Investor Update

Basel, 21 December 2017

European Commission approves Roche's Alecensa (alectinib) as first-line treatment in ALK-positive lung cancer

- **Alecensa provides a new treatment option for people with newly diagnosed ALK-positive NSCLC**
- **Approval based on phase III ALEX data showing Alecensa reduced the risk of disease progression or death by more than half versus crizotinib**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission (EC) has granted a marketing authorisation for 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). The approval is based on results from the phase III ALEX study, which showed Alecensa significantly reduced the risk of disease worsening or death (progression-free survival, PFS) by 53% (hazard ratio (HR)=0.47, 95% confidence interval (CI): 0.34-0.65, p<0.001) compared to crizotinib. The study also showed that Alecensa reduced the risk of tumours spreading to, or growing in the brain or central nervous system (CNS) compared to crizotinib by 84% (HR=0.16, 95% CI: 0.10-0.28, p<0.001). The safety profile of Alecensa was consistent with that observed in previous studies and compared favourably to crizotinib.[1]

"Many ALK-positive lung cancer patients see their disease progress within a year on current treatments," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The EU approval of Alecensa heralds a new era for these patients, who now have a treatment option available that halves the risk of disease progression compared with the previous standard of care, crizotinib and is also highly effective against brain metastases."

In addition to today's first-line approval, the EC also converted the conditional marketing authorisation of Alecensa in crizotinib failure to a standard marketing authorisation. Alecensa has also recently (6 November 2017) been approved by the US FDA, as well as Japan and Turkey as an initial (first-line) ALK-positive NSCLC treatment, and is already approved in Japan as well as in 18 countries in the crizotinib-failure setting.

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Results from the phase III ALEX study were simultaneously presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting and published in *The New England Journal of Medicine*. Subsequently, Alecensa was recommended in the US National Comprehensive Cancer Network (NCCN) guidelines as a treatment option for first-line ALK-positive metastatic NSCLC (*Category 1, Preferred*).[2]

ALK-positive NSCLC is a distinct form of lung cancer commonly affecting younger people (median age 52), and those with a light or non-smoking history.[3] Around 75,000 people are diagnosed with ALK-positive NSCLC every year.[4,5,6]

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. Overall survival (OS) data are currently considered immature with only about a quarter of events being reported.[7] Results include:

Summary of ALEX study key efficacy endpoints[1]		
	Alecensa n=152	**Crizotinib** n=151
Progression-free survival (PFS) as assessed by investigator (primary endpoint)		
Median PFS	NE	11.1 months
Hazard ratio (HR) (95% CI)	0.47 (0.34-0.65)	
p-value	p<0.001	
PFS as assessed by Independent Review Committee (secondary endpoint)		
Median PFS	25.7 months	10.4 months
HR (95% CI)	0.50 (0.36-0.70)	
p-value	p<0.001	

CNS efficacy (secondary endpoints)		
Patients with CNS progression	12%	45%
HR (95% CI)	0.16 (0.10-0.28)	
p-value	p<0.001	
12-month cumulative rate of first CNS progression	9.4%	41.4%

CI=confidence interval; CNS=central nervous system; NE=not estimable

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 AEs (≥10% absolute difference) were (Alecensa versus crizotinib): increased blood bilirubin (15% versus 1%) increased weight (10% versus 0%), decreased red blood cells (anaemia; 20% versus 5%) and myalgia (16% versus 2%). AEs leading to discontinuation (11% versus 13%), dose reduction (16% versus 21%) and dose interruption (19% versus 25%) were all lower in the Alecensa arm compared with the crizotinib arm.[1]

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. It is almost always found in people with a specific type of NSCLC called adenocarcinoma. Alecensa is approved in the United States, Turkey and Japan as an initial (first-line) treatment for ALK-positive, advanced NSCLC. In addition, Alecensa is approved in the United States, Europe, Japan, 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.

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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