Media Release

Roche to present first clinical data on novel anti-TIGIT cancer immunotherapy tiragolumab at ASCO

- **Phase II CITYSCAPE trial shows promising results adding tiragolumab to Tecentriq in people with PD-L1-positive metastatic non-small cell lung cancer**
- **Full results will be presented in an oral abstract session at the ASCO20 Virtual Scientific Program organised by the American Society of Clinical Oncology (ASCO)**

Basel, 14 May 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the Phase II CITYSCAPE trial, the first randomised study evaluating the efficacy and safety of tiragolumab plus Tecentriq® (atezolizumab) compared with Tecentriq alone as an initial (first-line) treatment for people with PD-L1-positive metastatic non-small cell lung cancer (NSCLC). Tiragolumab is a novel cancer immunotherapy designed to bind to TIGIT, an immune checkpoint protein expressed on immune cells. Both TIGIT and PD-L1 play an important role in immune suppression, and blocking both pathways could enhance anti-tumour activity. The full results will be presented in an oral abstract session (Abstract #9503) at the ASCO20 Virtual Scientific Program organised by the American Society of Clinical Oncology (ASCO), which will be held 29-31 May 2020.

"We are pleased to share these first randomised anti-TIGIT results, showing that tiragolumab, our novel cancer immunotherapy, has encouraging efficacy and safety in combination with Tecentriq," said Levi Garraway, M.D., Ph.D., chief medical officer and head of Global Product Development. "TIGIT, an immune checkpoint protein expressed on immune cells, was identified by our own scientists. By blocking both TIGIT and PD-L1 pathways simultaneously, we hope to deepen patient responses to immunotherapy and widen the circle of people who may benefit."

At the primary analysis, tiragolumab plus Tecentriq met both co-primary endpoints in the intention-to-treat (ITT) population, showing an improvement in the objective response rate (ORR) (31.3% vs 16.2%) and a 43% reduction in the risk of disease worsening or death (progression-free survival; PFS) (median PFS= 5.4 vs 3.6 months; hazard ratio (HR)=0.57, 95% CI: 0.37–0.90) compared with Tecentriq alone.

An exploratory analysis in people with high levels of PD-L1 (TPS ≥50%) showed a clinically meaningful improvement in ORR (55.2% vs 17.2%) and a 67% reduction in the risk of disease worsening or death (median PFS=not reached vs 3.9 months; HR=0.33, 95% CI: 0.15–0.72) with the combination compared with Tecentriq alone.[1]

The data suggest that the combination of tiragolumab plus Tecentriq was well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events (AEs) when combining the two immunotherapies compared with Tecentriq alone (41.8% vs 44.1%).

At a six-month follow-up, the improvement in the ORR and PFS in the tiragolumab plus Tecentriq arm persisted in both the ITT and the PD-L1-high populations, and no new safety signals were observed.

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As part of Roche's commitment to explore new immunotherapy options and combinations, the company recently initiated two Phase III clinical trials evaluating tiragolumab plus Tecentriq for people with certain types of lung cancer (SKYSCRAPER-01 and SKYSCRAPER-02). Tiragolumab is also being evaluated in other solid tumours as well as in hematological cancers. Additional Phase 1a/b results in solid tumours will be presented at an upcoming medical meeting.

About CITYSCAPE study [1]

CITYSCAPE is a global Phase II, randomised and blinded study evaluating tiragolumab plus Tecentriq 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 ORR and PFS. Secondary endpoints include safety and overall survival.

Efficacy results

	ITT (TPS≥1%) N=135		PD-L1-high (TPS≥50%) N=58		PD-L1-low (TPS1-49%) N=77	
Arms	tiragolumab + Tecentriq (n=67)	placebo + Tecentriq (n=68)	tiragolumab + Tecentriq (n=29)	placebo + Tecentriq (n=29)	tiragolumab+ Tecentriq (n=38)	placebo + Tecentriq (n=39)
ORR, % (95% CI)	31.3 (19.5, 43.2)	16.2 (6.7, 25.7)	55.2 (35.3, 75.0)	17.2 (1.8, 32.7)	13.2 (1.15, 25.2)	15.4 (2.8, 28.0)
Odds ratio (95% CI)	2.57 (1.07,6.14)*		5.91 (1.76,19.81) †		0.83 (0.23, 3.00) †	
Median PFS (95% CI)	5.4 (4.2, NE)	3.6 (2.7, 4.4)	NE (5.4, NE)	3.9 (2.1, 4.7)	4.1 (1.6, 5.6)	3.6 (1.5, 5.0)
HR (95% CI)	0.57 (0.37,0.90)*		0.33 (0.15, 0.72) †		0.85 (0.49, 1.48) †	

*stratified

†unstratified

At a six-month follow-up, the improvement in ORR (37.3% vs 20.6%) and PFS (median PFS=5.6 month versus 3.9 months) in the tiragolumab plus Tecentriq arm persisted in the ITT population. Results in the PD-L1-high population were also consistent with the first analysis and the median PFS was still not reached.

Safety results

	tiragolumab + Tecentriq n=67	placebo + Tecentriq n= 68
All Grade 3-5 AEs	41.8%	44.1%
Treatment- related AEs (TRAEs)	80.6%	72%
Grade ≥3 TRAEs	14.9%	19.1%
AEs leading to treatment withdrawal	7.5%	10.3%

About tiragolumab and TIGIT [5]
Tiragolumab is a monoclonal antibody designed to bind with TIGIT, a protein receptor on immune cells [2 3.] 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 6 7].

About Tecentriq
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 and small cell lung cancer, certain types of metastatic urothelial cancer, and in PD-L1-positive metastatic triple-negative breast cancer.

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 NSCLC
Lung cancer is the leading cause of cancer death globally [8]. Each year 1.76 million people die as a result of the disease; this translates into more than 4,800 deaths worldwide every day [8]. Lung cancer can be broadly divided into two major types: NSCLC and small cell lung cancer. NSCLC is the most prevalent type, accounting for around 85% of all cases [9]. NSCLC comprises non-squamous and squamous-cell lung cancer, the squamous form of which is characterised by flat cells covering the airway surface when viewed under a microscope [9].

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 eleventh 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.

References

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