# Assessment of the safety and tolerability of Gelesis100 in subjects who reached a body mass index below 27 $kg/m^2$ in the pivotal GLOW study

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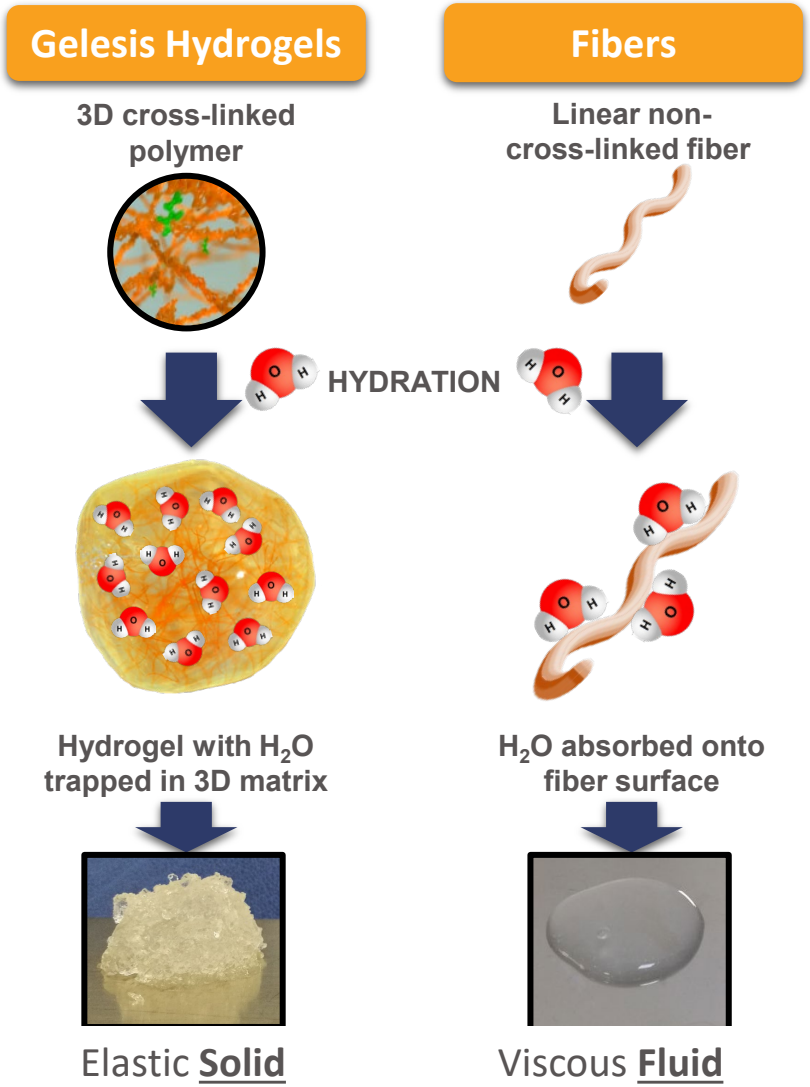
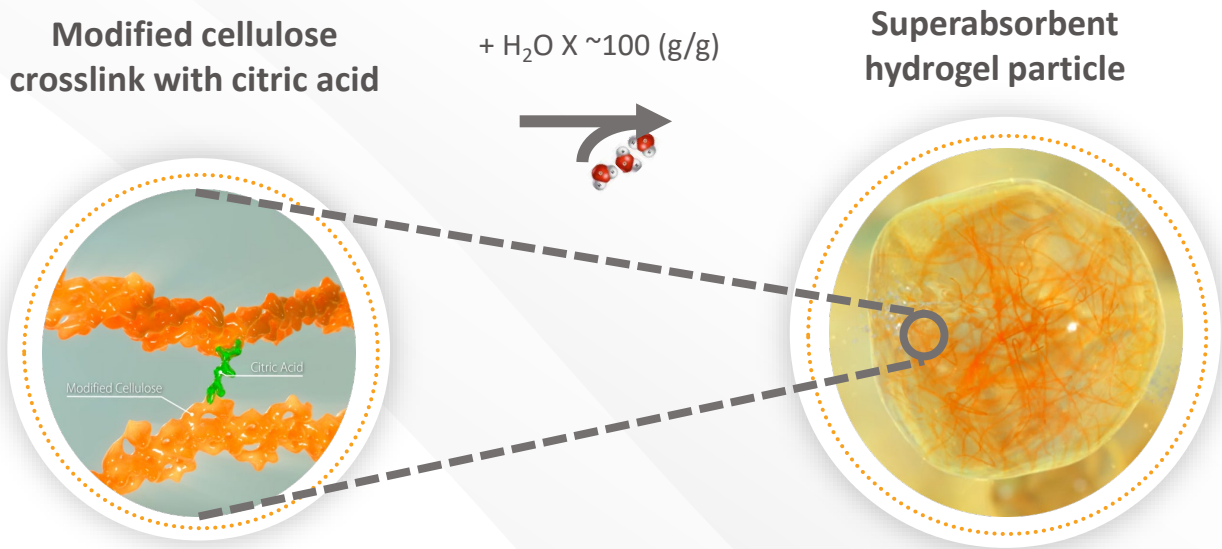
# Disclosures

