PureTech's Affiliate Gelesis Presents Data Supporting Lead Product Candidate's Positive Effect on People with Prediabetes, Untreated Diabetes, and Elevated Insulin Resistance

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Individuals with prediabetes and those with untreated type 2 diabetes had six times higher odds to achieve ≥10% weight loss compared to placebo

Individuals with high insulin resistance achieved significant drop in HOMA-IR levels on treatment independent of their level of weight loss

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 today presented clinical data at ENDO 2019, the Endocrine Society's annual meeting, suggesting that elevated fasting plasma glucose could be a useful and unique predictor to identify individuals who have higher adjusted odds to achieve significant weight loss with the Company's lead product candidate, Gelesis100.

Furthermore, individuals with high insulin resistance, as measured by HOMA-IR, at the start of the trial had a statistically significant reduction in HOMA-IR over the six-month treatment period – an effect observed both among those who lost significant weight while taking Gelesis100 and those who did not. Elevated insulin resistance is a significant driver of diabetes.

Gelesis100 is a superabsorbent hydrogel in development for the potential treatment of overweight and obesity. Data shared at ENDO 2019 show that individuals with prediabetes and untreated type 2 diabetes were particularly responsive to Gelesis100 in the pivotal GLOW study. They had six times higher odds of achieving ≥10% weight loss over six months, compared to placebo. Across the entire treatment group in the GLOW study, baseline fasting plasma glucose was correlated with greater weight loss (R =-0.24, P = 0.0144). The pronounced weight loss effect of Gelesis100 treatment in this population, which is at higher clinical risk, was also observed in a previous pilot study.

Eric Elenko, PhD, chief innovation officer at PureTech Health, said: "These findings suggest that Gelesis100 could be an important new tool for aiding in weight management in patients at high risk of diabetes or who have diabetes and are not yet on medication. Additional study is needed, but these data suggest that baseline measures of fasting plasma glucose could help predict which individuals are most likely to respond to Gelesis100 with significant weight loss of greater than 10% of their body weight. Gelesis100 could also be a compelling option for people with high insulin resistance. These data are particularly exciting given that obesity and diabetes are tremendous public health concerns and areas of high unmet medical need."

The full text announcement from Gelesis is as follows:

Gelesis Presents Expanded Data Showing Impact of Gelesis100 Hydrogel on Patients with Prediabetes, Untreated Diabetes, and Elevated Insulin Resistance

Individuals with prediabetes and those with untreated type 2 diabetes had six times higher odds to achieve ≥10% weight loss compared to placebo

Individuals with high insulin resistance achieved significant drop in HOMA-IR levels on treatment independent of their level of weight loss

BOSTON, March 25, 2019 —Gelesis, a biotechnology company developing first-in-class mechanotherapeutics to treat obesity and other chronic diseases related to the gastrointestinal (GI) pathway, today announced clinical data from its pivotal GLOW study suggesting that elevated fasting plasma glucose could be a useful and unique predictor to identify individuals who have higher adjusted odds to achieve significant weight loss with Gelesis100. As observed in a previous pilot study, participants with prediabetes or untreated type 2 diabetes were particularly responsive to its lead product candidate for weight management, Gelesis100. In addition, participants with high insulin resistance improved their insulin sensitivity significantly on treatment, including the non-responders (defined as those achieving less than 5% total body weight loss). The data were presented in two posters at ENDO 2019, the Endocrine Society's annual meeting.

"These findings provide compelling data that Gelesis100 may have particularly pronounced benefits for patients with elevated fasting blood glucose and diabetes. While additional studies with a longer time period need to be done, the metabolic and weight loss effects observed in the GLOW study support the concept that Gelesis100 could be an option for patients with high insulin resistance," said Harry L. Leider, M.D., MBA., FACPE, Chief Medical Officer of Gelesis. "We have already demonstrated that Gelesis100 is an effective tool for weight management. We now have data suggesting that the hydrogel may modulate the endocrine and metabolic systems to positive effect. We are eager to continue exploring the mechanisms behind these findings."

The data presented at ENDO 2019 come from subgroup analysis of the Gelesis Loss of Weight (GLOW) study, a pivotal multicentre, double-blind, placebo-controlled study of Gelesis100. The overarching study showed statistically significant separation from placebo in the ITT population and found that nearly 6 in 10 people treated with Gelesis100 were responders who lost, on average, 10% (about 22 pounds) of their body weight over six months.

In this subgroup analysis, researchers found that 44% of patients with elevated fasting blood glucose or untreated type 2 diabetes were "super-responders," meaning they lost at least 10% of their body weight (30 pounds on average) when treated with Gelesis100 (adjusted OR = 6.1, P = 0.007). Interestingly they had six times the odds of being super-responders, compared to placebo. Across the entire treatment group in the GLOW study, baseline fasting plasma glucose was correlated with greater weight loss (R =-0.24, P = 0.0144). The pronounced weight loss effect of Gelesis100 treatment in this population, which is at higher clinical risk, was also observed in the previous FLOW pilot study. The repeated findings suggest that Gelesis100 may be a new tool for aiding in weight management in patients at high risk of diabetes or diabetes-related complications.

