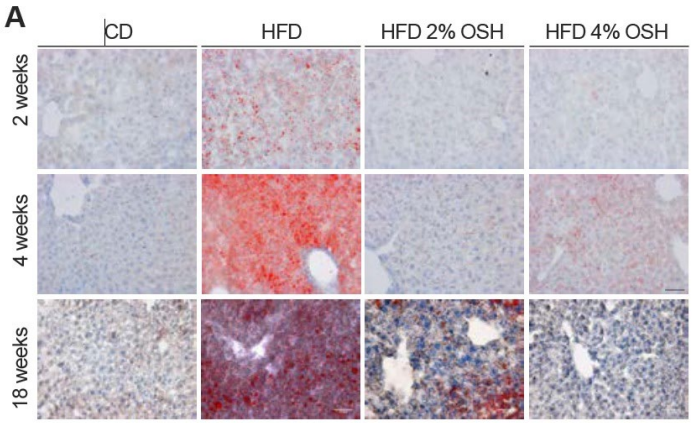
Published in the Journal of Hepatology

- Increases endogenous Glucagon-Like Peptide 1 (GLP-1)
- Protects against High Fat Diet-induced obesity, diabetes, NAFLD and NASH
- Restores gut barrier function (healing of leaky gut)

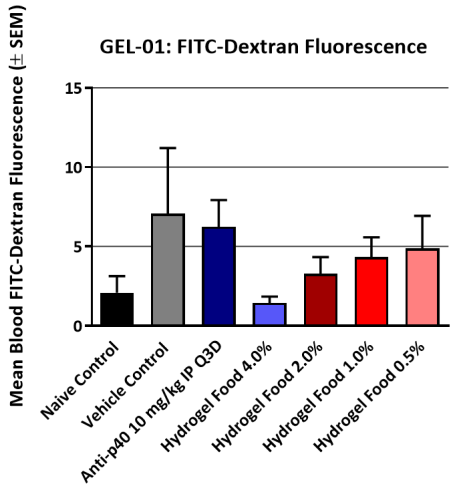
GS200 administration increased GLP-1 serum levels



GS200 prevented triglyceride accumulation in liver



GS200 reduced the translocation of 40 kDA Dextran molecules into circulation



Silvestri, A. et al. 2019. Journal of Hepatology 70:e157-158.

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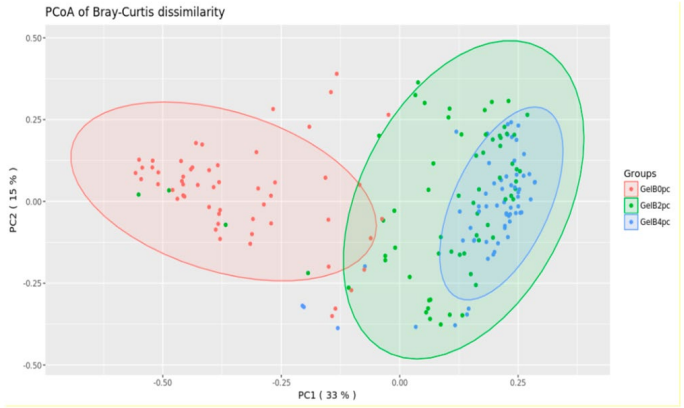
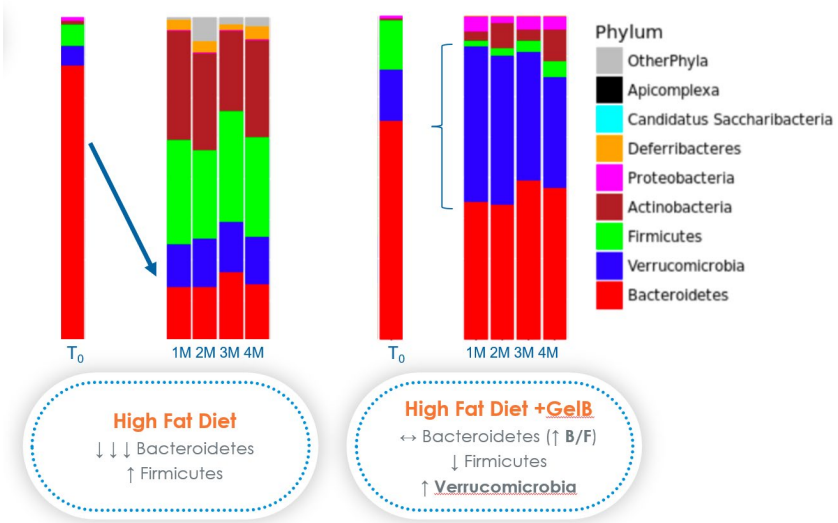
Additional Pre-Clinical Findings: GS200 Elicits Remarkable Shift in Microbiome with Known Therapeutic Effects