- 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



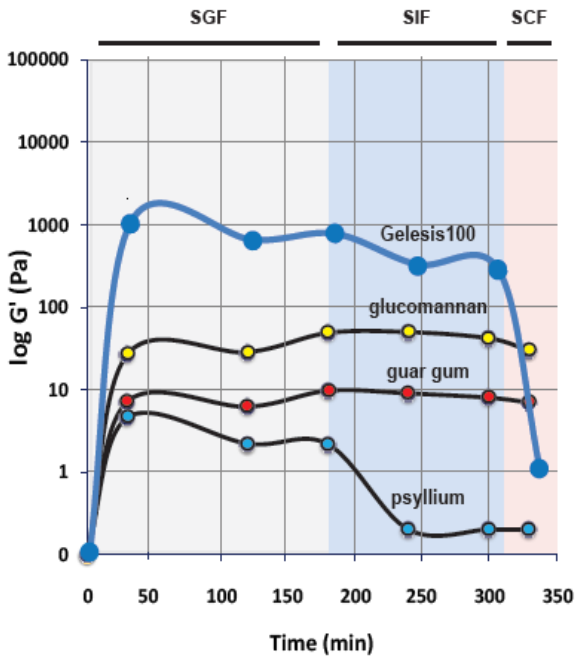




- Only superabsorbent made from **food-grade building blocks**
- **Biocompatible and biodegradable**
- Able to **absorb** amount of **water ~100x** its dry weight (superabsorbent)
- In fully hydrated state, ~1-2mm diameter with **elasticity/firmness** like leafy vegetables (eg, **lettuce)**
- Particles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

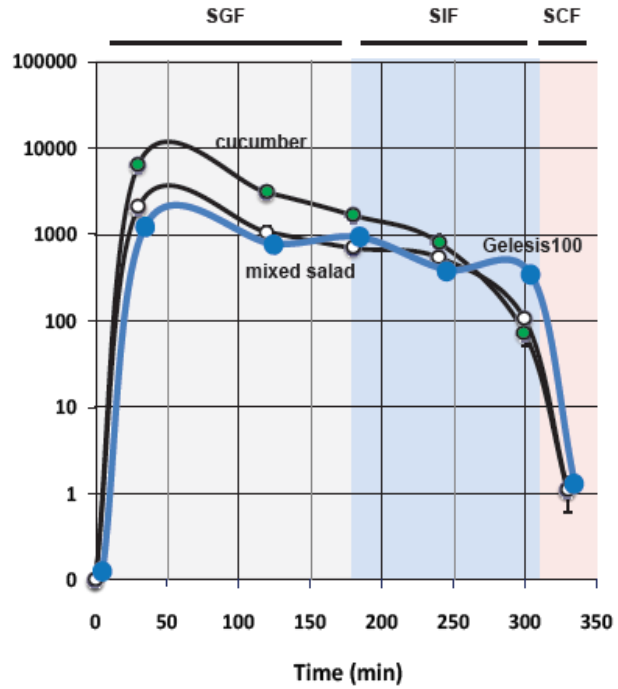
# Gelesis Hydrogels have similar mechanical properties to cellulosic vegetables

