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Follow-up phase III data showed Roche's Alecensa helped people with ALK-positive metastatic non-small cell lung cancer live a median of almost three years without their disease worsening or death

- **Investigator-assessed longer follow-up of the ALEX study demonstrated sustained benefit in the reduction of the risk of disease progression or death (57%) for people treated with Alecensa**
- **Alecensa more than tripled median progression-free survival (PFS) (34.8 months compared to 10.9 months for crizotinib)**
- **Investigator-assessed median PFS for people without CNS metastases at baseline was 34.8 months with Alecensa versus 14.7 months with crizotinib, while the median PFS for people with CNS metastases at baseline was 27.7 months with Alecensa versus 7.4 months with crizotinib**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced follow-up data from the phase III ALEX study, showing that, as an initial treatment, Alecensa® (alectinib) significantly reduced the risk of disease progression or death (progression-free survival; PFS) by 57% (hazard ratio [HR]= 0.43, 95% CI: 0.32-0.58) compared to crizotinib after two years of follow-up in people with anaplastic lymphoma kinase (ALK)-positive metastatic (advanced) non-small cell lung cancer (NSCLC), as assessed by the investigator.¹ The median PFS for people who received Alecensa was more than tripled compared to those who received crizotinib (34.8 months [95% CI: 17.7 months-NE] versus 10.9 months [95% CI: 9.1-12.9 months]), respectively, as assessed by the investigator. The safety profile for Alecensa was consistent with that observed in previous studies.

“Follow-up results from the ALEX study demonstrate the significant sustained benefit of Alecensa, showing that people with metastatic ALK-positive non-small cell lung cancer lived for almost three years without their disease progressing,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “These results further support the use of Alecensa as a standard of care for people who are newly diagnosed with this form of lung cancer.”

The longer-term analysis also included follow-up data for secondary endpoints of the ALEX study. Alecensa demonstrated superior efficacy compared to crizotinib regardless of the presence of central nervous system (CNS) metastases at baseline. Investigator-assessed median PFS for people without CNS metastases at

baseline was 34.8 months with Alecensa (95% CI: 22.4-NE) versus 14.7 months (95% CI: 10.8-20.3) with crizotinib (HR=0.47, 95% CI: 0.32-0.71). Investigator-assessed median PFS for people with CNS metastases at baseline was 27.7 months in the Alecensa arm (95% CI: 9.2-NE) versus 7.4 months (95% CI: 6.6-9.6) in the crizotinib arm (HR=0.35, 95% CI: 0.22-0.56).¹ The duration of response (DOR) for people who received Alecensa was 33.3 months (95% CI: 31.3-NE) compared to 11.1 months (95% CI: 7.5-13.0 months) for people who received crizotinib.¹

The data will be presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting on Sunday, 3 June, 2018 at 08:00 – 11:30 am CDT (Abstract #9043).

Alecensa is now approved in more than 45 countries as an initial (first-line) treatment for ALK-positive, advanced NSCLC, including in the United States, Europe and Japan.

About the ALEX study²

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 was PFS as assessed by the investigator, and secondary endpoints include: Independent Review Committee (IRC)-assessed PFS, time to CNS progression, objective response rate (ORR), DOR and overall survival (OS). The multicentre study was conducted in 303 people across 161 sites in 31 countries. OS data are currently considered immature with only about a third of events being reported.

Primary data from the ALEX study were previously presented at the 2017 ASCO Annual Meeting and published in the *New England Journal of Medicine*.³ Follow-up results from the ALEX study analysis to be presented at the 2018 ASCO Annual Meeting showed¹:

- After a further 10 months of follow-up, Alecensa reduced the risk of disease worsening or death (PFS) by 57% compared to crizotinib (HR=0.43, 95% CI: 0.32-0.58). Median follow-up was 27.8 months versus 22.8 months for Alecensa-treated patients and crizotinib-treated patients, respectively.
- Investigator-reported median PFS (the primary endpoint) was 34.8 months in the Alecensa arm (95% CI: 17.7-NE) versus 10.9 months (95% CI: 9.1-12.9 months) in the crizotinib arm.
- ORR for people treated with Alecensa was 82.9% (95% CI: 75.95-88.51) compared to 75.5% (95% CI: 67.84-82.12) for people treated with crizotinib, as assessed by the investigator.