Presented at the World of Microbiome

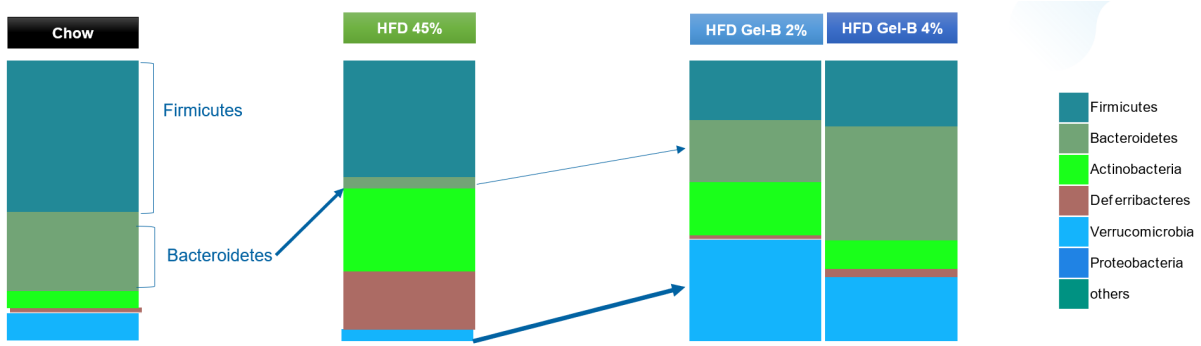
- Increases “Good” Bacteroidetes and decreases “Bad” Firmicutes
- Decreases “Bad” Actinobacteria
- Increases “Good” Verrucomicrobia, driven exclusively by “Good” *Akkermansia muciniphila*



GS200 protects against high fat diet-induced changes in microbiome



GS200 induces gut microbiota changes associated with improved metabolic outcomes



Microbiota in obesity

Increase in *Firmicutes* phylum

Reduced abundance of *Bacteroidetes*

A higher level of *Actinobacteria* phylum

Lower proportion of *Verrucomicrobia*

Gelesis Hydrogel induced microbiota changes

Decrease in *Firmicutes* phylum

Increased abundance of *Bacteroidetes*

A lower level of *Actinobacteria* phylum

Higher proportion of *Verrucomicrobia*

Gil Gomez, A. et al. Presented at the World of Microbiome Meeting 2022.

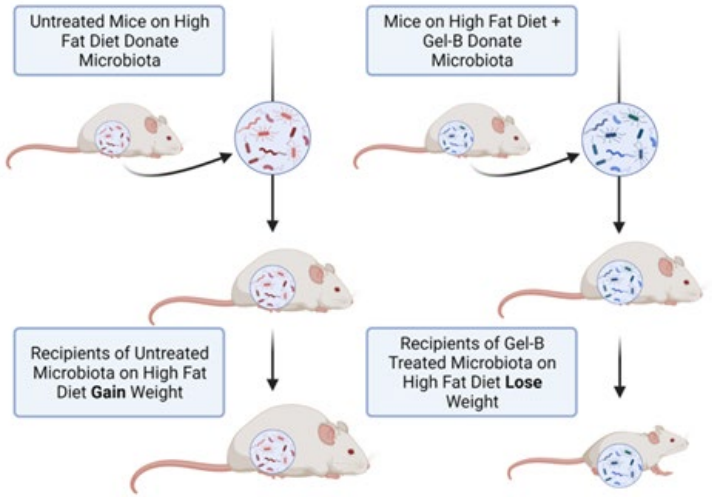
GELESIS

Microbiota Transplantation Confirms that Metabolic Effects are Induced by the GS200 Microbiota Shift

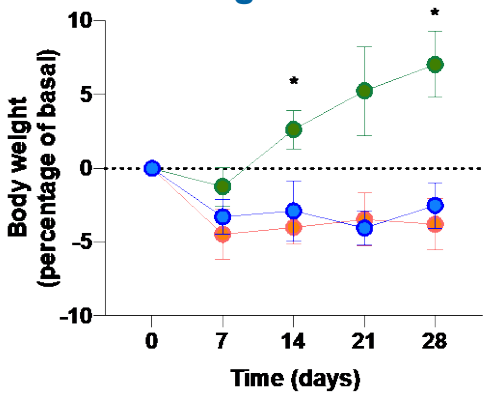
Presented at the American Diabetes Association

Microbiota transplantation was produced from feces of mice with metabolic disease, induced by high fat and high cholesterol diet (HFHCC), and treated with GS200 (**Donors**).

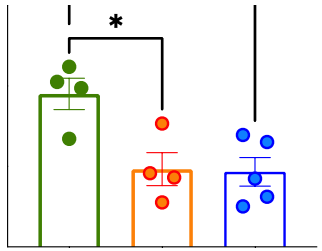
The **Recipients** were mice with the same metabolic disease, which never received GS200. The transplantation had a strong therapeutic effect as shown below.