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

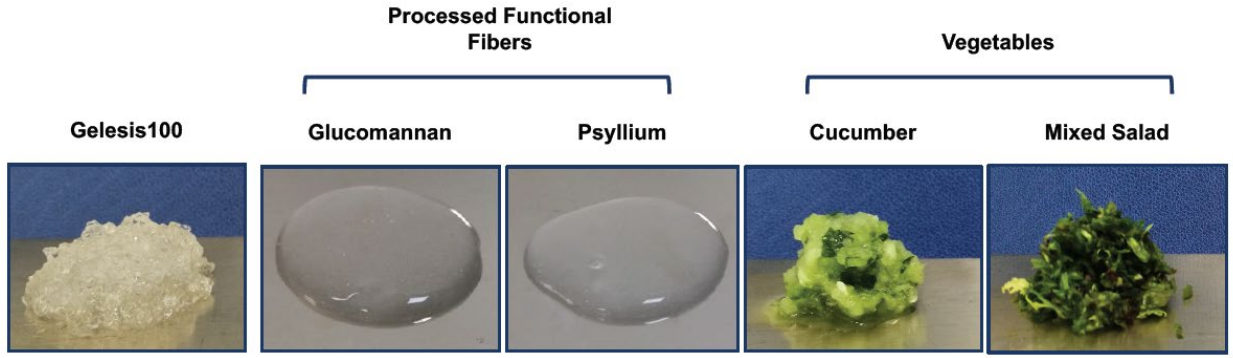
**A. Gelesis100 vs. Processed Functional Fibers**




**B. Gelesis100 vs. Vegetables**



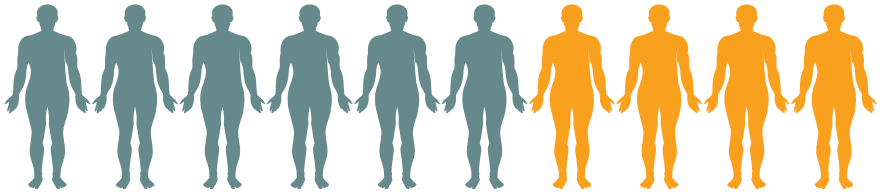

Visual comparison of Gelesis100, processed functional fibers, and vegetables following hydration or mastication



# GLOW: Key Findings

## RESPONDERS

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



**6 in 10 adults**

- 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

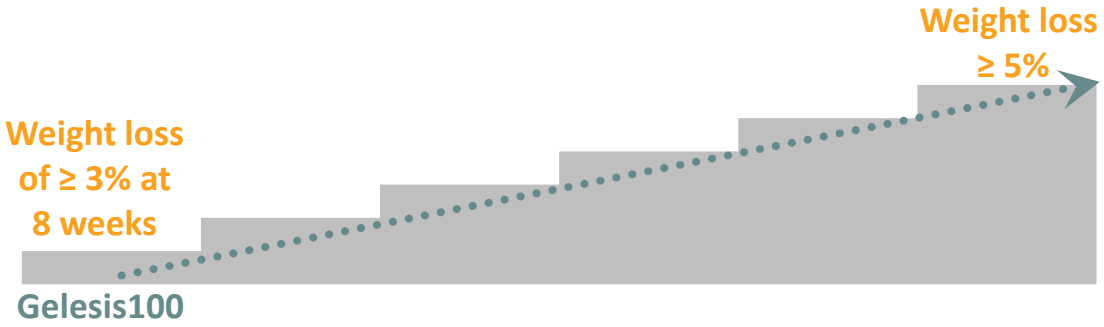
Adults **achieving 10% or greater** weight loss

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

**Coprimary endpoint –** Study results demonstrated statistically superior weight loss with Gelesis100 compared with the 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 vs 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 nonresponders 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%

Gelesis100 [package insert]. Gelesis. Boston, MA; 2019. Greenway FL, 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 significant 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.

