PureTech Founded Entity Karuna Therapeutics Announces Positive Results from Phase 3 EMERGENT-2 Trial of KarXT in Schizophrenia

August 8, 2022
RNS Number : 2831V
PureTech Health PLC
08 August 2022

08 August 2022

PureTech Health plc

PureTech Founded Entity Karuna Therapeutics Announces Positive Results from Phase 3 EMERGENT-2 Trial of KarXT in Schizophrenia

Trial met primary endpoint, with KarXT demonstrating a statistically significant 9.6-point reduction in PANSS Total Score compared to placebo at Week 5 (p<0.0001)

Trial also met key secondary endpoints, demonstrating statistically significant reductions in positive and negative symptoms of schizophrenia, as measured by the PANSS positive, PANSS negative and PANSS negative Marder factor subscales

KarXT was generally well tolerated, with a side effect profile substantially consistent with prior trials of KarXT in schizophrenia

Karuna plans to submit a New Drug Application (NDA) with the U.S. Food & Drug Administration (FDA) in mid-2023

Conference call and webcast to take place today at 8:00 a.m. EDT / 1:00 p.m. BST

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company, noted today that its Founded Entity, Karuna Therapeutics, Inc. (NASDAQ: KRTX) ("Karuna") announced positive topline results from its Phase 3 EMERGENT-2 trial evaluating the efficacy, safety, and tolerability of its lead investigational therapy, KarXT (xanomeline-trospium), in adults with schizophrenia. The trial met its primary endpoint, with KarXT demonstrating a statistically significant and clinically meaningful 9.6-point reduction in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo (-21.2 KarXT vs. -11.6 placebo, p<0.0001) at Week 5 (Cohen's d effect size of 0.61). KarXT also demonstrated an early and sustained statistically significant reduction of symptoms, as assessed by PANSS total score, starting at Week 2 and maintained such reduction through all timepoints in the trial.

Karuna will hold a webcast and conference call this morning at 8:00 a.m. ET to share results from an interim analysis of its Phase 3 EMERGENT-2 trial of KarXT for the treatment of schizophrenia. A live webcast of the presentation will be available on the Investor Relations page of Karuna's website at investors.karunatx.com. A replay of the webcast will also be archived for up to 30 days on Karuna's website following the conference.

As of August 3, 2022, PureTech owned approximately 5.5% of Karuna's outstanding stock. A founder of Karuna and co-inventor of the KarXT program, PureTech has a right to royalty payments of 3% of net sales of any commercialized product covered by the license agreement, as well as 20% sublicense income covered by the license agreement. The license agreement covers key territories including the United States, European Union, and Japan. PureTech is also eligible to receive certain milestone payments upon the achievement of regulatory approvals.

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

Karuna Therapeutics Announces Positive Results from Phase 3 EMERGENT-2 Trial of KarXT in Schizophrenia

Trial met primary endpoint, with KarXT demonstrating a statistically significant 9.6-point reduction in PANSS Total Score compared to placebo at Week 5 (p<0.0001)

Trial also met key secondary endpoints, demonstrating statistically significant reductions in positive and negative symptoms of schizophrenia, as measured by the PANSS positive, PANSS negative and PANSS negative Marder factor subscales

KarXT was generally well tolerated, with a side effect profile substantially consistent with prior trials of KarXT in schizophrenia

The Company plans to submit a New Drug Application (NDA) with the U.S. Food & Drug Administration (FDA) in mid-2023

Conference call and webcast to take place today at 8:00 a.m. ET

BOSTON-- 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 positive topline results from its Phase 3 EMERGENT-2 trial evaluating the efficacy, safety, and tolerability of its lead investigational therapy, KarXT (xanomeline-trospium), in adults with schizophrenia. The trial met its primary endpoint, with KarXT demonstrating a statistically significant and clinically meaningful 9.6-point reduction in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo (-21.2 KarXT vs. -11.6 placebo, p<0.0001) at Week 5 (Cohen's d effect size of 0.61). KarXT also demonstrated an early and sustained statistically significant reduction of symptoms, as assessed by PANSS total score, starting at Week 2 and maintained such reduction through all timepoints in the trial.

