Comprehensive analysis of safety and tolerability of Gelesis100 in overweight and obesity in the pivotal GLOW study

Luzi L[1], Raben A[2], Astrup A[2], Matejkova E[3], Svacina S[4], Gnessi L[5], Navas-Carretero S[6], Martinez JA[7], Fujioka K[8], Greenway FL[9], Aronne LJ[10], Apovian CM[11], Kaplan LM[12], Hill JO[13], Still CD[14], Urban LE[15], Leider H[15], Heshmati HM[15]

[1]University of Milan, [2]University of Copenhagen, [3]Health & Care, [4]General Hospital in Prague, [5]Sapienza University of Rome, [6]University of Navarra, [7]CIBERobn, [8]Scripps Clinic, [9]Pennington Biomedical Research Center, [10]Weill Cornell Medicine, [11]Boston University, [12]Massachusetts General Hospital, [13]University of Alabama at Birmingham, [14]Geisinger Obesity Institute, [15]Gelesis, Inc

INTRODUCTION

- Gelesis100 (Plenity™) is an oral, 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.

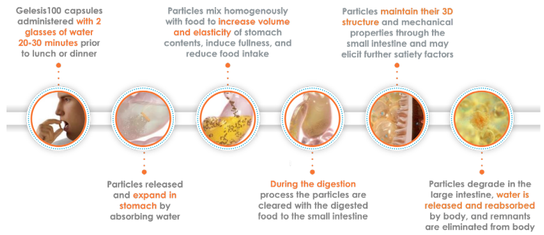
OBJECTIVE

- The objective of the GLOW study was to evaluate the safety and efficacy of Gelesis100 in patients with overweight or obesity.
- This presentation provides a comprehensive analysis of the safety data of the GLOW study.

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 (2.25 g twice daily) or placebo (sucrose) arm (2.70 g 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).
- The safety and tolerability were assessed by recording adverse events (AEs) and serious AEs (SAEs), and monitoring results from physical examination, vital signs, and fasting laboratory tests, including hematology, blood chemistry, and serum vitamins.

Figure 1. Gelesis100 hydrogel in the gastrointestinal tract



RESULTS

436 subjects were randomized in the GLOW study and constituted the intention-to-treat (ITT) population (223 in the Gelesis100 arm, 213 in the placebo arm) **(Table 1)**.

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

Parameter	Gelesis100 (n = 223)	Placebo (n = 213)	P value
Female, n (%)	125 (56.1)	120 (56.3)	NS
Age (years)*	48.2 ± 9.9	47.8 ± 10.9	NS
Weight (kg)*	97.6 ± 14.4	100.6 ± 15.3	0.0348
BMI (kg/m^2)*	33.5 ± 3.2	34.1 ± 3.2	NS
Overweight, n (%)	26 (11.7)	21 (9.9)	NS
Obese Class I, n (%)	129 (57.8)	108 (50.7)	NS
Obese Class II, n (%)	68 (30.5)	84 (39.4)	NS
Waist circumference (cm)*	108.3 ± 10.7	110.7 ± 11.0	0.0249

*Mean ± SD; NS: non-significant.

The mean (± SD) body weight losses from baseline to the end of treatment were 6.4 ± 5.8% and 4.4 ± 5.5% (P = 0.0007), in the Gelesis100 and placebo arms, respectively.

No significant differences between the Gelesis100 and placebo arms were observed in the overall rate of AEs **(Table 2)**.

Table 2. AEs characteristics in the safety population.

Parameter	Gelesis100 (n = 223)	Placebo (n = 211)
Subjects with any AE, n (%)	159 (71.3)	149 (70.6)
Subjects with severe AE, n (%)	8 (3.6)	10 (4.7)
Subjects with moderate AE, n (%)	88 (39.5)	83 (39.3)
Subjects with mild AE, n (%)	124 (55.6)	117 (55.5)
Subjects withdrawal due to AE, n (%)	8 (3.6)	7 (3.3)
Subjects with any SAE, n (%)	0 (0.0)	1 (0.5)

Gastrointestinal (GI)-related AEs were reported more frequently in the Gelesis100 arm (P = 0.0248) **(Table 3)**.

Table 3. Overview of treatment-related AEs in the safety population.