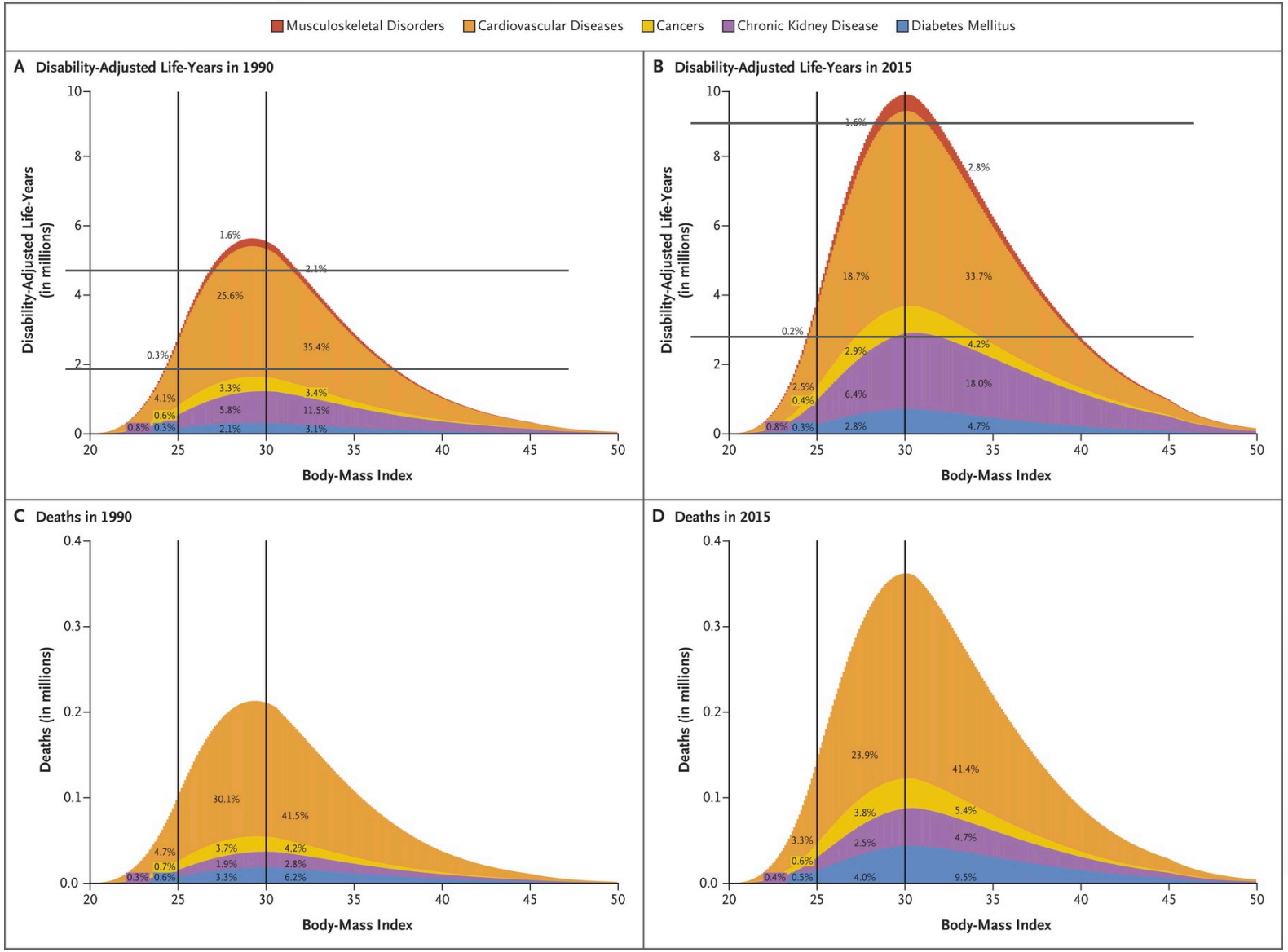
PLENITY [PACKAGE INSERT]. GELESIS. BOSTON, MA; 2019. HTTPS://WWW.FDA.GOV/MEDICAL-DEVICES/CLASSIFY-YOUR-MEDICAL-DEVICE/PRODUCT-MEDICAL-DEVICE

