

## **New data from the phase II CITYSCAPE trial show encouraging results with Roche's novel anti-TIGIT tiragolumab plus Tecentriq**

- **After 2.5 years median follow-up, pre-planned exploratory analyses in the PD-L1-high population show clinically meaningful results, with overall survival not yet reached and continued progression-free survival improvement for the combination compared with Tecentriq alone**
- **CITYSCAPE is the first randomised phase II trial of an anti-TIGIT therapy and is investigating tiragolumab in PD-L1-positive metastatic non-small cell lung cancer**
- **Tiragolumab is the first anti-TIGIT therapy to be granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration**
- **CITYSCAPE forms the basis of a broad tiragolumab development programme across multiple settings and tumour types**

Basel, 10 December 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new follow-up efficacy, safety and patient-reported outcomes (PROs) data from the phase II CITYSCAPE trial, investigating the novel anti-TIGIT cancer immunotherapy 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). The full results are being featured as an oral presentation in the Proffered Paper session 2 (Abstract LBA2) at the European Society for Medical Oncology (ESMO) Immuno-Oncology Congress 2021, taking place 8-11 December.<sup>1</sup>

“These encouraging results suggest that combining anti-TIGIT and anti-PD-L1 cancer immunotherapies such as tiragolumab and Tecentriq could potentially represent a novel approach to address unmet needs in cancer,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “With tiragolumab, we have the largest and most advanced anti-TIGIT clinical programme, and we look forward to the results of our phase III trials in lung cancer and other challenging tumour types.”

After 2.5 years median follow-up, tiragolumab plus Tecentriq continued to show an improvement in the intention-to-treat (ITT) population (n=67), driven by the PD-L1-high population (TPS ≥ 50%) (n=29). In the ITT population, the combination reduced the risk of disease worsening or death (progression-free survival; PFS) by 38% (median PFS=5.6 vs. 3.9 months; hazard ratio (HR)=0.62, 95% CI: 0.42-0.91) and improved overall response rates (ORR) (38.8% vs. 20.6%) compared with Tecentriq alone. A predefined exploratory analysis in the PD-L1-high population showed a 71% reduction in the risk of disease worsening or death (median PFS=16.6 vs. 4.1 months; HR=0.29, 95% CI: 0.15-0.53) and a clinically meaningful improvement in ORR (69% vs. 24.1%) with the combination compared with Tecentriq alone.<sup>1</sup>

The analysis also showed that tiragolumab plus Tecentriq improved overall survival (OS), a secondary endpoint of the study, in the ITT population, which was driven by the PD-L1-high

population. After 2.5 years median follow-up, median OS was 23.2 vs. 14.5 months (HR=0.69, 95% CI: 0.44-1.07) in the ITT population. The exploratory data in the PD-L1-high population showed a clinically meaningful OS improvement. The median was not reached for the tiragolumab regimen and is projected to be greater than 30.3 months based on the lower confidence interval (NE (30.3-NE) vs. 12.8 months (4.7-24.2); HR=0.23, 95% CI: 0.10-0.53).<sup>1</sup>

Data suggest that the combination was generally well-tolerated, showing similar rates of Grade 3-4 treatment-related adverse events (AEs) when adding tiragolumab to Tecentriq compared with Tecentriq alone (22.4% vs. 25%). The most common all cause AEs (rate greater than 5% difference between study groups) seen with the combination were infusion-related reactions, stiffness, dry skin, fatigue and rash. After longer follow-up, no new safety signals were observed with the combination. Patients generally reported minimal-to-moderate symptoms and generally maintained their quality of life compared with the start of treatment. PRO data from this exploratory analysis showed that lung symptoms, such as dyspnoea and pain, did not appear to deteriorate with the addition of tiragolumab to Tecentriq.<sup>1</sup>

CITYSCAPE study forms the basis of an industry-leading development programme across multiple settings and tumour types.<sup>3</sup>

The phase III SKYSCRAPER-01 trial is currently ongoing to confirm these results in the PD-L1-high population, with the goal of bringing this treatment option to patients. Earlier this year, tiragolumab was granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration – representing the first anti-TIGIT therapy to be granted this designation and the 37th BTD for Roche’s portfolio of medicines. Since 2020, Roche has initiated five phase III trials evaluating tiragolumab plus Tecentriq in early and metastatic disease in lung (SKYSCRAPER-01, SKYSCRAPER-02, SKYSCRAPER-03) and oesophageal cancers (SKYSCRAPER-07, SKYSCRAPER-08). Tiragolumab is also being evaluated in other solid tumours as well as in haematological cancers.

### About the CITYSCAPE study<sup>1</sup>

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 (ORR) and progression-free survival (PFS). Secondary endpoints include safety, overall survival (OS) and patient-reported outcomes (PROs). PRO results were assessed with EORTC QLQ-C30, a questionnaire developed to assess the quality of life of people with cancer, administered at baseline and throughout study treatment.