"Participants with elevated fasting blood glucose and untreated type 2 diabetes had higher odds of achieving loss of at least 10% of their body weight. This was an important result as this population almost invariably has lesser weight loss in behavioural and medication trials," said Scott Kahan, M.D., MPH, director of the National Center for Weight and Wellness and a physician specializing in obesity.

A separate analysis found that patients with high insulin resistance – a significant driver of diabetes – had positive metabolic responses to treatment with Gelesis100. Insulin resistance was measured by homeostatic model assessment – insulin resistance (HOMA-IR). Patients with high IR at the start of the clinical trial (mean baseline HOMA= 5.0) had a statistically significant reduction in HOMA-IR over the six-month treatment period (-22.3 +/- 9.5%, P= 0.021). Importantly this reduction was observed both in patients that were weight loss responders (with 5% or greater weight loss) and also in non-weight loss responders. The HOMA-IR decrease in the subgroup overall was driven by a significant reduction in fasting serum insulin.

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. The study had two predefined co-primary endpoints: at least 35% of patients taking Gelesis100 achieving ≥ 5% weight loss (categorical endpoint) and placebo adjusted weight loss to be assessed in two ways (super-superiority margin of 3% and also simple superiority). The study met and exceeded the pre-defined categorical endpoint, with 59% of adults in the treatment group achieving weight loss of 5% or greater. As previously announced, the study did not meet the 3% super-superiority endpoint but demonstrated superiority of the Gelesis100 treatment over the placebo group (–6.4% vs. –4.4%, P=0.0007). Gelesis100-treated individuals 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).

The overall incidence of adverse events in the Gelesis100 treatment group was no different than placebo (71% in both groups). The most common AEs were gastrointestinal disorders (186 AEs in 96 [43%] subjects in the Gelesis100 arm, compared to 134 events in 72 [34%] subjects receiving placebo), infections and infestations (94 events in 74 [33%] subjects with Gelesis100 and 101 events in 70 [33%] subjects with placebo), and musculoskeletal and connective tissue disorders (38 events in 31 [14%] subjects with Gelesis100 and 45 in 34 [16%] subjects with placebo). There were no serious adverse events (SAE) in the Gelesis100 treatment group, whereas there was one (1) SAE in the placebo treatment group.

Gelesis100 has been extensively evaluated in clinical studies and has been submitted to the U.S. Food and Drug Administration for review.

About Gelesis 100

Gelesis100 is a non-systemic, superabsorbent hydrogel in development for the potential treatment of overweight or obesity. It is made by cross linking two naturally-derived building blocks, modified cellulose and citric acid, that create a three-dimensional matrix. Gelesis100 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 (firmness) of solid plant-based foods (e.g., vegetables) without caloric value. The Gelesis100 hydrogel mass increases the volume and elasticity of the stomach and small intestine contents, promoting fullness and potentially increasing satiety to help patients lose weight. 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 a mechanical mode of action. 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 demonstrating a strong efficacy, tolerability and safety profile. 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. For more information, visit gelesis.com.

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 chronic diseases. The company's lead product candidate, Gelesis100, has been submitted to the FDA for review as a weight management aid. Additionally, Gelesis is developing its second candidate, 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 through a pipeline in other GI inflammatory conditions where gut barrier and gut permeability potentially play a role, such as 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, materials science, chronic disease research and commercialisation. Gelesis was co-founded by PureTech Health (LSE: PRTC), a biopharmaceutical company focused on the Brain-Immune-Gut (BIG) axis. For more information, visit gelesis.com or connect with us on Twitter @GelesisInc.

About PureTech Health

PureTech Health (LSE: PRTC) is an advanced biopharmaceutical company developing BIG medicines for dysfunctions of the Brain-Immune-Gut axis. The Company has gained deep insights into the connection between these systems and the resulting role in diseases that 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 with an unbiased, non-binary, and capital efficient R&D model across its affiliates and its internal labs. PureTech's affiliates include seven clinical-stage platforms with two product candidates that have been filed with the US Food and Drug Administration (FDA) for review and other novel pre-clinical programmes. The PureTech Health pipeline includes ground-breaking platforms and therapeutic candidates that were developed in collaboration with some of the world's leading experts.

PureTech's internal research and development is centred on tissue-selective immunomodulation for the treatment of oncology, autoimmune, and CNS-related disorders, with a near-term focus on targeting newly-discovered, foundational immunosuppressive mechanisms in oncology and novel approaches that harness the lymphatic infrastructure.

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.