Plenity™

Instructions for Use

Rx Only

Gelesis, Inc.

Contents

1. PRODUCT DESCRIPTION

Plenity™ is an oral capsule that promotes fullness and may help to increase satiety to help patients manage their weight. Plenity is nonsystemic and works directly in the gastrointestinal (GI) tract. Plenity is made from two natural ingredients, cellulose and citric acid, that form a three-dimensional matrix designed to occupy volume in the stomach and small intestine, to create a sensation of fullness.

Each Plenity capsule contains thousands of superabsorbent hydrogel particles (0.75 grams [g] per capsule), and each particle is approximately the size of a grain of salt. Patients consume three (3) capsules (2.25 g/dose) with water before both lunch and dinner.

The capsules disintegrate in the stomach and release the Plenity particles, which can hydrate up to 100 times their original weight. When fully hydrated, the individual nonclustering Plenity particles occupy about a quarter of average stomach volume. The gel particles mix with ingested foods, creating a larger volume with higher elasticity and viscosity in the stomach and small intestine, promoting satiety and fullness.

Plenity passes through the digestive system, maintaining its three-dimensional structure in the stomach and small intestine before breaking down in the colon. The water is then released and reabsorbed by the body. Plenity particles are eliminated through normal bowel movements (not absorbed).

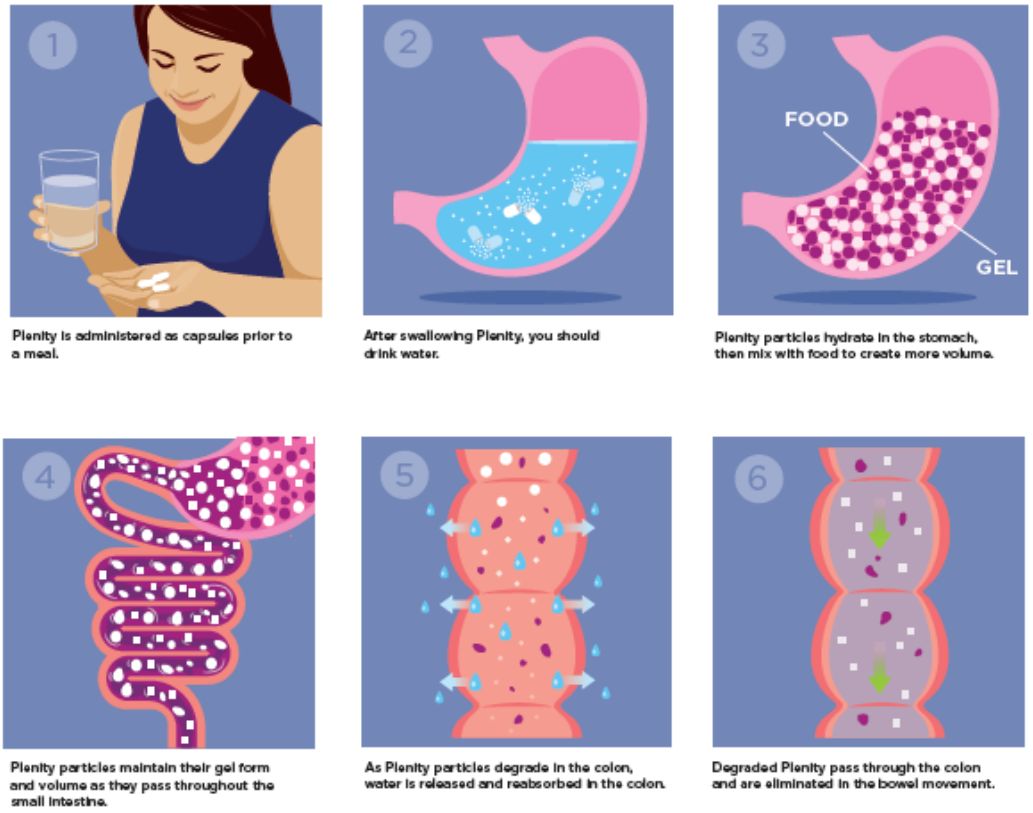


Figure 1. Ingestion and passage through GI tract

1.1. How Supplied

Plenity is supplied in double blister packs that, together, provide the two doses patients take daily. Each individual blister pack holds a single dose of three (3) capsules, to be administered with water before lunch and dinner.

Seven (7) double blister packs are supplied in a weekly package.

Figure 2. Double blister pack, front and back

1.2. Storage

- Blister packs should be kept closed and stored at room temperature between 5° Celsius (C) and 30°C [41°-86° Fahrenheit (F)].
- **Plenity should be kept in its original blister packs until use to avoid humidity causing hydration before ingestion.**

2. INDICATIONS FOR USE

Plenity is indicated to aid in weight management in overweight and obese adults with a Body Mass Index (BMI) of 25-40 kg/m^2, when used in conjunction with diet and exercise.

3. CONTRAINDICATIONS

Plenity is contraindicated in the following conditions:

- Pregnancy
- History of allergic reaction to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium oxide

4. WARNINGS

Read this package insert in its entirety before using Plenity.

Keep out of reach of children.

Plenity may alter the absorption of medications. Please review Section 6 and 8.3 carefully.

Do not use Plenity after the expiration date printed on the product packaging.

5. PRECAUTIONS

- Patients should contact a healthcare provider (HCP) immediately if a severe or continued adverse event occurs. If a severe allergic reaction, severe abdominal pain, or severe diarrhea occurs, patients should discontinue the product until speaking with an HCP.
- Patients with symptoms of dysphagia that may affect ability to swallow capsules are likely to have difficulty swallowing the capsule.
- Patients should not consume Plenity if the package is damaged.
- If any capsules are broken, crushed, or damaged, they should be discarded.
- Use with caution in patients with active gastrointestinal conditions such as gastro-esophageal reflux disease (GERD), ulcers, or heartburn.
- Avoid using in patients with the following conditions:
  - Esophageal anatomic anomalies, including webs, diverticuli, and rings.
  - Suspected strictures (such as patients with Crohn's disease).
  - Complications from prior gastrointestinal surgery that could affect GI transit and motility.
- Plenity is NOT a food substitute. It is not absorbed by the body and therefore has no nutritional or caloric value.
- Plenity should be taken under the direction of an HCP as part of a structured weight loss program. Failure to adhere to prescribed dietary and exercise instructions may result in failure to lose weight.

6. DIRECTIONS FOR USE

Plenity should be taken with water twice a day, 20-30 minutes before lunch and 20-30 minutes before dinner. Each dose includes 3 capsules of Plenity provided in a single blister pack.

For each dose, patients should follow these steps:

1. Swallow 3 capsules with water.
2. After taking the capsules, drink 2 additional glasses of water (8 fl oz/250 mL each).
3. Wait 20-30 minutes to begin the meal.

If a pre-meal dose is missed, instruct the patient to take Plenity during or immediately after that meal.

To avoid impact on the absorption of medications:

- The effect of concurrent use of Plenity on all medications is not known. Therefore, all medications that are taken once daily should be taken in the morning (fasting or with breakfast) or at bedtime as prescribed by your physician.
- If a patient is taking the medication with meals or close to meals, the prescriber should consider the known effect of concurrent use with metformin as a guide to determine if the risk of incorrect dosing, especially for narrow therapeutic drugs, is outweighed by the potential benefit from Plenity
- For all medications that should be taken with food, the medication should be taken after the meal has started.
- As is prudent with changes to diet or medication, for those patients who take metformin with meals it is recommended that glycemic control is monitored after initiation of Plenity to determine if a dose change is required.
  The pharmacokinetic profile of metformin, administrated with and without Plenity, both with food and in a fasted state, is shown in Section 8.3, Table 15 and Figure 7a and b.

