

## Roche's investigational personalised medicine entrectinib shrank tumours in people with NTRK fusion-positive solid tumours

- Entrectinib showed response irrespective of tumour type or 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, 21 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results from an integrated analysis of the pivotal phase II STARTRK-2, phase I STARTRK-1 and phase I ALKA-372-001 trials that showed the investigational personalised medicine entrectinib shrank tumours (objective response rate; ORR) in more than half (57.4%) of people with neurotrophic tropomyosin receptor kinase (NTRK) fusion-positive solid tumours. Objective responses to entrectinib were seen across ten different solid tumour types (median duration of response [DOR]=10.4 months), including in people with and without central nervous system (CNS) metastases at baseline.<sup>[1]</sup> Importantly, entrectinib shrank tumours that had spread to the brain in over half of people (intracranial response; IC ORR=54.5%), with more than a quarter of these people having a complete response.<sup>[1]</sup> The safety profile of entrectinib was consistent with that seen in previous analyses.<sup>[1]</sup>

“These data demonstrate the potential of entrectinib to treat a range of difficult-to-treat and rare cancers regardless of their site of origin,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Entrectinib has the potential to redefine personalised medicine, which can utilize tests such as next-generation sequencing, to find the right treatment for each individual patient. People with NTRK fusion-positive solid tumours need more options, and we look forward to working with health authorities to bring this potential treatment to patients as soon as possible.”

Roche is leveraging its expertise in developing personalised medicines and advanced diagnostics, in conjunction with Foundation Medicine, to develop a novel diagnostics approach using next-generation sequencing that will help identify people with NTRK gene fusions likely to benefit from entrectinib.<sup>[2;3]</sup>

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 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.<sup>[4]</sup> These designations are reserved for medicines that demonstrate substantial improvements over existing therapies or where there are unmet medical needs.

These NTRK fusion-positive results will be presented at the European Society for Medical Oncology (ESMO) 2018 Congress in Munich, Germany on 21 October 2018, 11:24-11:36 am CEST (LBA17). Follow Roche on Twitter via @Roche and keep up to date with ESMO 2018 congress news and updates by using the hashtag #ESMO2018.

Roche also recently presented positive results at the IASLC 19<sup>th</sup> World Conference on Lung Cancer (WCLC) that showed entrectinib shrank tumours (ORR) in 77.4% of people with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC).<sup>[5]</sup> In addition, entrectinib demonstrated a durable response of more than two years (DOR=24.6 months).<sup>[5]</sup> Importantly, entrectinib was shown to shrink tumours in more than half of people with cancer in the CNS (IC ORR=55.0%).<sup>[5]</sup> The safety profile of entrectinib was consistent with that seen in previous analyses.<sup>[5]</sup>

Roche plans to submit results from these integrated analyses to global health authorities for the treatment of NTRK fusion-positive solid tumours and ROS1-positive NSCLC.

#### **About the integrated analysis**

The integrated analysis included data from 54 people with locally advanced or metastatic NTRK 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.<sup>[4]</sup> The studies enrolled people across 15 countries and more than 150 clinical trial sites. Tumour types evaluated in the studies to date included breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers.

- **STARTRK-2** is a phase II, global, multicentre, open-label basket study in people with solid tumours that harbour an NTRK1/2/3, ROS1 or ALK-positive gene fusion.<sup>[6]</sup> The primary endpoints are ORR and DOR is a secondary endpoint.<sup>[6]</sup> Other secondary outcome measures include time to response, clinical benefit rate, intracranial tumour response, progression-free survival (PFS), CNS PFS and overall survival (OS).<sup>[6]</sup>
- **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, ROS1 or ALK gene fusions in the US and South Korea.<sup>[7]</sup> The trial assessed the safety and tolerability of entrectinib via a standard dose escalation scheme and determined the recommended phase II dose.<sup>[7]</sup>
- **ALKA-372-001** 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 TrkA/B/C, ROS1 or ALK gene fusions in Italy.<sup>[8]</sup>

Overall, entrectinib was well tolerated and the majority of adverse events were Grade 1-2, reversible, and managed with treatment interruption or dose reduction.<sup>[1]</sup> Treatment-related adverse events leading to discontinuation occurred in 3.9% of patients.<sup>[1]</sup> The most common treatment-related adverse events were altered sense of taste (dysgeusia), fatigue, and dizziness.<sup>[1]</sup>

### **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 TRK A/B/C and ROS1 proteins, whose activating fusions drive proliferation in certain types of cancer. <sup>[2,3]</sup> Entrectinib can block ROS1 and NTRK kinase activity and may result in the death of cancer cells with ROS1 or NTRK gene fusions. <sup>[2,3]</sup>

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. <sup>[6-8]</sup>

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### **About NTRK gene fusions**

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 signalling 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, and have been identified a broad range of solid tumour types, including breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers. <sup>[1]</sup> There is a high unmet medical need for treatments for people with life-threatening NTRK fusion-positive tumours.

### **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](http://www.roche.com).

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#### References

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