Zai Lab Partner 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

Karuna 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 with the FDA is scheduled for early second quarter of 2023

SHANGHAI and CAMBRIDGE, Mass., March 20, 2023 (GLOBE NEWSWIRE) -- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688) today announced that the company's partner, Karuna Therapeutics, Inc. (NASDAQ: KRTX), reported 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 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 to the FDA 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. Karuna is on track to submit an NDA to the FDA in mid-2023, with a potential launch in the second half of 2024 in the United States, if approved.

Zai Lab is on track to initiate a bridging study for the treatment of patients with schizophrenia in China in mid-2023.

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.

Zai Lab has an exclusive license agreement with Karuna Therapeutics for the development, manufacturing, and commercialization of KarXT in Greater China, including mainland China ("China"), Hong Kong, Macau, and Taiwan (collectively "Greater China").

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.

More than 8 million people in China are living with schizophrenia, yet fewer than half are receiving treatment, and even fewer are obtaining adequate symptom improvement using the current treatment of antipsychotics. Like patients globally, there is a significant need for more effective therapies with improved safety to treat serious psychiatric conditions for patients with schizophrenia in Greater China.

About Zai Lab
Zai Lab (NASDAQ: ZLAB; HKEX: 9688) is an innovative, research-based, commercial-stage biopharmaceutical company based in China and the United States focused on bringing transformative medicines for oncology, autoimmune disorders, infectious diseases, and neurological disorders to patients in China and around the world. Our goal is to leverage our competencies and resources to positively impact human health worldwide.

For additional information about Zai Lab, please visit www.zailaboratory.com or follow us at www.twitter.com/ZaiLab_Global.

Forward-Looking Statements
This press release contains forward-looking statements relating to our collaboration with Karuna Therapeutics, Inc., including specifically the results from the pivotal Phase 3 EMERGENT-3 trial of KarXT in schizophrenia and the potential to effectively treat patients in Greater China with schizophrenia that are suffering from serious psychiatric conditions. All statements, other than statements of historical fact, included in this press release are forward-looking statements, and can be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "possible," "potential," "will," "would," and other similar expressions. Such statements constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are not guarantees or assurances of future performance. Forward-looking statements are based on our expectations and assumptions as of the date of this press release and are subject to inherent uncertainties, risks, and changes in circumstances that may differ materially from those contemplated by the forward-looking statements. You should not place undue reliance on these forward-looking statements. Actual results may differ materially from those indicated by forward-looking statements as a result of various important factors, including but not limited to (1) the results of our clinical and pre-clinical development of our product candidates, (2) the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approvals of our product candidates, (3) the effects of the novel coronavirus (COVID-19) pandemic, including any government actions or lockdown measures taken in response, on our business and general economic, regulatory, and political conditions, (4) risks related to doing business in China, and (5) other factors identified in our most recent annual and quarterly reports and in other reports we have filed with the U.S. Securities and Exchange Commission. We anticipate that subsequent events and developments will cause our expectations and assumptions to change, and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise, except as may be required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

Our SEC filings can be found on our website at www.zailaboratory.com and on the SEC's website at www.sec.gov.

For more information, please contact:

Investor Relations: Lina Zhang
+86 136 8257 6943
lina.zhang@zailaboratory.com

Media: Jennifer Chang / Xiaoyu Chen
+1 (917) 446-3140 / +86 185 0015 5011
jennifer.chang@zailaboratory.com / xiaoyu.chen@zailaboratory.com

Zai Lab Limited

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