# EP4.08 Oral administration of Gelesis200 significantly decreases body weight in people with prediabetes or type 2 diabetes with overweight or obesity: results of the LIGHT-UP study

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## OBJECTIVES

Overweight and obesity are worldwide pandemics causing increased morbidity and mortality. There is a need for alternative therapies that result in meaningful weight loss in addition to diet and exercise, without an increased safety risk, especially in people with type 2 diabetes (T2D) since they typically face increased challenges losing weight and have higher risk of comorbidities.

## MATERIALS-METHODS

LIGHT-UP (NCT03058029), a multicenter, double-blind, randomized, placebo-controlled study, assessed the effects of Gelesis200, a non-systemic, investigational superabsorbent hydrogel, in people with a body mass index (BMI) between 27 and 40 kg/m2, with prediabetes (PD) or T2D (untreated or treated) over 25 weeks.

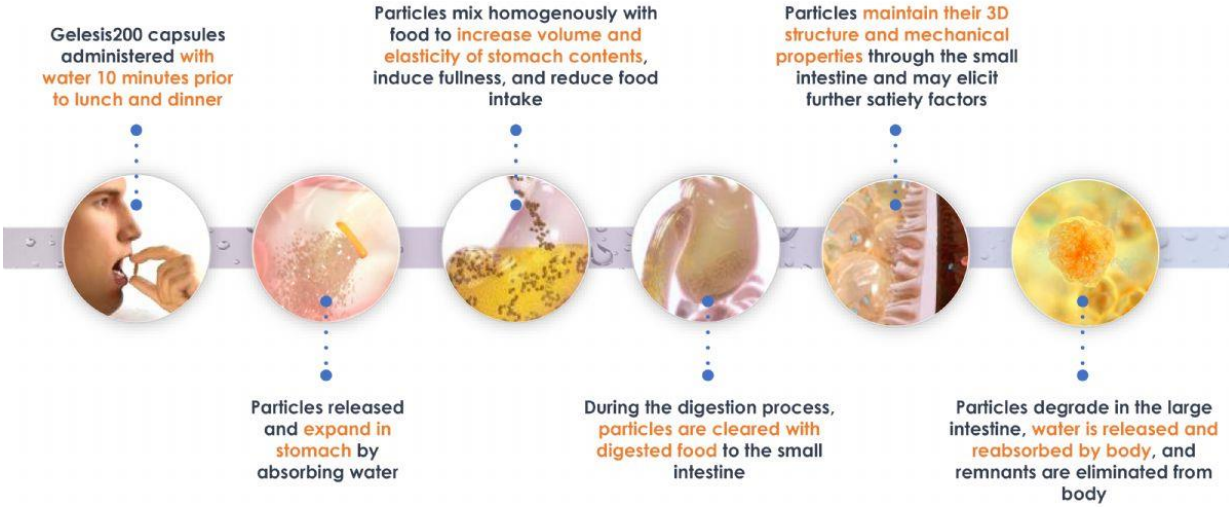
Participants were randomized to 2.10 g of Gelesis200 or placebo in capsules taken with water 10 minutes before lunch and dinner while given advice to support a 300 kcal/day energy-deficit diet with moderate-intensity physical activity (Figure 1).

Co-primary efficacy endpoints were percent of participants with body weight (BW) loss ≥ 5% (Responders at 5%) and percent change in BW from baseline.

Additional efficacy endpoints included Responders at 7.5% and 10% and changes in BMI, excess BW, and waist circumference (WC).

Data were analyzed using Logit models and analysis of covariance with multiple imputation (MI).

**Figure 1**




*Gelesis200 hydrogel in the gastrointestinal tract.*

## RESULTS

The intention-to-treat (ITT) population included 254 adults (males 40.2%, females 59.8%, mean age 49.6 years, mean BMI 34.7 kg/m2, PD 50.8%, untreated T2D 4.3%, treated T2D 44.9%) from 36 investigational sites in Europe and North America (Table 1).

By using MI to include data from ITT population who did not complete the study, 55% of Gelesis200-treated participants were Responders for 5% weight loss vs. 34% in the placebo arm (P = 0.0004). Importantly, Gelesis200-treated participants had 2.83 higher adjusted odds as compared to placebo to become Responders at 5%, achieving the first primary endpoint of the study (Figure 2). The mean BW loss for Responders at 5% was 10.5% (10.6 kg) and their mean WC reduction was 14.3 cm.