"We are thrilled that these topline results from the Phase 3 EMERGENT-2 trial confirm what was seen in our Phase 2 EMERGENT-1 trial and underscore the potential for KarXT, with its novel and unique mechanism of action, to redefine what successful treatment looks like for the 21 million people living with schizophrenia worldwide, and potentially usher in the first new class of medicine for these patients in more than 50 years," said Steve Paul, M.D., chief executive officer, president and chairman of Karuna Therapeutics. "These results represent our second positive registrational trial. We look forward to continuing to gather long-term safety data to support our submission of a New Drug Application with the U.S. Food and Drug Administration for KarXT as a treatment for schizophrenia, which we expect to occur in mid-2023."

KarXT also met key secondary endpoints in the Phase 3 EMERGENT-2 trial, demonstrating a statistically significant reduction in both positive symptoms (e.g., hallucinations or delusions) and negative symptoms (e.g., difficulty enjoying life or withdrawal from others) of schizophrenia as measured by the PANSS positive, PANSS negative and PANSS negative Marder factor subscales. Results at Week 5 include:

· 2.9-point reduction in the PANSS positive subscale with KarXT compared to placebo (-6.8 KarXT vs. -3.9 placebo, p<0.0001).

· 1.8-point reduction in the PANSS negative subscale with KarXT compared to placebo (-3.4 KarXT vs. -1.6 placebo, p=0.0055).

· 2.2-point reduction in the PANSS negative Marder factor subscale with KarXT compared to placebo (-4.2 KarXT vs. -2.0 placebo, p=0.0022).

KarXT was generally well tolerated. Overall discontinuation rates were similar between KarXT and placebo groups (25% vs. 21%). The overall treatment-emergent adverse events (TEAEs) rate for KarXT and placebo was 75% and 58%, respectively. Discontinuation rates related to TEAEs were similar between KarXT (7%) and placebo (6%). Equal rates of serious TEAEs were observed between KarXT and placebo (2% in each group) and included suicidal ideation, worsening of schizophrenia symptoms, and appendicitis. None of the serious TEAEs were determined to be drug related. The most common TEAEs (>5%) in the KarXT arm were all mild to moderate in severity and included constipation, dyspepsia, nausea, vomiting, headache, increases in blood pressure, dizziness, gastroesophageal reflux disease (acid reflux), abdominal discomfort, and diarrhea. Mean blood pressure measures were similar between KarXT and placebo throughout the trial, and no syncopal events were observed. In the subset of patients with a TEAE of blood pressure increases, mean blood pressure at endpoint was similar to baseline and did not lead to trial discontinuation. Similar to prior trials, an increase in heart rate was associated with KarXT treatment and decreased in magnitude by the end of the trial. Consistent with EMERGENT-1, KarXT was not associated with common problematic side effects of current treatments, including sedation (somnolence), weight gain, and extrapyramidal symptoms.

"Despite the number of available treatment options, there continues to be a tremendous unmet need in the treatment of schizophrenia, placing an immense burden on both patients and their caregivers," said Rishi Kakar, M.D., chief scientific officer, Segal Trials and lead investigator of the Phase 3 EMERGENT-2 trial. "These data build on the growing body of clinical evidence supporting the potential of KarXT as a new and differentiated approach for schizophrenia, demonstrating notable improvements across both positive and negative symptoms, while not being associated with common problematic side-effects of current therapies, such as weight gain, sedation and movement disorders. This unique profile of KarXT has the potential to provide a new meaningful treatment option for our patients and their families beyond the current standard of care."

The EMERGENT program consists of the completed positive Phase 2 EMERGENT-1 and Phase 3 EMERGENT-2 trials, as well as three ongoing trials evaluating the acute efficacy and long-term safety of KarXT (EMERGENT-3, EMERGENT-4, and EMERGENT-5). Topline data from the Phase 3 EMERGENT-3 trial are expected in the first quarter of 2023. The data from our EMERGENT program will be used to support submission of an NDA with the U.S. FDA for KarXT as a treatment for schizophrenia, which is expected in mid-2023. Additional analysis of data from the Phase 3 EMERGENT-2 trial is ongoing, with plans to present these results at future medical meetings.

