PureTech Provides End of Year Report on Key Progress

December 22, 2022

RNS Number : 5452K
PureTech Health PLC
22 December 2022

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Rapid advancement of PureTech's Wholly Owned Pipeline, with three clinical trials now underway and five completed this year that demonstrated compelling safety and tolerability data for LYT-100 (deupirfenidone) and proof of principle, oral bioavailability and tolerability for LYT-300 (oral allopregnanolone). Robust dose escalation and safety data also announced from completed monotherapy portion of Phase 1 program for LYT-200 (anti-galectin-9 mAb)

Catalyst-rich 2023 anticipated, with results from late-stage trial of LYT-100 in idiopathic pulmonary fibrosis and Phase 1b trial of LYT-200 in leukemia. Initiation of clinical trials planned with LYT-300 and LYT-310 (oral cannabidiol) targeting neurological conditions as well as the combination portion of the Phase 1 trial of LYT-200 in solid tumors

Continued momentum across Founded Entities, including Karuna's positive Phase 3 results for KarXT in schizophrenia, commercial progress for Gelesis' Plenity® and Akili's EndeavorRx® and Vor's promising initial data in acute myeloid leukemia

Board composition and committee changes also noted

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 reported on the key progress made across its Wholly Owned Programs[1] and Founded Entities[2] in 2022.

Daphne Zohar, Founder and Chief Executive Officer of PureTech, commented: "2022 has been a particularly successful and productive year in both crystallizing value and shaping the future of PureTech. Our primary focus is to progress our Wholly Owned Pipeline to commercialization and deliver new classes of medicines for patients with serious, debilitating conditions. We are advancing toward this goal by deepening our commitment to programs with compelling clinical data that are moving into late-stage studies and that we believe have the potential for broad impact.

"Over the next 12 months, we anticipate multiple important catalysts that will further guide how we

prioritize our pipeline, informing our decisions regarding which programs we will drive to commercial launches ourselves and which programs could be most successfully advanced through other avenues such as a partnership, sale, or spinout into another entity."

PureTech's Wholly Owned Programs are centered on developing breakthrough medicines for patients with underserved and serious diseases. The Company's therapeutic candidates are being advanced for the potential treatment of devastating conditions including idiopathic pulmonary fibrosis (IPF), metastatic solid tumors, leukemia and certain neurological and neuropsychological indications.

Additionally, PureTech's Founded Entities are advancing 20 therapeutics and therapeutic candidates, of which two (Plenity® for weight management[3] and EndeavorRx® for treating inattention in ADHD ages 8-12[4]) have received both U.S. FDA clearance and European marketing authorization and a third (KarXT for schizophrenia) will soon be filed for FDA approval, as of the most recent update by the company. Key highlights include the following:

Key Wholly Owned Program Updates

- LYT-100 (deupirfenidone) is in development for the potential treatment of conditions involving inflammation and fibrosis, including IPF, for which current standards of care are associated with significant tolerability issues, resulting in approximately three out of four patients in the U.S. foregoing treatment with these otherwise efficacious medicines.[5] LYT-100 is a deuterated form of one of these treatments, pirfenidone, which has proven efficacy and has been shown to improve survival in these patients by approximately three years, but its side effects cause patients to discontinue or dose reduce, thereby limiting its effectiveness.[6]
  - Announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with PureTech's LYT-100 experienced gastrointestinal-related adverse events compared to subjects treated with pirfenidone.
  - Initiated a global, randomized double blind placebo-controlled trial of LYT-100 in patients with IPF. This trial is expected to serve as the first of two registration-enabling trials, and topline results are expected by the end of 2023.
  - Initiated a preclinical study of LYT-100 for the prevention and treatment of radiation induced fibrosis, an indication for which the United States government stockpiles medical countermeasures. This program is subject to the Animal Rule, which allows for the approval of drugs based on validated animal models when human efficacy studies are not feasible.[7]
  - Completed a Phase 2a trial of LYT-100 in patients with breast cancer-related, upper limb secondary lymphedema, which met the primary endpoint of safety and tolerability, adding to the growing body of data demonstrating a favorable tolerability profile for LYT-100. Secondary endpoints assessed exploratory biomarkers related to lymphedema, and the data did not provide support for a clear development path for this indication. Given the Company's current priorities in IPF, where the regulatory path is well-defined and there is a wealth of strong efficacy data with pirfenidone, the Company has deprioritized lymphedema as an indication.
  - PureTech is also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions, such as progressive fibrosing interstitial lung diseases, myocardial and other organ system fibrosis, based on the strength of existing clinical data around the use of

pirfenidone in these indications.

