

Roche's investigational medicine entrectinib showed a durable response of more than two years in people with a specific type of lung cancer

- **Entrectinib reduced tumours in people with ROS1-positive non-small cell lung cancer (NSCLC), including those whose disease had spread to the central nervous system (CNS)**
- **Data will be submitted to global regulatory authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA)**

Basel, 24 September 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results for its investigational medicine entrectinib, from an integrated analysis of the pivotal phase II STARTRK-2, phase I STARTRK-1 and phase I ALKA trials, which showed that entrectinib shrank tumours (objective response rate; ORR) in 77.4% of people with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC).^[1] In addition, entrectinib demonstrated a durable response of more than two years (duration of response [DoR] = 24.6 months).^[1] Importantly, entrectinib was shown to shrink tumours in more than half of people with cancer in the central nervous system (CNS) (intracranial ORR: 55.0%).^[1] The safety profile of entrectinib was consistent with that seen in previous analyses, and no new safety signals were identified.^[1] Based on the integrated analysis of these studies, Roche plans to submit these data to global health authorities.

“These results show the potential of precision medicines to deliver tailored and effective treatment options for people with non-small cell lung cancer, including those whose tumours have spread to the central nervous system,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are also investigating entrectinib in NTRK fusion-positive tumours across several different cancer types, and look forward to presenting those results in the near future.”

ROS1 gene fusions have been identified in 1-2% of people with NSCLC.^[2] NSCLC is the most common type of lung cancer and accounts for 85% of all lung cancer diagnoses.^[3] Approximately 30-40% of people with ROS1-positive NSCLC have brain metastases at time of diagnosis.^[4]

These ROS1 results will be presented at the 2018 World Conference on Lung Cancer (WCLC) in Toronto, Canada on Monday, 24 September 2018, from 10:30 – 10:40 a.m. EDT (Abstract 13903), and featured in the WCLC press programme on Monday, 24 September, from 9:45 – 10:30 a.m. EDT. Follow Roche on Twitter via @Roche and keep up to date with WCLC 2018 congress news and updates by using the hashtag #WCLC2018.

About the integrated analysis

The integrated analysis included data from 53 people with ROS1-activating gene fusions from the phase II STARTRK-2, phase I STARTRK-1 and phase I ALKA trials.^[1] The studies enrolled people across 15 countries and more than 150 clinical trial sites.^[1]

- **STARTRK-2** is a phase II, global, multicentre, open-label basket study in people with solid tumours that harbour an NTRK1/2/3 or ROS1-positive gene fusion. ^[5] The primary endpoint is ORR. ^[5] Secondary outcome measures include DOR, time to response, clinical benefit rate, intracranial tumour response, progression-free survival (PFS), CNS PFS and overall survival (OS). ^[5]
- **STARTRK-1** is a phase I, multicentre, open-label dose escalation study of a daily continuous dosing schedule in people with solid tumours with NTRK1/2/3 or ROS1 gene fusions in the US and South Korea. ^[6] The trial assessed the safety and tolerability of entrectinib via a standard dose escalation scheme and determined the recommended phase II dose. ^[6]
- **ALKA** is a phase I, multicentre, open-label dose escalation study of an intermittent and continuous entrectinib dosing schedule in people with advanced or metastatic solid tumours with ROS1 gene fusions in Italy. ^[7]

Adverse events were consistent with previous data. ^[1] The most commonly reported adverse events include those affecting the nervous system, as well as constipation, altered sense of taste (dysgeusia) and fatigue. ^[1]

About entrectinib

Entrectinib (RXDX-101) is an investigational, oral medicine in development for the treatment of locally advanced or metastatic solid tumours that harbour NTRK1/2/3 or ROS1 gene fusions. It is a selective, CNS-active tyrosine kinase inhibitor designed to inhibit the kinase activity of the TRKA/B/C and ROS1 proteins, whose activating fusions drive proliferation in certain types of cancer. ^[8,9] Entrectinib can block ROS1 and NTRK kinase activity and may result in the death of cancer cells with ROS1 or NTRK gene fusions. ^[8,9] Entrectinib is being investigated across a range of solid tumour types, including non-small cell lung cancer, pancreatic cancer, sarcomas, thyroid cancer, salivary cancer, gastrointestinal stromal tumours (GIST) and cancers of unknown primary (CUP). ^[5-7]

Entrectinib has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA); Priority Medicines (PRIME) designation by the European Medicines Agency (EMA); and Sakigake designation by the Japanese health authorities for the treatment of NTRK-positive, locally advanced or metastatic solid tumours in adult and pediatric patients who have either progressed following prior therapies or have no acceptable standard therapies. ^[7]

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. ^[2]

ROS1 gene fusions account for 1-2% of non-small-cell lung cancer (NSCLC). ^[2] Lung cancer is the leading cause of cancer-related death across the world. ^[10] 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. ^[10] NSCLC is the most common type of lung cancer and accounts for 85% of all lung cancer diagnoses. ^[3] 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. ^[2]

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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