Media Release

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FDA grants Roche's Alecensa (alectinib) accelerated approval for people with a specific type of lung cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) granted accelerated approval to Alecensa® (alectinib) for the treatment of people with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. In the pivotal studies, Alecensa shrank tumours in up to 44 percent of people with ALK-positive NSCLC who progressed on crizotinib (objective response rate [ORR] of 38 percent [95 percent CI 28-49] and 44 percent [95 percent CI 36-53]).

In a subset of people with tumours that spread to the brain or other parts of the central nervous system (CNS), Alecensa shrank CNS tumours in about 60 percent of people (CNS ORR of 61 percent [95 percent CI 46-74]).

"Alecensa is now approved as a new option for people with ALK-positive NSCLC who progress on or are intolerant to crizotinib," said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. "Sixty percent of people enrolled in our studies had tumours that had spread to their central nervous systems, and Alecensa shrank tumours in many people in a subset of patients with CNS disease."

Possible serious side effects with Alecensa include liver problems, lung problems, slow heartbeat, muscle pain, tenderness and weakness. The most common side effects of Alecensa include tiredness, constipation and swelling in the hands, feet, ankles and eyelids.

The FDA's Accelerated Approval Program allows conditional approval of a medicine that fills an unmet medical need for a serious condition based on early evidence suggesting clinical benefit. The indication for Alecensa is approved under accelerated approval based on tumour response rate and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland

Group Communications
Roche Group Media Relations

Tel. +41 61 688 88 88
Fax +41 61 688 27 75
www.roche.com

In addition, Alecensa is being studied for use as an initial (first-line) treatment for people with advanced ALK-positive NSCLC. ALEX is a global, randomised phase III study comparing Alecensa to crizotinib as an initial treatment for people with advanced NSCLC whose tumours were characterised as ALK-positive by a companion VENTANA ALK (D5F3) CDx Assay immunohistochemistry (IHC) test developed by Roche Diagnostics. This study is part of the company's commitment to convert the current accelerated approval in people with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib to a full approval as an initial treatment.

About NP28761 (Study 1) and NP28673 (Study 2)

Study 1 is a phase II North American, single-arm, open-label, multicentre trial evaluating the safety and efficacy of Alecensa (600 mg orally twice daily) in 87 people with ALK-positive NSCLC whose disease progressed on crizotinib. Study 2 is a phase I/II global, single-arm, open-label, multicentre trial evaluating the safety and efficacy of Alecensa (600 mg orally twice daily) in 138 people with ALK-positive NSCLC whose disease progressed on crizotinib. People in the phase II studies received 600 mg of Alecensa orally twice daily. In both trials, the primary endpoint was ORR according to Response Evaluation Criteria in Solid Tumours (RECIST v1.1), as evaluated by an Independent Review Committee (IRC). Secondary endpoints included DOR and efficacy against disease that had spread to the CNS (CNS ORR and CNS DOR). A summary of the efficacy and safety data from both studies that support this approval is included below.

Efficacy Parameter	Study 1 (North American) n=87		Study 2 (Global) n=138	
	IRC* Assessment	Investigator Assessment	IRC* Assessment	Investigator Assessment
Objective Response Rate (ORR, primary endpoint)				
ORR (%) (95% CI)	38 (28, 49)	46 (35, 57)	44 (36, 53)	48 (39, 57)
Number of Responders				
Number of responders	33	40	61	66
Duration of Response (DOR, secondary endpoint)				
DOR (median in months) (95% CI)	7.5 (4.9, Not Estimable)	NE (4.9, Not Estimable)	11.2 (9.6, Not Estimable)	7.8 (7.4, 9.2)
CNS Efficacy (secondary endpoints, based on a pooled analysis of 51 people in Studies 1 and 2 with measurable CNS lesions at baseline according to RECIST v1.1)**				
CNS ORR (%) (95% CI)	61 (46, 74)			
CNS complete response rate (%)	18			
CNS partial response rate (%)	43			
CNS DOR (median in months) (95% CI)	9.1 (5.8, Not Evaluable)			

*18 patients in Study 1 and 16 patients in Study 2 did not have measurable disease at baseline as per IRC assessment and were classified as non-responders in the IRC analysis.

**Of 51 people in the subgroup, 35 (69 percent) had received prior brain radiation, including 25 (49 percent) who completed radiation treatment at least six months before starting treatment with Alecensa.

The most common Grade 3 or higher adverse events in the pooled analysis of both studies were an increase in muscle enzymes (creatine phosphokinase; 4.6 percent), shortness of breath (dyspnea; 3.6 percent), increased liver enzymes (aspartate transaminase; 3.6 percent, and alanine transaminase; 4.8 percent), evidence of liver dysfunction (hyperbilirubinemia; 2.4 percent), increased blood glucose (hyperglycemia; 2 percent), decreased levels of minerals (hypokalemia; 4 percent, hypophosphatemia; 2.8 percent, and hyponatremia; 2 percent), decreased red blood cells (anemia; 2 percent) and decreased white blood cells (lymphopenia; 4.6 percent).

About Alecensa

Alecensa (RG7853/AF-802/RO5424802/CH5424802) is an investigational oral medicine created at Chugai and is being developed for people with NSCLC whose tumours are identified as ALK+. ALK+ 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.

Early studies with Alecensa have shown activity on 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 studies of Alecensa include a companion test developed by Roche. 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 two 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

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. 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 chemotherapy.

In 2014, the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 billion Swiss francs. 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 roche.com.

Additional information

-Roche in Oncology: www.roche.com/media/media_backgrounder/media_oncology.htm

Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: roche.mediarelations@roche.com

- Nicolas Dunant (Head)
- Ulrike Engels-Lange
- Nicole Rüppel
- Claudia Schmitt