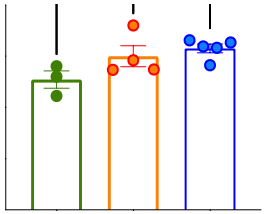
Weight Loss



Improved glucose control



Increased insulin sensitivity



Mice on HFHCC diet receiving microbiota from mice on:

- HFHCC
- HFHCC + 2% Gel B
- HFHCC + 4% Gel B

1. Gil Gomez, A. et al. Presented at the ADA Scientific Sessions 2022. 2. Gil Gomez, A. et al. Presented at the World of Microbiome Meeting 2022.

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GS200 Human Data Highlights

Presented Obesity Week

In the STAGE Clinical Study, GS200 Demonstrated Increased Satiety & Fulness Throughout the Day with Excellent Safety & Tolerability

- Short-term GS200 administration in clinical study was safe and well tolerated
- Administration of GS200 10 min before 3 meals increased self-reported feelings of fullness and satiety

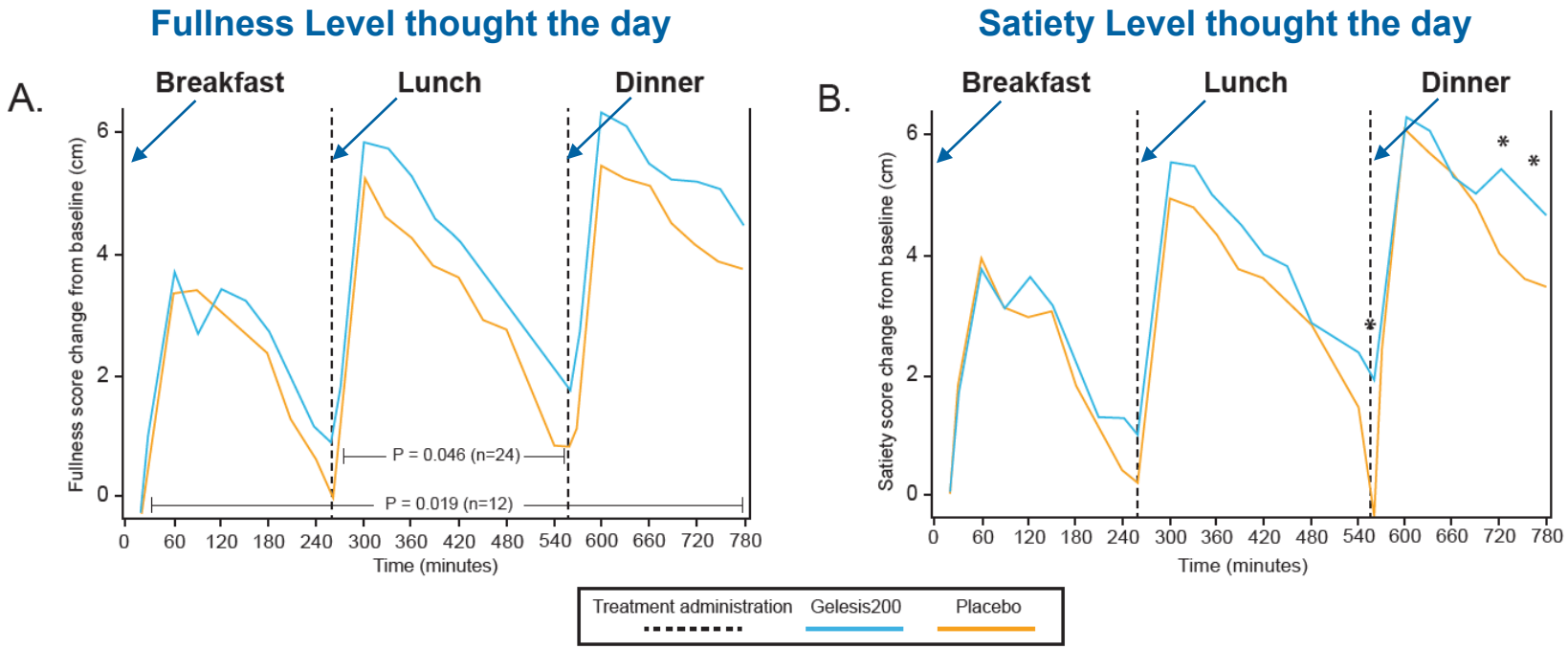


Figure 4: Changes in Fullness (Panel A) and Satiety (Panel B) Following Administration of Gelesis200 or Placebo 10 Min Prior to Meals.
*P = 0.017, 0.032, and 0.031 at 10 Min Prior to Dinner, and 150 and 180 Min After Dinner, Respectively.

Urban LE, et al. Presented at ObesityWeek 2016.

