Safety of Gelesis100 in Subjects Who Reached a BMI Below 27 kg/m^2 in the GLOW Study

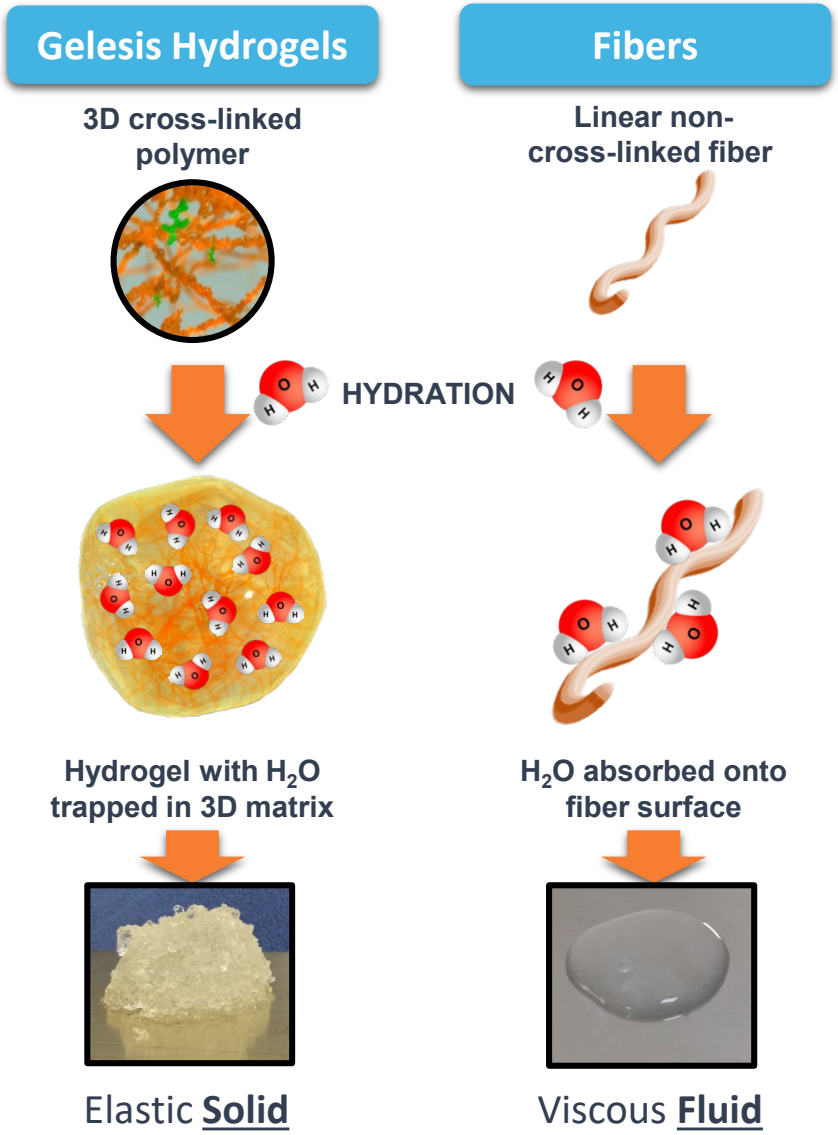
Louis J Aronne, MD, FACP

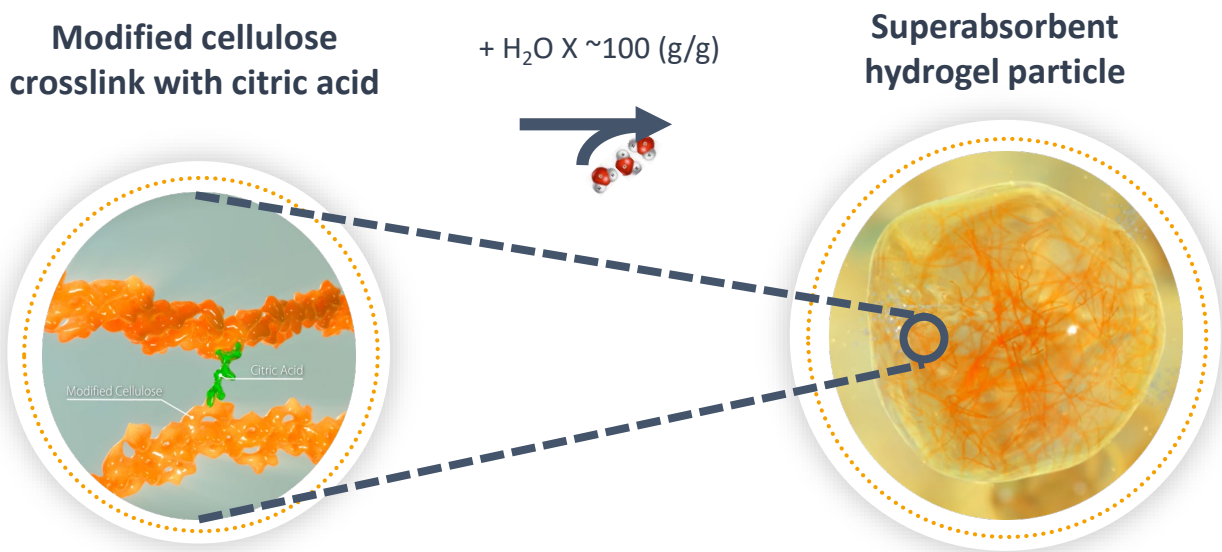
Sanford I. Weill Professor of Metabolic Research
Weill Cornell Medical College
New York, NY