7. POTENTIAL ADVERSE REACTIONS

Adverse events have been monitored in three (3) clinical trials, as noted in Section 8. In the GLOW pivotal trial, during the 24-week assessment period, the overall incidence of adverse events in the Plenity treatment group was no different than placebo (71% in both groups). In both treatment groups, most (>95%) adverse events were assessed by the investigator as mild or moderate in intensity. There were no serious adverse events (SAEs) in the Plenity treatment group, whereas there was one (1) SAE in the placebo treatment

group. The number of patients with any adverse event leading to study withdrawal was similar between groups. No deaths occurred during the trial.

Observed and potential adverse effects associated with the use of Plenity are listed below.

Table 1. Potential Adverse Events

Potential adverse events (rates observed compared to placebo)*		
Greater than placebo	**Equivalent to placebo**	**Not observed**
• All GI-related adverse events combined (98% mild or moderate)	• Abdominal distension • Abdominal pain • Bloating • Bowel movement irregularity • Changes to frequency and consistency of bowel movements • Constipation • Cramping • Diarrhea • Dyspepsia • Dysphagia • Eructation • Flatulence • Gastroesophageal reflux disease • Vomiting	• Adverse health consequences resulting from weight loss • Allergic Reaction • Bowel obstruction • Choking • Death • Dehydration • Electrolyte abnormalities • Fecal incontinence • GI atonia or hypomotility • Interactions with absorption of other ingested medication • Need for emergency surgery

*Rates observed in GLOW pivotal study.

8. CLINICAL STUDIES

The safety and effectiveness of Plenity were studied in the 6 month GLOW pivotal trial and supported by additional studies including the GLOW-EX 6 month extension trial and a drug-product interaction study.

8.1. GLOW (Gelesis Loss Of Weight) Pivotal Trial

8.1.1. Study Design

The Gelesis Loss Of Weight (GLOW) trial (ClinicalTrials.gov, NCT02307279) was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study assessing the safety and efficacy of 2.25g of Plenity on body weight over 24 weeks in 436

overweight and obese subjects (with and without type 2 diabetes). Subjects were randomized to 2.25g Plenity or placebo. All subjects were prescribed reduced caloric intake and exercise.

Enrollment included patients aged 22-65 years with BMI 27-40 kg/m^2. Those with BMI <30 kg/m^2 needed to have at least one of the following comorbidities: type 2 diabetes (untreated or metformin-treated), dyslipidemia, or hypertension. Fasting glucose was required to be between ≥90 mg/dL and ≤145 mg/dL (≥5.0 mmol/L and ≤8.1 mmol/L). Patients were excluded if pregnant, had known type 1 diabetes, or a known history of gastrointestinal or endocrine disease.

8.1.2. Study Endpoints

The co-primary effectiveness endpoints were included in an intent-to-treat, multiple imputation (ITT-MI) analysis of change in body weight from baseline to Day 171.

- Margin of 3% of the percent total body weight loss for the Plenity arm compared to the placebo arm
- More than 35% of subjects on Plenity achieving at least 5% total body weight loss (performance goal)

The safety endpoint was the incidence of all adverse events (AEs) and serious adverse events (SAEs) in an analysis of the safety population, defined as the cohort containing any subject receiving the treatment after randomization.

Secondary and tertiary endpoints were analyzed in a hierarchical fashion using a closed test procedure.

The ITT population is set of all randomized subjects. The ITT-multiple imputation (ITT-MI) population was the primary group analyzed for primary and secondary endpoints, and includes all randomized subjects with multiple imputation performed for missing primary and secondary endpoint data. The ITT-observed (ITT-Obs) population is the set of all randomized subjects who completed the study. This population was used to analyze the tertiary endpoints and for all exploratory analyses.

8.1.3. Study Population Demographics and Baseline Parameters

Between November 2014 and November 2016, 904 subjects were screened and enrolled in the GLOW study. From that group, 436 subjects were randomized 1:1 to take Plenity (n=223) or placebo (n=213). A total of 324 subjects completed the study, or 172/223 in the treatment group and 152/213 in the placebo group. Ninety-five subjects withdrew during the study; personal reasons were cited as being most common (Table 3).

Seventeen subjects, or 4% of all treated subjects [7 (3%) in treatment group, and 10 (5%) in placebo group] were lost to follow-up during the study treatment phase.

Demographics and baseline parameters were balanced between the groups, with 56% females in both groups, mean age of 48.2 in the Plenity group and 47.8 in the placebo group (range 24-65 years), and mean BMI of 33.5 in the Plenity group and 34.1 in the placebo group. The mean weight at enrollment was 215.2 lb in the Plenity group and 221.9 lb in the placebo group. Mean blood pressure in the Plenity group was 126.2/83.6 compared to 125.0/82.2 in the placebo group. The presence of diabetes and prediabetes, respectively, was 9% and 30% in the Plenity group, and 12% and 31% in the placebo group. Dyslipidemia was present in 69% of the Plenity group compared with 72% of the placebo group. Average waist circumference was 43 inches in for Plenity group and 44 inches in for placebo.

Table 2. Summary of Subject Demographics and Baseline Characteristics – ITT Population

	Plenity N=223	**Placebo N=213**	**Difference (95% CI) [1]**	**p-value**
Age (years), Mean ± SD (N)	48.2 ± 9.9 (223)	47.8 ± 10.9 (213)	0.34 (-1.62, 2.30)	0.7341
Gender, % (n/N)				1.0000
Female	56.1% (125/223)	56.3% (120/213)	-0.3% (-9.6%, 9.0%)	
Male	43.9% (98/223)	43.7% (93/213)	0.3% (-9.0%, 9.6%)	
Race, % (n/N)				0.9835
White	84.8% (189/223)	84.5% (180/213)	0.2% (-6.5%, 7.0%)	
Black Or African American	11.7% (26/223)	11.3% (24/213)	0.4% (-5.6%, 6.4%)	
Asian	1.8% (4/223)	1.9% (4/213)	-0.1% (-2.6%, 2.4%)	
Other	1.8% (4/223)	2.3% (5/213)	-0.6% (-3.2%, 2.1%)	
Hispanic Or Latino Ethnicity, % (n/N)	4.9% (11/223)	7.5% (16/213)	-2.6% (-7.1%, 2.0%)	0.3217
Weight (lb), Mean ± SD (N)	215.2 ± 31.7 (223)	221.9 ± 33.8 (213)	-6.64 (-12.80, -0.48)	0.0348
Height (in), Mean ± SD (N)	67.1 ± 3.7 (223)	67.5 ± 4.0 (213)	-0.48 (-1.21, 0.24)	0.1927
BMI (kg/m²), Mean ± SD (N)	33.5 ± 3.2 (223)	34.1 ± 3.2 (213)	-0.54 (-1.13, 0.06)	0.0784
Waist Circumference (in), Mean ± SD (N)	42.6 ± 4.2 (223)	43.6 ± 4.3 (213)	-0.92 (-1.73, -0.12)	0.0249
Weight Categories, % (n/N)				0.1457
Overweight	11.7% (26/223)	9.9% (21/213)	1.8% (-4.0%, 7.6%)	
Obese Class I	57.8% (129/223)	50.7% (108/213)	7.1% (-2.2%, 16.5%)	
Obese Class II	30.5% (68/223)	39.4% (84/213)	-8.9% (-17.9%, 0.0%)	
Comorbidities, % (n/N)				
Dyslipidemia	69.1% (154/223)	72.3% (154/213)	-3.2% (-11.8%, 5.3%)	0.4638