# 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**

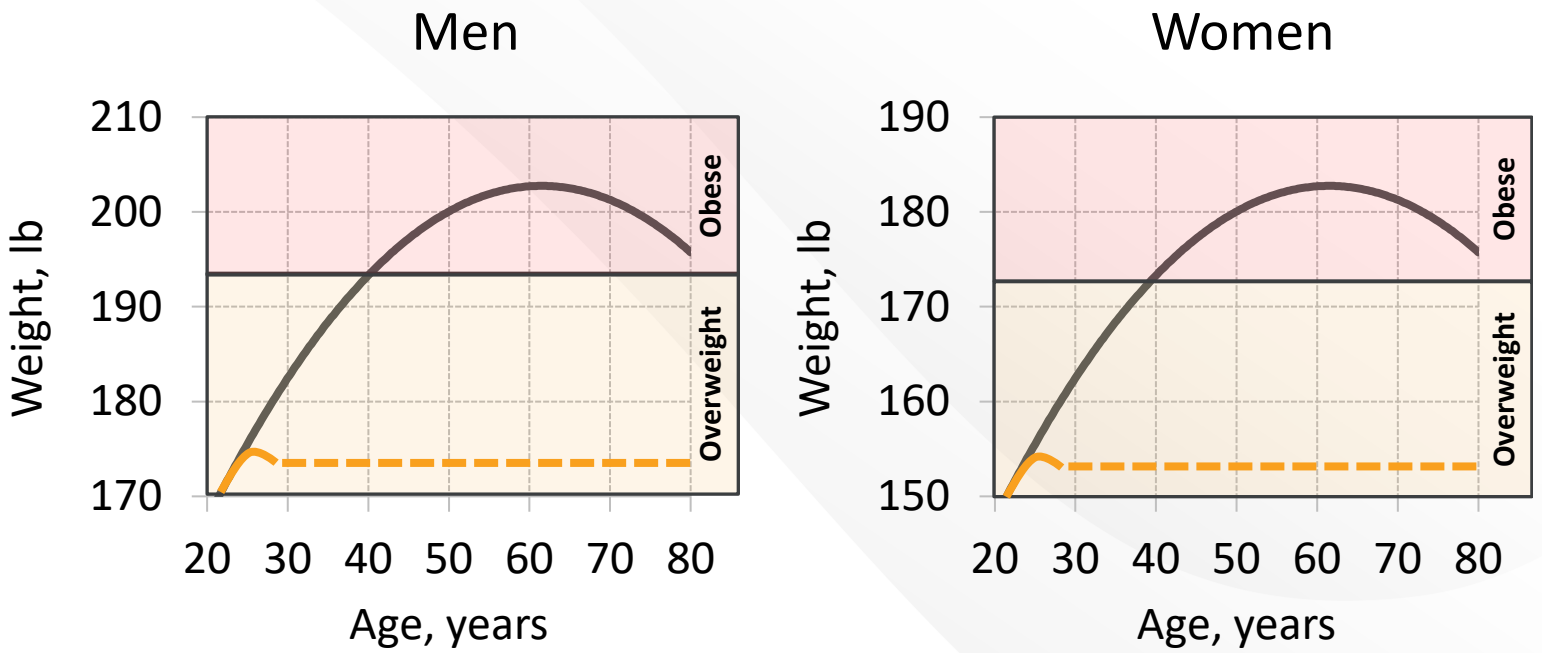
39% of deaths occurred in **overweight**