Disclosures

- Funding/grant support/honorarium
  - Gelesis
  - Allurion
  - Aspire Bariatrics, Inc.
  - Astra Zeneca
  - BMIQ
  - Eisai, Inc.
  - ERX
  - Jamieson Wellness
  - Janssen
  - Myos Corporation
  - Novo Nordisk
  - Pfizer
  - Sanofi
  - United Heath Group
  - Zafgen
- Owns Gelesis stock options as a scientific advisor

Gelesis Hydrogel Platform Technology…and how it is different than functional fibers



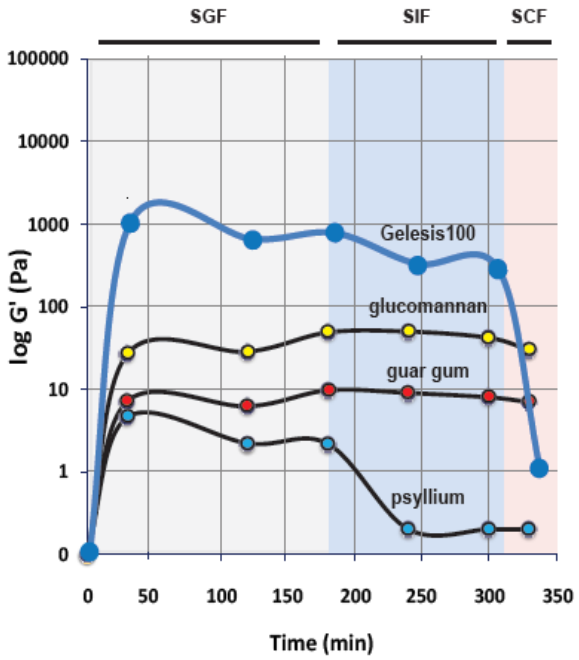


- Only superabsorbent made from **food-grade building blocks**
- **Biocompatible and biodegradable**
- Able to **absorb** amount of **water ~100x** its dry weight (superabsorbent)
- In fully hydrated state, ~1-2mm diameter with **elasticity/firmness** like leafy vegetables (eg, **lettuce)**
- Particles **don't cluster** and **maintain their 3D structure** in upper GI tract; however, partially **degrade in the large intestine**

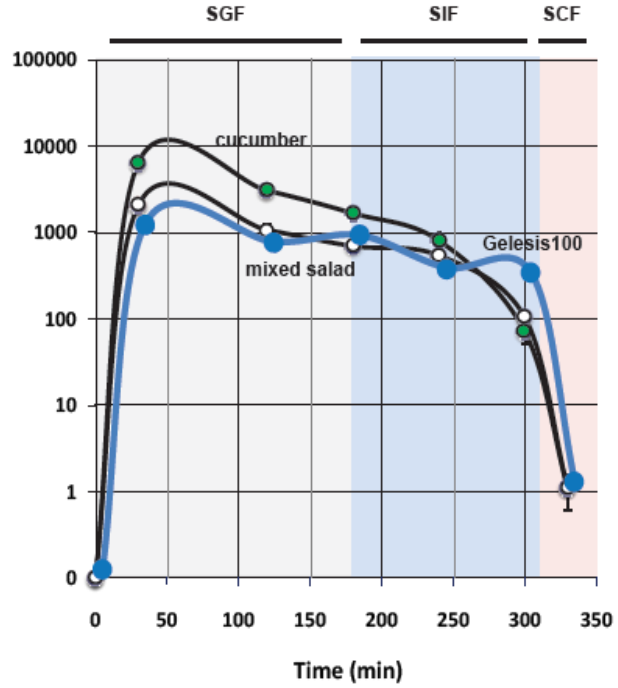
Gelesis Hydrogels have similar mechanical properties to cellulosic vegetables

