Assessment of Early Intervention with Gelesis100 in Overweight and Mild Obesity in the GLOW Study

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T-P-3542

INTRODUCTION

- Gelesis100 (Plenity™) is a non-systemic, superabsorbent hydrogel indicated to aid in weight management in overweight and obese adults with a BMI of 25-40 kg/m^2, when used in conjunction with diet and exercise **(Figure 1)**.
- Gelesis Loss Of Weight (GLOW; NCT02307279), a multicenter, double-blind, placebo-controlled pivotal study, demonstrated that Gelesis100 offers a compelling approach in the management of overweight and obesity given its safety and efficacy profile.

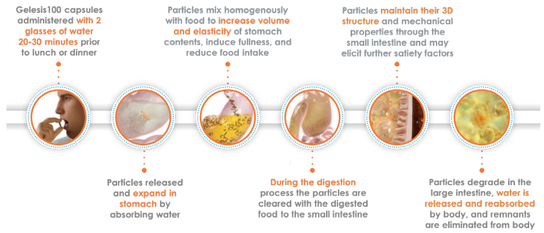
OBJECTIVE

The aim of this subanalysis of the GLOW study is to assess the efficacy, safety, and tolerability of Gelesis100 in subjects with a BMI below 35 kg/m^2.

METHODS

- The GLOW study assessed 436 overweight and obese subjects with BMI between 27 and 40 kg/m^2, with or without type 2 diabetes (T2D).
- Subjects were randomized to Gelesis100 arm (2.25g twice daily) or placebo (sucrose) arm (2.70g twice daily). Treatment was administered with 500 mL of water 20-30 minutes before lunch and dinner, in a double-blind, parallel-group fashion, over 24 weeks, in subjects on hypocaloric diet (-300 kcal/day).
- Co-primary efficacy endpoints were body weight (percent change) and body weight responders at 5% (percent subjects with ≥ 5% body weight loss).
- This subgroup analysis evaluated Gelesis100 specifically in subjects with a BMI < 35kg/m^2 at baseline

Figure 1. Gelesis100 hydrogel in the gastrointestinal tract



RESULTS

Of the 436 subjects who were randomized in the GLOW study and constituted the intention-to-treat (ITT) population (223 in the Gelesis100 arm, 213 in the placebo arm), 284 had a BMI below 35 kg/m^2 **(Table 1)**.

Table 1. Demographics and baseline characteristics of the ITT population.

Parameter	Gelesis100 (n = 155)	Placebo (n = 129)	P value
Female, n (%)	85 (55)	74 (57)	NS
Age (years)*	47.9 ± 10.3	48.9 ± 10.5	NS
Weight (kg)*	93.0 ± 12.3	94.3 ± 12.4	NS
BMI (kg/m^2)*	31.8 ± 1.9	32.0 ± 2.0	NS
Overweight, n (%)	26 (17)	21 (16)	NS
Obese Class I, n (%)	129 (83)	108 (84)	NS
Waist circumference (cm)*	105.3 ± 9.0	106.2 ± 9.3	NS
Postmenopausal, n (%)	39 (46)	34 (46)	NS
Current smokers, n (%)	16 (10)	11 (9)	NS
Dyslipidemia, n (%)	105 (68)	94 (73)	NS
Hypertension, n (%)	42 (27)	36 (28)	NS
Prediabetes, n (%)	36 (23)	35 (27)	NS
T2D, n (%)	13 (8)	14 (11)	NS

*Mean ± SD; NS: non-significant.

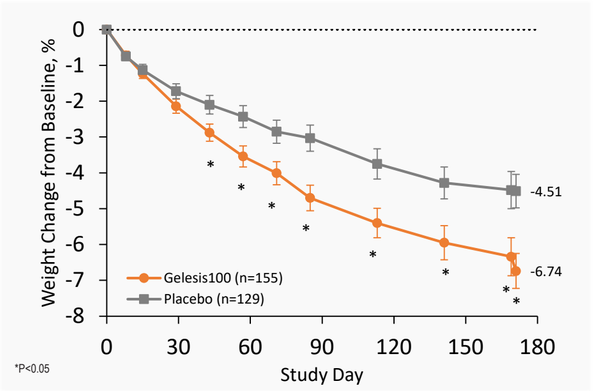
The mean (± SD) body weight losses from baseline to the end of treatment were 6.7 ± 6.1% and 4.5 ± 5.3%, with Gelesis100 and placebo, respectively **(Table 2 & Figure 2)**.

