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US FDA grants Breakthrough Therapy Designation for Roche's Alecensa (alectinib) for first-line treatment of people with ALK-positive NSCLC

- **This second Alecensa Breakthrough Therapy Designation granted is based on phase 3 J-ALEX study**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that it has received a second Breakthrough Therapy Designation (BTD) from the United States Food and Drug Administration (FDA) for its ALK inhibitor, Alecensa (alectinib). The latest BTD was granted for the treatment of adult patients with advanced anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) who have not received prior treatment with an ALK inhibitor.

“The J-ALEX study that supports the second Breakthrough Designation for Alecensa showed superior efficacy versus the standard of care, crizotinib, in Japanese people with advanced ALK-positive disease,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “The decision by the FDA to grant a second breakthrough therapy designation is recognition of the clinically meaningful improvement in efficacy and safety that Alecensa brings to the care of people with advanced ALK-positive lung cancer who have not received prior treatment with an ALK inhibitor.”

This second breakthrough therapy designation is based on the results of the open-label, randomised phase III J-ALEX study, which were presented at the American Society of Clinical Oncology (ASCO) 2016 Annual Meeting in June. J-ALEX compared the efficacy and safety of Alecensa with crizotinib in 207 Japanese people with ALK-positive, advanced or recurrent NSCLC who either had not been treated with chemotherapy or had received one prior line of chemotherapy. Results from the study demonstrated that Alecensa reduced the risk of disease worsening or death (progression-free survival, PFS) by 66% compared to crizotinib, whilst maintaining a favourable tolerability and safety profile consistent with that observed in previous studies.

The FDA's Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat serious diseases and to help ensure patients have access to them through FDA approval as soon as possible. Alecensa received its first FDA BTD in June 2013 for people with ALK-positive

NSCLC whose disease progressed on treatment with crizotinib.

Alecensa is currently available in the US and Israel to ALK-positive metastatic NSCLC patients who have progressed on or are intolerant to crizotinib, and in Japan to ALK-positive unresectable, recurrent or advanced NSCLC patients. In addition, an ongoing global, randomised phase III trial called ALEX is comparing Alecensa to Xalkori as an initial (first-line) treatment for people with advanced ALK-positive NSCLC.

About J-ALEX

The J-ALEX study conducted by Chugai is an open-label, randomised Phase III study that compared the efficacy and safety of Alecensa to crizotinib in Japanese people. The J-ALEX study enrolled 207 people with ALK-positive, advanced or recurrent NSCLC who had not been previously treated with an ALK inhibitor. People were randomised to the Alecensa group or the crizotinib group in a one-to-one ratio. Results include:

- Alecensa reduced the risk of disease worsening or death (PFS) by 66 percent compared to crizotinib (HR=0.34, 99 percent CI: 0.17-0.70, $p < 0.0001$).
- Median PFS was not reached in the Alecensa arm (95 percent CI: 20.3 months-not estimated) versus 10.2 months in the crizotinib arm (95 percent CI: 8.2-12.0).
- Grade 3-4 adverse events (AE) occurred with lesser frequency in the Alecensa arm compared to the crizotinib arm (27 percent vs. 51 percent).
- The most common AE occurring with > 30 percent frequency with Alecensa was constipation (36 percent). The most common AEs for crizotinib were nausea (74 percent), diarrhoea (73 percent), vomiting (59 percent), visual disturbance (55 percent), alteration in taste (dysgeusia, 52 percent), constipation (46 percent), and an elevation in liver enzymes called alanine transaminase (ALT, 32 percent) and aspartate transaminase (AST, 31 percent).

About Alecensa

Alecensa (RG7853/AF-802/CH5424802) is an oral medicine created at Chugai Research Laboratories and is being developed for people with NSCLC whose tumours are identified as ALK-positive. ALK-positive NSCLC is often found in younger people who have a light or non-smoking history. It is almost always found in people with a specific type of NSCLC called adenocarcinoma. Alecensa is currently approved in the United States for the treatment of people with advanced (metastatic) ALK-positive NSCLC whose disease has worsened after, or who could not tolerate treatment with, crizotinib.

In two key phase II studies, NP28761 and NP28673, Alecensa shrank tumours in up to 44% of people with ALK-positive NSCLC who progressed on crizotinib. Alecensa also demonstrated activity in brain metastases, indicating that the drug may be taken up in the brain. The brain is protected by the Blood-Brain Barrier, a network of tightly joined cells that line the inside of the blood vessels in the brain and spinal cord. One of the ways the Blood-Brain Barrier prevents molecules from affecting the brain is to actively eject them from the barrier through a process known as 'active efflux'. The active efflux system does not recognise Alecensa, which means that it may travel into and throughout brain tissue.

The global phase III studies of Alecensa include a companion test developed by Roche Diagnostics. Alecensa is marketed in Japan by Chugai Pharmaceutical, a member of the Roche Group.

About ALK-positive non-small cell lung cancer

Lung cancer is the biggest cancer killer, causing 1.59 million deaths globally each year. NSCLC is the most common type of lung cancer, and is the leading cause of cancer-related deaths in Europe and across the world, accounting for approximately 85% of lung cancer cases. ALK-positive NSCLC occurs in approximately 5% of patients with advanced NSCLC, translating to about 75,000 patients being diagnosed with the disease annually. It is almost always found in people with a specific type of NSCLC called adenocarcinoma, and is more common in light or non-smokers.

About Roche in lung cancer

Lung cancer is a major area of focus and investment for Roche, and we are committed to developing new approaches, medicines and tests that can help people with this deadly disease. Our goal is to provide an effective treatment option for every person diagnosed with lung cancer. We currently have three approved medicines to treat certain kinds of lung cancer and more than ten medicines being developed to target the most common genetic drivers of lung cancer or to boost the immune system to combat the disease.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. The

combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. Twenty-nine medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry eight years in a row by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2015 employed more than 91,700 people worldwide. In 2015, Roche invested CHF 9.3 billion in R&D and posted sales of CHF 48.1 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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Additional information

- Roche in Oncology: www.roche.com/media/media_backgrounduer/media_oncology.htm

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