# 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**

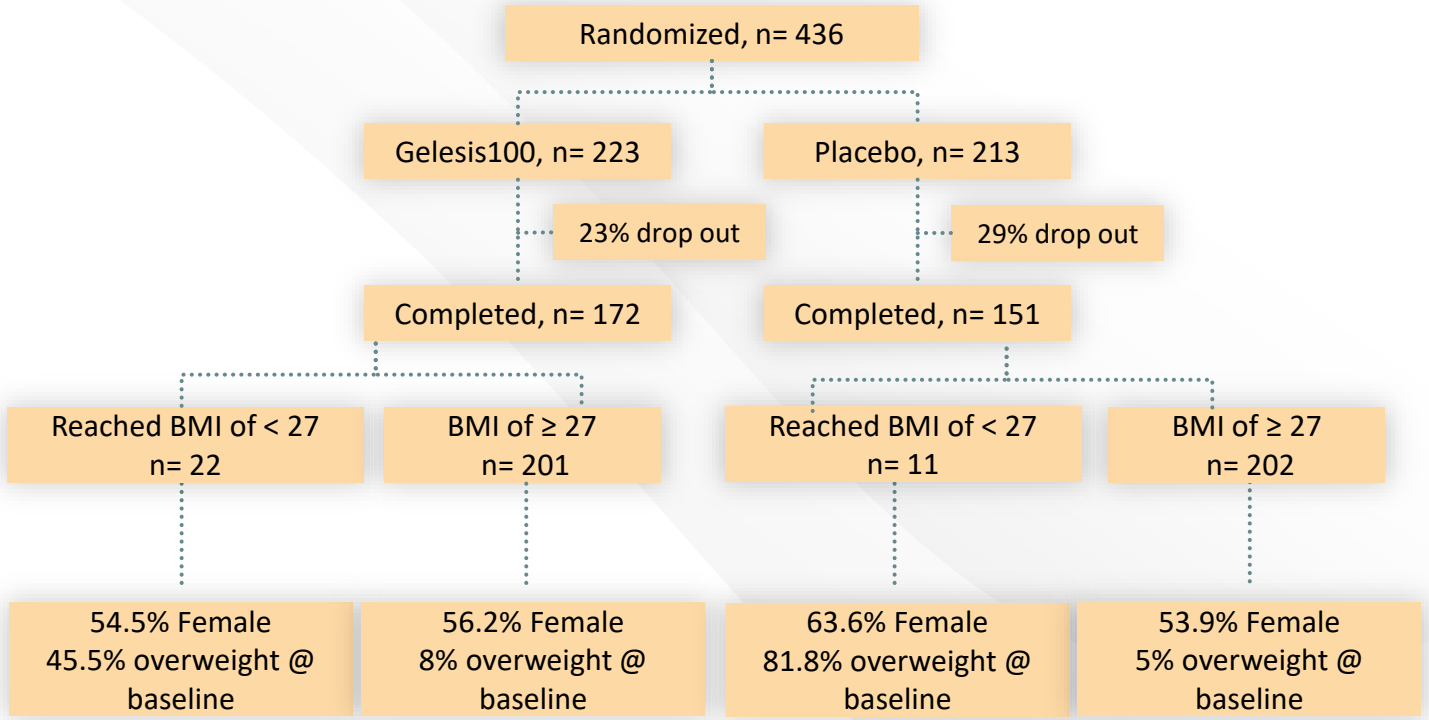



2007-2010 National health and Nutrition Examination Survey (CDC): https://www.cdc.gov/nchs/data/series/sr_11/sr11_252.pdf

1. Mozaffarian D, et al. *N Engl J Med*. 2011;364:2392-2404; 2. Wing RR, et al. *JAMA Intern Med*. 2016;176:755-762; 3. Umashanker D, et al. *Curr Atheroscler Rep*. 2017:19:35.