	Plenity N=223	Placebo N=213	Difference (95% CI) [1]	p-value
Hypertensive	30.0% (67/223)	28.2% (60/213)	1.9% (-6.7%, 10.4%)	0.6748
Type 2 Diabetes	9.4% (21/223)	11.7% (25/213)	-2.3% (-8.1%, 3.5%)	0.4406
Prediabetes	26% (59/223)	27% (58/213)	-1.4% (-10.0%, 7.2%)	0.7557
LDL Cholesterol (mg/dL), Mean ± SD (N)	134.7 ± 35.1 (220)	132.4 ± 33.2 (211)	2.34 (-4.13, 8.82)	0.4768
HDL Cholesterol (mg/dL), Mean ± SD (N)	52.5 ± 13.0 (220)	50.8 ± 13.7 (211)	1.71 (-0.82, 4.24)	0.1840
Systolic Blood Pressure (mmHg), Mean ± SD (N)	126.2 ± 14.4 (223)	125.0 ± 14.0 (211)	1.19 (-1.50, 3.87)	0.3846
Diastolic Blood Pressure (mmHg), Mean ± SD (N)	83.6 ± 9.1 (223)	82.2 ± 8.7 (211)	1.32 (-0.36, 3.00)	0.1240
Untreated fasting glucose (mg/dL) [2], Mean ± SD (N)[2, 3]	97.5 ± 11.5 (209)	98.1 ± 12.0 (195)	-0.58 (-2.87, 1.72)	0.6222
Tobacco Use				0.2614
Never	68.6% (153/223)	61.5% (131/213)	7.1% (-1.8%, 16.0%)	
Former	21.1% (47/223)	27.2% (58/213)	-6.2% (-14.2%, 1.9%)	
Current	10.3% (23/223)	11.3% (24/213)	-1.0% (-6.8%, 4.9%)	

[1] Difference taken for comparability between the two groups (T-C). 95% Confidence Interval and p-value for the difference in means (or proportions). Confidence intervals and p-values are not adjusted for multiple comparisons.
[2] Denominator represents number of subjects not on metformin in each treatment group.
[3] Inclusion criteria required mean fasting blood glucose ≥ 90 mg/dl.

8.1.4. Safety

The primary safety endpoint was an analysis of the safety population, defined as the cohort containing any subject receiving the treatment after randomization, for all AEs and SAEs (n = 223 for Plenity and n = 211 for placebo). Plenity was well tolerated, with fewer patient dropouts in the Plenity group than the placebo group, 23% (51) vs 29% (61) and equivalent dropout rates because of AEs 4% (8) vs 3% (7).

Table 3. Rates of Treatment Withdrawal, by Primary Reason – Safety Population

Parameter	Plenity (n=223) % (n)	Placebo (n=211) % (n)
Dropout	23% (51)	29% (61)
Adverse events	3.6% (8)	3.3% (7)
Lost to follow-up	3.1% (7)	4.2% (9)
Protocol deviation	3.6% (8)	3.8% (8)
Other	2.7% (6)	1.4% (3)
Withdrawal by subject	9.9% (22)	16% (34)

Table 4: Summary of AEs Resulting in Subject Withdrawal, based on MedDRA's System Organ Class (SOC) and Relatedness – Safety Population

	Plenity (n=223)	Placebo (n=211)
	Number Subjects with Event [% (n/N)]	**Number Subjects with Event [% (n/N)]**
All Adverse Events [1]	3.6% (8/223)	3.3% (7/211)
Gastrointestinal disorders	2.2% (5/223)	1.9% (4/211)
Related	2.2% (5/223)	1.9% (4/211)
General disorders and administration site conditions	0.9% (2/223)	0.0% (0/211)
Not related	0.9% (2/223)	0.0% (0/211)
Infections and infestations	0.9% (2/223)	0.5% (1/211)
Not related	0.9% (2/223)	0.5% (1/211)
Injury, poisoning and procedural complications	0.9% (2/223)	0.0% (0/211)
Not related	0.9% (2/223)	0.0% (0/211)
Investigations	0.4% (1/223)	0.0% (0/211)
Not related	0.4% (1/223)	0.0% (0/211)
Metabolism and nutrition disorders	0.0% (0/223)	0.5% (1/211)
Related	0.0% (0/223)	0.5% (1/211)
Musculoskeletal and connective tissue disorders	0.9% (2/223)	0.5% (1/211)
Related	0.4% (1/223)	0.0% (0/211)
Not related	0.4% (1/223)	0.5% (1/211)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.0% (0/223)	0.9% (2/211)
Not related	0.0% (0/223)	0.9% (2/211)
Psychiatric disorders	0.4% (1/223)	0.5% (1/211)
Not related	0.4% (1/223)	0.5% (1/211)
Renal and urinary disorders	0.4% (1/223)	0.0% (0/211)
Not related	0.4% (1/223)	0.0% (0/211)
Reproductive system and breast disorders	0.0% (0/223)	0.5% (1/211)
Not related	0.0% (0/223)	0.5% (1/211)
Skin and subcutaneous tissue disorders	0.0% (0/223)	0.5% (1/211)
Related	0.0% (0/223)	0.5% (1/211)
Vascular disorders	0.0% (0/223)	0.5% (1/211)
Not related	0.0% (0/223)	0.5% (1/211)
[1] Subjects with more than one AE are counted only once per SOC, using the strongest relatio nship.		

The overall incidence of adverse events in the Plenity treatment group was no different than placebo (71% in both groups). In both treatment groups, most (>95%) adverse events were assessed by the investigator as mild or moderate in intensity. There were no serious adverse events (SAE) in the Plenity treatment group, whereas there was one (1) SAE in the placebo treatment group. No deaths occurred during the trial. Overall, there were 540 mild AEs (282 in 124 subjects in the Plenity group and 258 in 117 subjects in the placebo group), 276 moderate AEs (143 in 88 subjects in the Plenity group and 133 in 83 subjects in the placebo group), and 24 severe AEs (11 events in 8 subjects in the Plenity and 13 events in 10 subjects in the placebo group).

Table 5: Summary of adverse events by treatment group – Safety Population

	Plenity (n=223)		**Placebo (n=211)**	
	Number Events	**Number Subjects with Event [% (n/N)]**	**Number Events**	**Number Subjects with Event [% (n/N)]**
Number of Subjects with any AE	436	71.3% (159/223)	404	70.6% (149/211)
Grade 3 (Severe)	11	3.6% (8/223)	13	4.7% (10/211)
Grade 2 (Moderate)	143	39.5% (88/223)	133	39.3% (83/211)
Grade 1 (Mild)	282	55.6% (124/223)	258	55.5% (117/211)
Number of Subjects with any SAE	0	0.0% (0/223)	1	0.5% (1/211)
Number of Subjects with AEs leading to withdrawal	29	3.6% (8/223)	21	3.3% (7/211)
Death	0	0.0% (0/223)	0	0.0% (0/211)

Overall, the most common AEs were gastrointestinal disorders (186 AEs in 96 [43%] subjects in Plenity, compared to 134 events in 72 [34%] subjects receiving placebo), infections and infestations (94 events in 74 [33%] subjects with Plenity and 101 events in 70 [33%] subjects with placebo), and musculoskeletal and connective tissue disorders (38 events in 31 [14%] subjects with Plenity and 45 in 34 [16%] subjects with placebo).

