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Chugai to Present Japanese Phase III Results on Alecensa® at ASCO

First Head-to-Head Study with Crizotinib Demonstrates Prolonged Progression Free Survival

TOKYO, May 19, 2016 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the results of the Japanese phase III study (J-ALEX) of Alecensa®, in *ALK* fusion gene positive non-small cell lung cancer (NSCLC) patients, will be presented at the annual meeting of the American Society of Clinical Oncology (ASCO) which will be held June 3 -7 in Chicago, IL (USA). Results from the J-ALEX study will be presented at the oral abstract sessions scheduled for June 6 (CDT).

Abstract #9008
Alectinib (ALC) versus crizotinib (CRZ) in ALK-inhibitor naïve ALK-positive non-small cell lung cancer (ALK+NSCLC): primary results from the J-ALEX study

The J-ALEX study was 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 either had not undergone chemotherapy or had undergone one chemotherapy regimen. The subjects were allocated to either the Alecensa arm or the crizotinib arm of the study 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, and other endpoints.

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 Estimated) 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 (36%) was an adverse event (AE) with >30% frequency, while in the crizotinib arm nausea (74%), diarrhea (73%), vomiting (59%), visual disturbance (55%), dysgeusia (52%), constipation (46%), ALT elevation (32%), and AST elevation (31%) were each seen in >30% patients. Grade 3-4 AEs occurred in 27% of the Alecensa arm and in 51% of the crizotinib arm, there were no treatment-related deaths in either arm.

In February, 2016, Chugai carried out a prospectively defined interim analysis, and had an independent data monitoring committee examine the results. Since the results showed that Alecensa significantly prolonged the PFS to a higher extent than anticipated, the committee decided to recommend an early discontinuation of the J-ALEX study.

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“It was found in Japan earlier than in any other country in the world that *ALK* fusion gene serves as a powerful carcinogenic factor for some types of lung cancer. Alecensa was created by Chugai as a drug selectively inhibiting the activity of *ALK* fusion gene, and it was first approved in Japan in 2014 based on the Japanese clinical study data. The J-ALEX study, comparing Alecensa therapy directly with standard therapy, demonstrated superiority of Alecensa over standard therapy for the first time in the world. This finding not only greatly encourages the patients suffering from *ALK* fusion gene positive NSCLC but also illustrates the high level of drug development progression from basic research to clinical studies in Japan,” said Chugai’s Director and Executive Vice President, Dr. Yutaka Tanaka. “Chugai is extremely proud of having developed Alecensa which has been shown to provide benefit to patients.”

As a top pharmaceutical company in the field of oncology in Japan, Chugai believes that early treatment using Alecensa in *ALK* fusion gene positive NSCLC is expected to prolong these patients’ PFS and enable them to face their disease with hope for the future.

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 “anaplastic lymphoma kinase (ALK) positive, metastatic non-small cell lung cancer (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.”

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 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.

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)

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