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

March 20, 2023

Third positive registrational trial met its primary endpoint, with KarXT demonstrating an 8.4-point reduction in PANSS total score compared to placebo at Week 5 (p<0.0001)

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

Company is on track to submit a New Drug Application (NDA) to the U.S. Food & Drug Administration (FDA) in mid-2023, with a potential launch in the second half of 2024, if approved

Pre-NDA meeting is scheduled for early second quarter of 2023

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

BOSTON--(BUSINESS WIRE)--Mar. 20, 2023-- 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-3 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 8.4-point reduction in Positive and Negative Syndrome Scale (PANSS) total score compared to placebo (-20.6 KarXT vs. -12.2 placebo; p<0.0001) at Week 5 (Cohen's d effect size of 0.60). Consistent with prior trials, KarXT demonstrated an early and sustained statistically significant reduction of symptoms from Week 2 (p<0.05) through the end of the trial as assessed by PANSS total score.

"KarXT has now demonstrated a robust and consistent reduction of symptoms across all three registrational trials, providing a compelling picture of the potential of KarXT in schizophrenia. With these data, we are one step closer to a potential treatment option that could provide the first new mechanism of action to treat schizophrenia in several decades," said Bill Meury, president and chief executive officer of Karuna Therapeutics. "We look forward to working closely with the FDA as we focus our attention on the regulatory process, including our upcoming pre-NDA meeting in early second quarter, and remain on track for an NDA submission in mid-2023. I would like to thank all of the participants in the EMERGENT trials and the study investigators – without their commitment and trust, none of this would be possible."

"Schizophrenia is a persistent and disabling condition that presents with symptoms which are often difficult to treat and manage. Despite the number of currently available treatments, there remains a significant need for new treatment options for the 21 million people living worldwide with schizophrenia," said David Walling, Ph.D., chief clinical officer at Cenexel - CNS and investigator on the EMERGENT-3 trial. "The results from the EMERGENT-3 trial add to the growing body of data which suggest KarXT could address the symptoms of schizophrenia without the common side effects we see with current treatment options."

KarXT also demonstrated reductions in positive and negative symptoms of schizophrenia as measured by PANSS positive, PANSS negative, and PANSS negative Marder factor subscales – secondary endpoints in the trial. KarXT demonstrated a clinically meaningful and statistically significant 3.5-point reduction in PANSS positive subscale compared to placebo at Week 5 (-7.1 KarXT vs. -3.6 placebo; p<0.0001). While not meeting the threshold for statistical significance at Week 5, KarXT did demonstrate a statistically significant reduction in PANSS negative subscale and PANSS negative Marder factor subscale compared to placebo at Week 4 (p<0.05).

KarXT was generally well tolerated, with a side effect profile substantially consistent with prior trials of KarXT. The overall discontinuation rate in the trial was 33% (37% KarXT vs. 29% placebo). The overall treatment emergent adverse event (TEAE) rates for KarXT and placebo were 70% and 50%, respectively. Discontinuation rates related to TEAEs were similar between treatment arms (6% KarXT vs. 5% placebo), consistent with the EMERGENT-1 and EMERGENT-2 trials. The only serious TEAE reported in the KarXT arm was related to gastroesophageal reflux disease (acid reflux) and deemed not to be related to study drug. There were no serious TEAEs reported in the placebo group. The most common KarXT TEAEs (≥5%) were nausea, dyspepsia, vomiting, constipation, headache, hypertension, diarrhea, and insomnia, which were all rated mild or moderate in severity. There were no discontinuations due to TEAEs of hypertension. Mean blood pressure measures were similar between KarXT and placebo, and no syncopal events were observed. Similar to prior trials, an increase in heart rate was associated with KarXT treatment and decreased in magnitude by the end of the trial. Measures of weight gain, somnolence, and extrapyramidal symptoms of KarXT were similar to placebo, consistent with prior trials of KarXT in schizophrenia.

The NDA submission for KarXT in schizophrenia will incorporate the efficacy and safety data from the three placebo-controlled registrational trials, EMERGENT-1, EMERGENT-2, and EMERGENT-3, in addition to long-term safety data from the ongoing EMERGENT-4 and EMERGENT-5 trials. The Company is on track to submit an NDA to the FDA in mid-2023, with a potential launch in the second half of 2024, if approved.

Conference Call and Webcast Information

Karuna will hold a webcast and conference call this morning at 8:00 a.m. ET to share topline results from its Phase 3 EMERGENT-3 trial of KarXT in 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 EMERGENT-3 Trial

The Phase 3 EMERGENT-3 trial is a double-blind, placebo-controlled, five-week, inpatient trial evaluating the efficacy, safety, and tolerability of our lead investigational therapy, KarXT, compared to placebo in adults with schizophrenia in the United States and Ukraine. 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. Prespecified 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 256 adults (between the ages of 18-65 years) with schizophrenia enrolled in the trial. Enrolled patients had a confirmed diagnosis of schizophrenia and were experiencing symptoms of psychosis at the time of enrollment.

Patients were randomized 1:1 to receive either a flexible dose of KarXT or placebo 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 on Day 8, patients had the option to increase to 125/30 BID based on tolerability. In the trial, 79% of patients on KarXT compared to 91% on placebo titrated to the highest dose level (125/30 BID).

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. KarXT is the first potential medicine of its kind with a truly new and unique dual mechanism of action. Unlike current therapies, KarXT does not rely on the dopaminergic or serotonergic pathways, and it is designed to harness the therapeutic potential of xanomeline while managing peripheral side effects through trospium. 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 persistent and often disabling mental illness affecting how a person 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 (deficits in memory, concentration, and decision-making) – all of which can severely impact functioning, 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 more than 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 approximately 75% 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, our liquidity and capital resources, 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, our ability to identify additional product candidates, 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, 2022. 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.

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