Table 6: All treatment emergent adverse events summarized by system organ class, relatedness and treatment group – Safety Population

	Plenity (n=223)		Placebo (n=221)	
	# Events	Number Subjects with Event [% (n/N)]	# Events	Number Subjects with Event [% (n/N)]
All Adverse Events	436	71.3% (159/223)	404	70.6% (149/211)
Related	174	39.5% (88/223)	122	30.3% (64/211)
Not related	262	59.6% (133/223)	282	60.7% (128/211)
Blood and lymphatic system disorders	1	0.4% (1/223)	1	0.5% (1/211)
Not related	1	0.4% (1/223)	1	0.5% (1/211)
Cardiac disorders	0	0.0% (0/223)	2	0.5% (1/211)
Not related	0	0.0% (0/223)	2	0.5% (1/211)
Ear and labyrinth disorders	0	0.0% (0/223)	3	0.9% (2/211)
Not related	0	0.0% (0/223)	3	0.9% (2/211)
Eye disorders	6	2.7% (6/223)	2	0.9% (2/211)
Related	0	0.0% (0/223)	1	0.5% (1/211)
Not related	6	2.7% (6/223)	1	0.5% (1/211)
Gastrointestinal disorders	186	43.0% (96/223)	134	34.1% (72/211)
Related	158	37.7% (84/223)	105	27.5% (58/211)
Not related	28	10.3% (23/223)	29	10.0% (21/211)
General disorders and administration site conditions	9	4.0% (9/223)	18	7.6% (16/211)
Related	1	0.4% (1/223)	1	0.5% (1/211)
Not related	8	3.6% (8/223)	17	7.1% (15/211)
Hepatobiliary disorders	1	0.4% (1/223)	0	0.0% (0/211)
Not related	1	0.4% (1/223)	0	0.0% (0/211)
Infections and infestations	94	33.2% (74/223)	101	33.2% (70/211)
Related	2	0.9% (2/223)	1	0.5% (1/211)
Not related	92	32.7% (73/223)	100	33.2% (70/211)
Injury, poisoning and procedural complications	23	9.9% (22/223)	15	5.7% (12/211)
Not related	23	9.9% (22/223)	15	5.7% (12/211)
Investigations	12	4.5% (10/223)	7	3.3% (7/211)
Related	3	1.3% (3/223)	3	1.4% (3/211)
Not related	9	3.1% (7/223)	4	1.9% (4/211)
Metabolism and nutrition disorders	3	1.3% (3/223)	6	2.8% (6/211)
Related	0	0.0% (0/223)	4	1.9% (4/211)

	Plenity (n=223)		Placebo (n=221)	
	# Events	Number Subjects with Event [% (n/N)]	# Events	Number Subjects with Event [% (n/N)]
Not related	3	1.3% (3/223)	2	0.9% (2/211)
Musculoskeletal and connective tissue disorders	38	13.9% (31/223)	45	16.1% (34/211)
Related	3	0.9% (2/223)	0	0.0% (0/211)
Not related	35	13.0% (29/223)	45	16.1% (34/211)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	0.4% (1/223)	5	1.4% (3/211)
Not related	1	0.4% (1/223)	5	1.4% (3/211)
Nervous system disorders	36	12.1% (27/223)	30	10.4% (22/211)
Related	4	1.8% (4/223)	2	0.9% (2/211)
Not related	32	11.2% (25/223)	28	10.0% (21/211)
Psychiatric disorders	4	1.8% (4/223)	3	1.4% (3/211)
Not related	4	1.8% (4/223)	3	1.4% (3/211)
Renal and urinary disorders	3	1.3% (3/223)	6	2.8% (6/211)
Related	1	0.4% (1/223)	0	0.0% (0/211)
Not related	2	0.9% (2/223)	6	2.8% (6/211)
Reproductive system and breast disorders	4	1.8% (4/223)	4	1.9% (4/211)
Related	0	0.0% (0/223)	1	0.5% (1/211)
Not related	4	1.8% (4/223)	3	1.4% (3/211)
Respiratory, thoracic and mediastinal disorders	7	2.7% (6/223)	14	6.2% (13/211)
Related	1	0.4% (1/223)	1	0.5% (1/211)
Not related	6	2.2% (5/223)	13	5.7% (12/211)
Skin and subcutaneous tissue disorders	5	2.2% (5/223)	6	2.4% (5/211)
Related	1	0.4% (1/223)	3	1.4% (3/211)
Not related	4	1.8% (4/223)	3	1.4% (3/211)
Vascular disorders	3	1.3% (3/223)	2	0.9% (2/211)
Not related	3	1.3% (3/223)	2	0.9% (2/211)

[1] Related includes events categorized as "Most probably related" and "Possibly related." Not related includes events categorized as "Probably not related" and "Not related."

Frequent treatment-emergent adverse events are defined as those events occurring with ≥5% incidence in any treatment group. No category of AE, categorized by severity, occurred at greater frequency in the Plenity group (Table **7**).

Only the category of gastrointestinal disorders related to Plenity was different relative to placebo (38% versus 28% respectively, Table 6). The majority of the events were assessed as mild (119 of 158 [75%] AEs with Plenity, 83 of 105 [79%] AEs with placebo) (Table 8). The gastrointestinal events considered to be either moderate or severe were no different between groups (39 events in 21 subjects in the Plenity group, 22 events in 15 subjects in the placebo group). This difference in overall GI adverse events is to be expected based on the mechanism of action of the product.

Table 7: Summary of Adverse Events by Severity (≥5% by SOC in Either Treatment Group) by Preferred Term, and Severity−Safety Population

	Plenity (n=223)		Placebo (n=211)	
	Number Events	**Number Subjects with Event [% (n/N)]**	**Number Events**	**Number Subjects with Event [% (n/N)]**
All Adverse Events	436	71.3% (159/223)	404	70.6% (149/211)
Gastrointestinal disorders				
Abdominal distension	27	11.7% (26/223)	14	6.6% (14/211)
Mild	20	8.5% (19/223)	12	5.7% (12/211)
Moderate	6	2.7% (6/223)	2	0.9% (2/211)
Severe	1	0.4% (1/223)	0	0.0% (0/211)
Abdominal pain	12	5.4% (12/223)	6	2.8% (6/211)
Mild	8	3.6% (8/223)	5	2.4% (5/211)
Moderate	4	1.8% (4/223)	1	0.5% (1/211)
Constipation[1]	13	5.4% (12/223)	11	5.2% (11/211)
Mild	10	4.0% (9/223)	6	2.8% (6/211)
Moderate	3	1.3% (3/223)	5	2.4% (5/211)
Diarrhea	31	12.6% (28/223)	20	8.5% (18/211)
Mild	19	7.6% (17/223)	14	6.2% (13/211)
Moderate	12	4.9% (11/223)	5	1.9% (4/211)
Severe	0	0.0% (0/223)	1	0.5% (1/211)
Flatulence	21	8.5% (19/223)	14	5.2% (11/211)
Mild	19	8.1% (18/223)	14	5.2% (11/211)
Moderate	2	0.4% (1/223)	0	0.0% (0/211)
Infrequent bowel movements[1]	24	9.4% (21/223)	12	4.7% (10/211)
Mild	21	8.1% (18/223)	9	3.8% (8/211)
Moderate	3	1.3% (3/223)	3	0.9% (2/211)
Nausea	12	4.9% (11/223)	12	5.2% (11/211)

	Plenity (n=223)		Placebo (n=211)	
	Number Events	**Number Subjects with Event [% (n/N)]**	**Number Events**	**Number Subjects with Event [% (n/N)]**
Mild	8	3.6% (8/223)	9	3.8% (8/211)
Moderate	3	0.9% (2/223)	2	0.9% (2/211)
Severe	1	0.4% (1/223)	1	0.5% (1/211)
Infections and infestations				
Nasopharyngitis	31	11.7% (26/223)	37	14.2% (30/211)
Mild	25	9.0% (20/223)	30	10.9% (23/211)
Moderate	6	2.7% (6/223)	7	3.3% (7/211)
Upper respiratory tract infection	9	3.6% (8/223)	14	5.7% (12/211)
Mild	8	3.1% (7/223)	14	5.7% (12/211)
Moderate	1	0.4% (1/223)	0	0.0% (0/211)
Musculoskeletal and connective tissue disorders				
Arthralgia	9	3.1% (7/223)	13	6.2% (13/211)
Mild	6	2.2% (5/223)	4	1.9% (4/211)
Moderate	3	0.9% (2/223)	7	3.3% (7/211)
Severe	0	0.0% (0/223)	2	0.9% (2/211)
Nervous system disorders				
Headache	23	7.2% (16/223)	26	8.5% (18/211)
Mild	19	5.4% (12/223)	12	3.8% (8/211)
Moderate	3	1.3% (3/223)	12	3.8% (8/211)
Severe	1	0.4% (1/223)	2	0.9% (2/211)

[1] Coded by investigator verbatim terms using Medical Dictionary for Regulatory Authorities [MedDRA] version 17.1

Table 8: Summary of Gastrointestinal AEs by Severity Deemed Possibly or Most Probably Related to Investigational Product – Safety Population

	Plenity (n=223)		Placebo (n=211_	
	Number Events	Number Subjects with Event [% (n/N)]	Number Events	Number Subjects with Event [% (n/N)]
Gastrointestinal Disorders [1]	158	37.7% (84/223)	105	27.5% (58/211)
Mild	119	28.3% (63/223)	83	20.4% (43/211)
Moderate	35	8.1% (18/223)	20	6.6% (14/211)
Severe	4	1.3% (3/223)	2	0.5% (1/211)
[1] Subjects with more than one AE are counted only once, at the worst severity.				