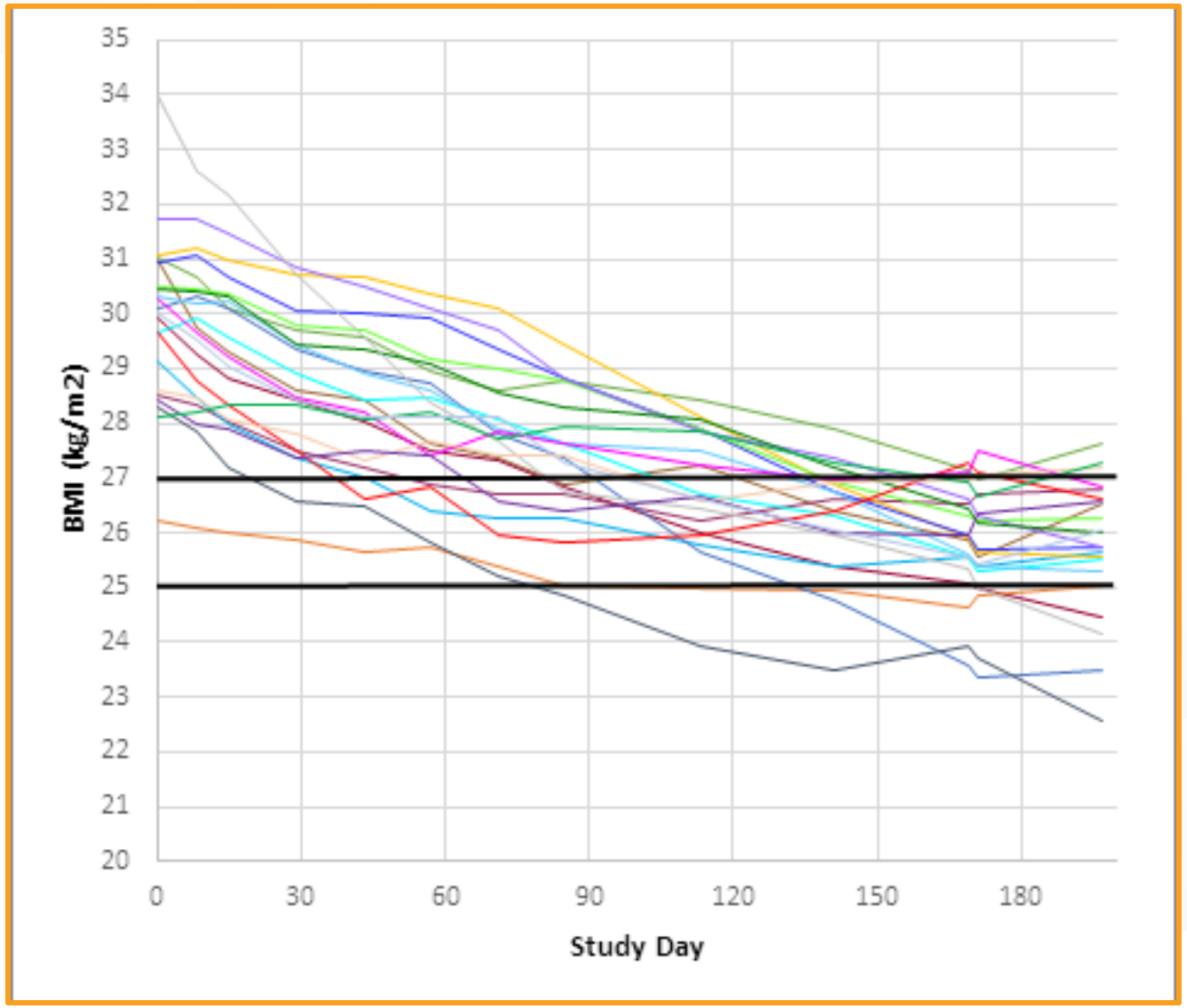
# Subgroup Analysis: BMI < 27 kg/m$^2$

- 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.