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PureTech Announces Publication of Phase 1 Results for LYT-100 in the Journal Clinical Pharmacology in Drug Development and Provides Timing Updates

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PureTech Announces Publication of Phase 1 Results for LYT-100 in the Journal *Clinical Pharmacology in Drug Development* **and Provides Timing Updates**

LYT-100 well-tolerated at all doses studied with a favorable PK profile; maximum tolerated dose not determined; additional studies underway to evaluate higher doses.

Phase 2 enrollment of LYT-100 in patients with Long COVID[1] respiratory complications expected to complete by year-end; results anticipated in 1H 2022.

Phase 1 healthy volunteer trials underway to further evaluate LYT-100 PK, dosing and tolerability to inform clinical development of LYT-100 across multiple indications; results anticipated in Q1 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 that the results from a Phase 1 trial evaluating multiple ascending doses and the food effect of LYT-100 (deupirfenidone) were published in the journal *Clinical Pharmacology in Drug Development*. Topline results from this Phase 1 study were previously announced in November 2020 and demonstrated that LYT-100 was well-tolerated in healthy volunteers under both fed and fasting conditions.

LYT-100 is PureTech's wholly-owned therapeutic candidate that is being advanced for the potential treatment of conditions involving inflammation and fibrosis and disorders of lymphatic flow. It is currently being evaluated in two Phase 2 trials in patients with Long COVID respiratory complications and breast cancer-related, upper limb secondary lymphedema. Enrollment in the Long COVID respiratory trial is expected to be completed by the end of 2021, with topline results anticipated in the first half of 2022. Topline results from the breast cancer-related, upper limb secondary lymphedema trial are anticipated in 2022.

"The data set from the completed Phase 1 MAD study, including a favorable safety and tolerability profile, reaffirms our belief that LYT-100 has the potential to be an attractive therapeutic option across a range of conditions. There are substantial shortcomings with the current standards of care for patients living with

fibrotic lung disease, and we believe that the anti-fibrotic and anti-inflammatory properties along with the favorable tolerability profile demonstrated with LYT-100 to date could address this issue," said Michael Chen, Ph.D., Head of Innovation at PureTech Health. "We're encouraged by these results and look forward to the upcoming clinical readouts as we advance LYT-100 in multiple indications."

LYT-100 is a selectively deuterated form of pirfenidone that retains the pharmacologic properties of the parent compound but is expected to be metabolized at an attenuated rate. GI-related tolerability issues have historically been associated with pirfenidone and have limited its usage in patients at the therapeutic dose approved by the U.S. Food and Drug Administration (FDA) for the treatment of idiopathic pulmonary fibrosis (IPF). Despite a noted dose-efficacy response in clinical trials in patients with IPF, higher doses of pirfenidone have not been adequately explored due to limitations in tolerability. PureTech is currently exploring the pharmacokinetic (PK) and tolerability profile of LYT-100 across a range of doses in order to determine whether LYT-100 can achieve higher levels of systemic exposure than the currently FDA-approved dose of pirfenidone.

Multiple ascending dose and food effect study results

The Phase 1 multiple ascending dose and food effect study was a randomized, double-blind, placebo-controlled study designed to evaluate the safety, tolerability, PK profile and food effect of LYT-100 in healthy volunteers in both fed and fasting states. Plasma concentrations of LYT-100 and its metabolites were measured to determine PK parameters.

Part 1 assessed multiple ascending doses of LYT-100 administered in doses of 100 mg, 250 mg, 500 mg, 750 mg and 1000 mg BID over five days without dose titration. Part 2 assessed the effect of fed versus fasting conditions on the PK profile of LYT-100 following a single 500 mg dose. No dose limiting toxicities were noted, and a maximum tolerated dose was not determined.

All adverse events (AEs) that were possibly or probably related to LYT-100 were mild. Of the 40 participants, 37 (92.5%) completed part 1 of the study and eight participants who completed part 1 also completed part 2. The most common AEs across part 1 of the multiple ascending dose cohorts were headache, abdominal distension and nausea. There were no tolerability issues after administration of a single dose of 500 mg given with or without food.

A dose-proportional PK profile was observed with LYT-100 throughout the range of doses studied. As with pirfenidone, LYT-100 exposure was affected by food, with fed conditions resulting in lower drug exposure compared to fasting conditions. The ratio of exposure during fed conditions was approximately 20% to 25% less than exposure during fasting. Fed conditions led to a 26% reduction in Cmax observed with LYT-100, while the Cmax reduction stated in the ESBRIET® (pirfenidone) U.S. Prescribing Information is 49%.

The therapeutic dose of pirfenidone approved by the FDA for the treatment of IPF is 801 mg three times a day. LYT-100 is designed to potentially improve upon this regimen. In a previously conducted single-dose crossover study, an 801 mg dose of LYT-100 resulted in greater drug exposure than an 801 mg dose of pirfenidone. In part 1 of the multiple ascending dose study, LYT-100 was well-tolerated at a dose above 801 mg.

Additional Phase 1 studies and future development plans

Given that the maximum tolerated dose for LYT-100 was not determined in the original Phase 1 study,

PureTech initiated a second multiple ascending dose study earlier this year to evaluate higher doses of the drug in healthy volunteers. PureTech also initiated additional Phase 1 studies to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies are expected in the first quarter of 2022.

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 (e.g., IPF and potentially other PF-ILDs 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, kidney and other organ system fibrosis based on clinical data around the use of pirfenidone in these indications.

PureTech completed a Phase 1 multiple ascending dose and food effect study evaluating LYT-100 in healthy volunteers and found it to be well-tolerated at all doses tested. In the fourth quarter of 2020, PureTech initiated a Phase 2 trial evaluating LYT-100 as a potential treatment for Long COVID respiratory complications and related sequalae and a Phase 2a proof-of-concept study evaluating LYT-100 in patients with breast cancer-related, upper limb secondary lymphedema. PureTech has also initiated additional Phase 1 clinical trials to further explore the PK, dosing and tolerability of LYT-100 in healthy volunteers. Results from these trials are expected to provide additional supportive data to inform the clinical development of LYT-100 across multiple indications.

[1] 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).

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 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 our expectations regarding the potential therapeutic benefit and administration of LYT-100 in patients, including its ability to potentially address certain shortcomings with respect to current standards of care, expectations regarding the clinical development of LYT-100 and the timing for completing enrollment in, or generating data and results from, our current Phase 1 and 2 trials of LYT-100, the potential of clinical data to provide support for further development of LYT-100 across multiple indications, the timing of updates from the Company with respect to future development plans for LYT-100 or other product candidates, 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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