Plenity was therefore well tolerated with no significant safety concerns compared to placebo. The study resulted in only a single SAE, which occurred in the placebo group.

A sub-study (n = 30 for Plenity and n = 28 for placebo) was conducted at four select centers to learn of any interaction between Plenity and vitamin levels. Measurements were obtained at baseline, Day 85, and Day 171. Unadjusted analysis of available data included concentrations of vitamins A, B1, B2, B12, B6, B9, D, and E. There were no significant differences from baseline for Plenity or placebo for all vitamin levels measured. There were no AEs or SAEs associated with abnormalities related to vitamins. Table 9 summarizes the vitamin levels at each visit for both treatment groups.

Table 9. Vitamin Levels Over Time – Sub-study with Vitamin Levels Measured

Table 33 Vitamin Levels at Baseline, Visit 9 and Visit 13						
	Plenity			**Placebo**		
Vitamin	**Baseline Mean ± SD (N)**	**Visit 9 Mean ± SD (N)**	**Visit 13 Mean ± SD (N)**	**Baseline Mean ± SD (N)**	**Visit 9 Mean ± SD (N)**	**Visit 13 Mean ± SD (N)**
Vitamin A (µg/dL)	72.5 ± 33.5 (28)	71.0 ± 26.2 (25)	70.4 ± 29.8 (27)	69.7 ± 21.9 (27)	74.0 ± 22.0 (22)	97.5 ± 177.4 (27)
Vitamin B1 (nmol/L)	211.6 ± 50.2 (28)	213.2 ± 45.0 (25)	187.8 ± 36.1 (27)	218.3 ± 66.5 (27)	232.1 ± 57.8 (22)	199.3 ± 54.9 (27)
Vitamin B2 (ug/L)	250.3 ± 43.5 (28)	257.3 ± 36.3 (25)	238.7 ± 31.6 (27)	262.7 ± 33.4 (27)	266.0 ± 38.9 (22)	241.9 ± 47.2 (27)
Vitamin B12 (pg/mL)	309.7 ± 151.9 (30)	308.4 ± 147.4 (29)	353.4 ± 248.1 (30)	338.8 ± 127.9 (28)	328.7 ± 115.1 (27)	312.5 ± 108.1 (28)
Vitamin B6 (ug/L)	22.8 ± 7.9 (28)	22.9 ± 10.9 (25)	20.8 ± 21.3 (27)	20.4 ± 5.3 (27)	18.1 ± 6.1 (22)	15.4 ± 3.5 (27)
Vitamin B9 (ng/mL)	10.3 ± 10.5 (30)	9.5 ± 5.5 (29)	8.4 ± 4.2 (30)	7.7 ± 5.1 (28)	8.0 ± 4.5 (27)	6.0 ± 2.4 (28)
25 (OH) Vitamin D (ng/mL)	15.2 ± 5.8 (30)	21.3 ± 5.9 (29)	25.0 ± 11.4 (30)	17.6 ± 10.1 (28)	23.7 ± 12.4 (27)	22.3 ± 8.4 (28)
Vitamin E (mg/L)	14.6 ± 4.4 (28)	14.1 ± 3.7 (25)	15.9 ± 4.7 (27)	14.0 ± 3.1 (27)	15.4 ± 3.4 (22)	14.2 ± 3.4 (27)

No significant difference in unadjusted analyses of observed data was observed for serum electrolytes or hematocrit in either group (Table 10).

Table 10. Other Key Laboratory Values – Safety Population

	Plenity (n=223)			Placebo (n=211)		
Parameter	**Baseline Mean ± SD (N)**	**Visit 13 Mean ± SD (N)**	**Change from Baseline Diff (95% CI) [1]**	**Baseline Mean ± SD (N)**	**Visit 13 Mean ± SD (N)**	**Change from Baseline Diff (95% CI) [1]**
Sodium (mEq/L)	140.5 ± 2.4 (221)	139.9 ± 2.6 (192)	-0.5 (-0.9, -0.1)	140.5 ± 2.6 (210)	140.4 ± 2.7 (182)	0.0 (-0.5, 0.5)
Potassium (mEq/L)	4.4 ± 0.3 (221)	4.3 ± 0.4 (192)	0.0 (-0.1, 0.0)	4.4 ± 0.4 (210)	4.4 ± 0.3 (182)	0.0 (-0.0, 0.1)
Calcium (mg/dL)	9.4 ± 0.4 (221)	9.3 ± 0.4 (192)	0.0 (-0.1, 0.1)	9.3 ± 0.4 (210)	9.3 ± 0.4 (182)	0.0 (-0.1, 0.1)
Magnesium (mg/dL)	2.1 ± 0.2 (220)	2.1 ± 0.2 (192)	0.0 (0.0, 0.1)	2.0 ± 0.2 (210)	2.1 ± 0.2 (182)	0.0 (0.0, 0.1)
Hematocrit (%)	42.2 ± 3.4 (219)	41.9 ± 3.5 (193)	-0.2 (-0.5, 0.1)	42.2 ± 3.5 (210)	42.3 ± 3.6 (179)	0.1 (-0.3, 0.4)

[1] Difference taken as change from baseline for comparability within the groups (V13 - Baseline). 95% Confidence Interval for the difference in means provided.

8.1.5. Effectiveness

8.1.5.1. Primary Endpoint Analysis

The co-primary effectiveness endpoints were: an ITT-MI analysis of total body weight loss, defined as the percent change from baseline to Day 171 with a super-superiority margin of 3%; and body weight responders, defined as ≥5% total body weight loss from baseline to Day 171, with at least 35% of subjects in the active arm achieving ≥5% weight loss. The co-primary endpoint of percent change in total body weight demonstrated greater weight loss at six months in subjects assigned to Plenity: -6% vs. -4%, (least square [LS] mean difference from an ANCOVA model adjusted for stratification factors and baseline weight was -2%, p=0.0007, 95% CI, -3.2 to -0.9 [ITT-MI]) (Table 11). Though the Plenity group achieved statistically superior weight loss compared to placebo, it did not meet the predefined super-superiority margin of 3% to successfully meet this co-primary endpoint. No weight loss plateau was observed during the 6-month GLOW study, and weight loss was sustained during a twenty-four (24) week follow-up period (Figure 3).

Table 11. Percent Change in Total Body Weight Loss (TBWL) from Baseline to Day 171– ITT MI Population

ITT-MI Analysis Population	**Plenity (N=223)**	**Placebo (N=213)**
Percent TBWL [1]		
Mean ± SD	-6.41 ± 5.79	-4.39 ± 5.52
Median (min, max)	-5.80 (-26.40, 7.74)	-3.97 (-22.31, 15.90)
LS Mean Difference [2]		
Mean ± SE	-2.07 ± 0.59	
95% CI [3]	(-3.24, -0.90)	
p-value: Super Superiority [4]	0.1193	
p-value: Superiority [5]	0.0007	
PP Analysis Population	**Plenity (N=154)**	**Placebo (N=141)**
Percent TBWL		
Mean ± SD	-6.31 ± 6.01	-4.89 ± 5.40
Median (min, max)	-5.73 (-26.40, 7.74)	-4.15 (-19.25, 10.42)
Difference (95% CI)	-1.42 (-2.73, -0.10)	

[1] Endpoint data imputed for 22.9% (51/223) in Plenity group and 28.6% (61/213) in Sham group.

