Roche's novel anti-TIGIT tiragolumab granted FDA Breakthrough Therapy Designation in combination with Tecentriq for PD-L1-high non-small cell lung cancer

- **Tiragolumab is the first anti-TIGIT therapy to be granted Breakthrough Therapy Designation (BTD) and marks the 37th BTD for Roche's portfolio of medicines**
- **BTD is based on the randomised phase II CITYSCAPE study that showed encouraging efficacy and safety with tiragolumab plus Tecentriq (atezolizumab) in people with PD-L1-positive metastatic non-small cell lung cancer**
- **Broad tiragolumab development programme is ongoing across various settings in different tumour types, including lung, oesophageal and cervical cancers**

Basel, 5 January 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA), in combination with Tecentriq® (atezolizumab) for the first-line treatment of people with metastatic non-small cell lung cancer (NSCLC) whose tumours have high PD-L1 expression with no EGFR or ALK genomic tumour aberrations. Tiragolumab is the first anti-TIGIT molecule to be granted BTD from the FDA, and the designation is based on randomised data from the phase II CITYSCAPE trial. CITYSCAPE provides the first evidence that targeting both immune inhibitory receptors, TIGIT and PD-L1, may enhance anti-tumour activity by potentially amplifying the immune response.[1]

"We have been researching TIGIT as a novel cancer immunotherapy target for almost ten years and we are pleased that the FDA has acknowledged the potential of tiragolumab to substantially improve outcomes for people with certain types of lung cancer," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to advancing our tiragolumab development programme, which includes chemotherapy-free combinations and trials in early stages of disease across multiple cancer types with high unmet need."

BTD is designed to accelerate the development and review of medicines intended to treat serious or life-threatening conditions, with preliminary evidence that indicates they may demonstrate a substantial improvement over existing therapies. This marks the 37th BTD for Roche's portfolio of medicines.

Tiragolumab in combination with Tecentriq has so far shown encouraging efficacy and safety in PD-L1-positive metastatic NSCLC based on data from the phase II CITYSCAPE trial, the first randomised study in the anti-TIGIT field.[1] Full results from CITYSCAPE, presented at the American Society of Clinical Oncology 2020 Virtual Scientific Program, showed that at an average of 10.9 months follow-up, the combination showed an improvement in the overall response rate (ORR; 37% vs. 21% with Tecentriq alone) and a 42% reduction in the risk of disease worsening or death (progression free survival; PFS) compared with Tecentriq alone.[1] An exploratory analysis in people with high levels of PD-L1 (tumour proportion score; TPS ≥ 50%)

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showed a clinically meaningful ORR vs. Tecentriq alone (66% vs. 24%) and median PFS was not reached (vs. 4.11 months with Tecentriq alone; HR=0.30, 95% CI: 0.15–0.61).[1] The data suggest that tiragolumab plus Tecentriq was generally well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events when combining the two immunotherapies compared with Tecentriq alone (48% vs. 44%).[1]

Roche is investigating the potential of tiragolumab in a broad development programme that builds on the benefit observed with Tecentriq while expanding into earlier stages of disease and new areas of unmet need. This includes randomised trials in metastatic NSCLC (SKYSCRAPER-01 and SKYSCRAPER-06) and small cell lung cancer (SKYSCRAPER-02), as well as exploration of tiragolumab in earlier stages, including stage III NSCLC (SKYSCRAPER-03) and locally advanced oesophageal cancer (SKYSCRAPER-07). Tiragolumab is also being investigated in metastatic oesophageal squamous cancer (SKYSCRAPER-08) and cervical cancer (SKYSCRAPER-04), with early trials in other tumour types.

Biomarker analyses from the CITYSCAPE study will be presented at the IASLC 2020 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer, taking place from 28-31 January 2021: Efficacy of Tiragolumab + Atezolizumab in PD-L1 IHC and TIGIT Subgroups in the Phase II CITYSCAPE Study in First-Line NSCLC.

Dual blockade of the TIGIT and PD-L1 pathways
TIGIT and PD-L1 are proteins that play a role in suppression of the immune system.[2] Blocking both pathways simultaneously with tiragolumab and Tecentriq® (atezolizumab) has the potential to increase anti-tumour activity by enhancing the body's immune response to cancer cells.[1] Targeting multiple immune pathways in this way has the potential to build upon previous advances in cancer immunotherapy, expand into earlier stages of disease and provide new treatment options in areas of high unmet need.

About the CITYSCAPE study[1]
CITYSCAPE is a global phase II, randomised and blinded study evaluating tiragolumab plus Tecentriq® (atezolizumab) compared with Tecentriq alone in 135 patients with first-line PD-L1-positive, locally advanced unresectable or metastatic non-small cell lung cancer. Patients were randomised 1:1 to receive either tiragolumab plus Tecentriq or placebo plus Tecentriq, until progressive disease or loss of clinical benefit. Co-primary endpoints are overall response rate and progression-free survival. Secondary endpoints include safety and overall survival.

About tiragolumab
Tiragolumab is a monoclonal antibody designed to bind with TIGIT, a protein receptor on immune cells.[2,3] Tiragolumab works as an immune amplifier, by potentially enhancing the body's immune response.[1] By binding to TIGIT, tiragolumab blocks its interaction with a protein called poliovirus receptor (PVR, or CD155) that can suppress the body's immune response.[4] Blockade of TIGIT and PD-L1 may synergistically enable the re-activation of T cells and enhance NK cell anti-tumour activity.[2,5,6]

About Tecentriq® (atezolizumab)
Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1, which is expressed on tumour cells and tumour-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, Tecentriq may enable the activation of T-cells. Tecentriq is a cancer immunotherapy that has the potential to be used as a foundational combination partner with other immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers. The development of Tecentriq and its clinical programme is based on our greater understanding of how the immune system interacts with tumours and how harnessing a person's immune system combats cancer more effectively.

Tecentriq is approved in the US, EU and countries around the world, either alone or in combination with targeted therapies and/or chemotherapies in various forms of non-small cell lung cancer, small cell lung cancer, certain types of metastatic urothelial cancer, in PD-L1-positive metastatic triple-negative breast cancer and for hepatocellular carcinoma. In the US, Tecentriq is also approved in combination with Cotellic® (cobimetinib) and Zelboraf® (vemurafenib) for the treatment of people with BRAF V600 mutation-positive advanced melanoma.

About Roche in cancer immunotherapy
Roche's rigorous pursuit of groundbreaking science has contributed to major therapeutic and diagnostic advances in oncology over the last 50 years, and today, realising the full potential of cancer immunotherapy is a major area of focus. With over 20 molecules in development, Roche is investigating the potential benefits of immunotherapy alone, and in combination with chemotherapy, targeted therapies or other immunotherapies with the goal of providing each person with a treatment tailored to harness their own unique immune system to attack their cancer. Our scientific expertise, coupled with innovative pipeline and extensive partnerships, gives us the confidence to continue pursuing the vision of finding a cure for cancer by ensuring the right treatment for the right patient at the right time.

In addition to Roche's approved PD-L1 checkpoint inhibitor, Tecentriq® (atezolizumab), Roche's broad cancer immunotherapy pipeline includes other checkpoint inhibitors, such as tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, individualised neoantigen therapies and T-cell bispecific antibodies. To learn more about Roche's scientific-led approach to cancer immunotherapy, please follow this link:
http://www.roche.com/research_and_development/what_we_are_working_on/oncology/cancer-immunotherapy.htm

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 twelfth consecutive year, Roche has been recognised as one of the most sustainable companies 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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