Zai Lab Partner Mirati Therapeutics Presents Late-Breaking Results Evaluating Concurrent Adagrasib and Pembrolizumab in First-Line Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC)

December 5, 2022

- *Adagrasib* in combination with pembrolizumab demonstrates favorable tolerability and promising preliminary efficacy in patients with first-line advanced/metastatic NSCLC harboring a $KRAS^{G12C}$ mutation
- Findings will be presented on December 7 at the 2022 ESMO Immuno-Oncology Annual Congress, as an oral presentation from 2:05 p.m.-2:15 p.m. CET / 8:05 a.m.-8:15 a.m. ET (Presentation #LBA4) during the “Proffered Paper session 1” session

SHANGHAI and CAMBRIDGE, Mass., Dec. 05, 2022 (GLOBE NEWSWIRE) -- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688), a patient-focused, innovative, commercial-stage, global biopharmaceutical company, today announced that the company’s partner Mirati Therapeutics, Inc. (NASDAQ: MRTX), a clinical-stage oncology company reported preliminary results from the KRYSTAL-7 Phase 2 trial and KRYSTAL-1 Phase 1b cohort evaluating *adagrasib* (400mg twice daily) concurrently combined with pembrolizumab in patients for the treatment of first-line NSCLC harboring a $KRAS^{G12C}$ mutation across all PD-L1 subgroups. These data are the first to demonstrate the potential tolerability and feasibility of a concurrent combination regimen of a $KRAS^{G12C}$ inhibitor and a PD-1/L1 checkpoint inhibitor.

Summary of Clinical Results

- The KRYSTAL-7 and KRYSTAL-1 trials represent the largest dataset evaluating a $KRAS^{G12C}$ inhibitor in combination with a PD-1/L1 checkpoint inhibitor as a first-line treatment for patients with NSCLC harboring a $KRAS^{G12C}$ mutation.
- 75 patients were enrolled and evaluable for safety with a median follow-up of 3.5 months (duration of treatment: 2 months). Treatment-related adverse events (TRAEs) were Grade 1–2 (39%), Grade 3 (40%) and Grade 4 (4%); there were no Grade 5 TRAEs observed. TRAEs led to discontinuation of both *adagrasib* and pembrolizumab in 2 patients and only pembrolizumab in 2 patients; there were no patients who discontinued only *adagrasib* due to a TRAE.
- Increases in alanine transaminase (ALT) / aspartate transaminase (AST) were consistent with either agent as a monotherapy with Grade 3 TRAEs being highest grade and total incidence of Grade 3 liver function test (LFT) increases of 9%. Median time from onset to an increase in ALT and AST was 26 and 37 days, respectively, and only 1 patient experienced new onset treatment-related ALT/AST increase after 3 months.
- Of patients who were clinically evaluable and received at least one on-study scan (n=53), *adagrasib* and pembrolizumab demonstrated promising preliminary clinical activity across all PD-L1 subgroups with an objective response rate (ORR) of 49%.
- In a subset of response-evaluable patients enrolled at least 6 months prior to the data cutoff date, 6 of 26 clinical responses occurred at second on-study scan or later, and the ORR was 56%.
- 7 evaluable patients enrolled in the KRYSTAL-1 Phase 1b cohort (with a median follow-up of 19.3 months) reported an ORR of 57% and a disease control rate (DCR) of 100%. The four patients who responded maintained response for over nine months while two continued to receive treatment and remain in response beyond 18 months.
- Safety in the KRYSTAL-1 Phase 1b cohort was consistent with what has been observed in KRSTYAL-7 and demonstrated a manageable safety profile with no Grade 4–5 TRAEs.

“Initial results across all cohorts suggest the concurrent combination of *adagrasib* and pembrolizumab may provide a chemotherapy-free option for treatment-naïve NSCLC with a manageable safety profile and encouraging clinical activity,” said Pasi A. Jänne, MD, PhD, Dana Farber Cancer Institute. “Across all evaluated cohorts, liver-related TRAEs were predominantly low grade and occurred early in treatment, with limited new onset after 3 months.”

The data (Presentation #LBA4) will be presented in an oral presentation on Dec. 7 at 2:05 p.m.-2:15 p.m. CET / 8:05 a.m.–8:15 a.m. ET during the “Proffered Paper session 1” at the European Society for Medical Oncology Immuno-Oncology (ESMO IO) Congress 2022.

“We are delighted to see the data that further underscores the potential of adagrasib as a well-tolerated treatment option for patients in the first-line setting,” said Josh Smiley, chief operating officer, Zai Lab. “Lung cancer is the most common cancer in China, and we look forward to continuing our collaboration with Mirati to develop adagrasib for patients with cancer who harbor the $KRAS^{G12C}$ mutation around the world.”

In August 2022, Zai Lab treated the first patient in Greater China for the KRYSTAL-7 Phase 2 trial.

About *Adagrasib* (MRTX849)

Adagrasib is an investigational, highly selective, and potent oral small-molecule inhibitor of $KRAS^{G12C}$ that is optimized to sustain target inhibition, an attribute that could be important to treat $KRAS^{G12C}$-mutated cancers, as the $KRAS^{G12C}$ protein regenerates every 24-48 hours. Studies of *adagrasib* have shown that the drug has a long half-life and extensive tissue distribution, and is well tolerated. In clinical trials, *adagrasib* also has shown, central nervous system penetrance and single-agent responses in non-small cell lung cancer (NSCLC), colorectal cancer, pancreatic cancer and other solid tumors with $KRAS^{G12C}$ mutations. *Adagrasib* is being evaluated in several clinical trials in combination with other anti-cancer therapies in patients with advanced solid tumors. Registration-enabling studies are ongoing in NSCLC and colorectal cancer. For more information visit Mirati.com/science.

Virtual Investor Event

Mirati Therapeutics will host an Investor Event on Wednesday, December 7, 2022, at 5:00 p.m. CET / 11:00 a.m. ET.

Mirati company executives will provide an overview of the *adagrasib* and pembrolizumab combination data presented 2022 ESMO Immuno-Oncology Annual Congress.

About NSCLC in China

$KRAS^{G12C}$ is the most common KRAS mutation in NSCLC. The mutation is a biomarker of poor prognosis in Chinese patients with NSCLC. Lung cancer consists of NSCLC in approximately 85% of cases and small cell lung cancer (SCLC) in approximately 15% of cases. According to the World Health Organization, the incidence of lung cancer in China in 2020 was 815,563 cases, with 714,699 deaths.

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.

Zai Lab Forward-Looking Statements

This press release contains forward-looking statements relating to future expectations, plans, and prospects, including, without limitation, statements relating to the potential benefits, safety, and efficacy of adagrasib; the treatment of lung cancer; and clinical trial data, data readouts, and presentations. These forward-looking statements include, without limitation, statements containing 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 nor are they 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) the effects of the novel coronavirus (COVID-19) pandemic on our business and general economic, regulatory, and political conditions, (6) risks related to doing business in China, and (7) 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.

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