- Alecensa demonstrated superior efficacy compared to crizotinib regardless of the presence or absence of CNS metastases at baseline. Investigator-assessed median PFS for people without CNS metastases at baseline was 34.8 months with Alecensa (95% CI: 22.4-NE) versus 14.7 months (95% CI: 10.8-20.3) with crizotinib (HR=0.47, 95% CI: 0.32-0.71). Investigator-reported median PFS for people with CNS metastases at baseline was 27.7 months in the Alecensa arm (95% CI: 9.2-NE) versus 7.4 months (95% CI: 6.6-9.6) in the crizotinib arm (HR=0.35, 95% CI: 0.22-0.56).
- Improvements were observed in the time between first response to treatment and disease worsening (DOR): 33.3 months with Alecensa versus 11.1 months with crizotinib.
- Grade 3-5 adverse events (AEs) were less frequent in the Alecensa arm (44.7%) compared to the crizotinib arm (51.0%). The most common Grade 3-4 AEs were increased liver enzymes (aspartate transaminase; 5.5%, and alanine transaminase; 4.6%) and increased muscle enzymes (creatine phosphokinase; 3.3%). Serious adverse reactions reported in $\geq 2\%$ of people treated with Alecensa were acute kidney injury (2.6%) and decreased red blood cells (anaemia; 2.0%).
- AEs leading to dose reduction (16.4% versus 20.5%) and dose interruption (22.4% versus 25.2%) were lower in the Alecensa arm compared with the crizotinib arm. AEs leading to discontinuation were equal in both arms (13.2%).

The FDA approval of Alecensa for the treatment of people with ALK-positive metastatic NSCLC was based on results from the phase III ALEX study from the primary data cutoff in February 2017. Results showed that:

- Alecensa significantly reduced the risk of disease worsening or death (PFS) by 47% (HR=0.53, 95% CI: 0.38-0.73, $p < 0.001$) compared to crizotinib as assessed by an IRC.
- The median PFS was 25.7 months (95% CI: 19.9-NE) for people who received Alecensa compared with 10.4 months (95% CI: 7.7-14.6) for people who received crizotinib as assessed by an IRC.
- Alecensa significantly reduced the risk of the cancer spreading to, or growing in, the brain or CNS compared to crizotinib by 84% (HR=0.16, 95% CI: 0.10-0.28, $p < 0.0001$). 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%).
- The safety profile of Alecensa was consistent with that observed in previous studies.
- Grade ≥ 3 adverse reactions were reported for 41% of people treated with Alecensa. The most common Grade 3-4 adverse reactions ($\geq 3\%$) were evidence of kidney dysfunction (increased creatinine; 4.1%), evidence of liver dysfunction (hyperbilirubinemia; 5%), low levels of sodium (hyponatremia; 6%),

increased liver enzymes (aspartate transaminase; 6%, and alanine transaminase; 6%), and decreased red blood cells (anaemia; 7%). Serious adverse reactions reported in $\geq 2\%$ of people treated with Alecensa were pneumonia (4.6%) and renal impairment (3.9%).

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 now approved in over 45 countries as an initial (first-line) treatment for ALK-positive, metastatic NSCLC, including in the United States, Europe, Japan, Turkey, Cuba, Peru, Thailand, Australia, the Dominican Republic, India, Israel, Paraguay, Switzerland, Bolivia, Serbia, South Korea and Singapore. In addition, Alecensa is approved in the United States, Europe, Japan, Kuwait, Israel, Hong Kong, Canada, South Korea, Switzerland, India, Bolivia, Australia, Singapore, Taiwan, Thailand, Liechtenstein, Argentina, United Arab Emirates, Saudi Arabia, Peru, New Zealand, Cuba, the Dominican Republic, Qatar, Oman, Serbia, Paraguay 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.

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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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: media.relations@roche-global.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow

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