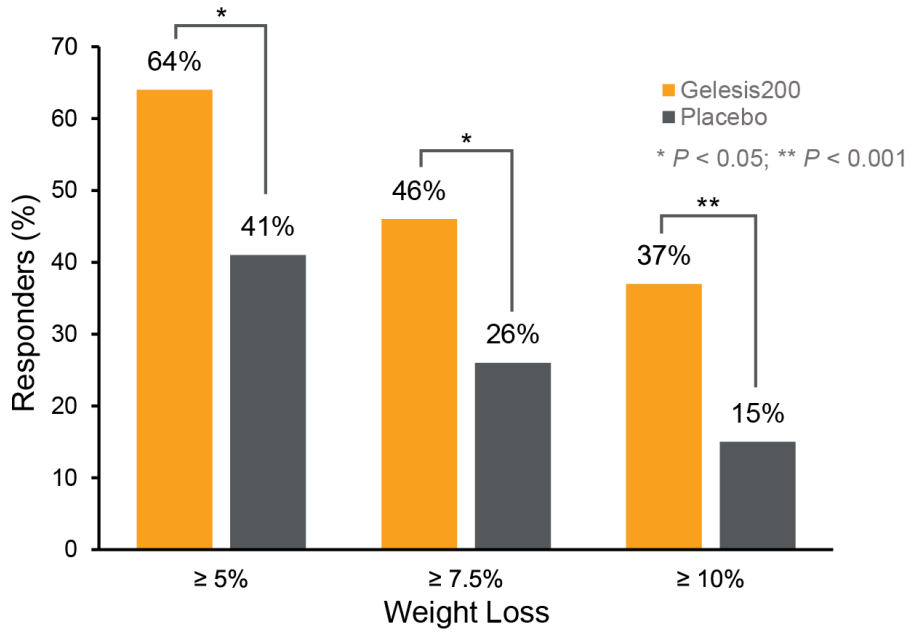
GELESIS

GS200 Effect on Body Weight in Humans with Overweight/Obesity and Prediabetes/Type 2 Diabetes: LIGHT-UP 6 Month Study

Published in the European Journal of Obesity

- Multicenter, double-blind, randomized, placebo-controlled study
- 254 subjects with prediabetes or type 2 diabetes
- 127 per arm, GS200 2.1 g twice daily or placebo, 25 weeks, BMI 27-40 kg/m^2 mean 34.7 kg/m^2
- GS200 taken with water 10 minutes pre-lunch & dinner with light diet (300-kcal deficit), behavior & walking program
- Mean weight loss was 7.1% for GS200 vs. 4.6% for placebo (*P*=0.003) †

Categorical weight loss GS200 vs. placebo LIGHT-UP†



† Per protocol population

Greenway F, et al. Obesity Facts. 2022;15(Suppl 1):1-240. DOI: 10.1159/000524469.

GELESIS

Strong and Early Separation Between Responders and Non-Responders as Early as 6 Weeks on Treatment
(LIGHT-UP Study)

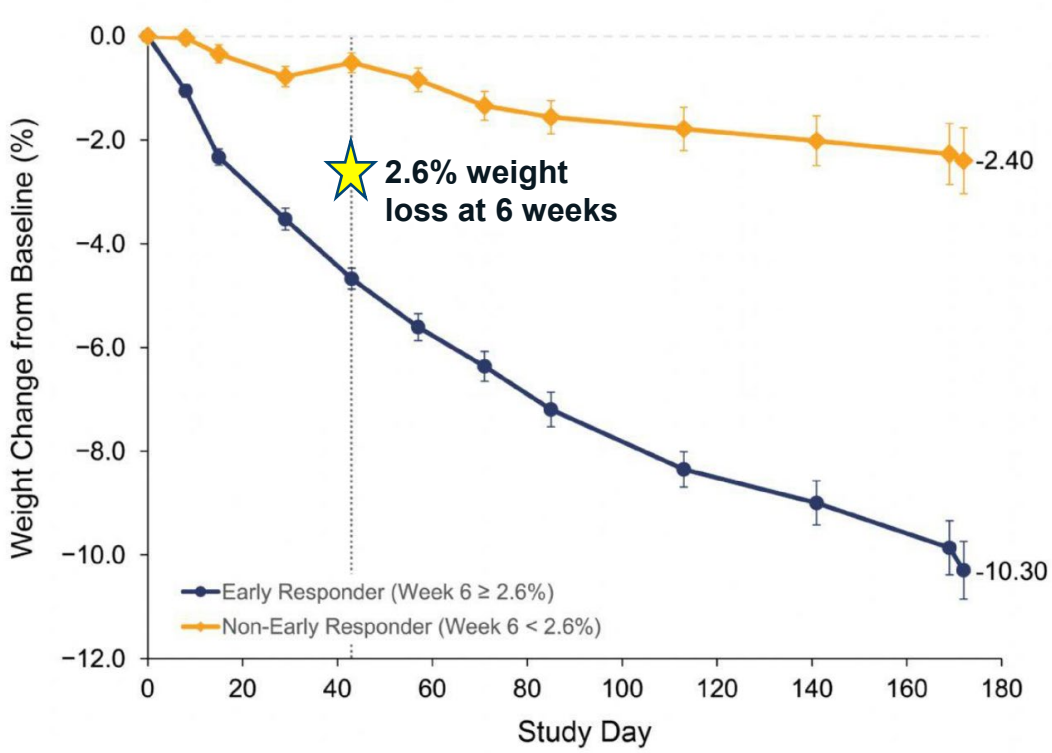
Published in the European Journal of Obesity

AUC ROC analysis showed that early response to GS200 (≥ 2.6% as early as 6 weeks) is highly predictive of clinically meaningful weight loss (≥ 5%, and average of 10.3%) after 25 weeks (≥ 85%).

