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EU Follows US and Approves Chugai's ALK Inhibitor "Alecensa®" as First Line Therapy for ALK-Positive Non-Small Cell Lung Cancer

- Alecensa Now Available in Japan, the United States and Europe for the Treatment of Advanced Lung Cancer -

TOKYO, December 21, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that F. Hoffmann-La Roche Ltd. obtained approval from the European Commission, for Alecensa® as monotherapy indicated for "the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)". In addition, the EU marketing authorisation for Alecensa has been switched from conditional approval (given in February 2017) to a full approval for the treatment of people with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib (second-line).

"Following approval for first line treatment in the US in November 2017, it is a great pleasure for Chugai that Alecensa has been approved for primary treatment in the EU. An improvement in prognosis is expected in patients with ALK-positive advanced NSCLC who receive treatment with Alecensa at an early stage," said Dr. Yasushi Ito, Chugai's Senior Vice President, Head of Project & Lifecycle Management Unit. "In addition to the J-ALEX study (JapicCTI-132316) conducted in Japan, results of the ALEX study (NCT02075840) conducted overseas also showed that this will be great news for patients. We are convinced that Alecensa can contribute to the treatment of many patients in the world."

This additional approval is based on results from the phase III ALEX study (NCT02075840).
The ALEX study (NCT02075840) evaluates the efficacy and safety of Alecensa compared with crizotinib in people with ALK-positive NSCLC who had not received prior systemic therapy (first-line). In the study, Alecensa significantly reduced the risk of disease worsening or death by 53% (HR=0.47, 95%CI: 0.34-0.65, stratified log-rank test, p<0.001) compared to crizotinib as assessed by investigators. Median progression-free survival (PFS) was 25.7 months (95%CI: 19.9-not estimable) for people who received Alecensa compared with 10.4 months (95%CI: 7.7-14.6) for people who received crizotinib as assessed by independent review committee. The safety profile of both drugs was consistent with that observed in previous studies, with no new findings.

In addition, Alecensa significantly reduced the risk of the cancer spreading to or growing in the brain or central nervous system (CNS) compared to crizotinib by 84% (HR=0.16, 95%CI: 0.10-0.28, stratified log-rank test, p<0.001). This was based on a time to CNS progression analysis in which there was a lower risk of progression in the CNS as the first site of disease progression for people who received Alecensa (12%) compared to people who received crizotinib (45%).

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About Alecensa

Alecensa is a highly selective oral ALK inhibitor discovered 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. Alecensa is able to remain active in the central nervous system and has proven activity against brain metastases.

Outside of Japan, Alecensa is currently approved in the United States, Europe, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India, Australia, Singapore, Taiwan, Thailand, Liechtenstein, Argentina, United Arab Emirates, Saudi Arabia and Turkey for the treatment of people with metastatic (advanced) ALK-positive NSCLC whose disease has worsened after, or who could not tolerate treatment with, crizotinib and in the US, EU and Turkey for the treatment of first line therapy on ALK-positive metastatic NSCLC.

In Japan, Alecensa 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 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)

Note: The dosage and administration of the ALEX study is "600mg alectinib administered orally twice daily," which is different from the Japanese dosage and administration.

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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