- LYT-200 (anti-galectin-9 mAb) is in development for the potential treatment of metastatic solid tumors that have poor survival rates as well as hematological malignancies, such as acute myeloid leukemia (AML), where more than 50% of patients either don't respond to initial treatment or experience relapse after responding to initial treatment.[8]
  - o Completed the bi-monthly and weekly monotherapy dose escalation portion of the Phase 1 program assessing the safety and tolerability of escalating doses of LYT-200 as a potential treatment for metastatic solid tumors. No dose-limiting toxicities were reported, and the full results will be presented in an upcoming scientific forum. Evaluation of LYT-200 in combination with tislelizumab is expected to begin in the first quarter of 2023.
  - o Shared new preclinical data supporting the clinical potential of LYT-200 as a therapeutic agent for the treatment of leukemia in a scientific poster at the American Society of Hematology (ASH) 64th Annual Meeting. The data presented support the role of galectin-9 in multiple types of leukemia and the ability of anti-galectin-9 antibodies to provide effective anti-tumor activity in these cancers. Based on these and other compelling preclinical data generated with LYT-200 in blood cancers, PureTech initiated a clinical trial to evaluate LYT-200 as a single agent for the treatment of AML, with results expected in 2023.
  - o Given the expansion of the clinical evaluation of LYT-200, the Company has deprioritized preclinical development of LYT-210.

- LYT-300 (oral allopregnanolone) is in development for the potential treatment of neurological and neuropsychological conditions where there is a need for more effective treatments that work quickly, have more favorable tolerability and can be administered conveniently.
  - o Completed the multi-part Phase 1 trial of LYT-300, which demonstrated oral bioavailability in healthy adults, achieving blood levels of allopregnanolone at or above those associated with therapeutic effect and ninefold greater than orally administered allopregnanolone, based on third-party published data.[9] The data also demonstrated target engagement with $GABA_A$ receptors, which are known to regulate mood and other neurological conditions. LYT-300 was generally well-tolerated with no treatment-related severe or serious adverse events observed. A Phase 1b/2a trial is expected to begin in the first half of 2023.

- LYT-310 (oral cannabidiol [CBD]) is in development to expand the therapeutic application of CBD across a range of neurological disorders.
  - o Announced nomination of a new therapeutic candidate, LYT-310, which is expected to enter the clinic in Q4 of 2023. As with LYT-300, PureTech scientists applied the Glyph™ **Platform** to enable advantages such as oral capsule dosing and the potential for improved safety and tolerability. These differentiated features of LYT-310 could expand CBD use across a broad range of patient populations (such as adolescents and adults) and indications, including rare and common forms of epilepsy as well as other central nervous system disorders. LYT-310 has the potential to be a readily scalable and consistent product that can be produced in a cost-effective manner.

- **LYT-503/IMB-150** (partnered non-opioid pain program) is being advanced through a collaboration for the potential treatment of interstitial cystitis/bladder pain syndrome, a chronic bladder condition that consists of discomfort or pain in the bladder or surrounding pelvic region that is not adequately

controlled for many patients.
    - First patient, first visit was achieved in the Phase 1 clinical trial evaluating LYT-503/IMB -150 as a potential non-opioid treatment for female patients with Interstitial Cystitis/Bladder Pain Syndrome.

- **LYT-510** (oral inflammation-targeting formulation of tacrolimus) is in development for the potential treatment of chronic pouchitis and inflammatory bowel disease (IBD), a condition for which current treatments require multiple injections over time and are associated with several limitations, including dose-limiting adverse events, loss of efficacy over time, a lack of efficacy entirely and the potential for opportunistic infections or malignancies.
    - **LYT-510** is the lead candidate generated from the **Alivio™ Platform,** with two others, **LYT-503/IMB-150** and **LYT-500**, also developed using PureTech's proprietary inflammation-targeting technology. PureTech will prioritize the development of **LYT-510** ahead of **LYT-500.**

- PureTech's **technology platforms,** which include the **Glyph, Alivio** and **Orasome-™ platforms**, contribute to the Company's advancement by generating new wholly-owned candidates **(Glyph: LYT-300** and **LYT-310)** and enabling strategic partnerships **(Alivio: LYT-503/IMB-150).** As part of its pipeline prioritization, the Company may opportunistically enter into additional strategic partnerships or spinout programs into new entities around one or several of its platforms or related candidates, especially as resources are increasingly dedicated to late-stage clinical development.

