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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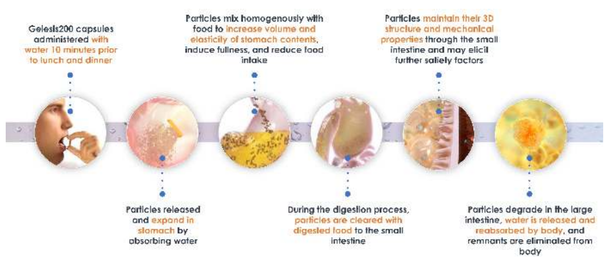
OBJECTIVES

- 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/m^2, 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/m^2, PD 50.8%, untreated T2D 4.3%, treated T2D 44.9%) from 36 investigational sites in Europe and North America (Table 1).

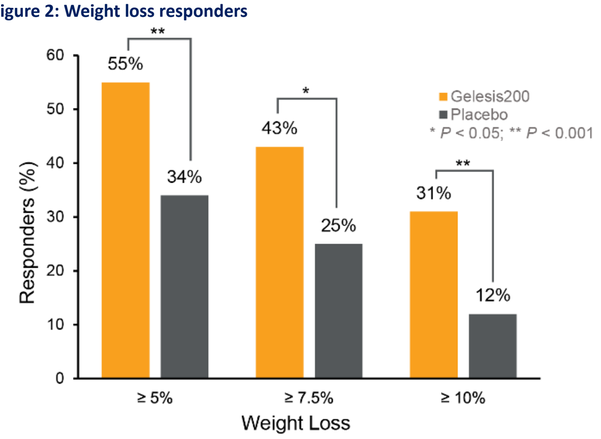
Table 1: Baseline characteristics of the intention-to-treat population

Parameter	Gelesis200 (n = 127)	Placebo (n = 127)	*P* value
Female, n (%)	76 (59.8)	76 (59.8)	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
Obesity, n (%)	114 (89.8)	114 (89.8)	NS
WC (cm)*	114.3 ± 11.4	113.1 ± 12.4	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.

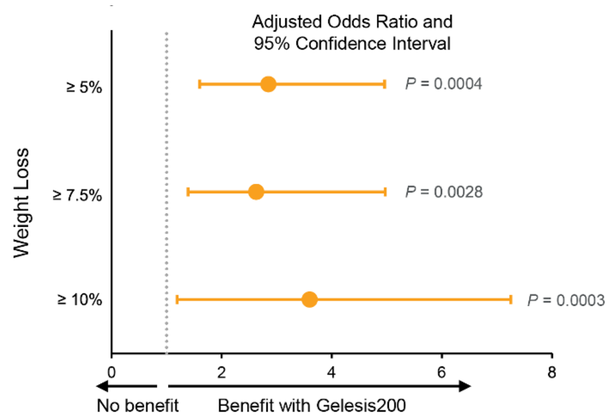
- Regarding weight loss categorical response, 55% of Gelesis200-treated participants were Responders for 5% weight loss vs. 34% in the placebo arm (*P* = 0.0004) (Figure 2).
- The mean BW loss for Responders at 5% was 10.5% (10.6 kg) and their mean WC reduction was 14.3 cm.

Figure 2: Weight loss responders



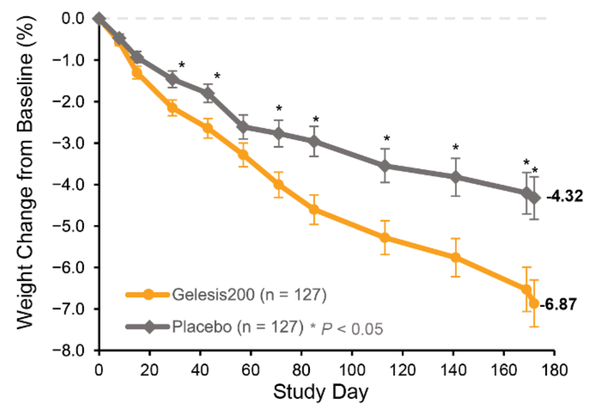
- Importantly, Gelesis200-treated participants had 2.83 higher adjusted odds as compared to placebo to become Responders at 5% (Figure 3).

Figure 3: Adjusted odds ratio



- 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) (Figure 4).

Figure 4: Weight loss over time



- Changes in weight-related parameters are reported in Table 2.

Table 2: Change from baseline of weight-related parameters in the intention-to-treat population

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.

- The most common treatment-emergent adverse events (TEAEs) by system organ class in the safety population are reported in Table 3.
- 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 3: Overall TEAE profile and the most common TEAEs by system organ class in the safety population.

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.

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.

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