Among the 171 participants who completed the study protocol requirements [per protocol (PP) population], 64% of Gelesis200-treated participants were Responders for 5% weight loss vs. 41% in the placebo arm (P = 0.0010) (Figure 3).

With respect to BW loss, the entire Gelesis200 treatment arm (including both Responders and non-Responders for 5% weight loss) demonstrated superiority over placebo after 25 weeks (BW loss of 6.9% vs. 4.3%, P = 0.0011 in the ITT population and 7.1% vs. 4.6%, P = 0.0029 in the PP population), thereby achieving the second primary endpoint (Figure 2 and Figure 3). Weight loss was similar between people with PD and T2D.

Changes in weight-related parameters are reported in Table 2 and Table 3, for the ITT and PP populations, respectively.

The most common treatment-emergent adverse events (TEAEs) by system organ class in the safety population are reported in Table 4. Overall, there were no significant differences in the incidence and severity of TEAEs between the 2 arms except for the incidence of constipation which was higher with Gelesis200 vs. placebo (14.3% vs. 3.9%) but with no severe cases. No serious TEAEs related to Gelesis200 were observed. Less than 2% of the Gelesis200-treated participants dropped out of the study due to TEAEs, which was similar to the dropout rate in the placebo arm.

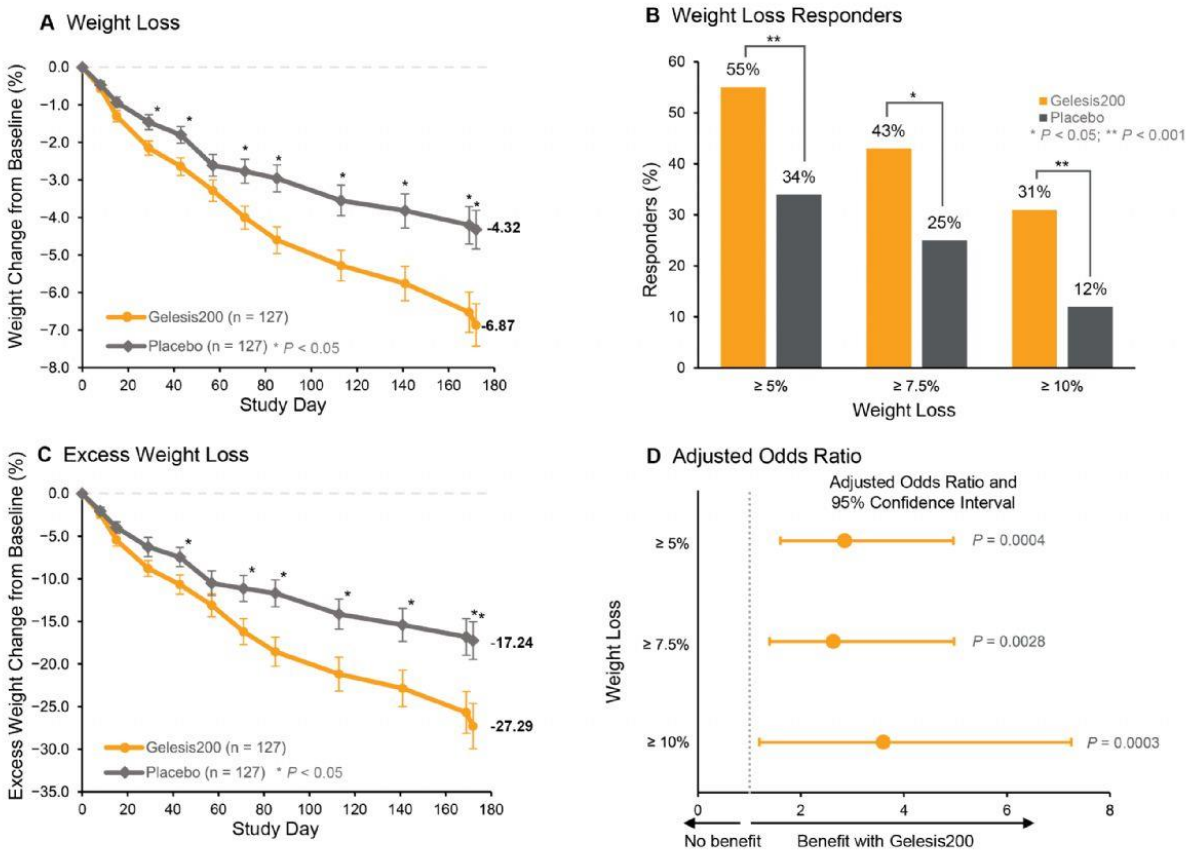
**Table 1**

| Parameter | Gelesis200 (n = 127) | Placebo (n = 127) | *P* value |
|---|---|---|---|
| Female, n (%) | 76 (59.8) | 76 (59.8) | NS |
| Postmenopausal, n (%) | 28 (22.0) | 30 (23.6) | NS |
| Age (years)* | 50.1 ± 10.7 | 49.1 ± 10.8 | NS |
| BW (kg)* | 100.7 ± 15.5 | 101.0 ± 17.4 | NS |
| BMI ($kg/m^2$)* | 34.8 ± 3.4 | 34.6 ± 3.4 | NS |
| Overweight, n (%) | 13 (10.2) | 13 (10.2) | NS |
| Obese, n (%) | 114 (89.8) | 114 (89.8) | NS |
| WC (cm)* | 114.3 ± 11.4 | 113.1 ± 12.4 | NS |
| Current smokers, n (%) | 23 (18.1) | 19 (15.0) | NS |
| Dyslipidemia, n (%) | 59 (46.5) | 62 (48.8) | NS |
| Hypertension, n (%) | 29 (22.8) | 30 (23.6) | NS |
| PD, n (%) | 63 (49.6) | 66 (52.0) | NS |
| Untreated T2D, n (%) | 6 (4.7) | 5 (3.9) | NS |
| Treated T2D, n (%) | 58 (45.7) | 56 (44.1) | NS |

N: Number of subjects; BW: Body weight; BMI: Body mass index; WC: Waist circumference; PD: Prediabetes; T2D: Type 2 diabetes; NS: Non-significant; *Mean ± SD.

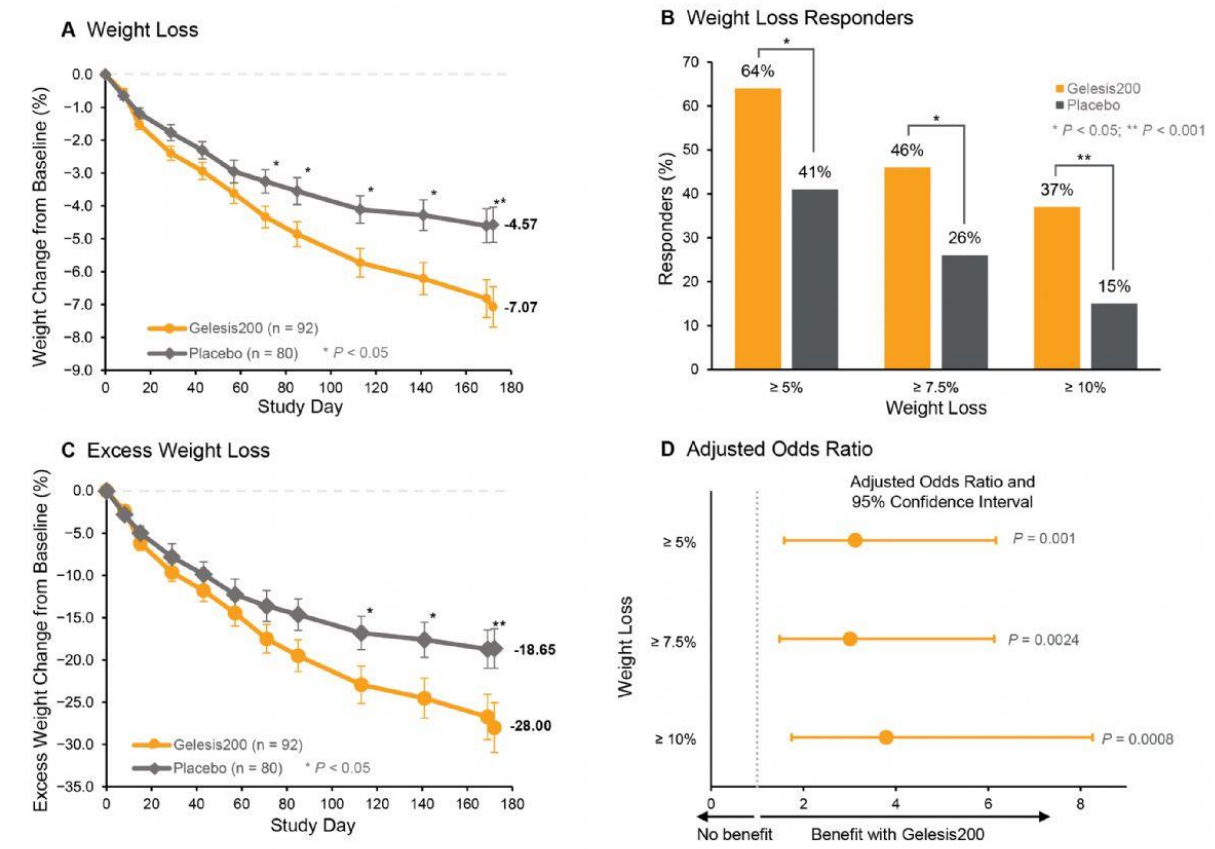
*Baseline characteristics of the intention-to-treat population.*