Key Founded Entity Updates:

- **Karuna** (Nasdaq: KRTX)
    - Announced positive topline Phase 3 data evaluating the efficacy, safety and tolerability of KarXT in adults with schizophrenia, meeting its primary endpoint and key secondary endpoints. Karuna plans to submit a New Drug Application (NDA) for KarXT in schizophrenia with the U.S. FDA in mid-2023, as of the most recent update by the company.
    - Announced the initiation of its Phase 3 ADEPT program, which is evaluating KarXT for the treatment of psychosis related to Alzheimer's Disease (AD.)

- **Gelesis** (NYSE: GLS)
    - Generated $36.8M in revenue and obtained 185,000 customers since the launch of Plenity.[3]
    - Announced that based on the extensive safety data and differentiation due to affordability, broad label and safety profile, it is preparing an application to the FDA to broaden the classification of Plenity in the U.S. from prescription-only to over the counter. Gelesis plans to submit the application to the FDA during the first quarter of 2023 and could receive market clearance by the third quarter of 2023.

- **Vor** (Nasdaq: VOR)
    - Announced initial clinical data from VBP101, Vor's Phase 1/2a multicenter, open-label, first-in-human study of tremtelectogene empogeditemcel or "trem-cel" (formerly VOR33) in patients with AML. The data observed from the first treated patient support the potential of a trem-cel transplant to be successfully manufactured, to engraft normally and to maintain blood counts following treatment with the CD33-targeted therapy Mylotarg. The clinical trial continues to enroll patients and additional data are expected in 2023.

- **Akili** (Nasdaq: AKLI)
  - Deployed first wave of its EndeavorRx[4] go-to-market sales force in 14 priority territories across the U.S. with a focus on Integrated Behavioral Health Centers and pediatric providers.
  - Announced that Highmark, the fourth largest Blue Cross Blue Shield organization, included EndeavorRx in its medical policy for the reimbursement of prescription digital therapeutics.
  - Announced that its partner, Shionogi, started a pivotal Phase 3 randomized, controlled study of SDT-001 in children with attention-deficit hyperactivity disorder (ADHD).

- **Vedanta**
  - Opened a new facility designed to manufacture clinical and commercial supply for its therapeutic portfolio, including for the planned Phase 3 study (expected to begin in the first half of 2023) and potential commercial launch of lead candidate, VE303, in *Clostridioides difficile* infection. Vedanta believes it was the first company to manufacture CGMP-grade defined bacterial consortia in powdered form, which enables stable, consistent oral formulations.

Board Composition & Committee Changes:

- As noted in PureTech's 2022 Half-Year Report, Dame Marjorie Scardino, Senior Independent Director, chair of the Nomination Committee and member of the Audit Committee, will retire as of the close of business on December 31, 2022. Raju Kucherlapati, Ph.D., will assume the role of PureTech's Senior Independent Director as well as the chair of its Nomination Committee, effective as of Dame Scardino's retirement.

- Christopher Viehbacher, Chair of PureTech's Board, was recently appointed President, Chief Executive Officer and a member of the Board of Biogen Inc. (Nasdaq: BIIB). Given the time commitment required by this new role, Mr. Viehbacher will not stand for re-election at the Company's 2023 Annual General Meeting. The Nomination Committee will initiate a process to identify a new Chair.

Mr. Viehbacher noted: "It has been truly rewarding to work with such a talented group of people who share a genuine passion for helping patients. Together, we have developed a pharmaceutical pioneer delivering innovative medicines with a proven track record that is truly differentiated across the industry. The foundation for these successes is supported by a strong cash position and unique business model to support continued growth. I'm proud of these collective accomplishments and I look forward to continuing to interact with my colleagues at PureTech in this next exciting phase for the company."

Ms. Zohar commented: "For nearly a decade, Chris has brought a balance of enthusiasm and skepticism to the PureTech Board that is emblematic of our approach. His commercial expertise, deal-making ethos and patient-centered focus have helped to shape our mission and laid the foundation for our future growth. I am grateful that Chris will remain a trusted advisor, and we wish him much success as he takes the helm at Biogen."