A summary of the results are as follows:

	ITT		PD-L1 TPS $\geq$ 50%		PD-L1 TPS 1-49%	
	Placebo plus Tecentriq	Tiragolumab plus Tecentriq	Placebo plus Tecentriq	Tiragolumab plus Tecentriq	Placebo plus Tecentriq	Tiragolumab plus Tecentriq
N	68	67	29	29	39	38
ORR, %	20.6	38.8	24.1	69.0	17.9	15.8
mDOR, mo (95% CI)	10.7 (6.0-18.8)	17.6 (9.1-26.1)	8.2 (5.6-10.4)	15.7 (9.1-NE)	18.8 (15.9-22.8)	17.8 (8.3-24.2)
mPFS, mo (95% CI)	3.9 (2.7-4.5)	5.6 (4.2-10.4)	4.1 (2.1-6.8)	16.6 (5.5-22.3)	3.6 (1.4-5.5)	4.0 (1.6-5.6)
HR (95% CI)	0.62* (0.42-0.91)		0.29 <sup>†</sup> (0.15-0.53)		1.07 <sup>†</sup> (0.67-1.71)	
mOS, mo (95% CI)	14.5 (9.6-20.4)	23.2 (14.1-31.5)	12.8 (4.7-24.2)	NE (30.3-NE)	14.5 (8.3-25.6)	13.3 (8.0-20.7)
HR (95% CI)	0.69* (0.44-1.07)		0.23 <sup>†</sup> (0.10-0.53)		1.16 <sup>†</sup> (0.70-1.94)	

\*Stratified; <sup>†</sup>Unstratified; NE = non-evaluable.

	Placebo plus Tecentriq n=68	Tiragolumab plus Tecentriq n=67
All cause AEs Grade 3-4	66 (97.1%)	66 (98.5%)

Grade 5	27 (39.7%) 7 (10.3%)	35 (52.2%) 3 (4.5%)
Treatment-related AEs	48 (70.6%)	55 (82.1%)
Grade 3-4	17 (25%)	15 (22.4%)
Grade 5	0	2 (3%)
Immune mediated AEs	32 (47.1%)	51 (76.1%)
Grade 3-4	11 (16.2%)	13 (19.4%)
AEs leading to withdrawal	9 (13.2%)	10 (14.9%)

### About tiragolumab

Tiragolumab is a first-in-class novel immune checkpoint inhibitor with an intact Fc region. Tiragolumab selectively binds to TIGIT, a novel inhibitory immune checkpoint which suppresses the immune response to cancer.<sup>1</sup> Based on preclinical research, tiragolumab is thought to work as an immune amplifier with other cancer immunotherapies such as Tecentriq.<sup>2</sup> The TIGIT pathway is distinct but complementary to the PD-L1/PD-1 pathway. Dual blockade with tiragolumab and Tecentriq may help overcome immune suppression and restore the immune response.<sup>1</sup>

### About Tecentriq® (atezolizumab)

Tecentriq is a monoclonal antibody designed to bind with a protein called Programmed Death Ligand-1 (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 NSCLC, SCLC, 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](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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, the company has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 thirteenth consecutive year, Roche has been recognised as one of the most sustainable companies in the pharmaceutical industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in

2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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).

All trademarks used or mentioned in this release are protected by law.

## References

[1] Cho BC, Rodriguez-Abreu D, et al. Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC. Presented at the European Society for Medical Oncology (ESMO) Immuno-Oncology Congress 2021; December 8-11. Abstract #LBA2.

[2] Johnston RJ, Comps-Agrar L, et al. Cancer Cell. 2014;26(6):923-937.

[3] National Institutes of Health. U.S. National Library of Medicine. Clinicaltrials.gov (NCT02794571; NCT03563716; NCT04294810; NCT04256421; NCT04513925; NCT04300647; NCT04832854; NCT04619797; NCT04543617; NCT04540211; NCT04665843; NCT03193190; NCT03281369; NCT03869190; NCT04524871; NCT04584112; NCT04045028). [Internet; cited 2021 December]. Available from: <https://clinicaltrials.gov/>.

## Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: [media.relations@roche.com](mailto:media.relations@roche.com)

### Dr. Nicolas Dunant

Phone: +41 61 687 05 17

### Sileia Urech

Phone: +41 79 935 81 48

### Dr. Barbara von Schnurbein

Phone: +41 61 687 89 67

### Karsten Kleine

Phone: +41 61 682 28 31

### Nina Mählitz

Phone: +41 79 327 54 74

### Nathalie Meetz

Phone: +41 61 687 43 05

## Roche Investor Relations

### Dr. Karl Mahler

Phone: +41 61 68-78503

e-mail: [karl.mahler@roche.com](mailto:karl.mahler@roche.com)

### Dr. Bruno Eschli

Phone: +41 61 68-75284

e-mail: [bruno.eschli@roche.com](mailto:bruno.eschli@roche.com)

### Dr. Sabine Borngräber

Phone: +41 61 68-88027

e-mail: [sabine.borngraeber@roche.com](mailto:sabine.borngraeber@roche.com)

### Dr. Gerard Tobin

Phone: +41 61 68-72942

e-mail: [gerard.tobin@roche.com](mailto:gerard.tobin@roche.com)

### Dr. Birgit Masjost

Phone: +41 61 68-84814

e-mail: [birgit.masjost@roche.com](mailto:birgit.masjost@roche.com)



## Investor Relations North America

**Loren Kalm**

Phone: +1 650 225 3217

e-mail: [kalm.loren@gene.com](mailto:kalm.loren@gene.com)