PureTech to Advance LYT-300 (Oral Allopregnanolone) for the Potential Treatment of Anxiety Disorders and Postpartum Depression

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A placebo-controlled, Phase 2a, proof-of-concept, social anxiety clinical trial in healthy volunteers is expected to begin in the first half of 2023, with results anticipated by the end of 2023

An open-label, Phase 2a, proof-of-concept clinical trial in women with postpartum depression is expected to initiate in the second half of 2023

In a healthy volunteer study, LYT-300 achieved blood levels of allopregnanolone at or above those associated with therapeutic effect in postpartum depression[1] and was generally well-tolerated

Allopregnanolone is a natural neurosteroid with proven efficacy that is currently only available as a 60-hour intravenous infusion

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company dedicated to changing the treatment paradigm for devastating diseases, today announced that it will advance LYT-300 (oral allopregnanolone) for the potential treatment of anxiety disorders and postpartum depression (PPD). A placebo-controlled, Phase 2a, proof-of-concept, social anxiety clinical trial in healthy volunteers is expected to begin in the first half of 2023, with results anticipated by the end of 2023. An open-label, Phase 2a, proof-of-concept clinical trial in women with PPD is expected to initiate in the second half of 2023.

"We believe LYT-300 is the most advanced oral prodrug of natural allopregnanolone and, as such, has the potential to unlock the full therapeutic benefit of allopregnanolone," said Julie Krop, M.D., Chief Medical Officer at PureTech. "Using our proprietary Glyph™ platform, we have made natural allopregnanolone orally bioavailable without permanently chemically modifying the natural neurosteroid. This differentiated approach, which harnesses the validated, fast-acting efficacy of allopregnanolone, may offer an enhanced therapeutic benefit to patients with a wide range of neurological and neuropsychiatric conditions, including anxiety and postpartum depression."

Social Anxiety Trial Design

The placebo-controlled, Phase 2a, proof-of-concept trial will evaluate short-term changes in anxiety-related patient reported outcomes in approximately 50 healthy volunteers. The trial will be conducted using a validated clinical model that simulates social anxiety.

Postpartum Depression Trial Design

The open-label, Phase 2a, proof-of-concept trial will evaluate LYT-300 in a small number of patients with moderate to severe PPD. It is designed to inform dose selection of LYT-300 in this population given the known efficacy of allopregnanolone in this population, and it will evaluate scores on the HAM-D scale as well as other relevant pharmacodynamic markers.

Topline results from a Phase 1 trial of LYT-300 were announced in December 2022 and showed that oral administration of LYT-300 achieved blood levels of allopregnanolone at or above those associated with therapeutic benefit in PPD and ninefold greater than orally administered allopregnanolone, based on third-party published data.[1] The results also demonstrated exposure-dependent target engagement with γ-aminobutyric-acid type A ($GABA_A$) receptors, which have been shown to regulate mood and other neurological conditions.

Allopregnanolone is a natural neurosteroid with well-validated biological effects. It has demonstrated a rapid onset of action for the treatment of depression, as well as the potential to treat other neurological conditions, including anxiety, but its poor oral bioavailability has limited its therapeutic potential. The United States Food and Drug Administration (FDA) has approved a 60-hour intravenous infusion formulation of allopregnanolone for the treatment of PPD, though this method of administration has inherent limitations. To overcome this, oral chemically modified analogs of allopregnanolone have been developed, though these may not capture the full therapeutic potential of natural allopregnanolone. To potentially harness the broad applicability of this natural neurosteroid through oral administration, PureTech has applied its Glyph platform, which is designed to enable the oral administration of certain therapeutics with low oral bioavailability due to first pass metabolism.

"I am exceptionally proud of the progress we've made with the Glyph platform, which has yielded two exciting therapeutic candidates to date, and I believe it will be a rich source of additional candidates for our Wholly Owned Pipeline going forward," said Joe Bolen, Ph.D., a member of PureTech's Research and Development Committee and recently retired Chief Scientific Officer. "PureTech's unique model includes moving resources toward the programs with the most promise. To that end, and with a focus on translational and clinical work, we have recently deprioritized our Orasome Technology Platform following a key go/no go experiment. I look forward to continuing to work with the team as a member of the R&D Committee to advance big ideas, and I am honored to be a part of such an innovative organization with a deep commitment to serving patients in need."

About Anxiety

Anxiety disorders are the most common mental disorder, affecting nearly 30% of adults.[2] There are several types of anxiety disorders, including generalized anxiety disorder, panic disorder and social anxiety disorder. They are characterized by feelings of excessive fear and may impact a person's ability to function normally.

About Postpartum Depression

Postpartum depression (PPD) is a debilitating condition that affects over 400,000 women who have given birth in the United States.[3] It is characterized by feelings of extreme sadness, changes in energy, sleep and appetite, and it can impact a mother's ability to care for her child.

About LYT-300

LYT-300 is a clinical therapeutic candidate that is in development as a potential treatment for anxiety and postpartum depression. Developed using PureTech's Glyph™ technology platform, LYT-300 is an oral prodrug of natural 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 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 orally administered 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. A placebo-controlled, Phase 2a, proof-of-concept, social anxiety clinical trial in healthy volunteers is expected to begin in the first half of 2023, with results anticipated by the end of 2023. An open-label, Phase 2a, proof-of-concept clinical trial in women with PPD is expected to initiate 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 biotherapeutics company dedicated to changing the treatment paradigm for devastating diseases. 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 26 therapeutics and therapeutic candidates, including two (Plenity® and EndeavorRx®) that have received both U.S. FDA clearance and European marketing authorization and a third (KarXT) that will soon be filed for FDA approval, as of the most recent update by the Company. 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 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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