PureTech Presents Preclinical Proof-of-Concept Data for LYT-300 (Oral Allopregnanolone) as Potential Treatment for Neurological and Neuropsychological Conditions

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Data demonstrating ability to achieve systemic exposure following oral administration shared at American College of Neuropsychopharmacology (ACNP) Annual Meeting

Results support potential of PureTech's Glyph™ technology platform to enable oral administration for a range of therapeutics

LYT-300 was recently advanced into a Phase 1 clinical study

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 the presentation of preclinical proof-of-concept data at the 60th American College of Neuropsychopharmacology (ACNP) Annual Meeting that support the clinical advancement 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 was recently advanced into a Phase 1 clinical study, which is designed to characterize the safety, tolerability and PK of orally administered LYT-300 in healthy volunteers and is expected to read out in the second half of 2022.

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. Synthetic oral analogs of allopregnanolone have had variable clinical success, and comparable activity with natural allopregnanolone remains to be established. Using PureTech's proprietary Glyph technology platform, 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.
The data presented at ACNP showed that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models of increasing complexity. In contrast, systemic levels of allopregnanolone were not observed following oral administration of natural unmodified allopregnanolone. These results demonstrate the potential of the Glyph technology platform to enhance the systemic absorption of natural bioactive molecules and other small molecules with poor oral bioavailability.

"We are pleased to present these data, which demonstrate the core mechanism that underpins the unique design of LYT-300, the first therapeutic candidate derived from our Glyph platform," said Joe Bolen, Ph.D., Chief Scientific Officer of PureTech. "As we advance LYT-300 into the clinic, we are encouraged that the Glyph platform continues to deliver a broad array of supportive data and peer-reviewed publications, underscoring the potential of this truly differentiated platform for rapid drug discovery."

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.

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](http://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 associated timelines, 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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