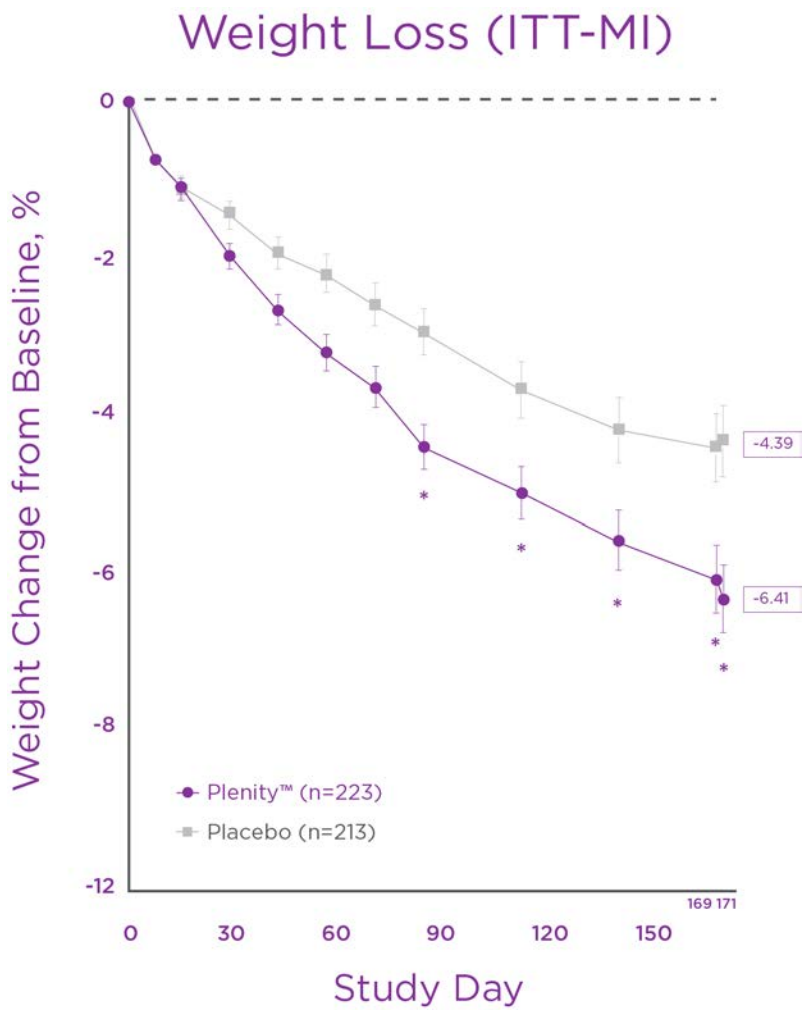
[2] Difference in adjusted means taken for comparability between the two groups.

[3] 95% Confidence Interval for the difference in LS means.

[4] p-value from ANCOVA model adjusted for stratification factors and Baseline weight, testing for super superiority (> 3% difference).

[5] p-value from ANCOVA model adjusted for stratification factors and Baseline weight, testing for superiority (difference > 0).

Figure 3: LS Mean Change (SE) in weight over the study period - ITT-MI population



The co-primary endpoint of body weight responders was achieved with significantly more subjects treated with Plenity achieving clinically meaningful weight loss vs placebo (ITT-MI, Table 12). The percent of responders with ≥5% weight loss was 59% with Plenity vs 42% with placebo (p=0.0008 from a logistic regression model adjusted for stratification factors and baseline weight).

Table 12: Summary of Body Weight Responders ≥ 5% at Day 171 – ITT MI Population

ITT-MI Analysis Population	Plenity (N=223)	Placebo (N=213)
Percent of body weight responders [1, 2]	58.6	42.2
95% CI	(52, 65)	
p-value [3]	<0.0001	
PP Analysis Population	**Plenity (N=154)**	**Placebo (N=141)**
Percent of body weight responders [2]	57.1	44.0
95% CI	(49, 65)	
p-value [3]	<0.0001	

ITT-MI Analysis Population	Plenity (N=223)	Placebo (N=213)
[1] Endpoint data imputed for 22.9% (51/223) in Plenity group and 28.6% (61/213) in Sham group.		
[2] Body weight responders defined as patients with ≥5% reduction in body weight.		
[3] p-value from binomial proportion test for % of responders in treatment group compared to 35% performance goal.		

8.1.5.2. Secondary Endpoint Analysis

The GLOW study included several secondary effectiveness endpoints to examine the impact of weight loss on other clinical outcomes. The statistical analysis plan dictated a closed test procedure to handle multiplicity in testing. The first secondary effectiveness endpoint, body weight in subjects with impaired plasma glucose at baseline, did not achieve statistical significance. Since the first secondary endpoint did not achieve $p<0.05$ significance level all the other secondary endpoints were evaluated only as descriptive statistics.

At the Day 171 assessment, BMI means (SD) in the ITT-MI population were 31.43 (3.66) and 32.57 (3.72) for the Plenity and placebo treatment groups, respectively. The mean changes (SD) in BMI from baseline to Day 171 were -2.12 kg/m^2 (1.92) and -1.51 kg/m^2 (1.90) for the Plenity and placebo treatment groups, respectively. The adjusted mean (SE) change in BMI from baseline to Day 171 for the treatment difference for Plenity versus placebo was -0.60 kg/m^2 (0.20) (95% CI; -1.00, -0.20) from an ANCOVA model adjusting for stratification factors and baseline BMI.

8.1.5.3. Additional Analysis

Multiple prespecified tertiary endpoints were measured in the ITT-Obs population, including 10% total body weight responders, estimated excess body weight loss, and change in waist circumference (Table 13). All differences between treatment groups and 95% CI's shown are from analyses adjusting for stratification factors and the corresponding baseline value for the respective endpoint. For 10% body weight responders, the Plenity arm had 26% (45/172) while the placebo arm had 16% (25/152), with the odds of being a 10% responder in the Plenity arm 1.88 (95% CI; 1.07, 3.30) times the odds in the placebo arm. For excess body weight loss, the Plenity arm had -28.96 (30.14) percent change while the placebo arm had -20.98 (25.69) percent change. The patients in the Plenity arm achieved more excess body weight loss than those in the placebo arm, the adjusted difference between groups was -6.44 (2.94) (95% CI; -12.2, -0.64). Similarly, the patients in the Plenity arm achieved greater reduction in waist circumference than those in the placebo arm: -2.64 inches (2.19) and -1.98 inches (2.32), respectively. The adjusted difference in change in waist circumference between the two groups was -0.73 in (0.25) with a 95% CI of (-1.22, -0.24).

Table 13: Tertiary Endpoints for Change or Percent Change from Baseline to Day 171 – ITT-Obs Population

Tertiary Endpoints	Plenity N = 172 Mean (SD)	Placebo N = 152 Mean (SD)	Difference [1]	95% CI [2]
Estimated excess body weight (% change)	-28.96 (30.14)	-20.98 (25.69)	-6.44 (2.94)	(-12.23, -0.64)
Waist circumference (change in inches)	-2.64 (2.19)	-1.98 (2.32)	-0.73 (0.25)	(-1.22, -0.24)

[1] Difference in adjusted means taken for comparability between the two groups (T - C).
[2] 95% Confidence Interval for the difference in LS means.

CI = confidence interval; ITT = intention-to-treat.

