PureTech's LYT-100 (Deupirfenidone) Achieves 50% Reduction in Healthy Older Adults Experiencing GI-Related Adverse Events Compared to Pirfenidone

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PureTech's **LYT-100 (Deupirfenidone) Achieves 50% Reduction in Healthy Older Adults Experiencing GI-Related Adverse Events Compared to Pirfenidone**

PureTech to initiate registration-enabling studies with LYT-100 for the treatment of IPF with a streamlined 505(b)(2) development path that includes a dose-ranging study in IPF patients and a Phase 3 study in IPF patients

Veteran IPF and pulmonary drug development expert, Paul Ford, M.D., Ph.D., joins PureTech as SVP Clinical Development to lead this program

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, today announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with PureTech's LYT-100 (deupirfenidone) experienced gastrointestinal (GI)-related adverse events (AEs) compared to subjects treated with pirfenidone (17.4% vs. 34.0%). Pirfenidone is approved by the U.S. Food and Drug Administration (FDA) for the treatment of idiopathic pulmonary fibrosis (IPF), an orphan disease that is chronic and progressive resulting in significant morbidity and mortality. Based on these results, additional data generated from PureTech's robust LYT-100 clinical program and recent regulatory feedback, the Company intends to advance LYT-100 into late-stage clinical development for the treatment of IPF, beginning with a dose-ranging study evaluating six months of treatment with LYT-100 initiating in the first half of 2022. PureTech believes the results of this study, together with a Phase 3 study, could serve as the basis for registration in the U.S.

LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically-validated anti-fibrotic and anti-inflammatory activity of pirfenidone with a differentiated pharmacokinetic profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies. Pirfenidone is one of the two standard of care treatments approved for IPF, along with nintedanib, both of which are efficacious but associated with significant GI-related tolerability issues.[1,2] Tolerability issues associated with pirfenidone result in treatment discontinuations and/or dose reductions below the FDA-approved dose of 801 mg three times a day (TID), thereby limiting its effectiveness in patients with IPF.[1]

"In the recently completed healthy older adult study, LYT-100 administration resulted in a clinically meaningful 50% reduction in the number of healthy older adults experiencing GI-related adverse events, compared to pirfenidone. This underscores the potential of LYT-100 to address a significant unmet need for patients with IPF by offering a more tolerable treatment option that may allow patients to continue on therapy, which is critical to address this serious condition," said Julie Krop, M.D., Chief Medical Officer of PureTech. "The ability to pursue a 505(b)(2) development path for LYT-100 based on the validated biology and known clinical benefits of pirfenidone significantly de-risks our path to approval and has the potential to make this important therapy available to patients faster."

Based on a recently published observational study and independent market research, only about 26% of IPF patients are treated with the current standard of care treatments despite their proven efficacy.[3] This suggests that a vast majority of IPF patients are not currently being treated, and further supports the significant need for new, tolerable treatment options. A previous clinical study comparing a lower dose of pirfenidone than the FDA-approved dose noted a dose-efficacy response, but whether doses higher than the marketed dose can achieve increased efficacy has not been adequately explored in patients with IPF. In the upcoming dose-ranging study, PureTech also plans to investigate LYT-100 in IPF patients at a dose with a higher total drug exposure than the currently approved dose of pirfenidone to see if higher exposure results in improved efficacy.

"Treatments that are both more effective and have fewer side effects are urgently needed in the fight against IPF," said Toby Maher, M.D., Ph.D., Professor of Medicine at Keck Medicine of USC Academic Medical Center at the University of Southern California. "LYT-100 builds on a wealth of existing clinical and biological knowledge and incorporates a novel modification that has now clearly been shown to improve tolerability and therefore treatment compliance - both of which are critical to improving outcomes for individuals with this chronic, progressive and inevitably fatal disease."

The double-blind, randomized, crossover study evaluated the tolerability of LYT-100 550 mg TID versus pirfenidone 801 mg TID in 49 healthy older adults aged 60-79, an age group consistent with that of the IPF patient population. The dose of LYT-100 used in this study was selected based on pharmacokinetics (PK) and modeling data from prior studies, which together suggest that 550 mg TID results in similar exposure levels achieved with 801 mg TID of pirfenidone. The study showed that 38% fewer subjects treated with LYT-100 experienced any AEs compared with those treated with pirfenidone (30.4% vs. 48.9%). Additionally, approximately 50% fewer subjects experienced GI-related AEs with LYT-100 compared with pirfenidone (17.4% vs. 34.0%), most notably nausea (15.2% with LYT-100 vs. 29.8% with pirfenidone), which is the most common AE associated with pirfenidone. No serious AEs were reported in the study, and there was one AE-related discontinuation in each arm. Though not powered to show statistical significance, this study provides evidence that LYT-100 has the potential to offer an important tolerability advantage over pirfenidone and helps to inform PureTech's development plans with this therapeutic candidate in IPF.

