Gelesis Presents New Data at ObesityWeek

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PureTech Founded Entity Gelesis Presents Three Poster Presentations at ObesityWeek® 2020

New data from Gelesis show that pre-diabetes and impaired beta cell function were associated with a dysfunctional gut barrier, a potential precursor to metabolic diseases

Additional analysis of Gelesis' pivotal GLOW study suggests fasting plasma glucose levels and insulin resistance could be strong predictors of weight loss with Plenity®

New in-vitro beverage interaction study finds that Plenity's hydrogel maintained its properties in the presence of alcoholic or acidic drinks

PureTech Health plc (LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company dedicated to discovering, developing and commercialising highly differentiated medicines for devastating diseases, is pleased to note that its Founded Entity, Gelesis, today announced the release of three poster presentations at ObesityWeek 2020, the annual congress of The Obesity Society.

The full text of the announcement from Gelesis is as follows:

Gelesis Presents Three Poster Presentations at ObesityWeek® 2020

New data show that pre-diabetes and impaired beta cell function were associated with a dysfunctional gut barrier, a potential precursor to metabolic diseases

Additional analysis of the company's pivotal GLOW study suggests fasting plasma glucose levels and insulin resistance could be strong predictors of weight loss with Plenity®

New in-vitro beverage interaction study finds that Plenity's hydrogel maintained its properties in the presence of alcoholic or acidic drinks

Boston, November 3, 2020 - Gelesis, a biotechnology company developing a novel hydrogel platform technology to treat overweight, obesity and other chronic metabolic diseases, announces the release of three poster presentations at ObesityWeek® 2020, the annual congress of The Obesity Society, including:

- For the first time, to the authors' knowledge, new data shows that impaired beta cell

function was associated with a dysfunctional gut barrier, a potential precursor to metabolic disease;

- Post-hoc analysis, utilising a novel statistical approach, of Gelesis' pivotal GLOW study suggests a connection between weight loss and glycaemic biomarkers; and
- An examination of the interaction between a variety of beverages and Plenity, an oral, non-systemic treatment cleared by the FDA as an aid for weight management in adults with a BMI of 25-40 kg/m^2, when used in conjunction with diet and exercise.

"This work presented at ObesityWeek highlights the interplay between the loss of intestinal barrier integrity and early beta-cell function, adding to the increased focus of the gut-pancreatic axis and its critical role on metabolic health," said Paresh Dandona, MD, PhD, Distinguished Professor in the Department of Medicine, Jacobs School of Medicine and Biomedical Sciences at SUNY Buffalo. "Gelesis is leading the field of research for intestinal barrier health with its hydrogel technology, with the goal of becoming a frontline treatment approach that targets the complex gut-host interaction."

The details of the presentations are as follows.

Poster Presentation (EP-234): Impaired Beta Cell Function is Associated with Evidence of Dysfunctional Gut Barrier; Husam Ghanim, PhD; State University of New York, Buffalo, NY
Impaired small intestinal permeability has been linked to metabolic diseases, including obesity, diabetes, and fatty liver disease. Intestinal permeability can be measured by drinking a solution containing various sugars that are typically too large to be absorbed through the gut barrier. The presence of these sugars (e.g. cellobiose) in the urine suggest an impairment in gut barrier function. This analysis is the first, to the authors' knowledge, to describe an association between increased small intestine permeability and a reduction in insulin-secreting pancreatic beta-cell function, as indicated by a reduced insulin response to a glucose stimulus. Diabetes is already known to have an association with impaired gut barrier. This new research also suggested a correlation between fasting plasma glucose (FPG) and gut permeability, proposing that pre-diabetes is potentially associated with impaired gut barrier as well. These data also suggest that intestinal barrier integrity may play an important role in the treatment of metabolic diseases.