Table 2. Change from baseline (mean ± SD) of weight-related parameters in the ITT population.

Parameter	Gelesis100 (n = 155)	Placebo (n = 129)	P value
BMI (kg/m^2)	-2.1 ± 1.9	-1.4 ± 1.7	0.0056
EEBW (%)*	-34.0 ± 33.3	-24.6 ± 28.6	0.0448
Waist circumference (cm)	-7.0 ± 5.6	-4.5 ± 6.0	0.0021

*EEBW is calculated as excess body weight over a BMI of 25.

Figure 2. Percent change in body weight from baseline by treatment group.

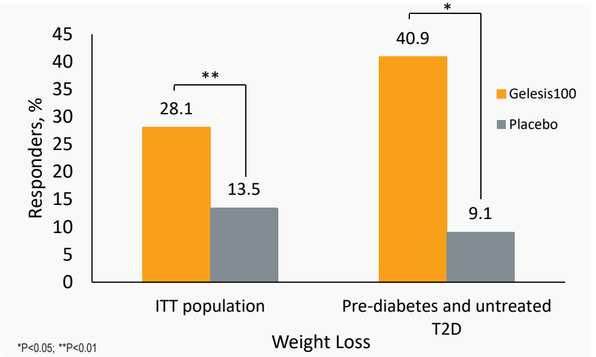


*P<0.05

Gelesis100-treated subjects had twice the odds of achieving ≥ 5% and ≥ 10% weight loss vs. placebo (adjusted OR: 1.9; P = 0.0269 and 2.8; P = 0.0064, respectively).

In completers with prediabetes and untreated T2D (22 in the Gelesis100 arm, 22 in the placebo arm) the adjusted odds of being super-responders (≥10% weight loss) were 8 times higher with Gelesis100 compared with placebo (40.9% vs. 9.1%, P = 0.0312) **(Figure 3).**

Figure 3. Percent responders with ≥ 10% weight loss



*P<0.05; **P<0.01

Safety and tolerability of Gelesis100 were similar to placebo, except for the incidences of overall gastrointestinal AEs and abdominal distention that were higher in the Gelesis100 arm **(Table 3)**.

Table 3. Subjects with the most common AEs in the ITT population.

Parameter	Gelesis100 (n = 155)	Placebo (n = 129)	P value
Any AE, n (%)	116 (75)	91 (71)	NS
Treatment-related (most probably or possibly) AE, n (%)	65 (42)	41 (32)	NS
Any SAE, n (%)	0 (0)	0 (0)	NS
Any gastrointestinal AE, n (%)	71 (46)	41 (32)	0.0204
Diarrhea, n (%)	21 (14)	12 (9)	NS
Abdominal distension, n (%)	20 (13)	7 (5)	0.0414
Flatulence, n (%)	13 (8)	6 (5)	NS
Infrequent bowel movements, n (%)	13 (8)	4 (3)	NS
Abdominal pain, n (%)	11 (7)	4 (3)	NS
Constipation, n (%)	8 (5)	6 (5)	NS
Nausea, n (%)	7 (5)	6 (5)	NS

NS: non-significant.

CONCLUSIONS

- **In subjects with overweight or mild obesity, despite not meeting the pre-defined super-superiority margin of 3%, treatment with Gelesis100 doubled the odds of achieving clinically meaningful weight loss (≥5%).**
- **In those with prediabetes and untreated T2D, the odds of being super-responders (≥10%) were 8 times higher with Gelesis100 compared with placebo.**
- **There were no differences in the incidence and severity of AEs between Gelesis100 and placebo arms except for the overall incidence of gastrointestinal AEs and the incidence of abdominal distension.**
- **Given its safety and efficacy profile, Gelesis100 offers a compelling approach to aid in weight management in overweight and obesity.**
- **Gelesis100 may shift the focus of weight management treatment towards lower BMI.**

DISCLOSURES

FLG, LJA, AR, AA, CMA, JOH, LMK, KF, EM, SS, LL, LG, SNC, JAM, and **CDS** are investigators/advisors and received financial support/honorarium/stock options from Gelesis. **HL** and **HMH** work for Gelesis and own Gelesis stock or stock options.

GELESIS

Presented at ObesityWeek 2019, Las Vegas, NV, November 7, 2019