In the placebo arm, similar sensitivity and specificity for predicting meaningful weight loss was not achieved until sometime between week 12 to week 16.

This early separation between Responders and Non-Responders demonstrates the strong binary effect of the treatment and could become a useful tool to motivate treatment compliance

Weight loss in early responders and non-early responders



Golub HL, et al. Obesity Facts. 2022;15(Suppl 1):1-240. DOI: 10.1159/000524469.

GELESIS

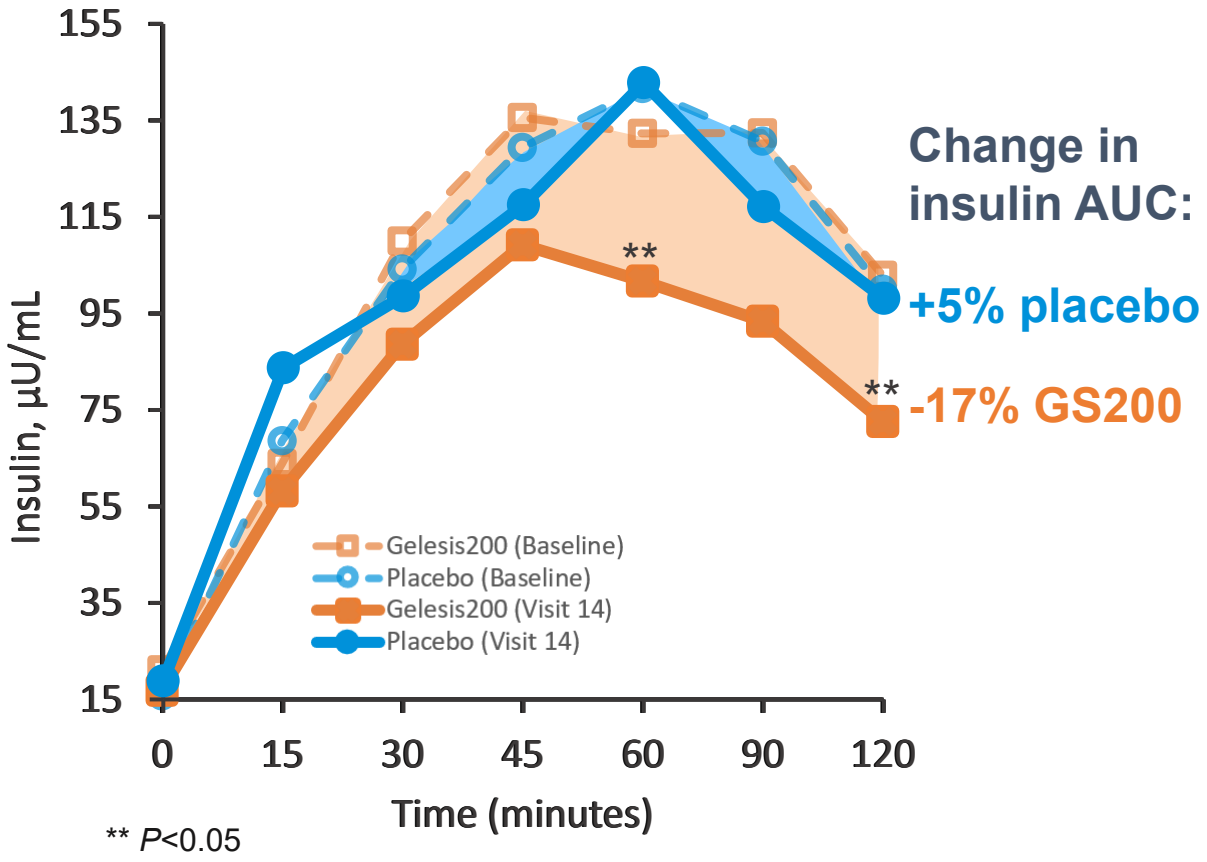
GS200 Elicits a Weight-Independent Reduction in Insulin Resistance in People with Prediabetes

Presented at the International Society of Endocrinology

For participants with prediabetes: At Week 25, insulin $AUC_{0\text{-}120}$ was significantly lower for participants on GS200 compared to placebo (mean difference: -22.0%, *P*=0.04).

- GS200 arm had a greater reduction in postprandial insulin during OGTT at T_{60} (-35.0 vs. -1.5 µU/mL for placebo, *P*=0.05) and T_{120} (-30.9 vs. 0.5 µU/mL for placebo, *P*=0.04).
- Participants on GS200 also had a greater reduction in insulin C_{max} vs. placebo (mean difference: -47.3 µU/mL, *P*=0.03).
- Data is consistent with previous pre-clinical studies and 2 other studies with GS 100 (Plenity).

