

Roche's Alecensa (alectinib) significantly reduced the risk of disease worsening or death as a first-line treatment in Asian patients with ALK-positive advanced or metastatic non-small cell lung cancer

- **Head-to-head phase III study of Alecensa versus crizotinib in Asian patient population showed a reduction in the risk of disease worsening or death by 78%**
- **Alecensa lowered the risk of tumour spread or growth in the brain or central nervous system by 86%**
- **Data add to a wealth of evidence, including the phase III ALEX and J-ALEX studies, supporting first-line use of Alecensa in multiple patient populations within ALK-positive non-small cell lung cancer and rapid worldwide regulatory approvals**

Basel, 22 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will today announce results from the phase III ALESIA study, showing that Alecensa® (alectinib) met its primary endpoint of investigator-assessed (INV) progression-free survival (PFS). Alecensa significantly reduced the risk of disease worsening or death by 78%, compared to crizotinib, when given as an initial (first-line) monotherapy treatment in Asian patients with anaplastic lymphoma kinase (ALK)-positive advanced or metastatic non-small cell lung cancer (NSCLC) (hazard ratio [HR]=0.22, 95% CI: 0.13-0.38).^[1] Median PFS reported by the investigators was not yet reached in patients who received Alecensa (95% CI: 20.3 months-not reached) versus 11.1 months (95% CI: 9.1-13.0 months) in those who received crizotinib.^[1] The safety profile of Alecensa was consistent with that observed in previous studies.^[1]

“The ALESIA study supports the use of Alecensa as the standard of care for newly diagnosed advanced or metastatic ALK-positive lung cancer across multiple populations,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Alecensa has received rapid regulatory approvals for first-line treatment in 65 countries to date, including in China.”

Median PFS reported by an independent review committee (IRC), a secondary endpoint, was not yet reached in patients who received Alecensa (95% CI: 16.7 months-not reached), versus 10.7 months (95% CI: 7.4 months-not reached) in patients who received crizotinib (HR=0.37, 95% CI: 0.22-0.61).^[1] The phase III ALESIA study also demonstrated that compared to crizotinib, Alecensa reduced the risk of disease progression in the central nervous system (CNS), another secondary endpoint in the study, by 86% (HR=0.14, 95% CI: 0.06-0.30).^[1]

The ALESIA data are being officially presented at the European Society for Medical Oncology (ESMO) 2018 Congress during a Presidential Symposium on 22 October at 16:30 (Abstract LBA10 Presidential Symposium).^[3]

This is the third phase III study to show that Alecensa as a first-line treatment significantly reduced the risk

of disease worsening or death (PFS) compared to crizotinib in patients with ALK-positive advanced or metastatic NSCLC.^[2,3;4] The results reinforce the findings of the phase III global ALEX study, which found that Alecensa significantly reduced the risk of disease progression or death (PFS) by 57% (HR=0.43, 95% CI: 0.32-0.58) compared to crizotinib after two years of follow-up in people with ALK-positive metastatic NSCLC, as assessed by the investigator.^[3] The ALEX study also showed that Alecensa more than tripled median PFS to nearly three years (34.8 months, 95% CI: 17.7 months-NE) compared to crizotinib (10.9 months, 95% CI: 9.1-12.9 months) and demonstrated superior efficacy compared to crizotinib regardless of the presence of CNS metastases at baseline, a secondary endpoint.^[3] INV median PFS for people without CNS metastases at baseline was 34.8 months with Alecensa (95% CI: 22.4 months-NE) versus 14.7 months (95% CI: 10.8-20.3 months) with crizotinib (HR=0.47, 95% CI: 0.32-0.71).^[3] INV median PFS for people with CNS metastases at baseline was 27.7 months in the Alecensa arm (95% CI: 9.2 months-NE) versus 7.4 months (95% CI: 6.6-9.6 months) in the crizotinib arm (HR=0.35, 95% CI: 0.22-0.56).^[3]

The ALESIA study was a bridging study, designed to show consistency with the phase III ALEX study and was not powered to show superiority vs crizotinib. It completes a post-approval agreement with the National Drug Administration of China (CNDA) to demonstrate consistency between the ALESIA and ALEX studies, following the priority review and rapid approval of Alecensa in August this year.^[5] The regulatory approval in China is one of the latest of 65 countries for the use of Alecensa as a first-line monotherapy for people with ALK-positive NSCLC.^[6]

About the ALESIA study^[7]

ALESIA (NCT02838420) is a randomised, multicentre, open-label phase III study evaluating the efficacy and safety of Alecensa versus crizotinib, and the pharmacokinetics of Alecensa in Asian patients with treatment-naïve ALK-positive advanced or metastatic NSCLC. Patients were randomised (2:1) to receive either Alecensa or crizotinib. The primary endpoint of the ALESIA study is PFS as assessed by the investigator using the RECIST v1.1 criteria. Secondary endpoints include: PFS, time to CNS progression and CNS ORR assessed by IRC, objective response rate and duration of response assessed by the investigator, overall survival, health-related quality of life and safety. The multicentre study was conducted in 187 patients across 21 sites in three countries.

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.^[6] ALK-positive NSCLC is often found in younger people who have a light or non-smoking history.^[8] It is almost always found in people with a specific type of NSCLC called adenocarcinoma.^[8] Alecensa is now approved in 65 countries as an initial (first-line) treatment for ALK-positive, metastatic NSCLC, including in the US, Europe, Japan and China.^[6]

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. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry 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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