Poster Presentation (EP-174): Evaluating Glucose and Insulin as Predictors of Weight Loss in GLOW: A Novel Statistical Approach; Mads Fiil Hjorth, PhD; University of Copenhagen, Frederiksberg, Denmark
In this post-hoc analysis of the Gelesis Loss of Weight (GLOW) study, researchers evaluated fasting plasma glucose (FPG) and fasting plasma insulin (FPI) levels as biomarker predictors for weight loss with Plenity. The results of this analysis suggest that for each 1mg/dL increase in FPG, people using Plenity lost 0.10kg more weight than those on placebo. Similar associations to weight loss were observed for fasting FPI and HOMA-IR for those individuals with elevated FPG. The authors conclude that FPG may be a predictor of weight loss with Plenity treatment, and FPI may also be an effective predictor, particularly in patients with an elevated FPG. The results of this analysis are consistent with the previously reported analysis of the FLOW pilot study, as well as studies that have demonstrated that patients with impaired FPG lost more weight than those with normal glycemia when exposed to diets higher in vegetables, fruits, and whole grains.

Poster Presentation (EP-175): Evaluating the Interaction of an Oral Superabsorbent Hydrogel with Alcohol and Acidic Beverages; Damian Bialonczyk, PharmD; Gelesis, Inc., Boston, MA
This presentation details the interaction of Plenity and the consumption of alcohol and acidic beverages during meals. Plenity is intended to be taken with 16 ounces of water 20-30 minutes prior to lunch and dinner. However, some patients may elect to consume beverages other than water with their meals (after consuming the recommended 16 oz of water with their Plenity capsules before the meal). The results of this in-vitro analysis suggest that the Plenity hydrogel maintains its firmness and water absorption capacity in the presence of a meal and various alcoholic and acidic beverages.

About the Gelesis Loss Of Weight (GLOW) clinical study
The Gelesis Loss Of Weight (GLOW) Study was a randomised, double-blind, placebo-controlled,

parallel-group study enrolling 436 adults with a body mass index (BMI) ≥ 27 and ≤ 40 kg/m^2, including those with prediabetes or type 2 diabetes. The 6-month study compared a 2.25 g dose of Plenity, administered twice daily, to placebo and was conducted at 33 sites across the United States and several European countries. Both the active and placebo arms also included a reduced calorie diet and daily physical activity. The study had two predefined co-primary endpoints: at least 35% of patients taking Plenity achieving ≥ 5% weight loss (categorical endpoint) and placebo-adjusted weight loss with a super-superiority margin of 3%. In addition, a prespecified analysis of simple superiority was also performed. The study met and exceeded the predefined categorical endpoint, with 59% of adults in the treatment group achieving weight loss of 5% or greater. The study did not meet the 3% super-superiority endpoint but demonstrated superiority of the Plenity treatment over the placebo group (-6.4% vs. -4.4%, P=0.0007). Plenity-treated individuals had twice the odds of achieving at least 5% weight loss vs. placebo (adjusted odds ratio [OR]: 2.0,P=0.0008). In addition, 26% of the adults who completed the treatment with Plenity were "super-responders," defined as achieving at least 10% weight loss. These super-responders achieved an average of about 14% weight loss or approximately 30 pounds. The overall incidence of adverse events (AEs) in the Plenity treatment group was no different from placebo. The most common treatment-related adverse events (TRAEs) were gastrointestinal disorders (158 TRAEs in 84 [38%] subjects in the Plenity arm, compared to 105 events in 58 [28%] subjects receiving placebo), infections and infestations (2 events in 2 [1%] subjects with Plenity and 1 events in 1 [1%] subjects with placebo), and musculoskeletal and connective tissue disorders (3 events in 2 [1%] subjects with Plenity and 0 in 0 [0%] subjects with placebo). There were no serious adverse events (SAE) in the Plenity treatment group, whereas there was one (1) SAE in the placebo treatment group.

