Roche presents exploratory data from the Phase III IMvigor010 study in early bladder cancer at the ESMO Immuno-Oncology Virtual Congress 2020

- **People with muscle-invasive urothelial cancer (MIUC) who had detectable circulating tumour DNA (ctDNA) were more likely to benefit from treatment with adjuvant (after surgery) Tecentriq monotherapy, compared with those without ctDNA**
- **The goal of current treatment in people with MIUC is to provide early intervention to reduce the risk of the disease recurring or spreading to other parts of the body**
- **Biomarker analysis from the negative IMvigor010 study broadens our knowledge of cancer immunotherapy in the adjuvant bladder cancer space and could help determine who may benefit most from adjuvant treatment and who may not benefit at all**

Basel, 10 December 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today presented an exploratory analysis from the Phase III IMvigor010 study evaluating Tecentriq® (atezolizumab), compared with observation, as an adjuvant (after surgery) monotherapy treatment for people with muscle-invasive urothelial cancer (MIUC) at the European Society for Medical Oncology Immuno-Oncology (ESMO IO) Virtual Congress, 9–12 December 2020.

Data from IMvigor010 show that in people with circulating tumour DNA (ctDNA), a benefit in disease-free survival (DFS) was seen in those receiving Tecentriq when compared with observation (median 5.9 months versus median 4.4 months, hazard ratio [HR]=0.58; 95% CI: 0.43–0.79). Overall survival (OS) at an interim analysis also favoured treatment with Tecentriq in the ctDNA-positive population, with a median of 25.8 months with Tecentriq, compared with 15.8 months for observation (HR=0.59; 95% CI: 0.41–0.86). Although these pre-specified analyses are exploratory and could not be formally tested per the statistical plan in the IMvigor010 study, the data further our understanding of the disease and will inform a new Phase III study in people with ctDNA-positive muscle-invasive bladder cancer.

“Bladder cancer is a complex and often difficult disease to treat, but as we continue to understand its biology, we are gaining greater clarity around new therapeutic avenues,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “By using ctDNA and other biomarkers, we hope to gain insights that enable a more personalised approach to treatment. We are applying these findings to our clinical development programme.”

As presented at the American Society of Clinical Oncology 2020 (ASCO20) Virtual Congress, IMvigor010 did not meet its primary endpoint of DFS compared with observation in people with high-risk MIUC in the intention-to-treat population (19.4 months with Tecentriq versus 16.6 months with observation [HR=0.89; 95% CI: 0.74–1.08; p=0.2446]). In an interim analysis of OS, the median was not reached in either treatment arm (HR=0.85). Safety data for Tecentriq were consistent with the known monotherapy safety profile, and no new safety concerns were identified.

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The goal of current treatment in people with MIUC is to provide early intervention to reduce the risk of the disease recurring or spreading to other parts of the body. As tumours grow, dying cells are replaced by new ones, releasing tumour DNA into the bloodstream. This DNA, known as ctDNA, can be utilised in different ways, including identifying people with minimal residual disease who may benefit the most from adjuvant therapy as well as those for whom adjuvant therapy may not provide benefit. In MIUC, ctDNA is a strong prognostic marker of disease recurrence.[1] More treatment options following surgery are needed because approximately half of people with MIUC will develop a recurrence of their disease within 2 years of surgery,[2] and with no predictive or prognostic biomarkers used in current clinical practice for MIUC,[1,3] there is a need for more personalised treatments for this disease.[1]

Roche has an extensive development programme for Tecentriq, including multiple ongoing and planned Phase III studies, across several types of lung, genitourinary, skin, breast, gastrointestinal, gynaecological, and head and neck cancers. This includes studies evaluating Tecentriq both alone and in combination with other medicines.

These data were presented at the ESMO IO Virtual Congress in the Proffered paper oral session on 10 December 2020, 13:50-14:02 CET.

About the IMvigor010 study
IMvigor010 is a global Phase III, open-label, randomised, controlled study designed to evaluate the efficacy and safety of adjuvant treatment with Tecentriq compared with observation in 809 people with MIUC, who are at high risk of recurrence following resection. The primary endpoint is DFS as assessed by investigator, which is defined as the time from randomisation to invasive urothelial cancer recurrence or death.

Key efficacy results from the exploratory analysis are below:

ctDNA-positive population (n=214, 37% of biomarker evaluable population, n=581)		
	Tecentriq (n=116)	**Observation (n=98)**
Median DFS (months) (95% CI)	5.9 (5.6–11.2)	4.4 (2.9–5.6)
DFS, HR (95% CI)	0.58 (0.43–0.79) p=0.0005	
Median OS at interim analysis (months)	25.8 (20.5–NR)	15.8 (10.5–19.7)

OS, HR (95% CI)	0.59 (0.41–0.86) p=0.0059
ctDNA-negative population (n=367, 63% of biomarker evaluable population, n=581)	
DFS, HR (95% CI)	1.14 (0.81–1.62) p=0.45
OS at interim analysis, HR (95% CI)	1.31 (0.77–2.23) p=0.32
ctDNA-positive and PD-L1-positive population (n=102)	
DFS, HR (95% CI)	0.52 (0.33–0.82)
ctDNA-positive and TMB-high population (n=69)	
DFS, HR (95% CI)	0.34 (0.19–0.60)

Note: p-values from exploratory analyses are provided for descriptive purposes. NR=not reached. TMB=tumour-mutational burden.

About bladder cancer and muscle-invasive urothelial cancer

In 2018, there were over half a million new cases of bladder cancer diagnosed globally, with approximately 200,000 deaths from the disease.[4] Urothelial cancer is the most common type of bladder cancer, accounting for about 90–95% of all cases.[5] MIUC is a type of urothelial cancer that has spread into the muscle of the bladder, ureter or renal pelvis.[6] Approximately 25% of new cases of bladder cancer are diagnosed with muscle-invasive disease,[7] which is associated with a poorer prognosis than non-MIUC.[6]

Roche will run a new Phase III study in people with ctDNA-positive muscle-invasive bladder cancer. More information is available here.

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 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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