**Figure 2**




*Weight loss data in the intention-to-treat population.*

**Figure 3**




*Weight loss data in the per protocol population.*

**Table 2**

| Parameter | Gelesis200 (n = 127) | Placebo (n = 127) | *P* value |
|---|---|---|---|
| BW (%)* | -6.9 ± 5.8 | -4.3 ± 5.2 | 0.0011 |
| BMI (%)* | -2.4 ± 2.1 | -1.5 ± 1.8 | 0.0011 |
| Excess BW (%)*, ** | -27.3 ± 27.4 | -17.2 ± 22.3 | 0.0042 |
| WC (cm)* | -9.7 ± 9.0 | -6.8 ± 6.4 | 0.0099 |

N: Number of subjects; BW: Body weight; BMI: Body mass index; WC: Waist circumference; *Mean ± SD; **Calculated as excess BMI over 25.

*Change from baseline of weight-related parameters in the intention-to-treat population.*

**Table 3**

| Parameter | Gelesis200 (n = 92) | Placebo (n = 80) | *P* value |
|---|---|---|---|
| BW (%)* | -7.1 ± 5.9 | -4.6 ± 4.7 | 0.0029 |
| BMI (%)* | -2.5 ± 2.1 | -1.6 ± 1.7 | 0.0023 |
| Excess BW (%)*, ** | -28.0 ± 28.2 | -18.7 ± 20.8 | 0.0160 |
| WC (cm)* | -10.3 ± 9.4 | -7.4 ± 6.1 | 0.0185 |

N: Number of subjects; BW: Body weight; BMI: Body mass index; WC: Waist circumference; *Mean ± SD; **Calculated as excess BMI over 25.

*Change from baseline of weight-related parameters in the per protocol population.*

**Table 4**

| Parameter | Gelesis200 (n = 126) | Placebo (n = 127) | *P* value |
|---|---|---|---|
| Any TEAEs, n (%) | 79 (62.7) | 79 (62.2) | NS |
| Any serious TEAEs, n (%) | 5 (4.0) | 2 (1.6) | NS |
| Infections and infestations, n (%) | 37 (29.4) | 35 (27.6) | NS |
| Gastrointestinal disorders, n (%) | 36 (28.6) | 30 (23.6) | NS |
| Musculoskeletal and connective tissue disorders, n (%) | 16 (12.7) | 14 (11.0) | NS |
| Nervous system disorders, n (%) | 15 (11.9) | 7 (5.5) | NS |
| Injury, poisoning and procedural complications, n (%) | 8 (6.3) | 8 (6.3) | NS |
| Vascular disorders, n (%) | 8 (6.3) | 4 (3.1) | NS |
| Investigations, n (%) | 6 (4.8) | 6 (4.7) | NS |
| Respiratory, thoracic and mediastinal disorders, n (%) | 4 (3.2) | 6 (4.7) | NS |

TEAE: Treatment-emergent adverse event; N: Number of subjects; NS: Non-significant.

*Overall TEAE profile and the most common TEAEs by system organ class in the safety population.*

## CONCLUSIONS

Gelesis200 is a promising new potential therapy for overweight and obesity in people with PD or T2D based on its favorable efficacy and safety data observed in the LIGHT-UP study.