Comparison of elastic modulus between Gelesis100 and processed functional fibers (A) and vegetables (B)

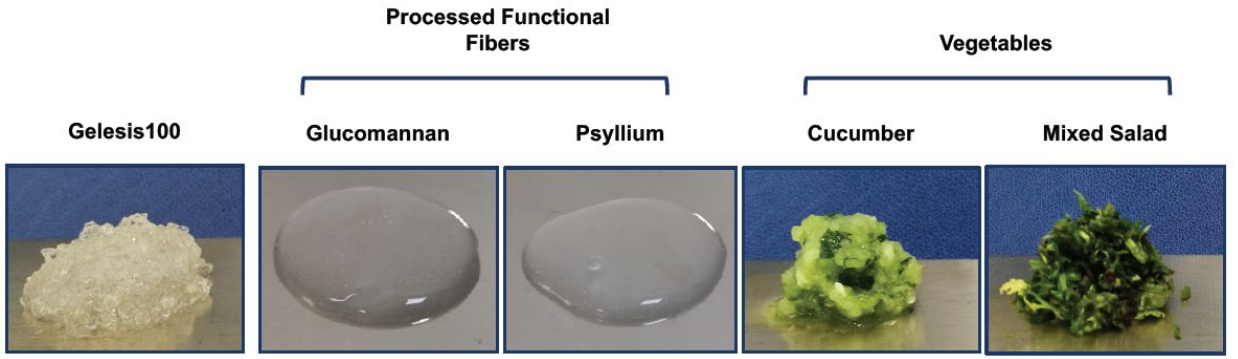
A. Gelesis100 vs. Processed Functional Fibers



B. Gelesis100 vs. Vegetables



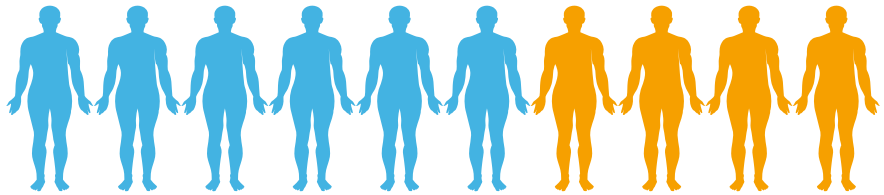
Visual comparison of Gelesis100, processed functional fibers, and vegetables following hydration or mastication



Key findings from the GLOW pivotal trial

RESPONDERS

Adults **achieving 5% or greater** weight loss



6 out of 10

- 59% of adults with overweight or obesity had a clinically meaningful response to Gelesis100, losing on average 10% of their weight (22 pounds) or ~3.5 inches from their waist
- Gelesis100 doubled the odds of achieving 5% or greater weight loss compared with placebo

SUPER RESPONDERS

Adults **achieving 10% or greater** weight loss

26% of adults with overweight or obesity were super-responders to **Gelesis100, losing on average 14% of their weight (30 pounds)**

Co-primary endpoint – The study also demonstrated statistically superior weight loss compared with placebo group (−6% vs −4%, respectively; P=0.0007) and did not meet the predefined super-superiority margin of 3%

Safety – Gelesis100 had no overall increased risks versus placebo, no serious adverse events and a lower dropout rate

IN A POST-HOC ANALYSIS, EARLY WEIGHT LOSS PREDICTED LONGER TERM BENEFIT

- Clear and early separation between responders and non-responders may allow for an early prediction of response
- Weight loss of ≥3% as early as after 8 weeks' treatment predicted weight loss ≥5% at 6 months, with sensitivity and specificity levels exceeding 80%

Greenway FL, Aronne LJ, Raben A, et al. *Obesity*. 2019;27:205-216.

Gelesis100 (Plenity™): A novel, superabsorbent hydrogel for weight management

- Made from GRAS (**G**enerally **R**ecognized **A**s **S**afe) and food-grade building blocks
- Defined by FDA as a device
  - Not absorbed
  - Not metabolized
  - Mechanical MOA
- No difference in tolerability or safety profile with Placebo in GLOW Pivotal trial

FDA cleared as an aid in weight management in adults with a BMI of **25–40 kg/m²**, when used in conjunction with diet and exercise.

