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PureTech Founded Entity Karuna Therapeutics Announces Results from Phase 1b Trial Evaluating the Safety and Tolerability of KarXT in Healthy Elderly Volunteers

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Karuna to initiate a Phase 2 trial evaluating KarXT in dementia-related psychosis in the first half of 2022

Results suggest that KarXT can be administered to elderly volunteers at doses which achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile

The majority of healthy elderly volunteers in the Phase 1b trial were titrated to xanomeline doses of 150 to 200 mg when dosed with KarXT

Safety and tolerability profile in Phase 1b trial in healthy elderly volunteers consistent with prior trials of KarXT

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, is pleased to note that its Founded Entity, Karuna, today announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT (xanomeline-trospium) in healthy elderly volunteers. Karuna had previously announced a preliminary analysis of data from the first two cohorts in the trial earlier this year. Based on results from the Phase 1b trial in healthy elderly volunteers, Karuna plans to initiate a Phase 2 trial evaluating KarXT in dementia-related psychosis in the first half of 2022.

As of April 30, 2021, PureTech's percentage ownership of Karuna was approximately 8.2 percent on an outstanding voting share basis. PureTech Health has a right to royalty payments as a percentage of net sales from Karuna.

The full text of the announcement from Karuna is as follows:

Karuna Therapeutics Announces Results from Phase 1b Trial Evaluating the Safety and Tolerability of KarXT in Healthy Elderly Volunteers

Company to initiate a Phase 2 trial evaluating KarXT in dementia-related psychosis in the first half of 2022

Results suggest that KarXT can be administered to elderly volunteers at doses which achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile

The majority of healthy elderly volunteers in the Phase 1b trial were titrated to xanomeline doses of 150 to 200 mg when dosed with KarXT

Safety and tolerability profile in Phase 1b trial in healthy elderly volunteers consistent with prior trials of KarXT

BOSTON--(BUSINESS WIRE)--Jun. 23, 2021-- Karuna Therapeutics, Inc. (NASDAQ: KRTX), a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions, today announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT (xanomeline-trospium) in healthy elderly volunteers. The Company had previously announced a preliminary analysis of data from the first two cohorts in the trial earlier this year. Based on results from the Phase 1b trial in healthy elderly volunteers, the Company plans to initiate a Phase 2 trial evaluating KarXT in dementia-related psychosis in the first half of 2022.

The placebo-controlled, inpatient Phase 1b dose-ranging trial consisted of three cohorts, each enrolling 16 healthy elderly volunteers, randomized 3:1 to receive KarXT or placebo. As part of the flexible dosing protocol, a volunteer's dose was increased if they were tolerating KarXT well at the time of the potential dose increase, as determined by a clinician. In the trial, the majority of healthy elderly volunteers were titrated to xanomeline doses of 150 to 200 mg when dosed with KarXT three times per day. As previously reported, pharmacokinetic data from Cohorts 1 and 2 demonstrated that healthy elderly volunteers achieved mean xanomeline blood levels comparable to, or slightly higher than, the mean xanomeline blood levels reported in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia. The Company plans to evaluate pharmacokinetic data from Cohort 3, once available. Previous trials of KarXT have demonstrated that the current formulation of KarXT results in xanomeline exposures, or blood levels, that are approximately 10% greater than blood levels seen in earlier trials of xanomeline alone.

The treatment-related adverse events (AEs) were similar to those observed in prior trials of KarXT, and a majority (>80%) were rated mild in severity. One serious AE of urinary retention was reported in Cohort 1. The Company believes the report of urinary retention was related to a higher dose of trospium used in Cohort 1 compared to doses used in Cohorts 2 and 3, where urinary retention was not observed. No serious or severe AEs were observed in Cohorts 2 and 3. Consistent with prior trials of KarXT, blood pressure in healthy elderly volunteers receiving KarXT was similar to placebo, and no syncopal events were observed. Heart rate increases observed in the trial were also consistent with prior trials of KarXT.
Data from the Phase 1b trial suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in Phase 1 trials in healthy adult volunteers and in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia, was better tolerated by healthy elderly volunteers.

"We are encouraged that the data from our Phase 1b healthy elderly volunteers trial suggest that potentially therapeutic doses of KarXT can be administered to elderly adults while maintaining a favorable tolerability profile," said Stephen Brannan, M.D., chief medical officer of Karuna Therapeutics. "Results from the third cohort provide additional data as we finalize the dosing and titration protocol for our Phase 2 trial in dementia-related psychosis."

"The results from the Phase 1b trial in healthy elderly volunteers, as well as a prior Phase 2 study demonstrating the potential of xanomeline to treat and prevent psychosis in patients with Alzheimer's disease, give us confidence in the potential utility of KarXT for the treatment of dementia-related psychosis," added Steve Paul, M.D., chief executive officer, president and chairman of the

board of Karuna Therapeutics. "These results support the progression of KarXT into a Phase 2 clinical trial for the treatment of dementia-related psychosis, which we plan to commence in the first half of 2022."

About KarXT

KarXT, a proprietary oral modulator of muscarinic cholinergic receptors, is Karuna's lead product candidate. It combines xanomeline, a novel muscarinic agonist, with trospium, an FDA-approved muscarinic antagonist that does not appreciably cross the blood-brain-barrier, to preferentially stimulate muscarinic receptors in the central nervous system. This novel product candidate, if approved, has the potential to usher in a new treatment paradigm and dramatically impact patients with schizophrenia and other psychotic disorders by providing a differentiated mechanism of action relative to current D2 dopamine and serotonin receptor-targeting antipsychotic drugs.

About Karuna

Karuna Therapeutics is a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions. At Karuna, we understand there is a need for differentiated and more effective treatments that can help patients navigate the challenges presented by these severe and disabling disorders. Utilizing our extensive knowledge of neuroscience, we are harnessing the untapped potential of the brain in pursuit of novel pathways to develop medicines that make meaningful differences in peoples' lives. For more information, please visit www.karunatx.com.

Forward Looking Statements

This press release contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about the timing of advancing of our planned clinical trials and regulatory filings, our goals to develop and commercialize our product candidates, and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to obtain necessary funding, our ability to generate positive clinical trial results for our product candidates and other risks inherent in clinical development, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, risks relating to business interruptions resulting from the coronavirus (COVID-19) pandemic, and other risks set forth under the heading "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2020. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

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 26 therapeutics and therapeutic candidates, including two that have received FDA clearance and European marketing authorization, as of the date of PureTech's most recently filed Annual Report on Form 20-F. 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 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, including statements that relate to the company's future prospects, developments, and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, expectations regarding the potential of KarXT and those risks and uncertainties described in the risk factors included in the regulatory filings for PureTech Health plc. 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, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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