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 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 without limitation those related to the Company's LYT-100 development program and the timing for results from ongoing clinical trials of LYT-100, the LYT-200 development program and the timing for results from ongoing clinical trials of LYT-200, the planned initiation of clinical trials for LYT-300 and LYT-310, the potential therapeutic benefits of the product candidates within Company's Wholly Owned Programs, the Company's plan related to the prioritization of programs and activities associated with its pipeline, the Company's approach to potential partnerships or spinouts of its platforms or candidates 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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[1] References to "Wholly Owned Programs" refer to the Company's six therapeutic candidates (LYT-100, LYT-200, LYT-300, LYT-310, LYT-510 and LYT-503/IMB-150), lymphatic and inflammation technology platforms and potential future therapeutic candidates and platforms that the Company may develop or obtain. References to "Wholly Owned Pipeline" refer to LYT-100, LYT-200, LYT-300, LYT-310, LYT-510 and LYT-503/IMB-150. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

[2]Founded Entities represent companies founded by PureTech in which PureTech maintains ownership of an equity interest and, in certain cases, is eligible to receive sublicense income and royalties on product sales. As of the date of this release, PureTech maintained control over Follica Incorporated, Vedanta Biosciences, Inc., and Entrega, Inc. by virtue of (a) majority voting control or (b) the right to elect representation to the entity's Board of Directors. As of the date of this release, PureTech did not have a controlling interest in Gelesis Holdings, Inc., Karuna Therapeutics, Inc., Akili, Inc., Sonde Health, Inc. and Vor Biopharma Inc.

[3] Important Safety Information about Plenity: Patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium dioxide should not take Plenity. To avoid impact on the absorption of medications: For all medications that should be taken with food, take them after starting a meal. For all medications that should be taken without food (on an empty stomach), continue taking on an empty stomach or as recommended by your physician. The overall incidence of side effects with Plenity was no different than placebo. The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence. Contact a doctor right away if problems occur. If you have a severe allergic reaction, severe stomach pain, or severe diarrhea, stop using Plenity until you can speak to your doctor. Rx Only. For the safe and proper use of Plenity or more information, talk to a healthcare professional, read the Patient Instructions for Use, or call 1-844-PLENITY.

[4] EndeavorRx is the first-and-only FDA-authorized treatment delivered through a video game experience. EndeavorRx is indicated to improve attention function as measured by computer-based testing in children ages 8 to 12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. Patients who engage with EndeavorRx demonstrate improvements in a digitally assessed measure Test of Variables of Attention (TOVA®) of sustained and selective attention and may not display benefits in typical behavioral symptoms, such as hyperactivity. EndeavorRx should be considered for use as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs, which further address symptoms of the disorder. EndeavorRx is available by prescription only. It is not intended to be used as a stand-alone therapeutic and is not a substitution for a child's medication. The most common side effect observed in children in EndeavorRx's clinical trials was a feeling of frustration, as the game can be quite challenging at times. No serious adverse events were associated with its use. EndeavorRx is recommended to be used for approximately 25 minutes a day, 5 days a week, over initially at least 4 consecutive weeks, or as recommended by your child's health care provider. To learn more about EndeavorRx, please visit EndeavorRx.com.

[5] Dempsey, T. M., Payne, S., Sangaralingham, L., Yao, X., Shah, N. D., & Limper, A. H. (2021). Adoption of the Antifibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. *Annals of the American Thoracic Society*, *18*(7), 1121-1128. https://doi.org/10.1513/AnnalsATS.202007-901OC

[6] Margaritopoulos, G. A., Trachalaki, A., Wells, A. U., Vasarmidi, E., Bibaki, E., Papastratigakis, G., Detorakis, S., Tzanakis, N., & Antoniou, K. M. (2018). Pirfenidone improves survival in IPF: results from a real-life study. *BMC pulmonary medicine*, *18*(1), 177. https://doi.org/10.1186/s12890-018-0736-z

[7] The use of the Animal Rule is intended for drugs and biological products developed to reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological or nuclear substances

[8] Walter, R. B., Othus, M., Burnett, A. K., Löwenberg, B., Kantarjian, H. M., Ossenkoppele, G. J., Hills, R. K., Ravandi, F., Pabst, T., Evans, A., Pierce, S. R., Vekemans, M. C., Appelbaum, F. R., & Estey, E. H. (2015). Resistance prediction in AML: analysis of 4601 patients from MRC/NCRI, HOVON/SAKK, SWOG and MD Anderson Cancer Center. *Leukemia*, 29(2), 312-320. https://doi.org/10.1038/leu.2014.242

[9] Brexanolone NDA 211371 Multi-disciplinary Review and Evaluation, FDA CDER, 2018.

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