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

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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

SHANGHAI and SAN FRANCISCO and CAMBRIDGE, Mass., Aug. 08, 2022 (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-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.

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.

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 the 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.

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 Karuna's 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.

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.

About Schizophrenia in China
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. Currently, 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 Limited (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, including our products, business activities and partnerships, research, and other events or developments, 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-2 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.

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