Changes in postprandial insulin for GS200 compared to placebo



** *P*<0.05

Luzi L, et al. 2022. Presented at the International Congress of Endocrinology 2022. Virtual.
AUC= area under the curve; OGTT = oral glucose tolerance test

GELESIS

In LIGHT-UP, Elevated Waist-to-Height Ratio was Associated with Greater Weight Loss with GS200

Presented at the International Society of Endocrinology

- Waist-to-Height ratio (**WHR)** is strongly correlated with fat mass and insulin resistance
- High **WHR** (≥ median of 0.67) achieved greater weight loss than those with low **WHR** (< 0.67). Weight losses were 8.1% vs. 5.5%, respectively (P = 0.03)
- **For each 0.05 increase in baseline WHR**, subjects on GS200 experienced a **greater weight change of -1.4 kg** compared to -0.7 kg for placebo (P=0.03)
- **WHR** could potentially become a useful tool to predict weight loss response with pre-diabetes or diabetes for GS200 treatment

Figure 2A: Predicted probabilities for being a Responder (body weight loss ≥ 5%) with 95% confidence limits in Gelesis200 arm

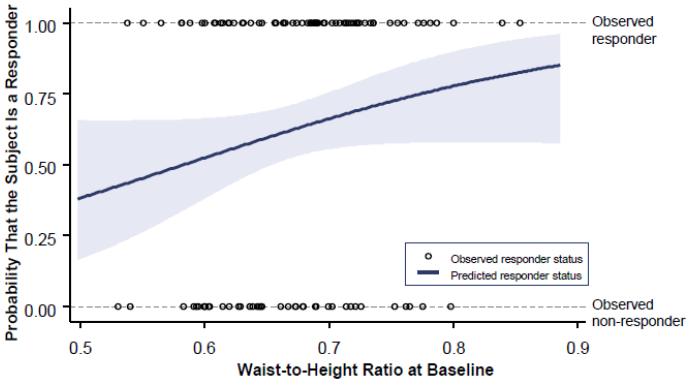
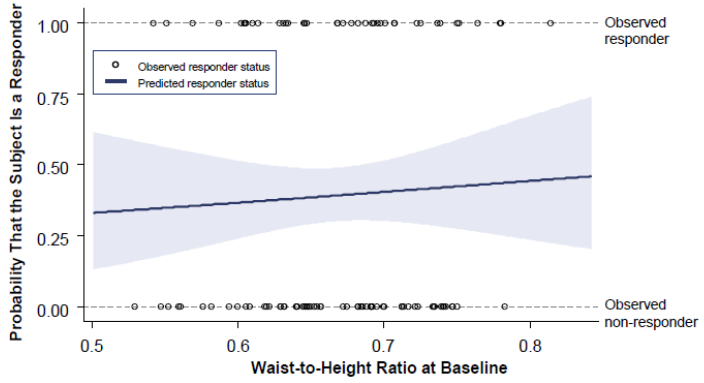
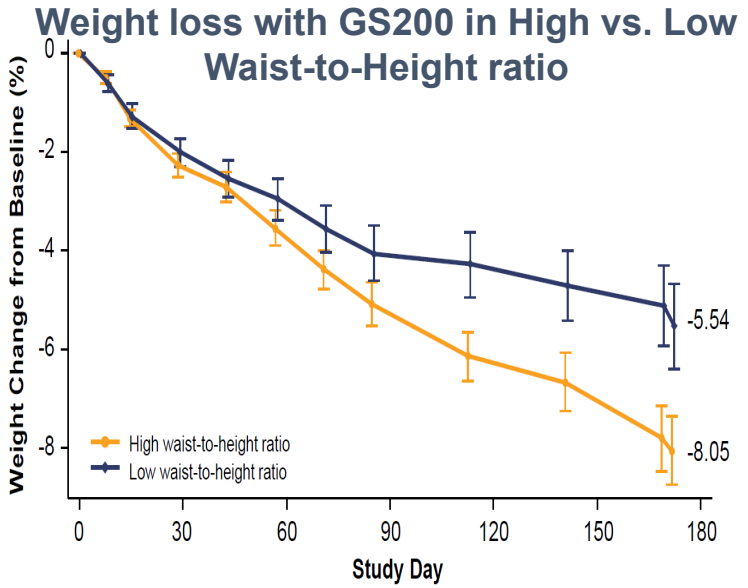


Figure 2B: Predicted probabilities for being a Responder (body weight loss ≥ 5%) with 95% confidence limits in placebo arm





Luzi L, et al. 2022. Presented at the International Congress of Endocrinology 2022. Virtual.
WHtR = waist-to-height ratio

GELESIS

GS200 Reduces Colonic Transit Time in Patients with Chronic Idiopathic Constipation, in a Pilot Study