BMI=body mass index.

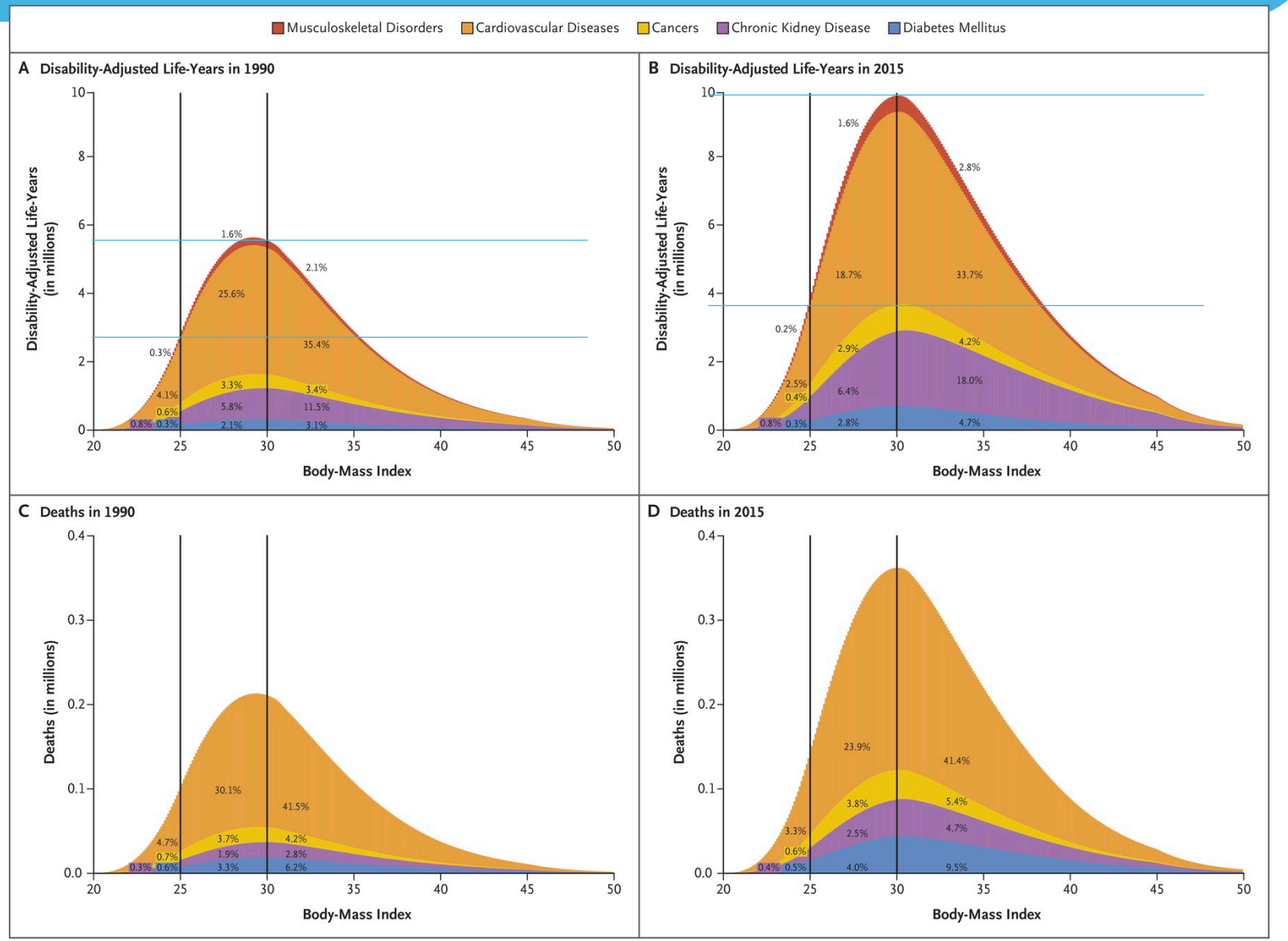
Plenity [package insert]. Gelesis. Boston, MA; 2019. https://www.fda.gov/medical-devices/classify-your-medical-device/product-medical-device

Disease burden is significant in overweight (BMI 25 – 30 kg/m^2), not just obesity

From 1990 through 2015, there was a relative increase of 28.3% in the global rate of death related to high BMI, from 41.9 deaths per 100,000 population in 1990 to 53.7 deaths per 100,000 population in 2015

