PureTech Initiates Late-Stage Clinical Study of Wholly-Owned Candidate LYT-100 (Deupirfenidone) in IPF and Advances LYT-200 (Anti-Galectin-9 mAb)

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IPF study will evaluate efficacy of two doses of LYT-100, one with comparable exposure to FDA-approved dose of pirfenidone and one with higher exposure, vs. placebo, as well as relative tolerability and efficacy vs. pirfenidone

Bi-monthly, monotherapy dose escalation portion of Phase 1/2 study of LYT-200 for the potential treatment of solid tumors has completed; evaluation of weekly doses of LYT-200 as a monotherapy has begun, and combination cohorts with chemotherapy or an anti-PD-1 to begin later this year

Company also plans to initiate studies with LYT-200 in leukemia by end of 2022

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 the initiation of a clinical study of LYT-100 (deupirfenidone), PureTech's wholly-owned therapeutic candidate for the potential treatment of idiopathic pulmonary fibrosis (IPF), to support its registration-enabling package. LYT-100 is a selectively deuterated form of pirfenidone. Pirfenidone is a proven therapy for IPF, a devastating condition where the favorable tolerability, safety and potentially higher exposure of LYT-100 could have an important impact on patient adherence and outcomes.

"The initiation of this study is supported by substantial clinical data demonstrating favorable safety and tolerability of LYT-100," said Julie Krop, M.D., Chief Medical Officer of PureTech. "The unique profile of LYT-100, coupled with the established efficacy of pirfenidone, has the potential to significantly improve care for these patients. We believe that enabling patients to stay on a therapeutic dose longer - even at a dose with comparable exposure to the FDA-approved dose of pirfenidone - has the potential to drive better efficacy. In addition, achieving higher exposure levels than the FDA-approved dose of pirfenidone has the potential to offer even better efficacy, which is our rationale for pursuing a higher dose of LYT-100 in this study. We are excited to be taking this important step towards our goal of helping patients with this devastating condition."

IPF is a chronic orphan condition that causes progressive scarring of the lungs, and approximately 130,000 people in the U.S. are living with the disease. The prognosis of IPF is poor, with the median survival after diagnosis generally estimated at two to five years. Pirfenidone is approved by the U.S. Food and Drug Administration (FDA) for IPF, yet there are serious limitations to pirfenidone's clinical use, primarily due to severe gastrointestinal (GI)-related tolerability issues.[1,2]

"Pirfenidone has proven efficacy to slow the decline in lung function in patients with IPF. However, many patients with IPF who start pirfenidone have side effects that cause them to either discontinue therapy or reduce their dose," said Kevin Flaherty, M.D., Professor of Internal Medicine at the University of Michigan specializing in IPF and other interstitial lung diseases and an advisor to PureTech. "I am excited by the safety and tolerability data generated to date with LYT-100, particularly the most recent data demonstrating how well-tolerated it was in a relatively sick, older patient population with multiple comorbidities, as I believe it could represent great potential in patients with IPF."

LYT-100 is designed to retain the potent and clinically validated anti-fibrotic and anti-inflammatory activity of pirfenidone but has demonstrated a highly

differentiated pharmacokinetic (PK) profile that has translated into improved tolerability in PureTech's ongoing clinical development program. To date, LYT-100 has been studied in more than 400 subjects and demonstrated a favorable safety and tolerability profile. In a crossover study in healthy older adults with similar median age to patients with IPF, PureTech showed that approximately 50% fewer subjects experienced GI-related adverse events (AEs) with LYT-100 compared with pirfenidone (17.4% vs. 34.0%) and substantially fewer subjects experienced AEs with LYT-100 vs. pirfenidone. PureTech also recently showed that LYT-100 can be safely dosed with a higher total drug exposure than the currently approved dose of pirfenidone, which could translate into improved efficacy over pirfenidone.

The global, randomized, placebo-controlled registration-enabling study is designed to evaluate the efficacy, tolerability, safety and dosing regimen of LYT-100 to help inform the study design for a potential pivotal study and to assess the relative efficacy of LYT-100 compared to pirfenidone. A total of approximately 240 patients will be randomized 1:1:1:1 to receive either one of two dose levels of LYT-100, the FDA-approved dose of pirfenidone, or a placebo. One of the LYT-100 arms will evaluate 550 mg three times a day (TID) of LYT-100, which has previously demonstrated the comparable exposure as the currently approved dose of pirfenidone (801 mg TID), and the other arm will evaluate an 825 mg TID dose of LYT-100, which has demonstrated higher exposure than the currently approved dose of pirfenidone with the potential for improved efficacy. The primary objective of the study is to demonstrate a statistically significant and clinically meaningful difference in the slope of decline in a measure of lung function, Forced Vital Capacity (FVC), in the LYT-100 treatment arms compared to placebo over 6 months. The study will also evaluate safety, tolerability and the slope of FVC decline in the LYT-100 treatment arms compared to pirfenidone, though this analysis is not powered to demonstrate strict non-inferiority. FVC is an established measure of pulmonary function in IPF and has served as the basis for FDA approval of the currently marketed treatments for IPF. Topline results from the study are expected by the end of 2023.

