Zai Lab Announces Approval of AUGTYRO™ (repotrectinib) for Patients with ROS1-positive NSCLC by China's NMPA

May 13, 2024

The approval is based on the pivotal TRIDENT-1 trial, in which AUGTYRO achieved a high response rate and durable responses, including robust intracranial responses

SHANGHAI & CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 12, 2024-- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688) today announced that the National Medical Products Administration (NMPA) in China has approved the New Drug Application (NDA) for AUGTYRO™ (repotrectinib) for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small-cell lung cancer (NSCLC). The approval is based on the pivotal TRIDENT-1 study, an open-label, single-arm, Phase 1/2 trial that evaluated repotrectinib in TKI-naïve and TKI-pretreated patients with *ROS1*-positive NSCLC.

"We are pleased with NMPA's approval of AUGTYRO for the treatment of patients with *ROS1*-positive NSCLC in China. There is a significant unmet need for these patients given the limited durability of benefit due to the emergence of resistance with existing therapies, eventually leading to tumor progression," said Rafael G. Amado, M.D., President, Head of Global Oncology Research and Development at Zai Lab. "We appreciate the NMPA for their thorough assessment of AUGTYRO, recognizing its potential to address the unmet medical need in China."

"Despite existing earlier generation TKIs for *ROS1*-positive NSCLC, there remains an unmet need for new treatment options that support important clinical goals, such as durable therapeutic response," said Dr. Shun Lu, M.D., Ph.D., Chief of Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiaotong University. "The TRIDENT-1 study showed that treatment with repotrectinib results in high response rates with promising durability in patients with *ROS1*-positive NSCLC, across TKI-naïve and TKI-pretreated settings, including in the presence of intracranial disease. Based on this study, repotrectinib has the potential to become a new standard of care for these patients."

In June 2023, China's NMPA accepted the NDA for AUGTYRO for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive NSCLC, with priority review granted in May 2023.

Zai Lab contributed to the pivotal TRIDENT-1 study and dosed the first patient in Greater China in May 2021, and the results were published in the *New England Journal of Medicine* in January 2024. The topline efficacy and safety data of Chinese subpopulation is consistent with that of global population, demonstrating robust response rates and durable clinical activity in patients with *ROS1*-positive NSCLC. Treatment with AUGTYRO was generally well tolerated with a manageable safety profile.

About AUGTYRO

AUGTYRO (repotrectinib) is a next-generation tyrosine kinase inhibitor targeting the *ROS1* and *NTRK* oncogenic drivers. Patients with solid tumors, including NSCLC, harboring *ROS1* and *NTRK* gene fusions treated with approved targeted therapies often develop resistance mutations that limit binding of these drugs to their target. Ultimately, this leads to shortened duration of response and tumor progression. AUGTYRO is the first next-generation ROS1 and TRK TKI uniquely designed to improve durability of benefit, including in the brain.

In November 2023, AUGTYRO was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC.

AUGTYRO has been granted three Breakthrough Therapy Designations from the U.S. Food and Drug Administration in: *ROS1*-positive metastatic NSCLC patients who have not been treated with a ROS1 TKI; *ROS1*-positive metastatic NSCLC patients who have previously been treated with one ROS1 TKI and who have not received prior platinum-based chemotherapy; and patients with advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with one or two prior TRK TKIs, with or without prior chemotherapy, and have not had satisfactory alternative treatments. Additionally, AUGTYRO was previously granted four Fast-Track designations in patients with: *ROS1*-positive advanced NSCLC who have not been treated with one ROS1 TKI; *ROS1*-positive advanced NSCLC who have been previously treated with one prior line of platinum-based chemotherapy and one prior ROS1 TKI; *ROS1*-positive advanced NSCLC pretreated with one prior ROS1 TKI without prior platinum-based chemotherapy; and advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with at least one prior line of chemotherapy and one or two prior TRK TKIs and have not had satisfactory alternative treatments. AUGTYRO was also granted an Orphan Drug designation in 2017.

