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Chugai's Alecensa® Met Its Primary Endpoint in the ALEX Study

- Following the Japanese Phase III Study, Alecensa Demonstrated Statistically Significant Improvement in PFS in a Global Phase III Head to Head Study with Crizotinib -

TOKYO, April 10, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that Alecensa as an initial (first-line) treatment showed that patients lived significantly longer without disease worsening (progression-free survival, PFS) compared to crizotinib in the ALEX Study, a global phase III study targeting *ALK* fusion gene positive non-small cell lung cancer (NSCLC), conducted by F. Hoffmann-La Roche Ltd. The safety profile of Alecensa was consistent with that observed in previous studies, with no new or unexpected adverse events.

"Following the Japanese phase III J-ALEX study, the ALEX study, the head to head trial with crizotinib, Alecensa demonstrated a significant prolongation of PFS compared to crizotinib. This finding greatly encourages the patients suffering from *ALK* fusion gene positive NSCLC," said Dr. Yasushi Ito, Senior Vice President, Head of Project & Lifecycle Management Unit. "We believe that Alecensa will also contribute to improving the outcomes for overseas patients from first line therapy in the future."

The ALEX study was an open-label, randomized global phase III study that compares the efficacy and safety between both monotherapy of Alecensa and crizotinib. The ALEX study enrolled treatment-naïve 303 patients with *ALK* fusion gene positive NSCLC. The subjects were allocated to either the Alecensa arm or the crizotinib arm in a one to one ratio. The primary endpoint of the ALEX study was PFS as assessed by the investigator. The secondary endpoints included Independent Review Committee-assessed PFS, overall survival, objective response rate, duration of response, safety, and other endpoints. The full data of the ALEX study will be presented at a future medical meeting and submitted to global health authorities, including the United States Food and Drug Administration.

Alecensa is a highly selective oral ALK inhibitor created by Chugai. It has been reported that approximately five 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 tumour cells and transforming the cells into tumour cells.[2, 3)] Alecensa exerts its anti-tumour effect by selectively inhibiting ALK kinase activity to inhibit tumour cell proliferation and induce cell death.[4)] In addition, Alecensa is not recognized by the active efflux system in the blood brain barrier which actively pumps molecules out of the brain. Thus, Alecensa is able to remain active in the central nervous system and has proven activity against brain metastases.

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Alecensa is currently approved in the United States, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India, the EU, Australia and Taiwan for the treatment of adult patients with ALK-positive, metastatic (advanced) NSCLC who have progressed on or those intolerant to crizotinib." In Japan, "Alecensa capsule 150mg" is available to patients with "*ALK* fusion gene positive unresectable, recurrent/advanced NSCLC" and is marketed by Chugai.

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)

Note: The description of Japanese package insert

- Dosage and administration for Japanese patients: "the usual adult dosage is 300mg alectinib administered orally twice daily."
- In the current Japanese package insert, it is described that "2. efficacy and safety of ALECENSA in chemotherapy-naïve patients have not been established."

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 2016 of Chugai totalled 491.8 billion yen and the operating income was 80.6 billion yen (IFRS Core basis).

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

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