8.2. GLOW-EX

The GLOW-EX Study (Clinicaltrials.gov, NCT03021291) was an open-label extension trial to study the safety of long-term exposure to Plenity and the effectiveness of Plenity in maintaining weight loss achieved after 6 months (combined with lifestyle modification). At that time, less than 20% (73 subjects) of the original cohort remained in the GLOW study. Of the remaining subjects, 52 had completed Visit 13 (Day 171) and had lost ≥3% body weight in either the treatment or control arm, which was required to be considered for GLOW-EX. Subjects who were assigned to placebo during GLOW crossed over to the Plenity arm (n=18), while the subjects who were assigned to Plenity during GLOW continued on Plenity for an additional 24 weeks (n=21).

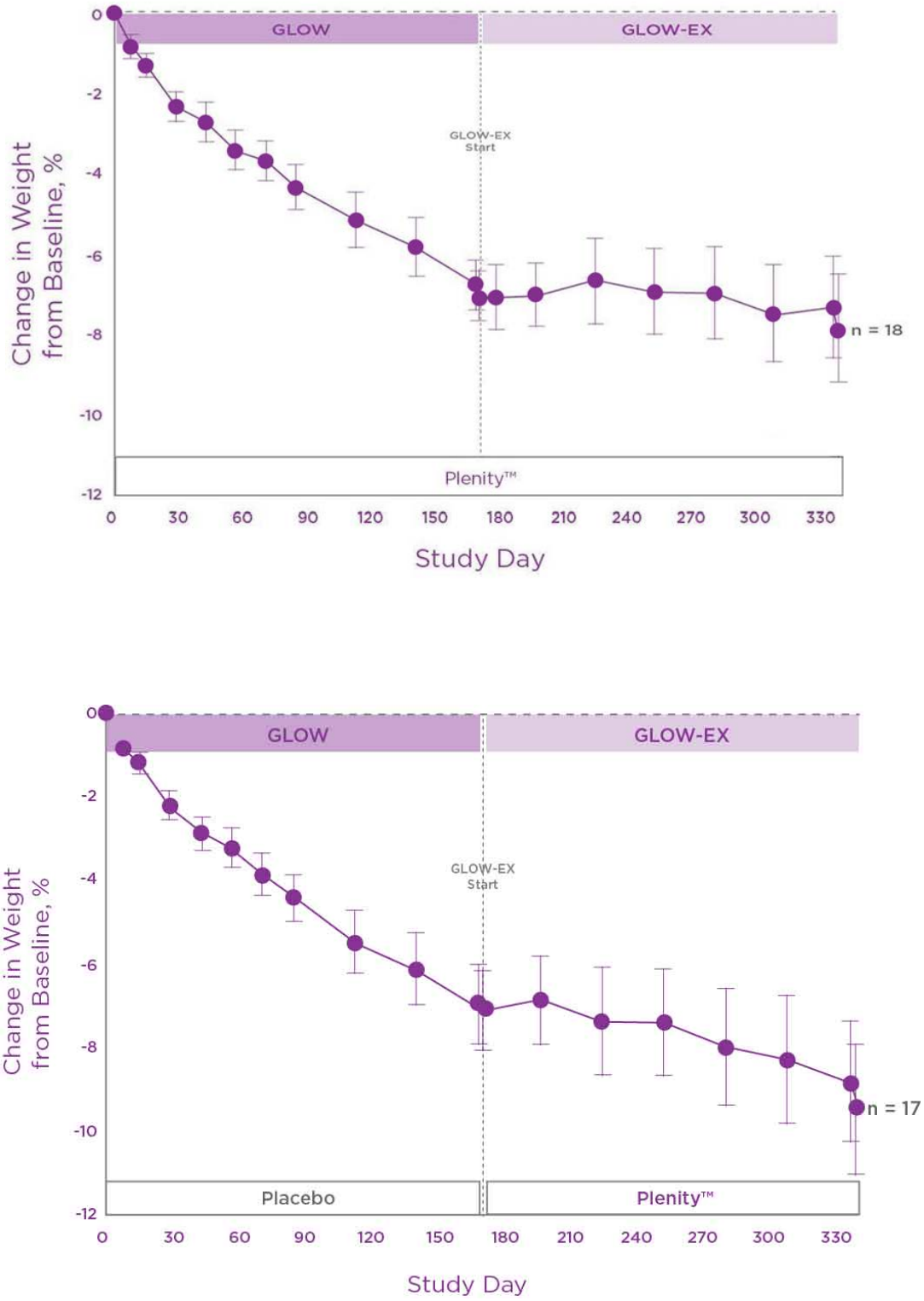
The daily dosing regimen was consistent with the GLOW study (3 capsules/2.25 g of Plenity taken before lunch and before dinner). The duration of the open-label treatment with Plenity 2.25 g was 165 days in the GLOW-EX Study.

The objectives are intended to evaluate 1) safety of one year exposure to Plenity, and 2) efficacy of Plenity to maintain weight loss achieved after 6 months of Plenity combined with diet and exercise.

At the time of enrollment in GLOW-EX, the subjects treated with Plenity during GLOW had already reached a mean (SD) weight loss of 7% ± 3% weight loss in 24 weeks. The additional six (6) months of exposure to Plenity provided an additional 0.8% ± 3% weight loss and demonstrated maintenance of the weight loss effect (Figure 6). The 18 subjects assigned to placebo in GLOW had lost 7% ± 4% during the GLOW study before starting on Plenity for 24 weeks. At the time when weight regain is expected, the subjects who successfully lost with lifestyle modification were able to lose an additional 3% ± 4% over the subsequent 24 weeks with the addition of Plenity treatment

The primary endpoint of weight maintenance was demonstrated as the unadjusted 95% confidence intervals at Day 171 (end of GLOW, 95% CI [-8.37 to -5.78]) and 339 (end of GLOW-EX, 95% CI [-10.54 to -5.22]) overlap. At the end of one year of therapy with Plenity, 67% of subjects achieved at least 5% weight loss.

Figure 6: GLOW-EX Results Demonstrating the Durability of Effect for the Plenity-Plenity Arm and Placebo-Plenity Arm



Approximately 58% of patients (11/19) maintained 80% or more of their initial weight loss during the following 6 months. At entry in the extension study, 15 of 21 subjects had reached at least 5% weight loss and, among that subset, almost all (12/15) maintained that weight threshold over the following 6 months. All 5 subjects who had achieved the 10% threshold by entry into the extension study maintained that threshold through 1 year.

The results also demonstrated that the safety profile for the extension phase of the study were consistent with the initial 6-month phase (Table 14). The events per patient month are similar during the first 6 months of exposure versus the last 6 months of exposure. There were no new AEs identified and the overall rates of each type of AE were similar to those seen during the blinded treatment phase of the study.

Table 14*:* Summary of AEs by SOC –Plenity Treated Subjects with AE in GLOW vs Plenity Treated GLOW Subjects with AE in GLOW-EX (Plenity-Plenity Group)

	Plenity Group During GLOW (n=223)			**Plenity-Plenity During GLOW-EX (n=21)**		
	# Events	**% Subjects with Event (n/N)**	**Events per Patient Month**	**# Events**	**% Subjects with Event (n/N)**	**Events per Patient Month**
All Adverse Events	436	71.3% (159/223)	0.3576	29	47.6% (10/21)	0.2375
Related	174	39.5% (88/223)	0.1427	11	19.0% (4/21)	0.0901
Not Related	262	59.6% (133/223)	0.2149	18	42.9% (9/21)	0.1474
Blood and lymphatic system disorders	1	0.4% (1/223)	0.0008	0	0.0% (0/21)	0
Eye disorders	6	2.7% (6/223)	0.0049	1	4.8% (1/21)	0.0082
Gastrointestinal disorders	186	43.0% (96/223)	0.1526	11	19.0% (4/21)	0.0901
General disorders and administration site conditions	9	4.0% (9/223)	0.0074	1	4.8% (1/21)	0.0082
Hepatobiliary disorders	1	0.4% (1/223)	0.0008	0	0.0% (0/21)	0
Infections and infestations	94	33.2% (74/223)	0.0771	3	9.5% (2/21)	0.0246
Injury, poisoning and procedural complications	23	9.9% (22/223)	0.0189	0	0.0% (0/21)	0
Investigations	12	4.5% (10/223)	0.0098	3	4.8% (1/21)	0.0246
Metabolism and nutrition disorders	3	1.3% (3/223)	0.0025	0	0.0% (0/21)	0
Musculoskeletal and connective tissue disorders	38	13.9% (31/223)	0.0312	2	9.5% (2/21)	0.0164
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	0.4% (1/223)	0.0008	0	0.0% (0/21)	0
Nervous system disorders	36	12.1% (27/223)	0.0295	4	14.3% (3/21)	0.0328