37% of disability adjusted life years occurred in **overweight**

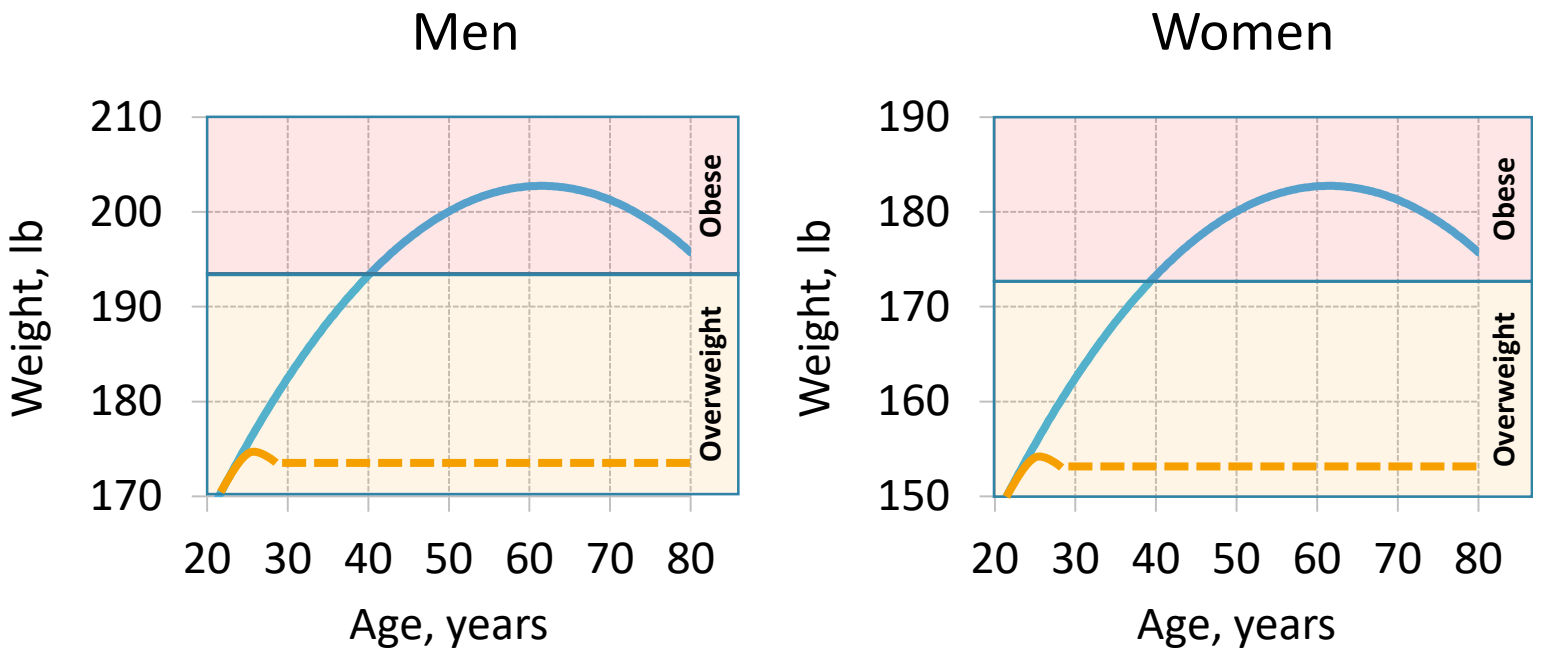
39% of deaths occurred in **overweight**



Should we break the cycle of weight gain in adults before they reach obesity?

- 120,877 US women and men who were free of chronic diseases followed from 1986 to 2006[1]
  - Within each 4-year period, participants gained an average of 3.35 lb (5th to 95th percentile, −4.1 to 12.4)
  - Corresponds to a weight gain of 16.8 lb over a period of 20 years
- Weight gain at ages between 18 to 35 years is strongly associated with critical outcomes such as cancer risk and mortality[2]
- *Should we treat overweight early, before presence of co-morbidities, just like treating hypertension at 140/90*[3]

