PureTech Founded Entity Gelesis Presents Study of Proprietary Hydrogel That Demonstrates How Gut Bacteria Contributes to Weight Loss and Beneficial Metabolic Effects

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PureTech Founded Entity Gelesis Presents Study of Proprietary Hydrogel That Demonstrates How Gut Bacteria Contributes to Weight Loss and Beneficial Metabolic Effects

New preclinical data presented at the American Diabetes Association's annual conference suggests that Gelesis' superabsorbent hydrogel causes changes to the microbiota leading to weight loss and improvements in glucose tolerance and insulin sensitivity

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company announced that its Founded Entity, Gelesis Holdings, Inc. (NYSE: GLS) ("Gelesis"), a consumer-focused biotherapeutics company and the maker of Plenity® for weight management, presented new preclinical data showing weight loss and additional metabolic benefits in mice receiving a microbiota transplant from another group of mice, treated with one of the company's proprietary hydrogels. These metabolic benefits occurred while both groups of mice, the donors of the microbiota transplant and the recipient mice, were on a high fat, high carbohydrate diet typically causing rapid weight gain, obesity, and diabetes. The findings were presented on Saturday at the American Diabetes Association's annual conference.

The study used intestinal microbiota transfer (IMT) to investigate the functional role of the gut microbiota to explain the metabolic effects associated with Gel-B treatment. Metabolic disease was induced in two cohorts of mice ("Donors" and "Recipients") via consumption of a high fat, high cholesterol, high carbohydrate (HFHCC) diet for 10 weeks. Donors either continued HFHCC or were treated with HFHCC plus Gel-B for 6 additional weeks. Fecal samples were processed from Donors every other day during weeks 2-6 of treatment. Recipients received either intestinal microbiota transfer from Gel-B-treated or untreated Donors. Recipients receiving IMT from untreated Donors continued to gain weight, while Recipients receiving IMT from Gel-B treated Donors lost weight, despite the continued consumption of HFHCC. Treating the recipients with intestinal microbiota of Gel B treated donors also resulted in improvement in glycemic control.

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

Microbiota Transplantation Demonstrates How Gut Bacteria Contributes to Weight Loss and Beneficial Metabolic Effects with Gelesis' Proprietary Hydrogel

New preclinical data presented today at the American Diabetes Association's annual conference suggests that the company's superabsorbent hydrogel causes changes to the microbiota leading to weight loss and improvements in glucose tolerance and insulin sensitivity

BOSTON, JUNE 4, 2022 - Gelesis (NYSE: GLS), the maker of Plenity for weight management, presented new preclinical data showing weight loss and additional metabolic benefits in mice receiving a microbiota transplant from another group of mice, treated with one of the company's proprietary hydrogels. These metabolic benefits occurred while both groups of mice, the donors of the microbiota transplant and the recipient mice, were on a high fat, high carbohydrate diet typically causing rapid weight gain, obesity, and diabetes. The findings were presented today at the American Diabetes Association's annual conference.

Gelesis' superabsorbent hydrogels are inspired by the composition (cellulose structures holding water) and mechanical properties (elasticity or firmness) of ingested raw vegetables. They are taken by capsules with water before a meal to create a much larger volume of small, non-aggregating hydrogel pieces that act locally in the digestive system without adding any additional calories. One of the hydrogels is commercially available as Plenity® to aid in weight management; others that utilize the same platform technology are in clinical and preclinical studies.

In April, Gelesis presented preclinical data at the World of Microbiome conference suggesting that adding superabsorbent hydrogel (Gel-B, an investigational candidate) to a high-fat "western-like" diet prevents unfavorable changes in the communities of gut bacteria associated with diet-induced weight gain. The study showed a striking effect on gut microbiota composition with enrichment of several key bacteria such as *Akkermansia muciniphila*, a bacterial species associated with gut health and weight loss. Importantly, an addible fiber (a modified cellulose), used as a positive control, did not support the growth of these species. This same type of modified cellulose is used to create Gelesis' proprietary hydrogels. The difference in bacterial growth between the linear fiber and the 3-dimensional hydrogel suggests that the effects of the hydrogel on the microbiota are mainly mechanical (i.e. elastic response or firmness). In previous studies, administration of one of these hydrogels, in addition to a high-fat diet, blunted weight gain, reversed gut atrophy, improved metabolic parameters, and restored gut barrier.