AUGTYRO has been granted four Breakthrough Therapy Designations by the CDE of China's NMPA in *ROS1*-positive metastatic NSCLC patients who have not been treated with a ROS1 TKI; *ROS1*-positive metastatic NSCLC patients who have previously been treated with one prior ROS1 TKI and who have not received prior platinum-based chemotherapy or immunotherapy; and *ROS1*-positive metastatic NSCLC patients who have previously been treated with one prior ROS1 TKI and one platinum-based chemotherapy; and patients with advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with one or two prior TRK TKIs, with or without prior chemotherapy, and have not had

satisfactory alternative treatments.

Zai Lab has an exclusive license agreement with Turning Point Therapeutics, Inc. (Turning Point Therapeutics, a Bristol Myers Squibb company) to develop and commercialize AUGTYRO in Greater China (Mainland China, Hong Kong, Taiwan, and Macau).

About TRIDENT-1

TRIDENT-1 is a global, multicenter, single-arm, open-label, multi-cohort Phase 1/2 clinical trial evaluating the safety, tolerability, pharmacokinetics and anti-tumor activity of AUGTYRO in patients with advanced solid tumors, including NSCLC.[1,2] Phase 1/2 includes patients with locally advanced or metastatic solid tumors harboring *ROS1* fusions.[2] Additional analyses of the trial are still being conducted; asymptomatic central nervous system (CNS) metastases are allowed.[1,2] The trial excludes patients with symptomatic brain metastases, among other exclusion criteria.[1] Phase 1 of the trial included the dose escalation that determined the recommended Phase 2 dose.[2]

Phase 2 of the trial has a primary endpoint of overall response rate (ORR).[1,2] Key secondary endpoints include duration of response (DOR) according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1) as assessed by Blinded Independent Central Review (BICR), progression-free survival (PFS), and intracranial response in six distinct expansion cohorts, including TKI-naïve and TKI-pretreated patients with *ROS1*-positive locally advanced or metastatic NSCLC.[1,2]

In TRIDENT-1, 79% (95% Confidence Interval [CI]: 68 to 88) of TKI-naïve patients (n=71) responded to treatment; 6% experienced complete responses and 73% experienced partial responses.[1] The median duration of response (mDOR) was 34.1 months.[1] Among TKI-pretreated patients, 38% (95% CI: 25 to 52) (n=56) responded to treatment; 5% experienced complete responses and 32% experienced partial responses and the mDOR was 14.8 months.[1] Among those who had measurable CNS metastases at baseline, responses in intracranial lesions were observed in 7 of 8 TKI-naïve patients and in 5 of 12 of those who were TKI-pretreated.[1]

The FDA-approved dosing for AUGTYRO is 160 mg orally once daily for 14 days, then increased to 160 mg twice daily until disease progression or unacceptable toxicity.[1]

About Non-Small Cell Lung Cancer in China

Lung cancer is the most commonly diagnosed cancer type and the leading cause of cancer death in China. There were approximately 871,000 new cases and 767,000 deaths of lung cancer in China in 2022, respectively.[3] NSCLC accounts for approximately 85% of lung cancer, and approximately 70% of NSCLC is locally advanced or metastatic at initial diagnosis. In China, *ROS1* rearrangements occur in 2-3% of patients with advanced NSCLC.[4]

[1] *Augtyro Prescribing Information. Augtyro U.S. Product Information. Last updated: November 2023. Princeton, NJ: Bristol Myers Squibb Company.*
[2] *ClinicalTrials.gov: NCT03093116. A study of repotrectinib (TPX-0005) in patients with advanced solid tumors harboring ALK, ROS1, or NTRK1-3 rearrangements (TRIDENT-1). Available at https://classic.clinicaltrials.gov/ct2/show/NCT03093116. Accessed November 4, 2023.*
[3] *Changfa Xia, et al. Cancer statistics in China and United States, 2022: profiles, trends, and determinants.*
[4] *Zhang, et al. Prevalence of ROS1 fusion in Chinese patients with non-small cell lung cancer, Thoracic Cancer January 2019.*

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, autoimmune disorders, infectious diseases, and neuroscience. 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.

Zai Lab Forward-Looking Statements

This press release contains forward-looking statements about future expectations, plans, and prospects for Zai Lab, including, without limitation, statements relating to the prospects of repotrectinib and the potential treatment of ROS1-positive NSCLC and NTRK-positive solid tumors in Greater China. 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 initiatives, (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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