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Data of Chugai's Alecensa® Presented at the American Society of Clinical Oncology on Global Phase III ALEX Study

- Alecensa® Demonstrates Statistically Significant Improvement in PFS and Reducing Risk of CNS Progression or Death -

TOKYO, June 6, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the results of the global phase III study (the ALEX study) of Alecensa®, conducted by F. Hoffmann-La Roche Ltd., 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) held in Chicago. The presentation will be held on oral abstract sessions on 6th June (Tue) 12:09-12:21 (CDT) as a late breaking subject.

Abstract LBA9008
Alectinib versus crizotinib in treatment-naive advanced *ALK*-positive non-small cell lung cancer (NSCLC): Primary results of the global phase III ALEX study.

"In the ALEX study comparing the efficacy and safety of first line therapy of Alecensa with crizotinib, Alecensa showed a significant prolongation of PFS and reduced the risk of disease progression or occurrence by 84% in patients with or without brain metastasis at baseline. The study also showed that Alecensa was well tolerated. These results will encourage the patients to fight cancer," said Dr. Yasushi Ito, Senior Vice President, Head of Project & Lifecycle Management Unit. "We believe that Alecensa will also contribute to improving the outcomes of many *ALK* fusion gene positive NSCLC patients not just in Japan but in overseas as well."

The ALEX study was an open-label, randomized global phase III study that compares the efficacy and safety between Alecensa and crizotinib in the first line therapy. 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 (IRC)-assessed PFS, IRC-assessed time to CNS progression, objective response rate, overall survival, safety and other endpoints.

Summaries of the ALEX study results

Efficacy:

- At the primary data cut-off, Alecensa arm demonstrated statistically significant improvement superiority vs crizotinib arm, reducing risk of progression or death by 53% (HR=0.47, 95%CI: 0.34-0.65, stratified log-rank test, p<0.0001) by investigators' assessment. Median PFS was not reached (95%CI: 17.7-not reached) in the Alecensa arm while it was 11.1 months (95%CI: 9.1-13.1) in the crizotinib arm.

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- According to independent review committee, Alecensa arm demonstrated statistically significant improvement superiority vs crizotinib arm, reducing risk of progression or death by 50% (HR=0.50, 95%CI: 0.36-0.70). Median PFS was 25.7 months (95%CI: 19.9-not reached) in the Alecensa arm while it was 10.4 months (95%CI: 7.7-14.6) in the crizotinib arm.
- Alecensa arm demonstrated improvement vs crizotinib arm, reducing risk of CNS progression by 84% (HR=0.16, 95% CI: 0.10-0.28).
- Overall survival data are currently considered immature with only about a quarter of events being reported.

Safety:

- Grade 3-5 adverse events (AEs) were less frequent with Alecensa arm, 41%, vs 50% with crizotinib arm.
- No new safety findings were observed in either arm.

About Alecensa

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.

Alecensa is currently approved in the United States, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India, the EU, Australia, Taiwan and Singapore 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.

The approved dosage and administration in Japan is "300mg alectinib is administered orally twice daily for adult patient."

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 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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