This new study aimed to investigate whether transferring the microbiota from Gel B-treated mice into the gut of mice fed a high fat, high carbohydrate, high cholesterol (HFHCC) diet for 10 weeks could alleviate the detrimental effects of their diet.

"This study provides strong evidence that the modulation of the gut microbiome by Gelesis' superabsorbent hydrogel likely plays a mechanistic role in the weight loss and metabolic impact of this intervention," said Maria Rescigno, PhD, Group Leader of the Mucosal Immunology and Microbiota Unit at Humanitas University in Milan, and one of the lead investigators on the study. "We found that the microbiota from animals with obesity consuming a high-fat diet can be modified with Gel-B treatment to become a 'lean microbiota.' We then found that this Gel-B induced lean microbiota was transmissible, as it caused weight loss in mice with obesity that were not treated by Gel-B."

The study used intestinal microbiota transfer (IMT) to investigate the functional role of the gut microbiota to explain the metabolic effects associated with Gel-B treatment. Metabolic disease was induced in two cohorts of mice ("Donors" and "Recipients") via consumption of a high fat, high cholesterol, high carbohydrate diet for 10 weeks. Donors either continued HFHCC or were treated with HFHCC plus Gel-B for 6 additional weeks. Fecal samples were processed from Donors every other day during weeks 2-6 of treatment. Recipients received either intestinal microbiota transfer from Gel-B-treated or untreated Donors. Recipients receiving IMT from untreated Donors continued to gain weight, while Recipients receiving IMT from Gel-B treated Donors lost weight, despite the continued consumption of HFHCC. Treating the recipients with intestinal microbiota of Gel B treated donors also resulted in improvement in glycemic control.

An interview with study author Dr. Rescigno is available at https://youtu.be/AsmUo7lnQbs.

About Gelesis

Gelesis Holdings Inc. (NYSE: GLS) ("Gelesis") is a consumer-centered biotherapeutics company and the maker of Plenity®, which is inspired by nature and FDA cleared to aid in weight management. Our first-of-their-kind non-systemic superabsorbent hydrogels are made entirely from naturally derived building blocks. They are inspired by the composition and mechanical properties of raw vegetables, taken by capsule, and act locally in the digestive system, so people feel satisfied with smaller portions. Our portfolio includes Plenity® and potential therapies in development for patients with Type 2 Diabetes, Non-alcoholic Fatty Liver Disease (NAFLD)/Non-alcoholic Steatohepatitis (NASH), and Functional Constipation. For more information, visit gelesis.com, or connect with us on Twitter @GelesisInc.

Plenity® is indicated to aid weight management in adults with excess weight or obesity, a Body Mass Index (BMI) of 25-40 kg/m², when used in conjunction with diet and exercise.

Important Safety Information about Plenity

- Patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium

dioxide should not take Plenity.

- To avoid impact on the absorption of medications:
  - For all medications that should be taken with food, take them after starting a meal.
  - For all medications that should be taken without food (on an empty stomach), continue taking on an empty stomach or as recommended by your physician.
- The overall incidence of side effects with Plenity was no different than placebo. The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence.
- Contact a doctor right away if problems occur. If you have a severe allergic reaction, severe stomach pain, or severe diarrhea, stop using Plenity until you can speak to your doctor.

Rx Only. For the safe and proper use of Plenity or more information, talk to a healthcare professional, read the Patient Instructions for Use, or call 1-844-PLENITY.