Published in the Journal of Neurogastroenterology and Motility

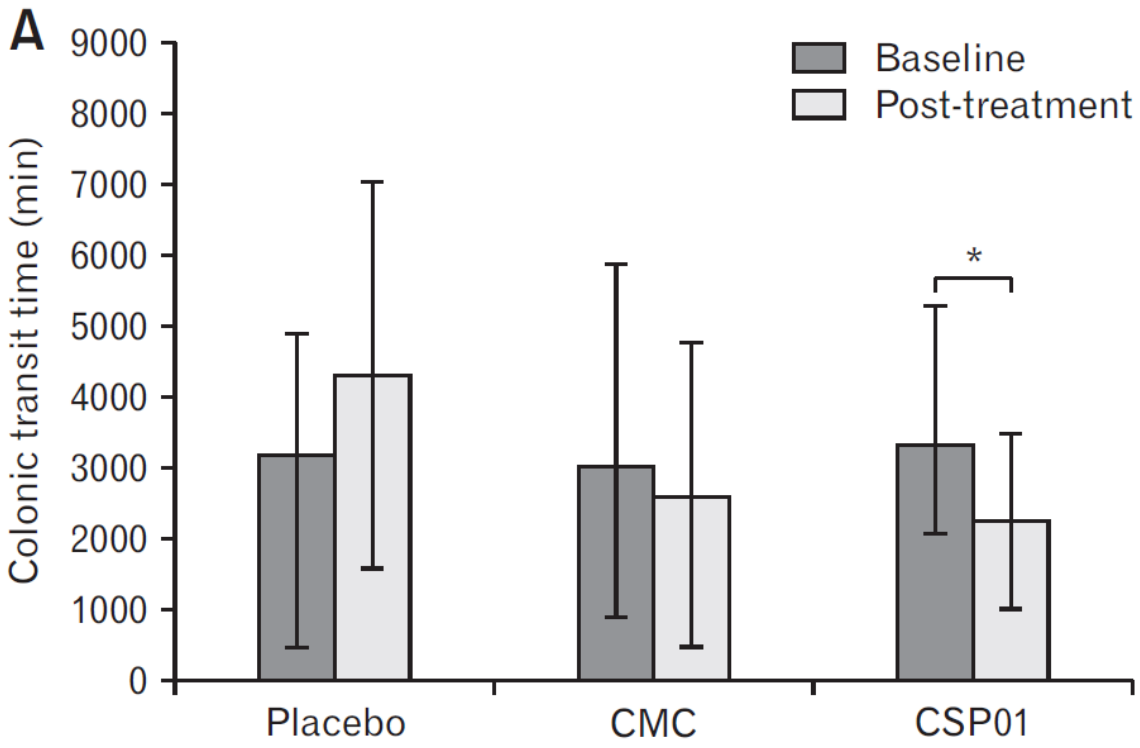
A pilot study at Mass General Hospital in Boston comparing change in colonic transit time (CTT) among patients with chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C) treated for 21 days with either GS200 hydrogel, active control (CMC) or placebo.

CTT was measured using wireless motility capsule.

GS200 significantly decreased CTT compared to placebo among patients with CIC, but not in patients with IBS-C.

Although GS200 is made from CMC, CMC which doesn't have the same structure and elasticity, didn't have any effect on CTT

GS200 is a promising agent in CIC. Further randomized trials are warranted to determine whether GS200 could become a treatment option for CIC.



Colonic transit times for patients with chronic idiopathic constipation (A). CSP01- GS200, CMC, carboxymethylcellulose *P < 0.05.

Staller K, et al. J Neurogastroenterol Motil. 2020 Sep 9;26(4):496.

GELESIS

Presented Obesity Week

LIGHT-UP Study Showed Favorable Tolerability Profile

	LIGHT-UP Patients[1], n (%) GS200 = 126	Placebo =127	Difference 95%	P-value	Plenity[2] Patients, n (%) Plenity = 223	Placebo = 211	Difference 95%	P-value
Any AE probably or possibly related to device	27 (21.4)	16 (12.6)	18.8	0.067	88 (39.5)	64 (30.3)	9.1	0.056
Gastrointestinal	**26 (20.6)**	**14 (11.0)**	12.0	**0.040**	**84 (37.7)**	**58 (27.5)**	10.2	**0.0250**
General disorders	1 (0.8)	0 (0.0)	0.8	0.498	1 (0.4)	1 (0.5)	–0.0	1.000
Infections and infestations	0 (0.0)	0 (0.0)			2 (0.9)	1 (0.5)	0.4	1.000
Investigations	1 (0.8)	3 (2.4)	1.6	0.622	3 (1.3)	3 (1.4)	–0.1	1.000

Gastrointestinal AEs in subjects on GS200 were more common than placebo, but the rate is ~50% of the GI AEs found in our GLOW/Plenity study, which received FDA Non-Significant Risk status (NSR)

1. Gelesis Loss of Weight in Subjects Without or With Type 2 Diabetes (LIGHT-UP) Clinical Study Report GS-200-002. December 2022. Data on File.
2. Greenway FL, et al. Obesity. 2019;27:205-216

*Table displays categories of AE's that have at least 1 GS200 subject reporting an AE

