Basel, 21 February 2017

Roche receives EU approval of Alecensa (alectinib) for people with previously treated ALK-positive non-small cell lung cancer

- Alecensa provides an efficacious, systemic treatment option for people with ALK-positive NSCLC, which is also active in patients with brain metastases, who have been previously treated with crizotinib

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Commission has granted a conditional marketing authorisation for Alecensa® (alectinib) as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib. Most people with ALK-positive NSCLC develop resistance to the current standard of care within one year of treatment, and approximately 60% will develop metastases in the central nervous system (CNS).1,2

“Every year, an estimated 75,000 people are diagnosed with ALK-positive NSCLC worldwide,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “Development of resistance to the current standard of care underlines the need for alternative treatments. Today’s approval provides the promise of a new treatment option for people in Europe with this devastating disease.”

The conditional approval is based primarily on data from the pivotal phase II NP28673 and NP28761 studies, which showed that Alecensa shrank tumours in up to 52.2% (95% CI: 39.7%, 64.6%) of people with advanced ALK-positive NSCLC whose disease had progressed following treatment with crizotinib (overall response rate; ORR).3,4 The studies also showed that Alecensa extended the time that people lived without their disease worsening or death (progression-free survival, PFS) by up to 8.9 months (95% CI: 5.6, 12.8).2,3 In addition, a pooled analysis of the two studies showed that Alecensa shrank CNS tumours that were measurable in 64% of patients (95% CI: 49.2%, 77.1%), and 22% (n=-29) achieved a complete response of their measurable and non-measurable CNS tumours.4
Conditional approval is granted to a medicinal product that fulfils an unmet medical need where the benefit of immediate availability outweighs the risk of less comprehensive data than normally required. Under the provisions of the conditional approval, Roche will provide additional data on first-line Alecensa in ALK inhibitor naïve ALK-positive NSCLC patients from an ongoing phase III study ALEX, comparing Alecensa to crizotinib. The ALEX study is expected to report data in the first half of 2017.

Alecensa is already approved for ALK-positive NSCLC in eight countries in the crizotinib failure setting, and also in Japan for people whose tumours were advanced, recurrent or could not be removed completely through surgery (unresectable). In addition to ALEX, Alecensa is also being explored as a first-line treatment option with the phase III J-ALEX study comparing Alecensa to crizotinib in Japanese patients. Results from the J-ALEX study were presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting and showed that Alecensa reduced the risk of disease worsening or death (PFS) by 66% (hazard ratio [HR]=0.34, 99% CI: 0.17-0.70, p<0.0001) compared to crizotinib in this specific form of lung cancer.

Each year lung cancer causes 1.59 million deaths worldwide, more than any other cancer. 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 the NP28673 study**

- NP28673 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.
- The study showed by assessment of an independent review committee an ORR of 50.8% (95% CI: 41.6%, 60.0%), as measured by RECIST criteria.
  - An investigator assessment also showed tumours shrank in 51.4% of people who received Alecensa (95% CI: 42.8%, 60.0%)
  - In addition, the people whose tumours shrank in response to Alecensa continued to respond for a median of 15.2 months (95% CI: 11.2, 24.9) (duration of response, DOR)
  - The median PFS for people who received Alecensa was 8.9 months (95% CI: 5.6, 12.8)
- Alecensa demonstrated a safety profile consistent with that observed in previous studies.
• The following events were reported in ≥2% of patients: dyspnoea (4%); anaemia (3%); fatigue, INR increased, pulmonary embolism and hyperbilirubinemia (each 2%).

About the NP28761 study

• NP28761 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.
• The study showed by assessment of an independent review committee an ORR of 52.2% (95% CI: 39.7%, 64.6%) as measured by RECIST criteria.
  o An investigator assessment showed tumours shrank in 52.9% of people who received Alecensa (95% CI: 41.9%, 63.7%).
  o In addition, the people whose tumours shrank in response to Alecensa continued to respond for a median of 14.9 months (95% CI: 6.9, NE) (DOR).
  o The median PFS for people who received Alecensa was 8.2 months (95% CI: 6.3, 12.6).
• Alecensa demonstrated a safety profile consistent with that observed in previous studies.
• The most common (occurring in at least 2% of people) Grade 3 or higher adverse events were an increase in muscle enzymes (increased blood levels of creatine phosphokinase; 8%), increased liver enzymes (alanine aminotransferase; 6%, and aspartate aminotransferase; 5%), shortness of breath (dyspnoea; 3%), elevated levels of triglyceride (hypertriglyceridaemia), decreased potassium level (hypokalaemia) low levels of phosphate in the blood (hypophosphatemia; 3%), partial blood thickening (thromboplastin; 2%) time prolonged.

About Alecensa

Alecensa (RG7853/AF-802/RO5424802/CH5424802) is an oral medicine created at Chugai Kamakura 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, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland and India for the treatment of advanced (metastatic) ALK-positive NSCLC whose disease has worsened after, or who could not tolerate treatment with, crizotinib and in Japan for ALK positive NSCLC patients.

In a pooled analysis of CNS endpoints from studies NP28673 and NP28761, Alecensa 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 ALEX study of Alecensa includes a companion test developed by Roche Diagnostics. Alecensa is marketed in Japan by Chugai Pharmaceutical, a member of the Roche Group.

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 four 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. 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.

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. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims for improving patient access to medical innovations by working with all relevant stakeholders. 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 (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of
CHF 50.6 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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Roche Group Media Relations
Phone: +41 - 61 688 8888 / e-mail: roche.mediarelations@roche.com
- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow

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