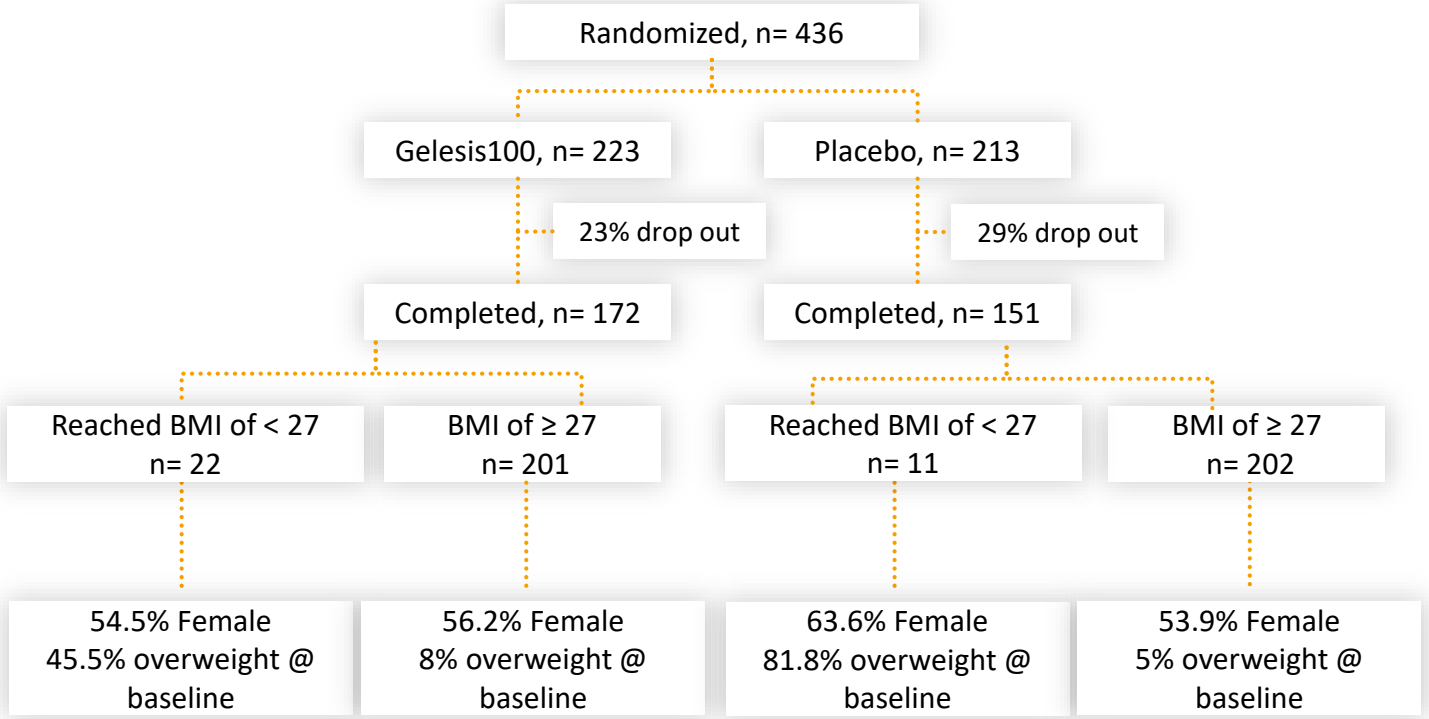
Average Weight by Age for American Men and Women



2007-2010 National health and Nutrition Examination Survey (CDC): https://www.cdc.gov/nchs/data/series/sr_11/sr11_252.pdf

