

Roche's personalised medicine entrectinib shrank tumours harbouring NTRK, ROS1 or ALK gene fusions in children and adolescents

- **Phase I/II study of entrectinib, an investigational medicine, showed responses in all paediatric tumour types harbouring neurotrophic tyrosine receptor kinase (NTRK), ROS1 or anaplastic lymphoma kinase (ALK) fusions, including those in the central nervous system**
- **Data featured in the ASCO presscast on Wednesday, 15 May, and will be presented at the 2019 ASCO Annual Meeting on Sunday, 2 June**

Basel, 16 May 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive data from the Phase I/II STARTRK-NG study, evaluating the investigational medicine entrectinib in children and adolescents with recurrent or refractory solid tumours with and without neurotrophic tyrosine receptor kinase (NTRK), ROS1 or anaplastic lymphoma kinase (ALK) gene fusions. The study showed entrectinib shrank tumours (objective response rate; ORR) in all children and adolescents who had NTRK, ROS1 or ALK fusion-positive solid tumours (11 of 11 patients), including two patients achieving a complete response.¹ Of the 11 patients, five patients with primary high-grade tumours in the central nervous system (CNS) had an objective response, including one patient with a complete response.¹ The safety profile of entrectinib was consistent with that seen in previous analyses.¹ Data will be presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago on Sunday, 2 June, 2019, from 8:00 – 8:12 am CDT (Abstract 10009), and was part of yesterday's official ASCO presscast.

“We are encouraged by the results we have seen with entrectinib in children with paediatric and adolescent cancers, including those with tumours in the brain,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “The STARTRK-NG study underscores the importance of combining comprehensive genomic profiling with targeted therapies and supports our approach to providing people with personalised medicines developed specifically for their type of cancer.”

Additional data for entrectinib across different tumour types and patient populations will also be presented at ASCO, highlighting the company's unique approach to personalised healthcare through advances in targeted therapies, diagnostics and data analytics:

- Initial results from an integrated analysis of the Phase II STARTRK-2, Phase I STARTRK-1 and Phase I ALKA-372-001 trials, evaluating the efficacy of entrectinib in adults with solid tumours and CNS metastases, will be presented on Saturday, 1 June, 2019, in a poster session from 3:00 – 4:30 pm CDT (Abstract 3017).
- Results from a Real World Data study, evaluating time-to-treatment discontinuation and progression-free survival as endpoints for comparative efficacy analysis of clinical trials of entrectinib

and crizotinib for the treatment of people with ROS1-positive non-small cell lung cancer (NSCLC), will be presented during a poster session on Sunday, 2 June, 2019, from 8:00 – 11:00 am CDT (Abstract 9070).

The FDA recently granted Priority Review for entrectinib for both the treatment of paediatric and adult patients with NTRK fusion-positive, locally advanced or metastatic solid tumours who have either progressed following prior therapies or as an initial therapy when there are no acceptable standard therapies, and for the treatment of people with metastatic ROS1-positive NSCLC.² These NDAs are based on results from the integrated analysis of the Phase II STARTRK-2, Phase I STARTRK-1 and Phase I ALKA-372-001 trials, and data from the STARTRK-NG study. The FDA is expected to make a decision on approval by 18 August, 2019.²

About the STARTRK-NG study

STARTRK-NG is a Phase I/II open-label dose-escalation and expansion study evaluating the safety and efficacy of entrectinib in children and adolescent patients with no curative first-line treatment option, recurrent or refractory extracranial solid tumours or primary CNS tumours, with or without NTRK, ROS1 or ALK fusions.¹ Response, assessed by Investigator, was classified as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD) using Response Assessment in Neuro-Oncology (RANO) for CNS tumours, Response Evaluation Criteria in Solid Tumors (RECIST), and Curie score (CS) for NBL.¹ The study enrolled 29 children and adolescents aged 4.9 months through to 20 years (median age of 7 years) who had recurrent or refractory solid tumours, and 28 were evaluated for response.¹ Of the 28 children and adolescents evaluated, 11 children were identified to have tumours with NTRK, ROS1 or ALK fusions and one with ALK F1174L-mutated neuroblastoma (NBL).¹ A summary of the results are included below.

- Complete responses were observed in 2 patients with tumours harbouring NTRK and ALK fusions: 1 with an NTRK fusion-positive primary CNS tumour and 1 with an ALK fusion-positive inflammatory myofibroblastic tumour. Another complete response was observed in 1 neuroblastoma patient with an ALK F1174L mutation.¹
- Partial responses were observed in 9 patients, 3 unconfirmed at the time of the clinical cut-off date, across NTRK, ROS1 and ALK fusion-positive primary CNS (n=4) and extracranial (n=5) solid tumours.¹
- Median duration of therapy for confirmed fusion-positive responders was 10.51 months (3.8 to 17.7 months), and median time to response was 1.89 months (1 to 1.9 months).¹
- The safety profile of entrectinib was consistent with that seen in previous analyses. Treatment-related adverse events were most frequently National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events Grade 1 or 2, leading to discontinuation in 6.9% of patients.¹

About NTRK fusion-positive cancer

Neurotrophic tyrosine receptor kinase (NTRK) 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 signaling pathways involved in proliferation of certain types of cancer. NTRK gene fusions are tumour-agnostic, meaning they 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.³

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 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.^{4,5} Entrectinib can block ROS1 and NTRK kinase activity and may result in the death of cancer cells with ROS1 or NTRK gene fusions.[4,5] Entrectinib is being investigated across a range of solid tumour types, including breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers.^{2,3}

Entrectinib has been granted Breakthrough Therapy Designation (BTD) by the FDA; Priority Medicines (PRIME) designation by the European Medicines Agency (EMA); and Sakigake designation by the Japanese health authorities for the treatment of NTRK fusion-positive, locally advanced or metastatic solid tumours in adult and paediatric patients who have either progressed following prior therapies or have no acceptable standard therapies.²

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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References

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