PureTech Advances Wholly-Owned Candidate LYT-300 (Oral Allopregnanolone) into Clinical Study for Potential Treatment of Neurological and Neuropsychological Conditions

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LYT-300 is the first candidate from the Glyph™ technology platform to enter the clinic, making it the third clinical-stage candidate from PureTech's pipeline

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, announced today the initiation of a clinical study of LYT-300 (oral allopregnanolone), PureTech's wholly-owned therapeutic candidate for the potential treatment of neurological and neuropsychological conditions, including depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. LYT-300 is the third clinical-stage, wholly-owned candidate from PureTech's pipeline.

LYT-300 is an oral form of allopregnanolone. Allopregnanolone is a natural neurosteroid that is a positive allosteric modulator of γ-aminobutyric-acid type A ($GABA_A$) receptors, which are known to play a key biological role in depression, epilepsy and other neurological and neuropsychological conditions. Natural allopregnanolone has poor oral bioavailability, thus limiting its development as a therapeutic. An injectable formulation of allopregnanolone is approved by the United States Food and Drug Administration (FDA) as a 60-hour infusion for the treatment of post-partum depression, though the method of administration has limitations. LYT-300 is designed to unlock the validated biology of allopregnanolone to potentially offer a new, oral treatment option for a range of conditions where there is significant patient need.

"Allopregnanolone is a powerful, natural regulator of mood disorders and other neurological conditions, but its therapeutic development has been limited by its poor oral bioavailability. Synthetic oral analogs of allopregnanolone have been developed, though the degree to which these compounds mimic the therapeutic effects of natural allopregnanolone remains to be seen," said Joe Bolen, Ph.D., Chief Scientific Officer of PureTech. "LYT-300 is designed to preserve the natural structure of allopregnanolone in an oral dosage form, which we believe could potentially offer much-needed treatment options in large indications, such as depression, anxiety and sleep, as well as for more rare conditions, including certain epileptic

disorders. Advancing LYT-300 into human clinical development offers the opportunity to potentially address many important psychiatric conditions without good treatment options, especially amid the growing mental health crisis in the United States wherein one in four adults report experiencing symptoms of depression or anxiety."

LYT-300 was developed from PureTech's proprietary Glyph technology platform, which generates novel prodrugs by reversibly linking small molecule drugs to dietary fat molecules. This linkage is designed to enable the transport of small molecule drugs directly into systemic circulation via the lymphatic system following oral administration, thereby bypassing first-pass liver metabolism. This platform also has the potential to deliver other drugs with poor bioavailability, including immune modulators that could directly target the mesenteric lymph nodes.

The Phase 1 study of LYT-300 involves multiple parts, including the evaluation of a single ascending dose, multiple ascending doses and the effect of food on oral absorption of the prodrug in healthy volunteers. Safety, tolerability and pharmacokinetics (PK) will be assessed. Given the $GABA_A$ receptor modulating activity of allopregnanolone, the study will also explore the impact of LYT-300 on b-EEG, a marker of $GABA_A$ target engagement, thus potentially providing early insights into the mechanistic effects of LYT-300. Results from the study are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

About LYT-300

LYT-300 is a clinical therapeutic candidate that is in development as a potential treatment for a range of neurological and neuropsychological conditions. Developed using PureTech's Glyph technology platform, LYT-300 is an oral prodrug of natural allopregnanolone. An IV formulation of allopregnanolone is approved by the U.S. FDA and administered as a 60-hour infusion for the treatment of post-partum depression. Allopregnanolone is a positive allosteric modulator of γ-aminobutyric-acid type A ($GABA_A$) receptors and has been shown to regulate mood and other neurological conditions. PureTech initiated a Phase 1 clinical study of LYT-300 in late 2021, which is designed to characterize the safety, tolerability and PK of orally administered LYT-300 in healthy volunteers.

About the Glyph™ Technology Platform

Glyph is PureTech's synthetic lymphatic-targeting chemistry platform which is designed to employ the lymphatic system's natural lipid absorption and transport process to enable the oral administration of therapeutics. Glyph reversibly links a drug to a dietary fat molecule, creating a novel prodrug. The linked fat molecule re-routes the drug's normal path to the systemic circulation, bypassing the liver and instead moving from the gut into the lymphatic vessels that normally process dietary fats. PureTech believes this technology has the potential to (1) enable direct modulation of the immune system via drug targets present in mesenteric lymph nodes and (2) provide a broadly applicable means of enhancing the bioavailability of orally administered drugs that would otherwise be reduced by first-pass liver metabolism. PureTech is leveraging validated biology to accelerate the development of a Glyph portfolio, prioritizing highly characterized drugs to enhance with the Glyph technology based on the potential value unlocked in improving their oral bioavailability or lymphatic targeting. PureTech's lead Glyph therapeutic candidate, LYT-300 (oral allopregnanolone), is being evaluated in a Phase 1 study, with results expected in the second half of 2022. PureTech has exclusively licensed the Glyph technology platform, which is based on the pioneering research of Christopher Porter, Ph.D., and his research group at the Monash Institute of

Pharmaceutical Sciences at Monash University. The Porter Research Group and collaborators have published research in *Nature Metabolism* and the *Journal of Controlled Release* supporting the Glyph platform's ability to directly target the lymphatic system with a variety of therapies.

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 the treatment potential of LYT-300, including possible additional indications, the applicability of clinical results to human subjects, the Phase 1 LYT-300 clinical study, including its design, associated timelines, and how it may inform future clinical studies, and our expectations regarding the Glyph™ technology platform. 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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