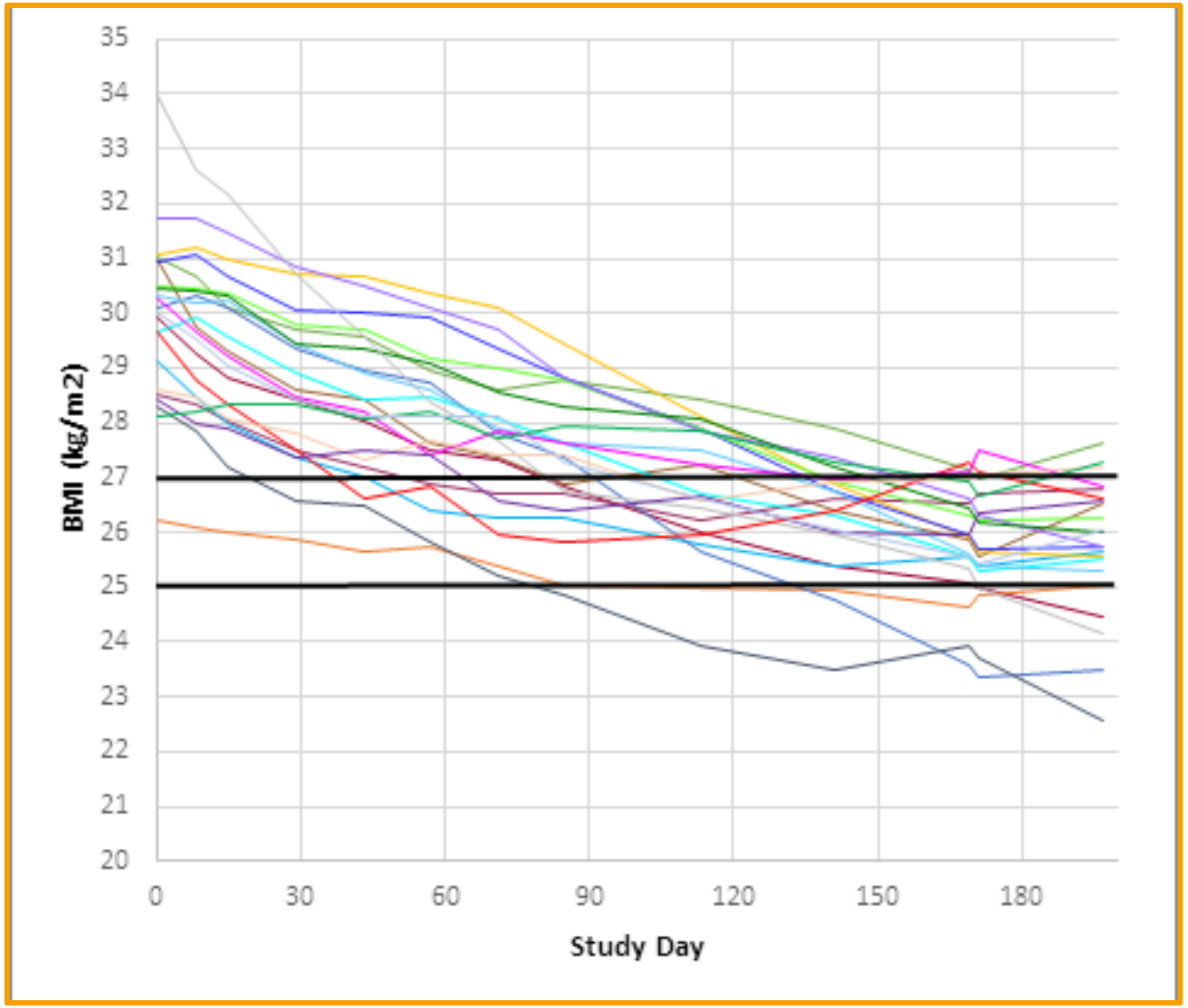
Subgroup Analysis: BMI < 27 kg/m^2

- Rationale
  - No prescribed options can address individuals who have BMI 25-27 kg/m^2 or have BMI 27-30 kg/m^2 without comorbidities
- Subgroup analysis
  - Assess safety of Gelesis100 administration in subjects who reached BMI<27 kg/m^2 during the study



Weight loss over time for Gelesis100-treated subjects who reached BMI < 27 kg/m^2

- Average time for subjects to reach BMI threshold of < 27 kg/m^2: 106 +- 49 days
- Average time exposed to Gelesis100 once subjects reached BMI< 27 kg/m^2: 60 days
- Total weight loss of 13.5% (95% CI -16% to -11%) while on Gelesis100
- Rate of weight loss tapered as it reached “normal BMI” goal



Gelesis100 Subjects With BMI <27 kg/m^2: No Increased Safety Risk

All AEs vs. GI-Related AEs – Safety Population

AEs	Gelesis100 Subjects with BMI < 27 kg/m^2		Placebo Subjects with BMI ≥ 27 kg/m^2		Difference		Gelesis Subjects with BMI ≥ 27 kg/m^2		Difference	
	# Events	#Subjects with Event [% (n/N)]	# Events	#Subjects with Event [% (n/N)]	95% CI[a]	p-value[a]	# Events	# Subjects with Event [% (n/N)]	95% CI[a]	p-value[a]
All	32	72.7% (16/22)	26	81.8% (9/11)	-9.1% (-36.7%, 28.4%)	0.69	404	71.1% (143/201)	1.6% (-22.4%, 18.7%)	1
GI-Related	10	31.8% (7/22)	7	27.3% (3/11)	4.6% (-33.0%, 35.0%)	1	176	44.3% (89/201)	-12.5% (-31.0%, 11.6%)	0.36

a. Difference taken for comparability between the 2 groups (T - C). 95% Newcombe Corrected CI and Fisher's Exact p-value for the difference in proportions.

AE = adverse event; CI = confidence interval; GI = gastrointestinal.

