Media Release

CHMP recommends EU approval of Roche's Tecentriq in combination with chemotherapy as an initial treatment of adults with extensive-stage small cell lung cancer

- **Decision based on results from first Phase III study to show a cancer immunotherapy-based combination significantly improved overall survival (OS) and progression-free survival (PFS) in over 20 years**

Basel, 26 July 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for Tecentriq® (atezolizumab) in combination with chemotherapy (carboplatin and etoposide) for the initial (first-line) treatment of adults with extensive-stage small cell lung cancer (ES-SCLC). This decision is based on results from the Phase III IMpower133 study, which showed that Tecentriq in combination with chemotherapy helped people live significantly longer compared with chemotherapy alone (median overall survival [OS]=12.3 vs. 10.3 months; hazard ratio [HR]=0.70, 95% CI: 0.54–0.91; p=0.0069) in the intention-to-treat (ITT) population.[1] The Tecentriq-based combination also significantly reduced the risk of disease worsening or death (progression-free survival, PFS) compared with chemotherapy alone (PFS=5.2 versus 4.3 months; HR=0.77, 95% CI: 0.62–0.96; p=0.017).

This is the first Phase III study to show that a cancer immunotherapy-based combination significantly improved OS and PFS in the first-line treatment of ES-SCLC. Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of Tecentriq.

"We are pleased to receive a positive opinion from the CHMP for our Tecentriq-based lung cancer combination for people living with extensive-stage small cell lung cancer," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The combination of Tecentriq and chemotherapy has the potential to address the high unmet need in this aggressive form of lung cancer where advances in survival have been very difficult to achieve."

Lung cancer is the leading cause of cancer death worldwide[2] and SCLC accounts for approximately 15% of all lung cancer cases, with the majority of patients (70%) diagnosed in the "extensive stage", often meaning a poor prognosis.[3] SCLC is distinguished from other lung cancer subtypes due to its aggressive nature, rapid growth and early development of metastatic disease.[3]

If the European Commission (EC) follows the EMA CHMP's recommendation, this Tecentriq-based combination could represent a potential new treatment option for people across Europe with ES-SCLC. Based on the CHMP positive opinion, a final decision regarding the approval of this Tecentriq-based combination is expected from the EC in the near future.

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About the IMpower133 study
IMpower133 is a Phase III, multicentre, double-blinded, randomised placebo-controlled study evaluating the efficacy and safety of Tecentriq in combination with chemotherapy (carboplatin and etoposide) vs. chemotherapy (carboplatin and etoposide) alone in chemotherapy-naïve adults with ES-SCLC.

The study enrolled 403 people who were randomised equally (1:1) to receive:

- Tecentriq in combination with carboplatin and etoposide (Arm A), or
- Placebo in combination with carboplatin and etoposide (Arm B, control arm)

During the treatment-induction phase, people received treatment on 21-day cycles for four cycles, followed by maintenance with Tecentriq or placebo until progressive disease (PD) as assessed by the investigator using Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1). Treatment could be continued until persistent radiographic PD or symptomatic deterioration was observed.

The co-primary endpoints were PFS as determined by the investigator using RECIST v1.1 and OS in the ITT population.

A summary of the ITT data from the IMpower133 study that support this recommendation is included below:[1]

- Tecentriq in combination with chemotherapy helped people live significantly longer, compared with chemotherapy alone (OS=12.3 vs. 10.3 months; HR=0.70, 95% CI: 0.54-0.91; p=0.0069) in the ITT population.
- The Tecentriq-based combination also significantly reduced the risk of disease worsening or death compared to chemotherapy alone (PFS=5.2 vs. 4.3 months; HR=0.77; 95% CI: 0.62-0.96; p=0.017).
- Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of Tecentriq.
- Serious adverse reactions occurred in 56.6% of people receiving Tecentriq plus chemotherapy compared to 56.1% of people receiving chemotherapy alone. The most common adverse reactions (≥20%) in people receiving Tecentriq plus chemotherapy were low white blood cell count (neutropenia; 23%), anaemia (14%), decreased neutrophil count (14%) and thrombocytopenia (10%).

About SCLC
Lung cancer is the leading cause of cancer death globally.[2] Each year 1.76 million people die as a result of the disease; this translates into more than 4,800 deaths worldwide every day.[2] Lung cancer can be broadly divided into two major types: NSCLC and SCLC, with SCLC accounting for approximately 15% of all lung cancer cases.[3]

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 (CIT) 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 triple-negative breast cancer.

About Roche in cancer immunotherapy
For more than 50 years, Roche has been developing medicines with the goal to redefine treatment in oncology. Today, we're investing more than ever in our effort to bring innovative treatment options that help a person's own immune system fight cancer.

By applying our seminal research in immune tumour profiling within the framework of the Roche-devised cancer immunity cycle, we are accelerating and expanding the transformative benefits with Tecentriq to a greater number of people living with cancer. Our cancer immunotherapy development programme takes a comprehensive approach in pursuing the goal of restoring cancer immunity to improve outcomes for patients.

To learn more about the Roche 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 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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

[1] Horn L et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med. 2018; DOI: 10.1056/NEJMoa1809064.
[2] GLOBOCAN 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. World Health Organization. Available from: http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf. Accessed July 2019.
[3] Paglialunga L et al. Immune checkpoint blockade in small cell lung cancer: is there a light at the end of the tunnel? ESMO Open 2016;1:e000022.

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