Media Release

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CHMP recommends EU approval of Roche's Alecensa (alectinib) as a first-line treatment for people with ALK-positive NSCLC

- **Positive opinion based on phase III results showing Alecensa reduced the risk of disease progression or death by more than half versus crizotinib**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Union's (EU) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the approval of Alecensa® (alectinib) as a monotherapy for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive, advanced non-small cell lung cancer (NSCLC). It has also simultaneously recommended the conversion of the current conditional marketing authorisation for Alecensa in crizotinib failure (second-line) to a full marketing authorisation.

The CHMP recommendation in first-line is based on results from the global phase III ALEX study, which showed Alecensa significantly reduced the risk of disease worsening or death (progression-free survival, PFS) by 53% (HR=0.47, 95% CI: 0.34-0.65, p<0.001) compared with crizotinib. The study also showed that Alecensa reduced the risk of tumours spreading to, or growing in, the brain or central nervous system (CNS) by 84% (HR=0.16, 95% CI: 0.10-0.28, p<0.001), compared with crizotinib. The safety and tolerability profile of Alecensa compared favourably to that of crizotinib despite the longer duration of treatment with Alecensa (17.9 vs. 10.7 months), and was consistent with that observed in previous studies.[1]

"This is more great news for people with this type of lung cancer, bringing them closer to benefiting from Alecensa's superior efficacy earlier in their treatment journey," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The results from ALEX clearly showed the significant benefits of Alecensa over crizotinib and we are pleased this has been recognised by the CHMP."

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The next step would be for the European Commission to make its final decision. A positive decision would mean approval for Alecensa across both the first-line and crizotinib failure settings in Europe. Alecensa was recently granted Priority Review by the U.S. Food and Drug Administration (FDA) in the first-line setting in the United States, and has been approved in the crizotinib failure setting since 2015.[2]

About the ALEX study

ALEX (NCT02075840/B028984) is a randomised, multicentre, open-label phase III study evaluating the efficacy and safety of Alecensa versus crizotinib in treatment-naïve people with ALK-positive NSCLC whose tumours were characterised as ALK-positive by the VENTANA ALK (D5F3) CDx Assay, a companion immunohistochemistry (IHC) test developed by Roche Tissue Diagnostics. People were randomised (1:1) to receive either Alecensa or crizotinib. The primary endpoint of the ALEX study is PFS as assessed by the investigator, and secondary endpoints include: Independent Review Committee (IRC)-assessed PFS, time to CNS progression, objective response rate (as defined by RECIST criteria), duration of response, overall survival, health-related quality of life and safety. The multicentre study was conducted in 303 people across 161 sites in 31 countries.[3] Results include:[1]

- Alecensa reduced the risk of disease worsening or death (PFS) by 53% compared to crizotinib (HR=0.47, 95% CI: 0.34-0.65, p<0.001).
- Investigator-reported median PFS (the primary endpoint) was not yet reached in the Alecensa arm (95% CI: 17.7 -not reached) versus 11.1 months (95% CI: 9.1-13.1 months) in the crizotinib arm.
- IRC-reported median PFS (a secondary endpoint) was 25.7 months (95% CI: 19.9-not estimable) in the Alecensa arm versus 10.4 months (95% CI: 7.7-14.6 months) in the crizotinib arm (HR=0.50, 95% CI: 0.36-0.70; p<0.001).
- Alecensa reduced the risk of progression in the CNS by 84% (HR=0.16, 95% CI: 0.10-0.28; p<0.001).
- The 12-month cumulative rate of CNS progression for people with or without existing CNS metastases at baseline was 9.4% (95% CI: 5.4-14.7%) for people treated with Alecensa and 41.4% (95% CI: 33.2-49.4%) for people treated with crizotinib.
- Overall survival (OS) data are still immature with only about a quarter of events being reported.
- Grade 3-5 adverse events (AEs) were less frequent in the Alecensa arm (41%) compared with the crizotinib arm (50%). In the Alecensa arm, the most common Grade 3-5 AEs (≥5%) were increased liver enzymes (alanine transferase and aspartate transferase; 5%) and decreased red blood cells (anaemia; 5%). AEs leading to discontinuation (11% vs. 13%), dose reduction (16% vs. 21%) and dose interruption (19% vs. 25%) were all lower in the Alecensa arm compared with the crizotinib arm.

About Alecensa

Alecensa (RG7853/AF-802/RO5424802/CH5424802) is a highly selective, CNS active, 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.[4] It is almost always found in people with a specific type of NSCLC called adenocarcinoma.[4] 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 advanced (metastatic) ALK-positive NSCLC whose disease has worsened after, or who could not tolerate treatment with, crizotinib and in Japan for people with ALK-positive NSCLC.

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 to improve patient access to medical innovations by working with all relevant stakeholders.

Thirty 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 nine 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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References

[1] Peters, S et al. Alectinib versus Crizotinib in Untreated ALK-Positive Non–Small-Cell Lung Cancer. NEJM 2017; http://www.nejm.org/doi/10.1056/NEJMoa1704795.

[2] FDA. FDA approves new oral therapy to treat ALK-positive lung cancer. [Internet; cited 2017 Oct 03]. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476926.htm.

[3] ClinicalTrials.gov. A Study Comparing Alectinib With Crizotinib in Treatment-Naive Anaplastic Lymphoma Kinase-Positive Advanced Non-Small Cell Lung Cancer Participants (ALEX) [Internet; cited 2017 Oct 03]. Available from: https://clinicaltrials.gov/ct2/show/NCT02075840.

[4] Gridelli C, et al. ALK inhibitors in the treatment of advanced NSCLC. Cancer Treatment Reviews. 2014;40:300-306.