Mostly Mild GI Adverse Events of Short Duration

- All AEs resolved without complications

Subject	Adverse Event Description	Severity	Relatedness	Duration
1	Flatulence	Mild	Possibly	4 months
2	Abdominal pain after intake for 10 min with looser stools than normal	Mild	Most probably	10 days
3	Bloating for 30min after meal	Mild	Most probably	5 months
4	Bloating without pain	Mild	Possibly	4 days
5	Diarrhea	Mild	Probably not	3 days
6	Bloating for 1 week	Moderate	Possibly	7 days
7	Inguinal Hernia	Mild	Not related	UNKN

Conclusions

- Consistent with the larger GLOW Cohort, Gelesis100 demonstrated no safety signal in this smaller subgroup who reached lower BMI. The tolerability and safety profile was no different from placebo
- There was no difference in GI-related adverse effects between groups
- Gelesis100 is FDA-cleared as an aid in weight management for patients who have a BMI as low as 25 kg/m^2 with or without co-morbidities
- A post-marketing registry is planned to prospectively collect more data on efficacy and safety in this population to further support these findings

Thank you

Back–up slides

Gelesis100 Subjects With BMI <27: No Increased Safety Risk

No difference in safety when compared to placebo subject who reached BMI <27 (n=11) or for the entire placebo cohort (n=211)

	Gelesis100 Subjects with BMI < 27 kg/m²		Gelesis100 Subjects with BMI > 27 kg/m²		Difference	
	Number Events	Number Subjects with Event [% (n/N)]	Number Events	Number Subjects with Event [% (n/N)]	95% CI[a]	p-value[a]
All AEs	32	72.7% (16/22)	404	71.1% (143/201)	1.6% (-22.4%, 18.7%)	1
Blood and lymphatic system disorders	1	4.5% (1/22)	0	0.0% (0/201)	4.5% (-0.4%, 24.9%)	0.0987
Eye disorders	0	0.0% (0/22)	6	3.0% (6/201)	-3.0% (-6.7%, 15.6%)	1
GI disorders	10	31.8% (7/22)	176	44.3% (89/201)	-12.5% (-31.0%, 11.6%)	0.3649
General disorders	1	4.5% (1/22)	8	4.0% (8/201)	0.6% (-5.3%, 21.0%)	1
Hepatobiliary disorders	0	0.0% (0/22)	1	0.5% (1/201)	-0.5% (-3.2%, 18.0%)	1
Infections and infestations	11	36.4% (8/22)	83	32.8% (66/201)	3.5% (-16.1%, 27.2%)	0.8125
Injury, poisoning and procedural complications	2	9.1% (2/22)	21	10.0% (20/201)	-0.9% (-10.0%, 21.0%)	1
Investigations	0	0.0% (0/22)	12	5.0% (10/201)	-5.0% (-9.2%, 13.7%)	0.6036
Metabolism and nutrition disorders	0	0.0% (0/22)	3	1.5% (3/201)	-1.5% (-4.7%, 17.0%)	1
Musculoskeletal and connective tissue disorders	4	18.2% (4/22)	34	13.4% (27/201)	4.7% (-8.7%, 28.0%)	0.52
Neoplasms benign, malignant, and unspecified (incl cysts and polyps)	0	0.0% (0/22)	1	0.5% (1/201)	-0.5% (-3.2%, 18.0%)	1
Nervous system disorders	2	9.1% (2/22)	34	12.4% (25/201)	-3.3% (-12.7%, 18.6%)	1
Psychiatric disorders	0	0.0% (0/22)	4	2.0% (4/201)	-2.0% (-5.3%, 16.6%)	1
Renal and urinary disorders	0	0.0% (0/22)	3	1.5% (3/201)	-1.5% (-4.7%, 17.0%)	1
Reproductive system and breast disorders	0	0.0% (0/22)	4	2.0% (4/201)	-2.0% (-5.3%, 16.6%)	1
Respiratory, thoracic, and mediastinal disorders	0	0.0% (0/22)	7	3.0% (6/201)	-3.0% (-6.7%, 15.6%)	1
Skin and subcutaneous tissue disorders	0	0.0% (0/22)	5	2.5% (5/201)	-2.5% (-6.0%, 16.1%)	1
Vascular disorders	1	4.5% (1/22)	2	1.0% (2/201)	3.6% (-1.7%, 23.9%)	0.2688

AE = adverse event, CI = confidence interval, GI = gastrointestinal.

a. Difference taken for comparability between the 2 groups (T - C). 95% Newcombe Corrected CI and Fisher's Exact p-value for the difference in proportions.