Based on the data generated to date and discussions with the FDA, PureTech plans to pursue a streamlined development program for LYT-100 in IPF, capitalizing on efficiencies of the 505(b)(2) pathway. The dose-ranging study, which is anticipated to begin in the first half of 2022, will enroll approximately 250 treatment naïve patients to evaluate LYT-100 efficacy relative to placebo and compare relative tolerability and efficacy for pirfenidone. The planned study will evaluate TID dosing of LYT-100 taken with meals. The TID regimen is designed to reduce the maximal drug concentration (Cmax), known to correlate with GI-related AEs with pirfenidone, while maintaining the same or higher overall systemic exposure (AUC) as pirfenidone. Pending positive clinical and regulatory feedback, the program will advance into a Phase 3 study.

To oversee the LYT-100 development program in IPF, Paul Ford, M.D., Ph.D., has joined PureTech as SVP of Clinical Development. Dr. Ford is an experienced clinical pulmonologist with more than 20 years of research and development expertise dedicated to IPF and other respiratory conditions. He has built and advanced programs from early to late-stage development at companies including Novartis, Galapagos and Galecto, and he has driven the recruitment and randomization of nearly 1,500 patients with IPF across several clinical studies.

"I am thrilled to be joining PureTech as we move LYT-100 into late-stage clinical development for the treatment of IPF. The data generated to date suggest LYT-100 may offer an important new treatment option for patients who are not currently on therapy or struggle to tolerate existing treatment options, which represent a substantial portion of the IPF patient population," said Dr. Ford. "I believe we have an efficient development path to support a compelling registration-enabling package in our pursuit to improve the treatment landscape for patients with IPF."

To date, LYT-100 has been studied in more than 400 subjects and demonstrated a favorable safety profile as part of PureTech's ongoing development work and indication prioritization. The company has conducted multiple Phase 1 studies to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults, the results of which have helped inform PureTech's development plans in IPF. These studies, as well as other ongoing studies, will also help to inform potential future development plans in other indications beyond IPF.

About LYT-100

LYT-100 is PureTech's most advanced therapeutic candidate from within its Wholly Owned Pipeline. A deuterated form of pirfenidone, an approved anti-inflammatory and anti-fibrotic drug, LYT-100 is being advanced for the potential treatment of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. PureTech is also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions such as myocardial and other organ system fibrosis based on the strength of existing clinical data around the use of pirfenidone in these indications.

In the fourth quarter of 2020, PureTech initiated a Phase 2 study evaluating LYT-100 as a potential treatment for Long COVID respiratory complications and related sequelae and a Phase 2a proof-of-concept study evaluating LYT-100 in patients with breast cancer-related, upper limb secondary lymphedema. Enrollment in the Long COVID study is complete, and topline results are anticipated in the first half of 2022. Topline results from the Phase 2a proof-of-concept breast cancer-related, upper limb secondary lymphedema study are anticipated in 2022. PureTech also expects to initiate a Phase 2 dose-ranging trial of LYT-100 in patients with IPF in the first half of 2022.

About Idiopathic Pulmonary Fibrosis (IPF)

Idiopathic Pulmonary Fibrosis (IPF) is an orphan condition that is progressive and characterized by irreversible scarring of the lungs that worsens over time and makes it difficult to breathe. The prognosis of IPF is poor, with the median survival after diagnosis generally estimated at two to five years. Currently available treatment options are associated with significant tolerability issues and dose-limiting toxicities, which can hamper treatment compliance and leaves patients and physicians needing new treatment options.

About the 505(b)(2) Regulatory Pathway

A 505(b)(2) is a type of New Drug Application (NDA) that a company may submit to the U.S. Food and Drug Administration (FDA) when seeking approval for an investigational therapeutic candidate. This application type allows a company to submit some of the required information based on studies not conducted by or for the applicant, which is intended to avoid unnecessary duplication of clinical studies and may therefore result in a less expensive clinical program and potentially shorter development timeline as compared to a traditional full NDA development path.

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 25 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 Half Year 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 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.

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 those related to our initiation of registration-enabling studies with LYT-100 for the treatment of IPF with a streamlined 505(b)(2) development path and the design and timing for the initiation of the dose-ranging and Phase 3 studies supporting the clinical development of LYT-100 for IPF in accordance with our development plan, our belief that the results of these studies could serve as the basis for registration of LYT-100 in the United States, the treatment potential of LYT-100, including its ability to address a significant unmet need for patients with IPF and certain shortcomings with respect to current standards of care, expectations regarding the potential of clinical data to support clinical development of LYT-100 for indications beyond IPF, the timing for topline results from our current Phase 2 Long COVID respiratory and 2a proof-of-concept breast cancer-related, upper limb secondary lymphedema studies of LYT-100, our product candidates and approach towards addressing major diseases, and our future prospects, developments 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, 2020 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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[2] Kato, M., Sasaki, S., Nakamura, T., Kurokawa, K., Yamada, T., Ochi, Y., Ihara, H., Takahashi, F., & Takahashi, K. (2019). Gastrointestinal adverse effects of nintedanib and the associated risk factors in patients with idiopathic pulmonary fibrosis. Scientific Reports, 9(1). https://doi.org/10.1038/s41598-019-48593-4.

[3] Dempsey, T. M., Payne, S., Sangaralingham, L., Yao, X., Shah, N. D., & Limper, A. H. (2021). Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Annals of the American Thoracic Society, 18(7), 1121-1128. https://doi.org/10.1513/AnnalsATS.202007-901OC.

[4] Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

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