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PureTech Founded Entity Karuna Therapeutics Announces New England Journal of Medicine Publication of Data from EMERGENT-1 Phase 2 Trial Evaluating KarXT in Schizophrenia

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Incidences of somnolence, weight gain and extrapyramidal symptoms were similar in KarXT and placebo treatment groups

KarXT is in Phase 3 clinical development for the treatment of psychosis in adults with schizophrenia

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 Therapeutics, Inc. (NASDAQ: KRTX), a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions, announced that results from the EMERGENT-1 Phase 2 clinical trial evaluating KarXT for the treatment of schizophrenia were published in the *New England Journal of Medicine (NEJM).*

The published manuscript titled "Muscarinic Cholinergic Receptor Agonist and Peripheral Antagonist for Schizophrenia" is available online and appears in the February 25, 2021 issue of *NEJM*.

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

Karuna Therapeutics Announces New England Journal of Medicine Publication of Data from EMERGENT-1 Phase 2 Trial Evaluating KarXT in Schizophrenia

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KarXT is in Phase 3 clinical development for the treatment of psychosis in adults with schizophrenia

BOSTON, February 24, 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 that results from the EMERGENT-1 Phase 2 clinical trial evaluating KarXT for the treatment of schizophrenia were published in the *New England Journal of Medicine (NEJM).*

"The publication of the EMERGENT-1 Phase 2 trial results in the peer-reviewed *New England Journal of Medicine* reinforces earlier clinical and preclinical data that KarXT's modulation of muscarinic receptor function in the brain improves the symptoms of psychosis in schizophrenia, and underscores the potential of KarXT to offer a novel approach to treating this serious and disabling condition," said Steve Brannan, M.D., chief medical officer of Karuna Therapeutics and lead author of the manuscript. "These findings support the potential for KarXT to treat symptoms of psychosis in schizophrenia without producing the common problematic side effects of current therapies, such as weight gain and extrapyramidal symptoms. Given these encouraging results, we have advanced KarXT into Phase 3 clinical development in our efforts to provide a meaningful, new, non-dopaminergic treatment option for this serious neuropsychiatric disorder affecting more than 21 million people worldwide."

The double-blind, placebo-controlled, five-week inpatient EMERGENT-1 Phase 2 trial enrolled 182 adults with an acute exacerbation of schizophrenia. In this trial, a twice-daily, flexible-dose treatment with KarXT demonstrated a statistically significant and clinically meaningful 11.6-point reduction in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo at Week 5, the primary outcome measure of the study, with an effect size of 0.75 ($p<0.0001$). Results published in *NEJM* also include data for pre-specified secondary outcome measures. Four of the five pre-specified secondary outcome measures, including PANSS positive symptom subscore, PANSS negative symptom subscore, PANSS Marder negative symptom subscore, and Clinical Global Impression - Severity frequency counts, showed statistically significant reductions following treatment with KarXT compared to placebo at Week 5 ($p<0.001$).

KarXT was generally well-tolerated, with similar discontinuation rates between KarXT and placebo arms, both overall (20% vs. 21%) and due to treatment-emergent adverse events (2% in both arms). The most common adverse events associated with KarXT, including constipation, nausea, dry mouth, dyspepsia and vomiting, were mild-to-moderate in severity and were not associated with treatment discontinuation. Rates of nausea, vomiting, and dry mouth decreased over the course of the trial, while rates of constipation remained essentially constant. Incidences of somnolence, weight gain and extrapyramidal symptoms, which are common problematic side effects of current antipsychotic therapies, were similar in the placebo and KarXT treatment groups.

"Many people living with schizophrenia have persistent symptoms, experience poor quality of life and impaired ability to function, despite treatment with current antipsychotic drugs," said Jeffrey Lieberman, M.D., professor and chairman of the Department of Psychiatry, Columbia University, College of Physicians and Surgeons, member of Karuna's scientific advisory board, and co-author of the manuscript. "The clinical trial results with KarXT highlight its potential to be a differentiated treatment option with a completely new mechanism of action for people living with schizophrenia, offering relief from acute psychotic symptoms without the debilitating side effects associated with the current standard of care."

The published manuscript titled "Muscarinic Cholinergic Receptor Agonist and Peripheral Antagonist for Schizophrenia," is available online, and will appear in the February 25, 2021 issue of *NEJM*.

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 Schizophrenia

Schizophrenia is a chronic and often disabling brain condition affecting how a person thinks, feels and behaves. It is estimated to affect more than 21 million people worldwide, and has a young age at onset, typically presenting during late adolescence to early adulthood. Symptoms of schizophrenia generally fall into three categories - positive (delusions, hallucinations, and difficulty organizing and expressing thoughts), negative (difficulty enjoying life and withdrawal from others) and cognitive (deficits in memory, concentration and decision making). Given the nature of these symptoms, schizophrenia can affect all areas of patients' lives. Many people living with schizophrenia have difficulty finding an effective treatment and continue to experience distressing symptoms. With the help of a dedicated treatment team, it is possible for people with schizophrenia to live full lives. New therapeutic options with different mechanisms of action will enable more patients to find an effective and safe treatment regimen.

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, 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, 2019 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 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 intractable cancers, lymphatic and gastrointestinal diseases, central nervous system disorders and inflammatory and immunological diseases, 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, as of the date of PureTech's most recently filed Registration Statement on Form 20-F, was comprised of 24 products and product candidates, including two that have received FDA clearance and European marketing authorization. All of the underlying programs and platforms that resulted in this pipeline of product 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, our expectations regarding the potential therapeutic benefits of our product candidates, our expectations regarding the results from Karuna's EMERGENT-1 Phase 2 clinical trial evaluating 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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