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Chugai's Alecensa® Receives Breakthrough Therapy Designation from FDA for First-Line Treatment of ALK Positive Non-Small Cell Lung Cancer

-- Alecensa's Second Designation and the Fourth Designation Overall for Three Chugai Originated Drugs --

TOKYO, October 4, 2016 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) for the first-line treatment of ALK positive non-small cell lung cancer (NSCLC) to Alecensa®, a highly selective ALK inhibitor created by Chugai. Alecensa® is approved in Japan and in the United States, and filed in Europe by Roche.

"We are pleased that Alecensa has received Breakthrough Therapy Designation for the second time, which also marks the fourth BTD for Chugai originated drugs," said Dr. Yasushi Ito, Chugai's Senior Vice President, Head of Project & Lifecycle Management Unit. "This designation underscores that the medical value of Alecensa is highly appreciated, and that the drug has great potential to the treatment of ALK positive NSCLC."

This designation is based on the J-ALEX study, conducted by Chugai, which is an open-label, randomized phase III study that compares the efficacy and safety between Alecensa and crizotinib. The J-ALEX study enrolled 207 ALK-inhibitor naïve patients with *ALK* fusion gene positive advanced or recurrent NSCLC, who had not undergone chemotherapy or had undergone one chemotherapy regimen. The subjects were allocated to either the Alecensa arm or the crizotinib arm in a one to one ratio. The primary endpoint of the J-ALEX study was progression free survival (PFS) as assessed by a blinded independent review board. The secondary endpoints included overall survival, objective response rate and safety. In February 2016, an independent data monitoring committee recommended to discontinue the J-ALEX study early for benefit based on the results of the predetermined interim analysis which was examined by the committee.

The PFS hazard ratio of the Alecensa arm to the crizotinib arm was 0.34, and Alecensa demonstrated significantly prolonged PFS (99.6826% CI: 0.17-0.70, stratified log-rank p<0.0001). Median PFS was not reached (95% CI: 20.3-Not reached) in the Alecensa arm while it was 10.2 months (95%CI: 8.2-12.0) in the crizotinib arm. In the Alecensa arm, constipation was an adverse event (AE) with >30% frequency, while in the crizotinib arm nausea, diarrhea, vomiting, visual disturbance, dysgeusia, constipation, ALT elevation and AST elevation were observed in >30% patients. Grade 3-4 AEs occurred in 27% of the Alecensa arm and in 51% of the crizotinib arm, with no treatment-related deaths in both arms.

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This is the fourth Breakthrough Therapy Designation for Chugai originated drugs following Alecensa (ALK positive, metastatic NSCLC in patients who have progressed on or those who are intolerant to crizotinib), Actemra (systemic sclerosis), and emicizumab (prophylactic treatment for 12 years or older patients with hemophilia A with factor VIII inhibitors).

Based on Chugai's business philosophy of "Innovation all for the patients," Chugai will collaborate with Roche and Genentech to receive approval for the early use of Alecensa in a number of countries around the world.

About Breakthrough Therapy Designation

The Breakthrough Therapy Designation was adopted as part of the FDA Safety and Innovation Act (FDASIA) enacted in July 2012 aiming at expediting the development and review of drugs for the treatment of severe or life-threatening diseases or symptoms. In order to grant Breakthrough Therapy Designation, preliminary clinical evidence is required demonstrating that the drug may have substantial improvement on at least one clinically significant endpoint over existing therapies. Breakthrough Therapy Designation includes the features of a Fast Track designation, with the addition of intensive guidance on efficient drug development as well organizational commitment from FDA.

About Alecensa

Alecensa is a highly selective ALK inhibitor discovered by Chugai. It has been reported that 2 to 5 percent of patients with NSCLC express a chromosomal rearrangement which leads to fusion of the ALK gene with another gene.[1)] ALK kinase signalling is constantly active in cells with such fusion genes, resulting in uncontrolled growth of tumor cells and transforming the cells into tumor cells.[2, 3)] Alecensa exerts its anti-tumor effect by selectively inhibiting ALK kinase activity to inhibit tumor cell proliferation and induce cell death.[4)] In addition, Alecensa is not recognized by the transporter proteins in the blood brain barrier that actively pump molecules out of the brain. Alecensa is active in the central nervous system and has proven activity against brain metastases.

In Japan, Alecensa is available to patients with "ALK fusion gene positive unresectable, recurrent/advanced NSCLC" and is marketed by Chugai. In the US, Alecensa was approved in December 2015 for the indication of "ALK positive, metastatic NSCLC in patients who have progressed on or those who are intolerant to crizotinib." In September 2015, Roche filed the MAA in Europe to the European Medicines Agency for the approval of "ALK fusion gene positive unresectable, recurrent/advanced NSCLC."

1) Biomarker committee of The Japan Lung Cancer Society, Guidelines for ALK gene tests in lung cancer patients
2) Soda et al., Nature. 448: 561-566 (2007)
3) Takeuchi et al., Clin Cancer Res. 15: 3143-3149 (2009)
4) Sakamoto et al., Cancer Cell. 19: 679-690 (2011)

About Chugai

Chugai Pharmaceutical is one of Japan's leading research-based pharmaceutical companies with strengths in biotechnology products. Chugai, based in Tokyo, specializes in prescription pharmaceuticals and is listed on the 1st section of the Tokyo Stock Exchange. As an important member of the Roche Group, Chugai is actively involved in R&D activities in Japan and abroad. Specifically, Chugai is working to develop innovative products which may satisfy the unmet medical needs, mainly focusing on the oncology area.

In Japan, Chugai's research facilities in Gotemba and Kamakura are collaborating to develop new pharmaceuticals and laboratories in Ukima are conducting research for technology development for industrial production. Overseas, Chugai Pharmabody Research based in Singapore is engaged in research focusing on the generation of novel antibody drugs by utilizing Chugai's proprietary innovative antibody engineering technologies. Chugai Pharma USA and Chugai Pharma Europe are engaged in clinical development activities in the United States and Europe.

The consolidated revenue in 2015 of Chugai totalled 498.8 billion yen and the operating income was 90.7 billion yen (IFRS Core basis).

Additional information is available on the internet at http://www.chugai-pharm.co.jp/english.

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