PureTech Health Affiliate Gelesis Announces Promising Pilot Clinical Data From Prototype of GS500 In Development for Chronic Idiopathic Constipation

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Investigational candidate developed by Gelesis demonstrated significant 16 hour reduction in colonic transit time in patients with chronic idiopathic constipation

First clinical study of programme's efficacy in common condition that affects up to 25% of US population

Data presented at Digestive Disease Week further supports proprietary hydrogel platform's potential across a variety of chronic diseases of the gastrointestinal pathway

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 announced promising clinical data from a pilot study of its GS500 prototype (GS500/ CSP01), which is being explored as a potential treatment for chronic idiopathic constipation (CIC). The data demonstrated that GS500 provided a significant reduction in colonic transit time in patients with CIC, relative to placebo. The data package was presented by Gelesis research collaborators from Brigham and Women's Hospital and Massachusetts General Hospital at Digestive Disease Week 2019, the world's largest gathering of physicians, researchers, and industry in the fields of gastroenterology, hepatology, endoscopy, and gastrointestinal surgery, held in San Diego, California.

The primary end-point of this randomised, double-blind study was the change in colonic transit time (CTT) from pre-treatment to post-treatment as measured by wireless motility capsules. Two populations were evaluated separately, 27 subjects with CIC and 13 subjects with irritable bowel syndrome with constipation (IBS-C). Patients were randomised into three treatment groups to receive 21 days of treatment with either GS500 (n=20), active control (modified cellulose, n=11) or placebo (n=9). Each subject's CTT was measured during the third week of treatment and compared to their baseline, collected during 7 days of pre-treatment. In the CIC population on treatment, colonic transit time was reduced by approximately 16 hours (~31%) compared to baseline (P=0.02 compared to placebo). No statistically significant change was observed in the placebo or the active control groups.

Gelesis' proprietary hydrogel product candidates are orally administered and synthesised from two naturally derived building blocks – modified cellulose cross-linked with citric acid – that create a three-dimensional matrix designed to achieve specific mechanical properties through the gastrointestinal system. Modulation of these properties allows hydrogel properties to be tailored to specific conditions. This pilot study provides the Company's first clinical data related to chronic idiopathic constipation.

The full text announcement from Gelesis is as follows:

Promising Clinical Data from Pilot Study of Gelesis' Novel Hydrogel GS500 Prototype for the Potential Treatment of Chronic Constipation Presented at Digestive Disease Week by Researchers from Massachusetts General Hospital and Brigham and Women's Hospital

Investigational candidate developed by Gelesis demonstrated significant 16 hour reduction in colonic transit time in patients with chronic idiopathic constipation

First clinical study demonstrating super-absorbent hydrogel platform's potential in this common condition

BOSTON, May 19, 2019 —Gelesis, a biotechnology company at the forefront of developing mechanobiology-based therapies to treat chronic diseases related to the gastrointestinal (GI) system, announced the presentation of data from a clinical study demonstrating that GS500 prototype (GS500/CSP01) provided a significant reduction in colonic transit time (CTT) in patients with chronic idiopathic constipation (CIC) relative to placebo. The data were presented at Digestive Disease Week 2019, held in San Diego, California.

"One out of seven adults throughout the world suffer from chronic idiopathic constipation. This condition can have a significant negative impact on quality of life," said Dr Braden Kuo, Gastrointestinal Unit in the Massachusetts General Hospital (MGH) Department of Medicine. "The safety and efficacy results of this study are intriguing and suggest further clinical evaluation in this very common, treatment resistant condition would be both warranted and welcome."

Gelesis' proprietary hydrogel product candidates are orally administered and synthesised from two naturally derived building blocks – modified cellulose cross-linked with citric acid – that create a three-dimensional matrix designed to achieve specific mechanical properties (high elastic response) through the gastrointestinal system. In order to assess the potential therapeutic benefits of the hydrogel's specific mechanical properties, modified cellulose, the main building block of GS500, was included as an active control. This modified cellulose is a widely used soluble dietary fiber but lacks the three dimensional structure of the superabsorbent hydrogel, and therefore creates significantly lower elastic response.

"The wireless motility capsule monitoring system allowed us to demonstrate that the superabsorbent hydrogel, in contrast to modified cellulose alone or placebo, accelerated colonic transit time," said Dr Kyle Staller, Center for Neurointestinal Health and Division of Gastroenterology at Harvard-affiliated Massachusetts General Hospital. "This finding suggests that the three-dimensional structure of Gelesis' hydrogel technology and specific elastic response may have contributed to the observed improvements in colonic transit time over the active fiber control in this study."

The primary end-point of this randomised, double-blind study was the change in CTT from pre-treatment to post-treatment as measured by wireless

motility capsules. The test involves swallowing a small data recording device which transmits information to a wireless data receiver.

Two populations were evaluated separately, 27 subjects with CIC and 13 subjects with irritable bowel syndrome with constipation (IBS-C). Patients were randomised into three treatment groups to receive 21 days of treatment with either GS500 (n=20), active control (modified cellulose, n=11) or placebo (n=9). Each subject's CTT was measured during the third week of treatment and compared to their baseline, collected during 7 days of pre-treatment. Secondary outcome measures included improvement of relevant gastro intestinal (GI) symptoms.

In the CIC population on treatment, colonic transit time was reduced by approximately 16 hours (~31%) compared to baseline (P=0.02 compared to placebo). No statistically significant change was observed in the placebo or the active control groups. No improvement was observed in the IBS-C population, as well as no change in the reported GI symptoms which were the secondary endpoints. Two randomised patients did not complete the study, one in the treatment group due to a GI related AE, and one in the placebo group due to a faulty monitoring device. No serious adverse events were reported.

This pilot study of 40 subjects was powered to detect improvement in CTT (the primary end-point). Recent data suggest that colonic transit time influences gut health and a longer faecal retention time is associated with CIC symptoms and less microbiome diversity. Further studies are required to assess the effect of Gelesis' hydrogel technology on symptom improvement.

About Chronic Idiopathic Constipation

Chronic idiopathic constipation (CIC) is a common gastrointestinal disorder. Its primary symptom is a low frequency of bowel movements, which can cause significant discomfort and negative impact on quality-of-life. CIC is estimated to affect between 15 and 25 percent of the general population in North America.

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. In April 2019, Gelesis received FDA clearance for its lead product candidate, PLENITY™. Gelesis is preparing to initiate a targeted US launch of PLENITY in the second half of 2019 and anticipates PLENITY will be broadly available by prescription in the US in 2020.

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 (GS300, GS400, GS500) 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). Recent preclinical data presented this year support the potential role of this novel hydrogel platform technology in restoring gut barrier function and intestinal tissue health.

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, including one product that has been cleared by the US Food and Drug Administration (FDA) and a second product candidate that has been filed with the FDA for review, and several other novel preclinical 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.