PureTech Awarded up to $11.4 Million from U.S. Department of Defense to Advance LYT-300 (Oral Allopregnanolone) for Fragile X-associated Tremor/Ataxia Syndrome

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Planning underway for Phase 2 trial of LYT-300 in Fragile X-associated Tremor/Ataxia Syndrome

LYT-300 is also being evaluated in a Phase 2a trial for anxiety disorders, and a Phase 2a in patients with postpartum depression is planned to initiate in second half of 2023

LYT-300, LYT-310 and additional preclinical programs for CNS indications have been produced from PureTech's Glyph™ technology platform for enhancing oral bioavailability

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 that the company has been awarded up to $11.4 million from the U.S. Department of Defense (DoD) to advance its therapeutic candidate, LYT-300 (oral allopregnanolone), for the treatment of Fragile X-associated Tremor Ataxia Syndrome (FXTAS). The funds will support a Phase 2 trial of LYT-300 in collaboration with the University of California, Davis (UC Davis).

LYT-300, an oral prodrug of allopregnanolone, is PureTech's wholly-owned therapeutic candidate for the potential treatment of anxiety disorders, postpartum depression, FXTAS and other neurological and neuropsychiatric indications. LYT-300 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.

FXTAS, which was discovered by Dr. Randi Hagerman and her colleagues at the University of California, Davis, is a devastating neurological condition that is closely related to, but distinct from, Fragile X syndrome (FXS). Both conditions are the result of repeated elements in the Fragile X Messenger Ribonucleoprotein Gene 1 (*FMR1*) gene. While FXS is associated with intellectual disability and autism, FXTAS leads to neurodegeneration in otherwise normally developed, aging individuals who carry a premutation of the *FMR1* gene.

"FXTAS is a devastating, late-onset neurodegenerative condition characterized by cognitive decline, tremors in the hands and balance problems. Currently, there are no primary treatments for FXTAS, though IV-administrated allopregnanolone has demonstrated therapeutic potential," said Dr. Randi Hagerman, M.D., F.A.A.P., Medical Director of the UC Davis MIND Institute, Chair in Fragile X Research and co-primary investigator for the LYT-300 trial. "I am

excited to be working with PureTech to evaluate their oral prodrug of allopregnanolone (LYT-300), and I am optimistic that this award will help accelerate the development of this potential first therapy for FXTAS."

An exploratory, open-label trial of six men with FXTAS, evaluated IV-administration of allopregnanolone across multiple neuropsychological and emotional tests. In addition to being well-tolerated, allopregnanolone showed signals of pharmacologic benefit across multiple neurological endpoints, including the Behavioral Dyscontrol Scale, which measures executive, cognitive and motor function, and demonstrated improvement compared to baseline ($p=0.009$).[1] IV administration is not feasible in most indications, especially for a chronic therapy, and there remains a need for treatments that can address this debilitating condition. PureTech plans to evaluate LYT-300 in a placebo-controlled trial to demonstrate the safety, tolerability and efficacy of the drug in people with FXTAS.

"This award from the DoD allows us to expand our evaluation of LYT-300, a candidate with a wide variety of potential indications, into FXTAS, an area of tremendous need where otherwise normally developed, aging individuals suffer from significant neurodegeneration," said Eric Elenko, Ph.D., Chief Innovation Officer at PureTech Health. "We look forward to collaborating with Dr. Randi Hagerman and her team at UC Davis to bring the potential of allopregnanolone to the thousands of individuals with FXTAS in need of a treatment."

PureTech's capital efficient strategy includes the pursuit of non-dilutive funding in the form of grants. This is the fourth DoD grant that PureTech has secured on behalf of its Wholly Owned Programs in addition to five grants secured on behalf of its Founded Entities. This work is supported by the Office of the Assistant Secretary of Defense for Health Affairs and the Defense Health Agency J9, Research and Development Directorate, or the U.S. Army Medical Research Acquisition Activity at the U.S. Army Medical Research and Development Command through the Peer Reviewed Medical Research Program (PRMRP) under Award No. HT94252310598, with a total program budget of up to $11.4 million for both the planning and clinical study phases. The PRMRP supports research across the full range of science and medicine, with an underlying goal of enhancing the health, care and well-being of military service members, veterans, retirees and their family members. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

In addition to LYT-300, which is being advanced in three indications, PureTech is progressing multiple CNS-focused programs derived from its Glyph platform. These include LYT-310, an oral form of cannabidiol that is expected to enter a Phase 1 clinical trial in the fourth quarter of 2023, as well as programs that are in various stages of preclinical development.

About Fragile X-associated Tremor/Ataxia Syndrome

Fragile X-associated Tremor/Ataxia Syndrome (FXTAS) was discovered at the MIND Institute by researcher Dr. Randi Hagerman and her colleagues in 2001. It is one of the most devastating of the Fragile X Spectrum Disorders, which result from a trinucleotide expansion in the *FMR1* gene. FXTAS is a late onset condition that can occur in up to 75% of males with the premutation by the eighth decade of life and in approximately 16% of females, but the clinical signs typically emerge when individuals are in their early 60s. The clinical features of FXTAS include tremor in the hands with action or at rest, balance problems (ataxia) that lead to frequent falling, and cognitive decline that is sometimes misdiagnosed as Alzheimer's disease. No specific treatment for FXTAS is efficacious, though a variety of medications may improve psychiatric issues or the severity of tremor. Carriers are common in the general population, occurring in 1 in 150 to 200 women and 1 in 400 men, but FXTAS is often mistakenly diagnosed as Parkinson's disease.

About LYT-300

LYT-300 is a clinical-stage therapeutic candidate that is in development as a potential treatment for neurological and neuropsychiatric conditions, including anxiety disorders, postpartum depression and Fragile X-associated Tremor/Ataxia Syndrome. Developed using PureTech's Glyph™ technology platform, LYT-300 is an oral prodrug of endogenous allopregnanolone that is designed to overcome its poor oral bioavailability. PureTech completed a Phase 1 clinical trial of LYT-300 in 2022, which demonstrated oral bioavailability, tolerability and γ-aminobutyric-acid type A

($GABA_A$) receptor target engagement in healthy volunteers.

Allopregnanolone is a positive allosteric modulator (PAM) of $GABA_A$ 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.[2] 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.

About the Glyph™ Platform

Glyph is PureTech's lymphatic-targeting 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) provide a broadly applicable means of enhancing the bioavailability of certain orally administered drugs that would otherwise be limited by first-pass liver metabolism and (2) enable direct modulation of the immune system via drug targets present in mesenteric lymph nodes. 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 trial using a validated clinical model of anxiety in healthy volunteers initiated in June 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 and planning is underway for a Phase 2 clinical trial in FXTAS. A second therapeutic candidate, LYT-310 (oral cannabidiol), is expected to enter the clinic in Q4 of 2023. PureTech has a robust intellectual property (IP) portfolio that includes licensed patents as well as wholly owned IP, 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, including for FXTAS, 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, 2022 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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