About Plenity®

Plenity is an oral, non-systemic, superabsorbent hydrogel which has received FDA clearance as an 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. Gelesis has also received approval to market Plenity in the European Economic Area. Plenity is made by cross-linking two naturally derived building blocks, modified cellulose and citric acid, that create a three-dimensional matrix. Plenity particles rapidly absorb water in the stomach and homogenously mix with ingested foods. Rather than forming one large mass, it creates thousands of small individual gel pieces with the elasticity and firmness of solid plant-based foods (e.g., vegetables) without caloric value. The Plenity hydrogel increases the volume and elasticity of the stomach and small intestine contents and induces a feeling of fullness and satiety. Once it arrives in the large intestine, the hydrogel is partially broken down by enzymes and loses its three-dimensional structure along with most of its absorption capacity. The released water is reabsorbed in the large intestine, and the remaining cellulosic material is eliminated through the body's natural digestive processes. Plenity is considered a medical device because it achieves its primary intended purpose through mechanical modes of action consistent with mechanobiology constructs. For more information, visit myplenity.com.

Important Safety Information

- Plenity is contraindicated in patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium dioxide
- Plenity may alter the absorption of medications. Read Sections 6 and 8.3 of the Instructions for Use carefully
- Avoid use in patients with: esophageal anatomic anomalies, including webs, diverticuli, and rings; suspected strictures (such as patients with Crohn's disease); and complications from prior gastrointestinal (GI) surgery that could affect GI transit and motility
- Use with caution in patients with active gastrointestinal conditions such as gastro-esophageal reflux disease (GERD), ulcers, or heartburn
- The overall incidence of AEs in the Plenity group was no different than the placebo group
- The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence.

For the safe and proper use of Plenity, refer to the U.S. Physician's Instructions for Use or the EU Physician's Instructions for Use.

About Gelesis

Gelesis is developing a novel hydrogel platform technology to treat overweight and obesity and chronic diseases related to the GI pathway. Gelesis' proprietary approach is designed to act mechanically in the GI pathway to potentially alter the course of certain chronic diseases. In April 2019, Gelesis received FDA clearance for its lead product candidate, Plenity®, as an aid for 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. It was also granted a CE Mark, which allows Gelesis to market Plenity in the European Economic Area. Plenity is currently available in limited release in the U.S. Additionally, Gelesis is developing additional investigational candidates such as Gelesis200, a hydrogel optimised for weight loss and glycaemic control in patients with type 2 diabetes and prediabetes. Novel hydrogel mechanotherapeutics based on the Gelesis platform technology are also being advanced in other GI inflammatory conditions, such as non-alcoholic steatohepatitis (NASH) and functional constipation. For more information, visit gelesis.com or connect with us on Twitter @GelesisInc.

About PureTech Health

PureTech is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercialising highly differentiated medicines for devastating diseases, including intractable cancers, lymphatic and gastrointestinal diseases, central nervous system disorders and inflammatory and immunological diseases, among others. The Company has created a broad and deep pipeline through the expertise of its experienced research and development team and its extensive network of scientists, clinicians and industry leaders. This pipeline, which is being advanced both internally and through PureTech's Founded Entities, is comprised of 24 products and product candidates, including two that have received US Food and Drug Administration (FDA) clearance and European marketing authorisation. All of the underlying programmes and platforms that resulted in this pipeline of product candidates were initially identified or discovered and then advanced by the PureTech team through key validation points based on the Company's unique insights into the biology of the brain, immune and gut, or BIG, systems and the interface between those systems, referred to as the BIG Axis.

For more information, visit www.puretechhealth.com or connect with us on Twitter @puretechh.

Forward Looking Statement

This press release contains statements that are or may be forward-looking statements, including statements that relate to the Gelesis' future prospects, developments, and strategies. The forward looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, our expectations regarding the potential therapeutic benefits of Plenity and those risks and uncertainties described in the risk factors included in the regulatory filings for PureTech Health plc. These forward-looking statements are based on assumptions regarding the present and future business strategies of the company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law and regulatory requirements, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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