Forward-Looking Statements

Certain statements, estimates, targets and projections in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws. The words "anticipate," "believe," continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "strive," "would" and similar expressions may identify forward-looking statements, but the absence of these words does not mean that statement is not forward looking. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. Forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding the future, including those relating to Gelesis' business combination with Capstar Special Purpose Acquisition Corp. ("Capstar") and its expected benefits, Gelesis' performance following the business combination, the competitive environment in which Gelesis operates, the expected future operating and financial performance and market opportunities of Gelesis and statements regarding Gelesis' expectations, hopes, beliefs, intentions or strategies regarding the future. In addition, any statements that refer to projections, forecasts, or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. Forward-looking statements speak only as of the date they are made. Readers are cautioned not to put undue reliance on forward-looking statements, and Gelesis assumes no obligation and does not intend to update or revise these forward-looking statements, whether as a result of new information, future events, or otherwise. Gelesis gives no assurance that any expectations set forth in this press release will be achieved. Various risks and uncertainties (some of which are beyond our control) or other factors could cause actual future results, performance or events to differ materially from those described herein. Some of the factors that may impact future results and performance may include, without limitation: (i) the size, demand and growth potential of the markets for Plenity® and Gelesis' other product candidates and Gelesis' ability to serve those markets; (ii) the degree of market acceptance and adoption of Gelesis' products; (iii) Gelesis' ability to develop innovative products and compete with other companies engaged in the weight loss industry; (iv) Gelesis' ability to finance and complete successfully the commercial launch of Plenity® and its growth plans, including new possible indications and the clinical data from ongoing and future studies about liver and other diseases; (v) failure to realize the anticipated benefits of the business combination, including as a result of a delay or difficulty in integrating the businesses of Capstar and Gelesis; (vi) the ability of Gelesis to issue equity or equity-linked securities or obtain debt financing in the future; (vii) the outcome of any legal proceedings instituted against Capstar, Gelesis, or others in connection with the business combination; (viii) the ability of Gelesis to maintain its listing on the New York Stock Exchange; (ix) the risk that the business combination disrupts current plans and operations of Gelesis as a result of Gelesis being a publicly listed issuer; (x) the regulatory pathway for Gelesis' products and responses from regulators, including the FDA and similar regulators outside of the United States; (xi) the ability of Gelesis to grow and manage growth profitably, maintain relationships with customers and suppliers and retain Gelesis' management and key employees; (xii) costs related to the business combination, including costs associated with the Gelesis being a publicly listed issuer; (xiii) changes in applicable laws or regulations; (xiv) the possibility that Gelesis may be adversely affected by other economic, business, regulatory and/or competitive factors; (xv) Gelesis' estimates of expenses and profitability; (xvi) ongoing regulatory requirements, (xvii) any competing products or technologies that may emerge, (xviii) the volatility of the telehealth market in general, or insufficient patient demand; (xix) the ability of Gelesis to defend its intellectual property and satisfy regulatory requirements; (xx) the impact of the COVID 19 pandemic on Gelesis' business; (xxi) the limited operating history of Gelesis; (xxii) the potential impact of inflation on our operating expenses and costs of goods; and (xxiii) other important factors discussed in the "Risk Factors" section of Gelesis' most recent Annual Report on Form 10-K, and in other filings that Gelesis makes with the Securities and Exchange Commission. These filings address other important risks and uncertainties that could cause actual results and events to differ materially from those contained in the forward-looking statements.

About PureTech Health

PureTech is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, 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 27 therapeutics and therapeutic candidates, including two that have received both U.S. FDA clearance and European marketing authorization, as of the date of PureTech's most recently filed Annual Report and corresponding Form 6-K. All of the underlying programs and platforms that resulted in this pipeline of therapeutic candidates were initially identified or discovered and then advanced by the PureTech team through key validation points based on unique insights in immunology and drug development.

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

Cautionary Note Regarding Forward-Looking Statements

This press release contains statements that are or may be forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements that relate to the business combination agreement between Gelesis and Capstar Special Purpose Acquisition Corp. (NYSE: CPSR) or matters related thereto, the potential of Gel-B to become a foundational treatment, and Gelesis' future prospects, development plans, and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks, uncertainties and other important factors that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks, uncertainties and other important factors described under the caption "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2021 filed with the SEC and in our other regulatory filings. 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, we disclaim any obligation to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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