Conference Call and Webcast Information

Karuna will hold a webcast and conference call this morning at 8:00 a.m. ET to share results from an interim analysis of its Phase 3 EMERGENT-2 trial of KarXT for the treatment of schizophrenia.

A live webcast of the presentation will be available on the Investor Relations page of Karuna's website at investors.karunatx.com. A replay of the webcast will also be archived for up to 30 days on Karuna's website following the conference.

About the Phase 3 EMERGENT-2 Trial

The Phase 3 EMERGENT-2 trial is a double-blind, placebo-controlled, five-week, inpatient trial evaluating the efficacy, safety, and tolerability of our lead investigational therapy, KarXT, as compared to placebo in adults with schizophrenia in the United States. The primary endpoint was change from baseline in Positive and Negative Syndrome Scale (PANSS) total score, a scale for measuring schizophrenia symptom severity, of KarXT compared to placebo at Week 5. Key secondary endpoints included change from baseline in PANSS positive, PANSS negative and PANSS negative Marder factor subscale of KarXT compared to placebo at Week 5.

A total of 252 adults (between the ages of 18-65 years) with a confirmed diagnosis of schizophrenia who were experiencing symptoms of psychosis enrolled in the trial. Patients were randomized 1:1 to receive either a flexible dose of KarXT (n=126) or placebo (n=126) two times a day (BID) for five weeks. On Days 1-2, patients received a dose of 50/20 KarXT (50mg xanomeline/20mg trospium) BID or matching placebo. On Day 3, patients escalated to a dose of 100/20 BID, and starting on Day 8, patients could increase to 125/30 BID based on tolerability. In the trial, 81% of patients on KarXT compared to 90% on placebo titrated to the highest dose level (125/30).

About KarXT

KarXT (xanomeline-trospium) is an oral, investigational M1/M4-preferring muscarinic agonist in development for the treatment of psychiatric and neurological conditions, including schizophrenia and psychosis in Alzheimer's disease. Comprised of muscarinic agonist xanomeline and muscarinic antagonist trospium, it is designed to preferentially stimulate muscarinic receptors in the central nervous system. KarXT is the first potential medicine

of its kind with a truly new and unique dual mechanism that does not rely on the dopaminergic or serotonergic pathway to treat symptoms of serious mental illness. This approach has the potential to provide a differentiated therapy, and, if approved, to beneficially impact the lives of millions of people with serious mental illness.

About Schizophrenia

Schizophrenia is a chronic and often debilitating mental illness that impacts how one thinks, feels, and behaves. It is characterized by positive symptoms (hallucinations and delusions), negative symptoms (difficulty enjoying life and withdrawal from others), and cognitive impairment. Together these symptoms can severely impact quality of life and productivity, with only 10% of people gainfully employed and many struggling to meet adult milestones - such as living independently. The life expectancy of people living with schizophrenia is reduced by 10-20 years compared to the general population. Schizophrenia affects approximately 21 million people worldwide and is most commonly treated with antipsychotics. Unfortunately, many people with schizophrenia continue to experience limited efficacy or problematic side effects while on antipsychotic therapy, and up to 74% of patients discontinue medication before 18 months. When schizophrenia treatment is discontinued, it can lead to impacts on health including relapse, hospitalization, and longer time to remission.

About Karuna Therapeutics

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 serious mental illness. 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 our ongoing and 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, 2021. 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 27 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 Annual 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 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 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, including those related to the Company's intentions as to the use of the proceeds from the Transaction and those related to royalties and other potential payments due to the Company, should be considered forward-looking statements. 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.

Contact:

PureTech

Public Relations

publicrelations@puretechhealth.com

Investor Relations

IR@puretechhealth.com

EU Media

Ben Atwell, Rob Winder

+44 (0) 20 3727 1000

ben.atwell@FTIconsulting.com

U.S. Media

Nichole Sarkis

+1 774 278 8273

nichole@tenbridgecommunications.com

END

DISBKLBBLVLLBBB