Advancement of LYT-200 Clinical Program

PureTech's LYT-200 program is also progressing through clinical development. Following the completion of the monotherapy dose escalation portion of the Phase 1 program, PureTech has begun to evaluate weekly doses of LYT-200 and will soon begin to enroll patients in cohorts designed to evaluate LYT-200 in combination with chemotherapy or an anti-PD-1 monoclonal antibody. Results from the single agent cohorts are expected by the end of 2022, and results from the combination cohorts are expected in 2023.

LYT-200 is a fully human IgG4 monoclonal antibody (mAb) designed to inhibit the activity of galectin-9, a key molecule expressed by tumors and immune cells and shown in preclinical models to suppress the immune system from recognizing and destroying cancer cells. The primary objective of the Phase 1 portion of the ongoing adaptive Phase 1/2 study is to assess the safety and tolerability of escalating doses of LYT-200 in order to identify an appropriate dose and dosing interval to carry forward into the Phase 2 portion of the trial. Six cohorts were treated with escalating, bi-monthly doses from 0.2-16 mg/kg, and no dose limiting toxicities were reported to date.

Additionally, compelling preclinical data have been generated with LYT-200 in leukemia models, which will be submitted for presentation in a scientific forum. Based on these data, PureTech plans to initiate a study of LYT-200 as a single agent in leukemia patients by the end of 2022.

"We are very pleased with the progress of our Phase 1 evaluation of LYT-200, which has demonstrated favorable safety and tolerability as a single agent at all doses studied to date without any dose limiting toxicities," said Aleksandra Filipovic, M.D., Ph.D., Head of Oncology at PureTech. "We look forward to the continued evaluation of this novel therapy as a potential treatment for metastatic solid tumors as well as the initiation of clinical studies in leukemia."

About LYT-100

LYT-100 is one of seven therapeutic candidates within PureTech's Wholly Owned Pipeline. It 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 supported by data from multiple human clinical studies. LYT-100 is being advanced for the potential treatment of conditions involving inflammation and fibrosis, including idiopathic pulmonary fibrosis and breast cancer-related, upper limb secondary 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.

About LYT-200

LYT-200 is a fully human IgG4 monoclonal antibody targeting a foundational immunosuppressive protein, galectin-9, for the potential treatment of solid tumors, including pancreatic ductal adenocarcinoma, colorectal cancer and cholangiocarcinoma, that are difficult to treat and have poor survival rates. PureTech has presented preclinical data demonstrating high expression of galectin-9 across breast cancer, pancreatic and cholangiocarcinoma samples and found that the highest levels of galectin-9 correlated with shorter time to disease relapse and poor survival. These data suggest that galectin-9 could be significant both as a therapeutic target for a range of cancers and as a cancer biomarker. Preclinical animal and patient-derived organoid tumor models also showed the potential efficacy of LYT-200 and the importance of galectin-9 as a target. LYT-200 is currently being evaluated in a Phase 1/2 adaptive design trial.

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 those related to our study of LYT-100 for the treatment of IPF and the timing for topline results from the study, the treatment potential of LYT-100 for patients with IPF, our LYT-200 development program and the timing of results for the Phase 1 portion of our Phase 1/2 study as well as our plans to initiate a study of LYT-200 as a single agent in leukemia patients, and our therapeutic 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, 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.

[1] Rubino, C. M., Bhavnani, S. M., Ambrose, P. G., Forrest, A., & Loutit, J. S. (2009). Effect of food and antacids on the pharmacokinetics of pirfenidone in older healthy adults. *Pulmonary pharmacology & therapeutics*, *22*(4), 279-285. https://doi.org/10.1016/j.pupt.2009.03.003

[2] Belhassen, M., Dalon, F., Nolin, M., & Van Ganse, E. (2021). Comparative outcomes in patients receiving pirfenidone or nintedanib for idiopathic pulmonary fibrosis. Respiratory research, 22(1), 135. https://doi.org/10.1186/s12931-021-01714-y

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