

FDA approves Roche's Rozlytrek™ (entrectinib) for people with ROS1-positive, metastatic non-small cell lung cancer and NTRK gene fusion-positive solid tumours

- **First FDA-approved treatment designed to target both ROS1 and NTRK that also shows response in cancer that has spread to the brain**
- **Roche's first FDA-approved tumour-agnostic medicine**

Basel, 16 August 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved Rozlytrek™ (entrectinib) for the treatment of adults with ROS1-positive, metastatic non-small cell lung cancer (NSCLC). The FDA has also granted accelerated approval to Rozlytrek for the treatment of adult and paediatric patients 12 years of age and older with solid tumours that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have progressed following treatment or have no satisfactory alternative therapy.¹

These approvals are based on results from the integrated analysis of the pivotal Phase II STARTRK-2, Phase I STARTRK-1 and Phase I ALKA-372-001 trials, and data from the Phase I/II STARTRK-NG study. In the integrated analysis, Rozlytrek was studied in several solid tumour types, including breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers. In ROS1-positive, metastatic NSCLC, Rozlytrek shrank tumours in 78% of people with the disease (overall response rate [ORR]; N=51) and the duration of response (DoR) ranged from 1.8 to 36.8+ months (N=40 out of 51).¹ Rozlytrek also shrank tumours in more than half of people with NTRK gene fusion-positive, locally advanced or metastatic solid tumours (ORR=57%; N=54), and objective responses were observed across 10 tumour types (DoR ranged from 2.8 to 26.0+ months; N=31 out of 54).¹ Objective responses to Rozlytrek were seen in people with central nervous system (CNS) metastases at baseline.¹

“Rozlytrek's FDA approval for two rare types of cancer is an important advance for patients, combining a targeted medicine and genomic testing to bring this new treatment option to patients who are waiting,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “Rozlytrek is the first FDA-approved treatment that selectively targets both ROS1 and NTRK fusions, and, importantly, has also shown responses in these rare cancer types that have spread to the brain.”

The most common adverse reactions (≥20 percent) with Rozlytrek were fatigue, constipation, altered sense of taste (dysgeusia), swelling (oedema), dizziness, diarrhoea, nausea, nervous system disorders (dysaesthesia), shortness of breath (dyspnoea), muscle pain (myalgia), cognitive impairment, increased weight, cough, vomiting, fever (pyrexia), joint pain (arthralgia) and vision disorders.¹

The FDA's Accelerated Approval Program allows conditional approval of a medicine that fills an unmet medical need for a serious or life-threatening disease or condition.² The accelerated approval for NTRK gene fusion-positive solid tumors is based on tumour response rate and durability of response, and continued approval may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Biomarker testing for ROS1 in NSCLC and NTRK gene fusions across all solid tumours is the only way to identify people who are eligible for treatment with Rozlytrek. Roche is leveraging its expertise in developing personalised medicines and advanced diagnostics, in conjunction with Foundation Medicine, to help identify people with ROS1 and NTRK gene fusions. Foundation Medicine will submit FoundationOne®CDx to the FDA for approval as a companion diagnostic for Rozlytrek. An FDA-approved companion diagnostic for Rozlytrek is not available at this time.

About the integrated analysis

This approval is based on an integrated analysis including data from 51 people with ROS1-positive NSCLC and 54 people with locally advanced or metastatic NTRK gene fusion-positive solid tumours (10 tumour types, >19 histopathologies) from the Phase II STARTRK-2, Phase I STARTRK-1 and Phase I ALKA-372-001 trials.¹ This approval is also based on data from the Phase I/II STARTRK-NG study in paediatric patients.¹ The studies enrolled people across 15 countries and more than 150 clinical trial sites. Safety was assessed from an integrated analysis of 355 people across these four trials.

About ROS1-positive non-small cell lung cancer (NSCLC)

ROS1 is a tyrosine kinase, which plays a role in controlling how cells grow and proliferate. When a ROS1 gene fusion occurs, cancer cells grow and proliferate in an uncontrolled manner. Blocking this abnormal signalling can cause tumour cells to shrink or die.³

ROS1 gene fusions account for 1-2% of non-small-cell lung cancer (NSCLC).³ Lung cancer is the leading cause of cancer-related death across the world.⁴ Each year, more than one and a half million people die as a result of the disease globally, equating to more than 4,000 deaths every day.⁴ NSCLC is the most common type of lung cancer and accounts for 85% of all lung cancer diagnoses.⁵ While the ROS1 gene fusion can be found in any patient with NSCLC, young never-smokers with NSCLC have the highest incidence of ROS1 gene fusions.³

About NTRK gene fusion-positive cancer

Neurotrophic tyrosine receptor kinase (NTRK) gene fusion-positive cancer occurs when the NTRK1/2/3 genes fuse with other genes, resulting in altered TRK proteins (TRKA/TRKB/TRKC) that can activate signalling pathways involved in proliferation of certain types of cancer. NTRK gene fusions are present in tumours irrespective of site of origin. These fusions have been identified in a broad range of solid tumour types, including breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers.⁶

About Rozlytrek

Rozlytrek (entrectinib) is an oral medicine for the treatment of adults with ROS1-positive, metastatic non-small cell lung cancer (NSCLC), as well as for the treatment of adult and paediatric patients 12 years of age

and older with solid tumours that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have progressed following treatment or have no satisfactory alternative therapy.¹ It is a selective tyrosine kinase inhibitor designed to inhibit the kinase activity of the TRK A/B/C and ROS1 proteins, whose activating fusions drive proliferation in certain types of cancer.^{7,8} Rozlytrek can block ROS1 and NTRK kinase activity and may result in the death of cancer cells with ROS1 or NTRK gene fusions.^{7,8}

Rozlytrek was first approved by Japan's Ministry of Health, Labour and Welfare (MHLW) on 18 June for the treatment of adult and paediatric patients with NTRK fusion-positive, advanced recurrent solid tumours. Prior to that, it was granted Sakigake designation for accelerated review by the MHLW. It has also been granted Priority Medicines (PRIME) designation by the European Medicines Agency (EMA).⁹

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 five 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. More than 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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