Parameter	Gelesis100 (n = 223)	Placebo (n = 211)	P value
Any AE probably or possibly related, n (%)	88 (39.5)	64 (30.3)	0.0557
Eye disorders, n (%)	0 (0.0)	1 (0.5)	0.4862
GI Disorders, n (%)	84 (37.7)	58 (27.5)	0.0248
General disorders and administration site conditions, n (%)	1 (0.4)	1 (0.5)	1.0000
Infections and infestations, n (%)	2 (0.9)	1 (0.5)	1.0000
Investigations, n (%)	3 (1.3)	3 (1.4)	1.0000
Metabolism and nutrition disorders, n (%)	0 (0.0)	4 (1.9)	0.0551
Musculoskeletal and connective tissue disorders, n (%)	2 (0.9)	0 (0.0)	0.4992
Nervous system disorders, n (%)	4 (1.8)	2 (0.9)	0.6860
Renal and urinary disorders, n (%)	1 (0.4)	0 (0.0)	1.0000
Reproductive system and breast disorders, n (%)	0 (0.0)	1 (0.5)	0.4862
Respiratory, thoracic, and mediastinal disorders, n (%)	1 (0.4)	1 (0.5)	1.0000
Skin and subcutaneous tissue disorders, n (%)	1 (0.4)	3 (1.4)	0.3599

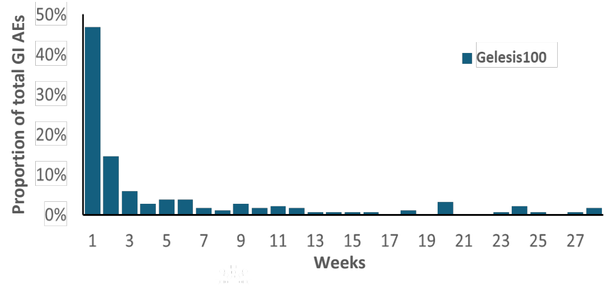
The most common GI-related AEs in the Gelesis100 arm were abdominal distension, diarrhea, infrequent bowel movements, flatulence, abdominal pain, and constipation **(Table 4)**.

Table 4. Individual GI-related AEs in the safety population.

Parameter	Gelesis100 (n = 223)	Placebo (n = 211)	P value
GI-related AEs, n (%)	84 (37.7)	58 (27.5)	0.0248
Abdominal distension, n (%)	24 (10.8)	12 (5.7)	0.0579
Diarrhea, n (%)	23 (10.3)	16 (7.6)	0.4015
Infrequent bowel movements, n (%)	20 (9.0)	10 (4.7)	0.0910
Flatulence, n (%)	19 (8.5)	10 (4.7)	0.1272
Abdominal pain, n (%)	11 (4.9)	6 (2.8)	0.3258
Constipation, n (%)	10 (4.5)	10 (4.7)	1.0000

Most GI-related AEs with Gelesis100 occurred within the first two weeks of therapy initiation **(Figure 2)** and the majority of them (62.4%) resolved within two weeks of onset.

Figure 2. Incidence of GI-related AEs in the Gelesis100 arm.



There were no differences in the changes in hematology, blood chemistry (including serum sodium, potassium, calcium, and magnesium), and serum vitamins (vitamins A, B1, B2, B6, B9, B12, D, and E) between the two arms.

CONCLUSIONS

- **Other than a small increase in the incidence of overall GI AEs, there were no differences in the incidence and severity of AEs between the Gelesis100 and placebo arms.**
- **No clinically-meaningful changes were observed in hematology or chemistry.**
- **Gelesis100 (Plenity™) is a safe and well-tolerated therapy to aid in weight management in overweight and obesity.**

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. **LEU, HL** and **HMH** work for Gelesis and own Gelesis stock or stock options.

GELESIS

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Poster Talk Track

- Introduction – Dr. Ken Fujioka, director of the Nutrition and Metabolic Research Center at Scripps Clinic, in San Diego, California.
- Title of presentation – Comprehensive analysis of safety and tolerability of Gelesis100 in overweight and obesity in the pivotal GLOW study.
- Gelesis100, which is known commercially by the brand name Plenity, is a non-systemic, superabsorbent hydrogel which has been FDA-cleared for weight management in patients with overweight and obesity with a BMI 25-40 kg/m2, when used in conjunction with diet and exercise.
- The objective of the Gelesis Loss of Weight study, or GLOW, was to demonstrate the safety and efficacy of Gelesis100 in patients with overweight or obesity. It was a double-blinded, placebo-controlled study of 436 patients with overweight and obesity and was 6 months in duration. This presentation focuses specifically on the safety data.
- At the end of the 6-month study period, the overall rate of adverse events and the severity of adverse events was not statistically different between patients randomized to Gelesis100 or placebo.
- Looking specifically at adverse events categorized by system organ class, we can see that gastrointestinal adverse events did occur more frequently in patients who used Gelesis100, the most common being abdominal distention, diarrhea, infrequent bowel movements, and flatulence. Although there was a numerical difference in the occurrence of these individual adverse events, none of these reached the level of statistical significance.
- Most gastrointestinal adverse events with Gelesis100 occurred within the first two weeks of therapy initiation and most resolved within two weeks of onset.
- Lastly, there were no clinically-meaningful changes between both groups in terms of abnormal hematology or clinical chemistries.
- Thank you for your attention.