Pivotal Weight Loss Data for Gelesis100 Published in Obesity, Including Predictors of Response

November 13, 2018

6 out of 10 of adults with overweight or obesity had a clinically meaningful response to Gelesis100, losing on average 10% of their weight (10 kilograms) and 9.3 centimetres from their waists. Adults treated with Gelesis100 had twice the odds of achieving > 5% and > 10% total body weight loss compared to placebo

Successful response to Gelesis100 may be predicted by elevated fasting plasma glucose or weight loss as early as week 8

Gelesis100 had a highly favourable safety and tolerability profile

PureTech Health plc (LSE: PRTC) ("PureTech Health"), an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis, is pleased to note that its affiliate, Gelesis, has published expanded data from the pivotal weight loss study of lead product candidate, Gelesis100. The data were published this week in the journal *Obesity* and presented as three posters and an oral session at ObesityWeek 2018, the annual combined congress of the American Society for Metabolic and Bariatric Surgery and The Obesity Society. Gelesis has submitted a medical device marketing application for Gelesis100 with the United States Food and Drug Administration (FDA).

Joe Bolen, PhD, Chief Scientific Officer at PureTech Health, said: "We are pleased that the results of the Gelesis100 pivotal study were selected for publication in *Obesity,* one of the field's leading peer-reviewed journals. The expanded data further emphasise the compelling safety and efficacy profile of Gelesis100 and provide compelling information around predictors of response. As obesity is a growing global health issue, we are committed to working with regulatory authorities around the world to potentially offer this first-in-class therapy for those struggling with overweight and obesity."

The full text announcement from Gelesis is as follows:

Pivotal Weight Loss Data for Gelesis100 Published in *Obesity*, Including Predictors of Response

6 out of 10 of adults with overweight or obesity had a clinically meaningful response to Gelesis100, losing on average 10% of their weight (22 pounds) and nearly 4 inches from their waists. Adults treated with Gelesis100 had twice the odds of achieving > 5% and > 10% total body weight loss compared to placebo

Successful response to Gelesis100 may be predicted by elevated fasting plasma glucose or weight loss as early as week 8

Gelesis100 had a highly favourable safety and tolerability profile

BOSTON, Nov. 13, 2018 —Gelesis, a biotechnology company developing first-in-class mechanotherapeutics to treat obesity and other chronic diseases related to the gastrointestinal (GI) tract, today announced expanded data from its Gelesis Loss of Weight (GLOW) clinical study, a pivotal multicentre, double-blind, placebo-controlled study of the Company's lead investigational candidate, Gelesis100, which is an oral, non-systemic approach to weight loss. The data were published this week in the journal *Obesity* and presented as three posters and an oral session at ObesityWeek 2018, the annual combined congress of the American Society for Metabolic and Bariatric Surgery and The Obesity Society.

The GLOW study was designed to assess change in body weight in adults with overweight or obesity after six months of treatment with Gelesis100. Topline results of the study were announced in September 2017. In the Intent To Treat (ITT) population, 59% of Gelesis100-treated adults achieved weight loss of at least 5% (achieving one primary outcome) vs. 42% in the placebo group. The new data show that Gelesis100-treated adults fell into two groups: responders, the 6 out of 10 who lost an average of 10% of their total body weight (about 22 pounds) and nearly 4 inches from their waists; and non-responders, those who lost an average of 1% of their total body weight (about 2 pounds). The complete Gelesis100 treatment group (including both responders and non-responders) demonstrated superiority compared to placebo (–6.4% vs. –4.4%, P=0.0007), and as previously announced, did not meet a co-primary outcome of 3% super-superiority over placebo.

In addition, 27% of the Gelesis100 ITT population compared to 15% of the placebo group 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. Gelesis100-treated individuals also had twice the odds of achieving at least 5% and at least 10% weight loss vs. placebo (adjusted odds ratio [OR]: 2.0, P=0.0008; adjusted OR: 2.1, P=0.0107, respectively).

Notably, there was a clear and early separation between responders and non-responders, which may allow for an early prediction of response to therapy. More specifically, weight loss of at least 3% as early as after eight weeks of treatment predicted clinically meaningful weight loss at six months, with sensitivity and specificity levels exceeding 80%. The paper published in *Obesity* noted that early prediction of response to therapy could allow more efficient use of resources and provide a key treatment milestone for clinicians and patients.

The study also showed that nearly half of the adults with pre-diabetes or drug-naive diabetes were super-responders. These individuals, who typically face greater challenges to lose weight, had six times greater odds of being super-responders, compared to placebo (adjusted OR: 6.1, P=0.0071). This is the second Gelesis100 clinical study to find an association between elevated fasting plasma glucose and a pronounced response to Gelesis100.

