Zai Lab Partner MacroGenics Announces FDA Approval of MARGENZA™ for Patients with Pretreated Metastatic HER2-Positive Breast Cancer

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- *MARGENZA (margetuximab-cmkb) is the first HER2-targeted therapy to have improved progression-free survival (PFS) versus Herceptin® (trastuzumab), both combined with chemotherapy, in a head-to-head Phase 3 clinical trial*
- *MARGENZA is approved, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease*
- *Product launch in U.S. anticipated in March 2021*

SHANGHAI and SAN FRANCISCO, Dec. 16, 2020 (GLOBE NEWSWIRE) -- Zai Lab Limited's (NASDAQ: ZLAB; HKEX: 9688) partner MacroGenics, Inc. (Nasdaq: MGNX), a biopharmaceutical company focused on developing and commercializing innovative monoclonal-antibody-based therapeutics for the treatment of cancer, today announced that the U.S. Food and Drug Administration (FDA) has approved MARGENZA, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. MARGENZA is being further developed by MacroGenics for the treatment of advanced gastric cancer, with support by Zai Lab in Greater China. The approval in breast cancer in the U.S. was based on safety and efficacy results from the pivotal Phase 3 SOPHIA trial.

"We congratulate our partner MacroGenics for this great success," said Samantha Du, Ph.D., Founder, Chairwoman and Chief Executive Officer of Zai Lab. "We look forward to bringing this important medicine to metastatic breast cancer patients in China as soon as possible. We are also participating in the global Phase 2/3 MAHOGANY clinical trial of margetuximab plus checkpoint blockade, with or without chemotherapy, as a potential first-line treatment for patients in front-line gastroesophageal cancer."

The approval for MARGENZA was based on data from SOPHIA, a randomized Phase 3 clinical trial. The study, which included 536 patients, showed a statistically significant 24% reduction in the risk of disease progression or death with MARGENZA plus chemotherapy compared with trastuzumab plus chemotherapy (hazard ratio [HR]=0.76; 95% CI, 0.59-0.98; P=0.033; median PFS 5.8 vs 4.9 months). The objective response rate for MARGENZA plus chemotherapy was 22% and for trastuzumab plus chemotherapy was 16%. The final Overall Survival (OS) analysis is expected in the second half of 2021.

Adverse reactions occurring in greater than twenty percent of patients with MARGENZA in combination with chemotherapy were fatigue/asthenia (57%), nausea (33%), diarrhea (25%), and vomiting (21%). The MARGENZA U.S. Prescribing Information has a BOXED WARNING for left ventricular dysfunction and embryo-fetal toxicity. In addition, MARGENZA can cause infusion-related reactions (IRRs). IRRs occurred in 13% of patients treated with MARGENZA, with the majority reported as Grade 2 or less. Grade 3 IRRs occurred in 1.5% of patients.

About the SOPHIA Study

The SOPHIA study (NCT02492711) is a randomized, open-label Phase 3 clinical trial evaluating MARGENZA plus chemotherapy compared to trastuzumab plus chemotherapy in patients with HER2-positive metastatic breast cancer, who have previously been treated with anti-HER2-targeted therapies. All study patients had previously received trastuzumab, all but one patient had previously received pertuzumab, and 91% had previously received ado-trastuzumab emtansine, or T-DM1.

The study enrolled 536 patients who were randomized 1:1 to receive either MARGENZA (n=266) given intravenously at 15 mg/kg every three weeks or trastuzumab (n=270) given intravenously at 6 mg/kg (or 8 mg/kg for loading dose) every three weeks in combination with one of four chemotherapy agents (capecitabine, eribulin, gemcitabine or vinorelbine) given at the standard doses. Intent-to-treat PFS analysis occurred after 265 PFS events.

The primary endpoints of the study are sequentially assessed PFS, determined by blinded, centrally reviewed radiological review, followed by OS. Additional key secondary endpoints are PFS by investigator assessment, ORR and Duration of Response. Tertiary endpoints include ORR by investigator assessment and safety. PFS and ORR were assessed according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1).