	Plenity Group During GLOW (n=223)			Plenity-Plenity During GLOW-EX (n=21)		
	# Events	% Subjects with Event (n/N)	Events per Patient Month	# Events	% Subjects with Event (n/N)	Events per Patient Month
Psychiatric disorders	4	1.8% (4/223)	0.0033	0	0.0% (0/21)	0
Renal and urinary disorders	3	1.3% (3/223)	0.0025	1	4.8% (1/21)	0.0082
Reproductive system and breast disorders	4	1.8% (4/223)	0.0033	1	4.8% (1/21)	0.0082
Respiratory, thoracic and mediastinal disorders	7	2.7% (6/223)	0.0057	1	4.8% (1/21)	0.0082
Skin and subcutaneous tissue disorders	5	2.2% (5/223)	0.0041	0	0.0% (0/21)	0
Vascular disorders	3	1.3% (3/223)	0.0025	1	4.8% (1/21)	0.0082

8.3. Drug-Product Interaction Study

A drug-product interaction study (ClinicalTrials.gov, NCT02524821) was conducted to evaluate the effect of Plenity capsules on the pharmacokinetics (PK) of metformin, administered as single dose in healthy overweight or obese subjects under fasting and fed conditions. A total of 24 healthy, overweight or obese adult non-smokers (12 males and 12 females) were included in this study.

Patients were instructed to take metformin with or without food and with or without Plenity as shown in Table 15 and Figure 7.

The results of this study demonstrate that when metformin is dosed as instructed in its labeling with food (condition C in Table 15) there is a decrease in the median AUC compared to dosed in a fasting state (condition A in Table 15). There is no significant difference when Plenity is added to metformin during a meal (condition D in Table 15 and Figure 7b). In contrast, there is a significant decrease in the median AUC when Plenity is added to metformin during the fasting state (condition B in Table 15 and Figure 7a). These results are consistent with the food effect on metformin (but not Glucophage XR) absorption described in the labeling and shows that Plenity does not significantly increase the effect added with the meal (Figure 7a and b).

Table 15: Summary of Pharmacokinetics Parameters for Metformin for each Treatment

Parameter (units)	Metformin 1 x 850 mg Tablet - Fasting (A)						
	N	Mean	SD	CV%	Median	Min	Max
AUC_{0-t} (h*ng/mL)	24	11764.22	3780.11	32.13	12153.33	6414.48	21405.81
C_{max} (ng/mL)	24	1937.83	639.66	33.01	1809.65	1080.62	3105.64
T_{max} (h)	24	2.60	0.828	31.8	2.33	1.33	4.49

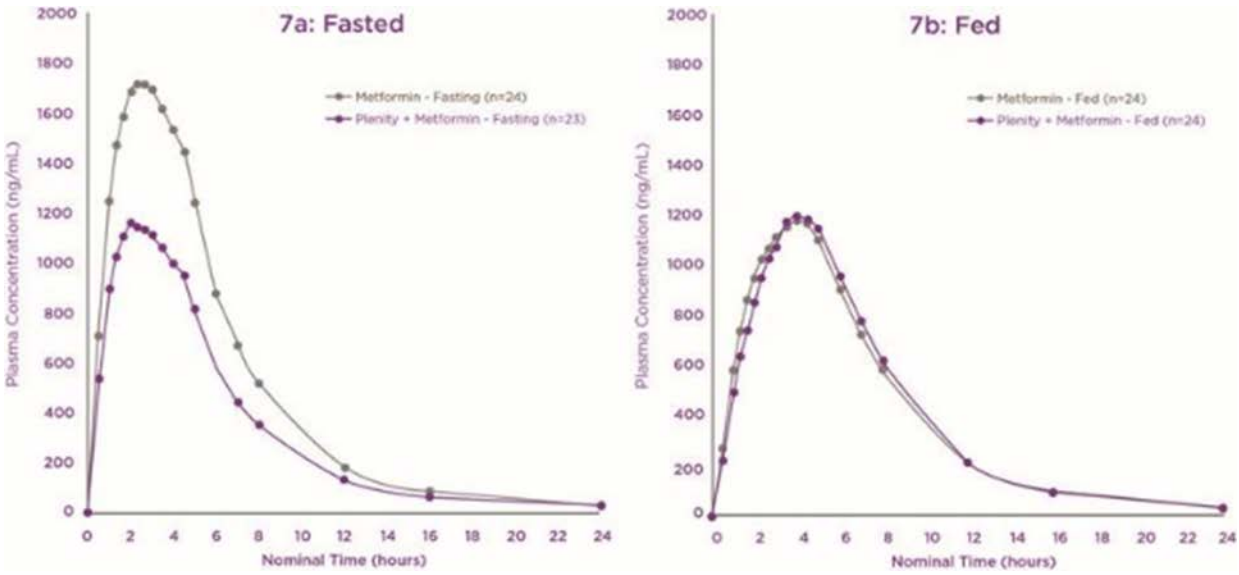
Parameter (units)	3 x 0.75 g Gelesis100 Capsules + Metformin - Fasting (B)						
	N	Mean	SD	CV%	Median	Min	Max
AUC_{0-t} (h*ng/mL)	23	8039.14	2909.08	36.19	7081.98	4575.55	14442.87
C_{max} (ng/mL)	23	1227.52	384.23	31.30	1071.13	796.65	2124.37
T_{max} (h)	23	2.32	0.869	37.5	1.99	0.995	4.50

Parameter (units)	Metformin 1 x 850 mg Tablet - Fed (C)						
	N	Mean	SD	CV%	Median	Min	Max
AUC_{0-t} (h*ng/mL)	24	9645.55	2338.89	24.25	10008.09	5454.81	14093.13
C_{max} (ng/mL)	24	1312.10	269.42	20.53	1263.58	785.54	1841.69
T_{max} (h)	24	3.38	1.26	37.3	3.25	1.33	6.01

Parameter (units)	3 x 0.75 g Gelesis100 Capsules + Metformin - Fed (D)						
	N	Mean	SD	CV%	Median	Min	Max
AUC_{0-t} (h*ng/mL)	24	9679.04	2615.09	27.02	9517.32	5472.55	15907.85
C_{max} (ng/mL)	24	1270.39	348.32	27.42	1266.35	672.16	2223.02
T_{max} (h)	24	3.79	1.00	26.4	4.00	1.99	5.00

Prescribers should consider the above information and review Section 6 (Directions for Use) when counselling patients on taking medications when using Plenity.

Figure 7a and b: Mean Concentration-time Profile for Metformin for each Treatment



Explanation of symbols

	Catalog number
	Batch code
	Use by date
	Manufacturer
	Keep dry
	Caution
	Consult instructions for use
	Do not use if package is damaged
	Prescription Use Only

Gelesis, Inc. 501 Boylston Street, Suite 6102 Boston, MA 02116 USA Info@gelesis.com (617) 456-4718	**Manufactured by**: Gelesis Srl. Via Giuseppe Verdi, 188 Calimera (LE) 73021 Italy