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Chugai's ALK Inhibitor "Alecensa®" Approved for the Treatment of First Line Therapy on ALK-Positive Non-Small Cell Lung Cancer in the US

TOKYO, November 8, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that Genentech Inc., a member of the Roche Group, obtained approval from the U.S. Food and Drug Administration (FDA), for Alecensa® in the treatment of "anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC)". In addition to this approval, the FDA also converted Alecensa's initial accelerated approval (given in December 2015) 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).

"In July 2014, Alecensa obtained its first approval globally in Japan. With the goal of contributing to many patients in the world, the development of Alecensa was progressed with a focus on speed in each country," said Dr. Yasushi Ito, Chugai's Senior Vice President, Head of Project & Lifecycle Management Unit. "The results of Phase III studies both in Japan and overseas showed that Alecensa could improve current treatment of ALK-positive NSCLC."

Alecensa received Breakthrough Therapy Designation from the FDA in September 2016 for the treatment of adults with advanced ALK-positive NSCLC who have not received prior treatment with an ALK inhibitor. Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat serious or life-threatening diseases and to help ensure people have access to them through FDA approval as soon as possible. Breakthrough Therapy designation was granted on the basis of the Japanese phase III J-ALEX study which was conducted prior to ALEX study.

The new approval is based on results from the phase III ALEX study.
The ALEX study 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 47% (HR=0.53, 95%CI: 0.38-0.73, stratified log-rank test, p<0.0001) compared to crizotinib as assessed by independent review committee. 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. 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<0.0001). 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%).

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL: +81-(0)3-3273-0881 E-mail: pr@chugai-pharm.co.jp
Investor Relations Group TEL: +81-(0)3-3273-0554 E-mail: ir@chugai-pharm.co.jp

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.

Alecensa is currently approved in the United States, Europe, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India, Australia, Singapore, Taiwan, Liechtenstein, Thailand, Argentina 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. 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.

Contact:
For Media
Chugai Pharmaceutical Co., Ltd.
Media Relations Group, Corporate Communications Dept.,
Koki Harada
Tel: +81-3-3273-0881
E-mail: pr@chugai-pharm.co.jp

For US media
Chugai Pharma USA Inc.
Casey Astringer
Tel: +1-908-516-1350
E-mail: pr@chugai-pharm.com

For Investors
Chugai Pharmaceutical Co., Ltd.
Investor Relations Group, Corporate Communications Dept.,
Toshiya Sasai
Tel: +81-3-3273-0554
E-mail: ir@chugai-pharm.co.jp