About HER2-positive Breast Cancer

Human epidermal growth factor receptor 2 (HER2) is a protein found on the surface of some cancer cells that promotes growth and is associated with aggressive disease and poor prognosis. Breast cancer is the most common cancer in Chinese women, with 272,400 newly diagnosed cases and 70,700 deaths in 2015. Approximately 25%-30% of all types of late-stage breast cancer in China are HER2-positive. Monoclonal antibodies targeting

HER2 have greatly improved outcomes; however, a significant number of patients progress to later lines of therapy. Effective treatments for metastatic HER2-positive breast cancer continue to remain an unmet need.

About MARGENZA

MARGENZA (margetuximab-cmkb) is an Fc-engineered, monoclonal antibody that targets the HER2 oncoprotein. HER2 is expressed by tumor cells in breast, gastroesophageal and other solid tumors. Similar to trastuzumab, margetuximab-cmkb inhibits tumor cell proliferation, reduces shedding of the HER2 extracellular domain and mediates antibody-dependent cellular cytotoxicity (ADCC). However, through MacroGenics' Fc Optimization technology, margetuximab-cmkb has been engineered to enhance the engagement of the immune system. *In vitro*, the modified Fc region of margetuximab-cmkb increases binding to the activating Fc receptor FCGR3A (CD16A) and decreases binding to the inhibitory Fc receptor FCGR2B (CD32B). These changes lead to greater *in vitro* ADCC and NK cell activation. The clinical significance of *in vitro* data is unknown.

Margetuximab-cmkb is also being evaluated in combination with checkpoint blockade in the Phase 2/3 MAHOGANY trial for the treatment of patients with HER2-positive gastroesophageal cancer (NCT04082364), and in combination with tebotelimab (PD-1 × LAG-3 bispecific DART® molecule) in various HER2-positive tumors (NCT03219268). For more information, please visit www.clinicaltrials.gov.

Most Common Adverse Reactions

The most common adverse drug reactions (≥10%) with MARGENZA in combination with chemotherapy are fatigue/asthenia, nausea, diarrhea, vomiting, constipation, headache, pyrexia, alopecia, abdominal pain, peripheral neuropathy, arthralgia/myalgia, cough, decreased appetite, dyspnea, infusion-related reactions, palmar-plantar erythrodysesthesia, and extremity pain.

Link to full Prescribing Information, including Boxed Warning

About Zai Lab

Zai Lab (NASDAQ:ZLAB; HKEX: 9688) is an innovative commercial-stage biopharmaceutical company focused on bringing transformative medicines for cancer and infectious and autoimmune diseases to patients in China and around the world. We aim to address significant unmet medical needs in large, fast-growing segments of the pharmaceutical market. To that end, our experienced team has secured partnerships with leading global biopharmaceutical companies in order to generate a broad pipeline of innovative marketed products and drug candidates. We have also built an in-house team with strong drug discovery and translational research capabilities and are establishing a pipeline of proprietary drug candidates with global rights. Our vision is to become a leading global biopharmaceutical company, discovering, developing, manufacturing and commercializing our portfolio in order to impact human health worldwide.

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

For more information, please contact:

ZAI LAB CONTACTS:

Zai Lab
Billy Cho, CFO
+86 137 6151 2501
billy.cho@zailaboratory.com

Media: Ryo Imai / Robert Flamm, Ph.D.
Burns McClellan, on behalf of Zai Lab
212-213-0006 ext. 315 / 364
rimai@burnsmc.com / rflamm@burnsmc.com

Investors: Pete Rahmer / Mike Zanoni
Endurance Advisors, on behalf of Zai Lab
415-515-9763 / 610-442-8570
prahmer@enduranceadvisors.com / mzanoni@enduranceadvisors.com

Zai Lab Limited

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