There were no statistically significant differences in the incidence and severity of adverse events (AEs) between the two groups except for the overall incidence of GI-related AEs, which was higher in the Gelesis100 group. Of the GI-related AEs, the largest difference in the incidence between the two

groups was abdominal distension (12% in the Gelesis100 group compared to 7% in the placebo group), a difference that was not statistically significant. The majority of GI-related AEs were mild and had short duration and full resolution. No serious adverse events were observed in the Gelesis100 group.

“More than 130 million Americans struggle with weight loss, making it one of the biggest public health issues facing our society. We believe Gelesis100 offers a compelling new potential approach given its strong safety and efficacy profile and, if cleared by the U.S. Food and Drug Administration, it could be an important addition to the clinical toolkit for treating overweight and obesity,” said Harry L. Leider, MD, MBA, FACPE, Chief Medical Officer of Gelesis. “There are no simple and well-established predictive indicators of response to weight-loss therapeutics, so these findings that may identify individuals more likely to be responders are exciting. We are also studying how the Gelesis hydrogel technology may modulate metabolic and inflammatory systems in a number of conditions related to gut barrier dysfunction including NAFLD, NASH, and IBD.”

“This thorough and well-designed study demonstrated that Gelesis100 has a promising safety and efficacy profile, and that it has the potential to serve as an important foundational therapy for treating individuals struggling with excess weight,” said Frank L. Greenway, MD, Medical Director and Professor at the Pennington Biomedical Research Center of the Louisiana State University.

Gelesis has submitted a medical device marketing application for Gelesis100 with the United States Food and Drug Administration (FDA) for review and is not available for sale.

About Gelesis100

Gelesis100 is a non-systemic, superabsorbent hydrogel in development for the potential treatment of overweight or obesity. It is made from two naturally derived building blocks, modified cellulose cross-linked with citric acid, that create a three-dimensional matrix. Orally administered in capsules with water before a meal, Gelesis100 particles rapidly absorb water in the stomach and homogenously mix with ingested foods. When hydrated, Gelesis100 occupies about one-fourth of the average stomach volume. Rather than forming one large mass, it creates thousands of small individual gel pieces with the elasticity (firmness) of solid ingested foods (e.g., vegetables) without caloric value. Gelesis100 maintains its three-dimensional structure and mechanical properties during transit through the small intestine. 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 expelled in the faeces. Gelesis100 is considered a medical device because it achieves its primary intended purpose through mechanical modes of action consistent with mechanobiology constructs. Gelesis100 received a Non-Significant Risk (NSR) determination by the FDA for the GLOW pivotal study.

This investigational product and its earlier prototypes have been studied in more than 450 patients (excluding patients treated by placebo) across five clinical studies throughout the United States, Canada, and Europe and in these studies has shown weight loss, increased satiety, and reduced hunger. Other than an increase in overall gastrointestinal adverse events (AEs), most of which were assessed as mild, there was no difference in the incidence and severity of AEs between the Gelesis100 and placebo groups. In both treatment groups, most AEs were mild or moderate in intensity. No serious adverse events were observed in the Gelesis100 group.

About Gelesis

Gelesis is developing a novel mechanobiology platform technology to treat obesity and other 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 chronic diseases. In September 2017, Gelesis completed a pivotal trial for weight loss evaluating its lead investigational product candidate Gelesis100. Additionally, Gelesis is conducting a proof-of-concept study for its second candidate, Gelesis200, which is 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 through a pipeline with preclinical studies in other GI-related conditions such as non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and inflammatory bowel disease (IBD).

The Gelesis executive and advisory team includes some of the world’s leading experts in obesity, chronic disease research, and materials science. Gelesis was co-founded by PureTech Health (PRTC.L), an advanced, clinical-stage biopharmaceutical company. For more information, visit www.gelesis.com or connect with us on Twitter @GelesisInc.

About PureTech Health

PureTech Health (LSE: PRTC) is an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis. The Company has developed deep insights into the connection between the individual components of these systems and the resulting role in many chronic diseases, which have proven resistant to established therapeutic approaches. By harnessing this emerging field of human biology, PureTech Health is developing new categories of medicines with the potential to have great impact on people with serious diseases.

PureTech Health is advancing a rich pipeline of innovative therapies across two divisions: the Affiliates division and the Internal division. Its Affiliates division includes two product candidates that have been filed with the US Food and Drug Administration (FDA) for review and several other novel clinical and pre-clinical programmes. These affiliates are developing ground-breaking platforms and therapeutic candidates in collaboration with some of the world’s leading experts.

PureTech’s Internal division is advancing a pipeline fuelled by recent discoveries in lymphatics and immune cell trafficking to modulate disease in a tissue-specific manner. These programmes leverage the transport and biodistribution of various immune system components for the targeted treatment of diseases with major unmet needs, including cancers, autoimmune diseases, and neuroimmune disorders.

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 company's 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, 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.