Zai Lab Reports Positive Topline Data from Phase 3 Bridging Trial Evaluating KarXT for the Treatment of Schizophrenia in China

10月 29, 2024

KarXT demonstrated a statistically significant 9.2-point reduction in PANSS Total score from baseline at Week 5 compared to placebo (p=0.0014)

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

KarXT has a tolerable safety profile with no new or unexpected safety signals

Based on these results, Zai is moving swiftly to submit New Drug Application (NDA) to China's National Medical Products Administration (NMPA) in early 2025

SHANGHAI & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 29, 2024-- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688) today announced positive topline results from the company's Phase 3 multi-center trial evaluating the safety and efficacy of KarXT (xanomeline and trospium chloride) in China. Consistent with previous global studies, the registrational bridging trial met its primary endpoint, with KarXT demonstrating a statistically significant 9.2-point reduction in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo at Week 5 (-16.9 KarXT vs. -7.7 placebo, p=0.0014).

The study also met all key secondary efficacy endpoints, demonstrating a significant improvement in PANSS positive symptom subscale score, PANSS negative symptom subscale score, PANSS negative Marder factor score, the Clinical Global Impression-Severity (CGI-S) scale at week five and percentage of PANSS responders at week five compared to placebo. Key secondary endpoints were formally tested sequentially in a predefined order.

Results at Week 5 include:

- 1.9-point reduction in the PANSS positive subscale with KarXT compared to placebo (-6.5 KarXT vs. -4.6 placebo, p=0.0474).
- 2.5-point reduction in the PANSS negative subscale with KarXT compared to placebo (-3.2 KarXT vs. -0.7 placebo, p=0.0062).

There were no safety signals that were new or unexpected in comparison with prior KarXT trials in schizophrenia. Treatment emergent adverse events in the treatment arm that occurred at ≥ 10% and at least twice the rate in placebo include vomiting, tachycardia, nausea, systemic hypertension, dizziness and diarrhea. Based on these results, Zai Lab is moving swiftly to submit a new drug application (NDA) to China's National Medical Products Administration (NMPA) for KarXT in schizophrenia in early 2025.

"The positive findings we observed in this bridging trial will contribute to a large global dataset for KarXT and demonstrate that this novel compound has the potential to be an important new treatment option for adults with schizophrenia in China," said Rafael G. Amado, M.D., President, Head of Global Research and Development, Zai Lab. "More than 8 million people in China live with schizophrenia, and fewer than half receive treatment, while many more do not get adequate symptom relief and suffer debilitating side effects from available antipsychotic therapies. This clinical trial is an example of Zai Lab's capabilities as a partner that helps to expand access to innovative treatments in collaboration with our global partners."

The Zai Lab Phase 3 multi-center, randomized, placebo-controlled trial (ZL-2701-001) evaluated the efficacy and safety of KarXT in 202 acutely psychotic hospitalized adult patients with schizophrenia in China. The study comprised two parts: a five-week double-blind part followed by a 12-week open-label extension part. Results shared today are from the five-week, double-blind trial segment.

"We see on a daily basis the need for more effective and tolerable treatment options for patients living with schizophrenia in Greater China," said Gang Wang, M.D., Director of National Clinical Research Center for Mental Disorders, Dean of Beijing Anding Hospital, Capital Medical University and the leading principal investigator in the Zai Lab Phase 3 trial. "We are encouraged that the data from this study further support KarXT as an impactful treatment option for these patients."

Full data from the trial will be presented at a future medical conference.

About KarXT

KarXT (xanomeline and trospium chloride) is a combination of an oral M1/M4-preferring muscarinic acetylcholine receptor agonist and a muscarinic acetylcholine receptor antagonist. This combination is in development for the treatment of psychiatric conditions, including schizophrenia and Alzheimer's-related psychosis. Xanomeline preferentially stimulates muscarinic receptors in the central nervous system implicated in these conditions, as compared to current antipsychotic medicines, which mostly target dopamine or serotonin receptors.

Zai Lab has an exclusive license from Karuna Therapeutics, Inc., a company later acquired by Bristol Myers Squibb, to develop, manufacture, and commercialize KarXT in Greater China (mainland China, Hong Kong, Macau, and Taiwan, collectively).

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 nearly 24 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. We are focused on discovering, developing, and commercializing innovative products that address medical conditions with significant unmet needs in the areas of oncology, immunology, neuroscience, and infectious disease. Our goal is to leverage our competencies and resources to positively impact human health in China and 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 future expectations, plans, and prospects, including, without limitation, statements relating to our collaboration with Bristol Myers Squibb, the potential benefits, safety, and efficacy of KarXT including the results from the pivotal Phase 3 EMERGENT-3 trial of KarXT in schizophrenia, and the potential treatment of psychiatric and neurological conditions including schizophrenia and dementia-related psychosis. These forward-looking statements may contain 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 statements of historical fact or 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. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including but not limited to (1) our ability to successfully commercialize and generate revenue from our approved products, (2) our ability to obtain funding for our operations and business decisions, (3) the results of our clinical and pre-clinical development of our product candidates, (4) the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approvals of our product candidates, (5) risks related to doing business in China, and (6) 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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Investor Relations:
Christine Chiou / Lina Zhang
+1 (917) 886-6929 / +86 136 8257 6943
christine.chiou1@zailaboratory.com / lina.zhang@zailaboratory.com

Media:
Shaun Maccoun/ Xiaoyu Chen
+1 (857) 270-8854 / +86 185 0015 5011
shaun.maccoun@zailaboratory.com / xiaoyu.chen@zailaboratory.com

Source: Zai Lab Limited