FDA approves Roche's Tecentriq in combination with Avastin and chemotherapy for the initial treatment of people with a specific type of metastatic lung cancer

- **Approval based on survival benefit of Tecentriq in combination with Avastin, paclitaxel and carboplatin (chemotherapy) in people with metastatic non-squamous non-small cell lung cancer (NSCLC) with no EGFR or ALK genomic tumour aberrations compared to Avastin plus chemotherapy**

Basel, 7 December 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) approved Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab), paclitaxel and carboplatin (chemotherapy), for the initial (first-line) treatment of people with metastatic non-squamous non-small cell lung cancer (NSCLC) with no EGFR or ALK genomic tumour aberrations.

"This Tecentriq regimen has demonstrated a significant survival benefit in the initial treatment of metastatic non-squamous non-small cell lung cancer," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "Today's approval supports our combination approach for Tecentriq in lung cancer and our vision to develop medicines that improve outcomes for patients with this complex disease."

This approval is based on results from the Phase III IMpower150 study, which showed that Tecentriq in combination with Avastin and chemotherapy helped people live significantly longer, compared to Avastin and chemotherapy (median overall survival [OS]=19.2 versus 14.7 months; hazard ratio [HR]=0.78; 95%, CI: 0.64–0.96; p=0.016) in the intention-to-treat wild-type (ITT–WT) population.[1] The safety profile of the Tecentriq combination was consistent with that observed in previous studies.

Roche is working with the FDA on post-marketing commitments (PMCs) to better understand and characterise the potential effects of Tecentriq-related anti-drug antibodies (ADAs) and neutralising antibodies (NAbs) across all of our studies. An analysis of ADAs in the IMpower150 study showed no impact on the efficacy of Tecentriq.

Tecentriq is also approved by the FDA to treat people with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy, and have progressed on an appropriate FDA-approved targeted therapy if their tumour has EGFR or ALK genetic alterations.

About the IMpower150 study
IMpower150 is a multicentre, open-label, randomised, controlled Phase III study evaluating the efficacy and safety of Tecentriq in combination with chemotherapy (carboplatin and paclitaxel) with or without Avastin in people with stage IV or recurrent metastatic non-squamous NSCLC who had not been treated with chemotherapy for their advanced disease. It enrolled 1,202 people, of whom 1,045 were in the ITT-WT subpopulation, which excluded those people with EGFR and ALK mutations. People were randomised (1:1:1) to receive:

- Tecentriq plus carboplatin and paclitaxel (Arm A), or
- Tecentriq and Avastin plus carboplatin and paclitaxel (Arm B), or
- Avastin plus carboplatin and paclitaxel (Arm C, control arm).

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Investor Relations email: investor.relations@roche.com
Tel. +41 61 68-88880 Fax +41 61 69-10014 www.roche.com

The co-primary endpoints comparing Arms B and C were OS and progression-free survival (PFS), as determined by the investigator using Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) and assessed in the ITT-WT subpopulation. Key secondary endpoints included investigator-assessed PFS, OS and safety in the ITT population.

A summary of the ITT-WT data from the IMpower150 study that support this approval is included below:[1]

- Tecentriq in combination with Avastin and chemotherapy helped people live significantly longer, compared to Avastin and chemotherapy (median OS=19.2 versus 14.7 months; HR=0.78; 95%, CI: 0.64–0.96; p=0.016).
- In addition, Tecentriq in combination with Avastin and chemotherapy reduced risk of disease worsening or death (PFS) by 29%, compared to Avastin and chemotherapy (HR: 0.71; 95%, CI: 0.59–0.85, p=0.0002).
- Tecentriq in combination with Avastin and chemotherapy shrank tumours (overall response rate [ORR]) in 55% of people (95%, CI: 49–60) compared to 42 percent of people (95 percent CI: 37-48) on Avastin and chemotherapy.
    - 4% of people receiving Tecentriq in combination with Avastin and chemotherapy experienced a complete response (CR), and 51% of people experienced a partial response (PR).
- The median duration of response (DoR) for people receiving Tecentriq in combination with Avastin and chemotherapy was 10.8 months (95%, CI: 8.4–13.9) compared to 6.5 months (95 percent CI: 5.6-7.6) for people on Avastin and chemotherapy.
- The most common adverse reactions (≥20%) in people receiving Tecentriq in combination with Avastin and chemotherapy were fatigue and lack of energy (asthenia; 50%), hair loss (alopecia; 48%), nausea (39%), diarrhoea (32%), constipation (30%), decreased appetite (29%), joint pain (arthralgia; 26%), hypertension (25%), and pain from nerve damage (peripheral neuropathy; 24%).

About NSCLC

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 small cell lung cancer. NSCLC is the most prevalent type, accounting for around 85% of all cases.[3] 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.[3]

About the Tecentriq (atezolizumab) and Avastin (bevacizumab) combination

There is a strong scientific rationale to support the use of Tecentriq plus Avastin in combination. The Tecentriq and Avastin regimen may enhance the potential of the immune system to combat first-line advanced NSCLC. Avastin, in addition to its established anti-angiogenic effects, may further enhance Tecentriq's ability to restore anti-cancer immunity, by inhibiting VEGF-related immunosuppression, promoting T cell tumour infiltration and enabling priming and activation of T cell responses against tumour antigens.

About Tecentriq (atezolizumab)

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1 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 has the potential to be used as a foundational combination partner with cancer immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers.

Currently, Roche has nine Phase III lung cancer studies underway, evaluating Tecentriq alone or in combination with other medicines.

Tecentriq is already approved in the European Union, United States and more than 80 countries for people with previously treated metastatic NSCLC and for people with locally advanced or metastatic urothelial cancer (mUC) who are not eligible for cisplatin chemotherapy, or who have had disease progression during or following platinum-containing therapy.

About Avastin (bevacizumab)
Avastin is a prescription-only medicine that is a solution for intravenous infusion. It is a biologic antibody designed to specifically bind to a protein called vascular endothelial growth factor (VEGF) that plays an important role throughout the lifecycle of the tumour to develop and maintain blood vessels, a process known as angiogenesis. Avastin is designed to interfere with the tumour blood supply by directly binding to the VEGF protein to prevent interactions with receptors on blood vessel cells. The tumour blood supply is thought to be critical to a tumour's ability to grow and spread in the body (metastasise).

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. 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.

References

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Roche Investor Relations

Dr. Karl Mahler
Phone: +41 61 68-78503
e-mail: karl.mahler@roche.com

Jon Kaspar Bayard
Phone: +41 61 68-83894
e-mail: jon_kaspar.bayard@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com

Dr. Lisa Tuomi
Phone: +1 650 467 8737
e-mail: tuomi.lisa@gene.com