PureTech Initiates Phase 2a Clinical Trial of LYT-300 (Oral Allopregnanolone) for the Potential Treatment of Anxiety Disorders

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Results from a validated clinical model of anxiety in healthy volunteers anticipated by the end of 2023

Phase 2a clinical trial of LYT-300 in patients with postpartum depression planned to initiate in second half of 2023

LYT-300 is derived from PureTech's Glyph™ platform, which is designed to enable oral administration of a range of therapeutics

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company dedicated to changing the lives of patients with devastating diseases, today announced the initiation of a Phase 2a proof-of-concept clinical trial of LYT-300 (oral allopregnanolone) in healthy volunteers using a validated clinical model of anxiety. LYT-300 is PureTech's wholly-owned therapeutic candidate for the potential treatment of neurological and neuropsychiatric disorders, including anxiety disorders and postpartum depression (PPD). LYT-300 is an oral prodrug of allopregnanolone that was developed using PureTech's Glyph™ platform, which harnesses the body's natural lipid absorption and transport process to enable the oral administration of certain therapeutics that otherwise cannot be administered orally.

"Anxiety disorders are the most common mental disorder,[1] impacting nearly 30% of adults at some point in their lives.[2] Despite this, there has been very little clinical development in the last 20 years - especially when compared to other psychiatric conditions," said Eric Elenko, Ph.D., Chief Innovation Officer at PureTech. "We believe that our Glyph technology platform is positioned to unlock the therapeutic potential of a range of molecules, beginning with allopregnanolone, and we look forward to the results of this study as well as the initiation of a study with LYT-300 in postpartum depression later this year."

In December 2022, PureTech announced positive topline results from the completed, multi-part Phase 1 study of LYT-300. The data showed that oral administration of LYT-300 achieved blood levels of allopregnanolone at or above those associated with therapeutic benefit in PPD and nine times greater than orally administered allopregnanolone, based on third-party published data.[3] LYT-300 also demonstrated dose-dependent target engagement with $GABA_A$ receptors, which are known to regulate mood and other neurological conditions.

Allopregnanolone and related endogenous neurosteroids have been recognized for their potential to treat depression and other neurological and neuropsychiatric indications with a rapid onset of action. The major hurdles associated with endogenous neurosteroids in the past have been the inability to create oral formulations and chronically administer them to patients. An intravenous formulation of allopregnanolone is approved by the U.S. Food and Drug Administration as a 60-hour infusion for the treatment of postpartum depression, though the method of administration has significant challenges and limits the scope of clinical translation with this class of compounds. To overcome this, medicinal chemistry approaches have been applied to synthesize orally bioavailable chemical analogs of allopregnanolone. These oral analogs may have different pharmacological effects than endogenous allopregnanolone and therefore may not capture its full therapeutic potential.

PureTech's Glyph platform is designed to address these issues by reversibly linking allopregnanolone to a lipid, creating a novel prodrug. The linked fat molecule re-routes the drug's normal pathway into the systemic circulation, bypassing the liver and instead moving directly from the gut into the lymphatic vessels that normally process dietary fats. This technology has the potential to provide a broadly applicable means of enhancing the bioavailability of certain drugs that would otherwise be limited by first-pass liver metabolism, including allopregnanolone.

Results for the placebo-controlled, Phase 2a, proof-of-concept trial using a validated clinical model of anxiety in healthy volunteers are anticipated by the end of 2023. Additionally, the open-label, Phase 2a, proof-of-concept clinical trial in patients with postpartum depression is expected to begin in the second half of 2023.

About LYT-300

LYT-300 is a clinical therapeutic candidate that is in development as a potential treatment of neurological and neuropsychiatric disorders, including anxiety disorders and postpartum depression. Developed using PureTech's Glyph™ technology platform, LYT-300 is an oral prodrug of endogenous allopregnanolone. An intravenous formulation of allopregnanolone is approved by the United States Food and Drug Administration and administered as a 60-hour infusion for the treatment of postpartum depression. PureTech completed a Phase 1 clinical trial of LYT-300 in 2022, which demonstrated oral bioavailability, tolerability and $GABA_A$ receptor target engagement in healthy volunteers. Allopregnanolone is a positive allosteric modulator (PAM) of γ-aminobutyric-acid type A ($GABA_A$) receptors and has been shown to regulate mood and other neurological conditions. Unlike benzodiazepines, allopregnanolone can provide both transient and longer-term normalization of overactive neural circuits because it also acts at GABA receptors outside of synapses.[4] Dual intra- and extra-synaptic GABA PAMs have been shown to not only improve sleep,[5] but also mood.[1]

About the Glyph™ Platform

Glyph is PureTech's 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 certain 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 certain drugs that would otherwise be limited by first-pass liver metabolism. PureTech is accelerating development of a Glyph portfolio that leverages validated efficacy, prioritizing highly characterized drugs to evaluate the ability of the Glyph technology to improve oral bioavailability or lymphatic targeting. PureTech's lead Glyph therapeutic candidate, LYT-300 (oral allopregnanolone), completed a Phase 1 clinical trial in 2022. Results from a placebo-controlled, Phase 2a, proof-of-concept, trial using a validated clinical model of anxiety in healthy volunteers are anticipated by the end of 2023. An open-label, Phase 2a, proof-of-concept clinical trial in patients with PPD is expected to begin in the second half of 2023. A second therapeutic candidate, LYT-310 (oral cannabidiol), is expected to enter the clinic in Q4 of 2023. PureTech has a robust intellectual property portfolio that includes licensed patents as well as wholly owned patents, covering 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*, *Angewandte Chemie* 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 giving life to new classes of medicine to change the lives of patients with devastating diseases. The Company has created a broad and deep pipeline through its experienced research and development team and its extensive network of scientists, clinicians and industry leaders that is being advanced both internally and through its Founded Entities. PureTech's R&D engine has resulted in the development of 27 therapeutics and therapeutic candidates, including two (Plenity® and EndeavorRx®) that have received both US FDA clearance and European marketing authorization and a third (KarXT) that is expected to be filed soon for FDA approval. A number of these programs are being advanced by PureTech or its Founded Entities in various indications and stages of clinical development, including registration enabling studies. 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.

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 those statements that relate to our expectations around the design of and the timelines and key milestones associated with clinical trials for LYT-300, the therapeutic potential of LYT-300, our expectations regarding the Glyph™ technology platform including the potential for new treatment applications, the applicability of preclinical results to human subjects, 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, 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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