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Low rate of early treatment withdrawal due to *AEs* in LIGHT-UP: *Only 2 (1.6%) of subjects on GS200 withdrew because of AEs*

Presented Obesity Week

Parameter	GS200 (n) N=127	Placebo (n) N=127
Drop-out Rates	**16.5% (21)**	**21.3% (27)**
Adverse events	**1.6% (2)**	**1.6% (2)**
Lost to follow-up	5.5% (7)	1.6% (2)
Protocol deviation	0.8% (1)	2.4% (3)
Withdrawal by subject	3.9% (5)	14.2% (18)
Other	4.7% (6)	1.6% (2)

Gelesis Loss of Weight in Subjects Without or With Type 2 Diabetes (LIGHT-UP) Clinical Study Report GS-200-002. December 2022. Data on File.

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Gelesis Patents

9

Patent Families

Gelesis products are protected by 9 families of patents and patent applications with more than 100 individual issued patents in major markets around the world, covering composition of matter, methods of use, and methods of production for product candidates and the platform technology, including **Plenity** (GS100), GS200, GS300, and GS500

Protection through at least 2035 with issued and pending patents (in US and ex-US) broadly covering compositions of matter, methods of use and methods of production, with potential for extensions

Composition

Patents covering Plenity (GS100) and GS200 composition of matter have been granted in US, Europe, China, Japan, Russia, Australia, and Canada (and are pending in additional territories)

Methods of Use

Uses of Gelesis hydrogels for treating obesity and reducing caloric intake are currently protected by three issued patents in the U.S. and corresponding patents have also been granted or allowed in Europe, Canada, China, Japan, Russia, Australia, Canada, and Mexico

Provisional Applications

One U.S. provisional application is also pending, which is directed to methods of treating GI-related metabolic diseases

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New Product Concepts

GS200 Could be Administered in Multiple Forms:

In capsules (gelatin or vegetarian) or sachets

As a single ingredient or in combination with other supplements

In dry foods such as food bars

Coating the GS200 particles with a moisture barrier prevents hydration in the mouth and delays the hydration until the food is in the stomach

In wet foods such as instant oatmeal

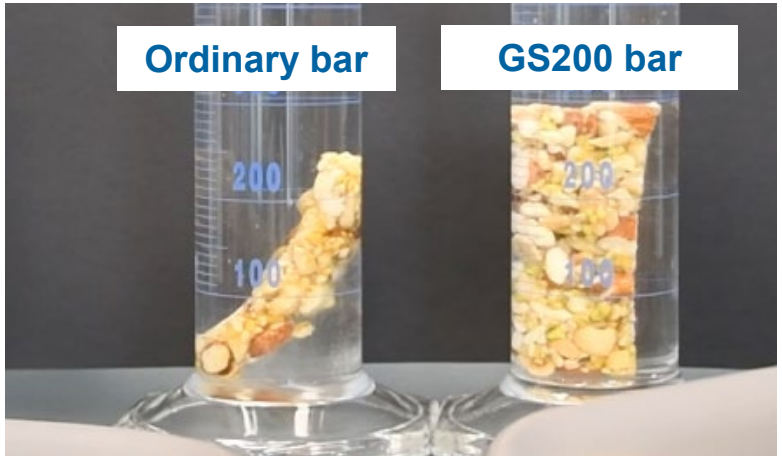
GS200 is hydrated during the preparation to create much larger volume without any additional calories

GS200 Food Bar Prototype

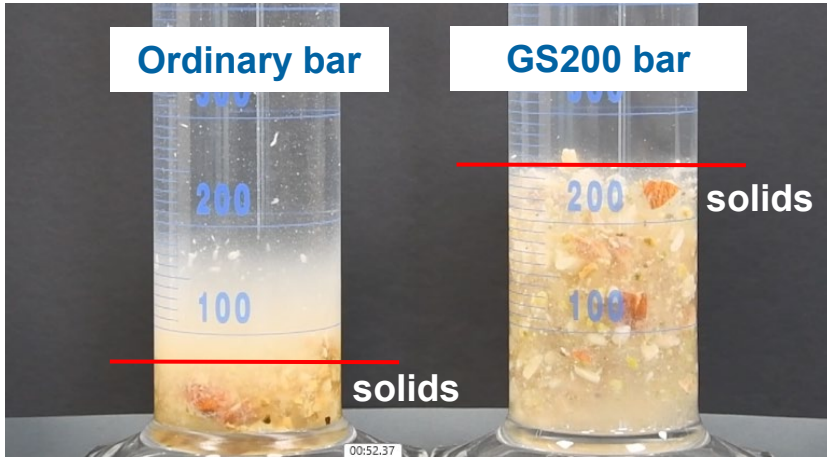
Food bars enhanced by GS200 have the same taste and texture, yet will create up to 5X more volume in the stomach without adding any calories

The 40g bar prototype in the photos has 2g of GS200. In the stomach it will create similar volume, firmness and composition, as ½ pound of ingested cucumbers

1



2



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