Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Chugai's ALK Inhibitor "Alecensa®" Approved in the EU

- Alecensa is Available Now in Japan, the United States and Europe -

TOKYO, February 21, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that F. Hoffmann-La Roche Ltd. obtained conditional marketing authorization from the European Commission (EC) , for the anti-cancer agent, alectinib hydrochloride (brand name: Alecensa®) for the treatment of adult patients with "anaplastic lymphoma kinase (ALK) positive, metastatic non-small cell lung cancer (NSCLC) who have progressed on or those intolerant to crizotinib."

"Alecensa was created by Chugai, and in July 2014, Japan became the first country in the world to receive regulatory approval. We believe that the approval of Alecensa by the EC will bring great hope for patients in the EU living with this disease," said Dr. Yasushi Ito, Chugai's Senior Vice President, Head of Project & Lifecycle Management Unit. "We are extremely pleased that Alecensa can contribute to the treatment of patients with ALK positive NSCLC in each country."

EU approval was based on two clinical phase I/II trials, as summarised below:

- The NP28761 study is a phase I/II North American, single arm, open-label, multicentre trial evaluating the safety and efficacy of Alecensa in 87 people with ALK positive NSCLC whose disease progressed on crizotinib. (Data cut-off: October 24, 2014)
- The NP28673 study is a phase I/II global, single arm, open-label, multicentre trial evaluating the safety and efficacy of Alecensa in 138 people with ALK-positive NSCLC whose disease progressed on crizotinib. (Primary data cut-off including safety: August 18, 2014, updated Independent Review Committee (IRC) data cut-off: January 8, 2015)
- People in the phase II studies received 600 mg of Alecensa orally twice daily. In both trials, the primary endpoint was objective response rate (ORR) according to Response Evaluation Criteria in Solid Tumours (RECIST v1.1), and evaluated by an IRC. Secondary endpoints included duration of response (DOR), progression-free survival (PFS) and safety.
- Efficacy Parameters

	The NP28761 study (N=87)		The NP28673 study (N=138)	
	IRC Assessment	Investigator Assessment	IRC Assessment	Investigator Assessment
ORR (%) (95% CI)	52.2 (39.7-64.6)	52.9 (41.9-63.7)	50.8 (41.6-60.0)	51.4 (42.8-60.0)
DOR (median in months) (95% CI)	14.9 (6.9-NE)	-	15.2 (11.2-24.9)	-
PFS (median in months) (95% CI)	8.0 (6.3-12.6)	-	8.9 (5.6-12.8)	-

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

- Alecensa demonstrated a safety profile consistent with that observed in previous studies.
- The most common Grade 3 or higher adverse events were an increase in muscle enzymes (increased blood levels of creatine phosphokinase; eight percent), increased liver enzymes (alanine aminotransferase; six percent, and aspartate aminotransferase; five percent) and shortness of breath (dyspnoea; three percent).

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.

Chugai has out-licensed the rights of Alecensa to Roche in overseas countries including Europe and the US. Alecensa is currently approved in the United States, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India and the EU for the treatment of advanced (metastatic) 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.

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.

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 European media
Chugai Pharma France SAS
Nathalie Leroy
Tel: +33-1-56-37-05-21
E-mail: pr@chugai.eu

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