Phase III IMmotion151 study showed Roche’s TECENTRIQ® (atezolizumab) and Avastin® (bevacizumab) reduced the risk of disease worsening or death by 26 percent in certain people with advanced kidney cancer

- TECENTRIQ and Avastin met co-primary endpoint of improvement in investigator-assessed progression-free survival (PFS) compared with sunitinib for people whose disease expressed PD-L1
- IMmotion151 is the second Phase III study to show positive PFS results for a treatment regimen including TECENTRIQ plus Avastin
- Data will be discussed with global health authorities, including the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results from the positive Phase III IMmotion151 study of TECENTRIQ® (atezolizumab) and Avastin® (bevacizumab) as a first-line treatment for advanced or metastatic renal cell carcinoma (mRCC). The study met its co-primary endpoint of investigator-assessed progression-free survival (PFS) in people whose disease expressed the PD-L1 (programmed death-ligand 1: expression ≥1%) protein. Those who received TECENTRIQ plus Avastin had a 26-percent reduced risk of disease worsening or death (PFS) compared to people treated with sunitinib (median PFS [mPFS]: 11.2 vs. 7.7 months; HR=0.74; 95% CI 0.57, 0.96; p=0.02). Initial observations from the co-primary endpoint of overall survival (OS) in the overall study population (intention-to-treat, ITT) were encouraging, but are still immature. Safety for the TECENTRIQ and Avastin combination appeared consistent with the known safety profile of the individual medicines and what was previously reported in the Phase II IMmotion150 study. No new safety signals were identified with the combination. The rate of treatment-related Grade 3-4 adverse events was lower with the TECENTRIQ and Avastin combination (40%) than with sunitinib alone (54%) in all treated patients.

Observations of a pre-specified subgroup analysis of the TECENTRIQ and Avastin combination indicated that, in people whose disease expressed PD-L1, a numerical difference in PFS favouring TECENTRIQ was seen across all patient risk factor groups (favorable, intermediate and poor) compared to sunitinib.
In addition, a pre-defined analysis of patient-reported outcomes (PRO) revealed that the combination of TECENTRIQ and Avastin markedly delayed the time to a worsening of disease symptoms that interfere with day-to-day life compared to sunitinib, (median time to deterioration: 11.3 vs 4.3 months; HR=0.56; 95% CI: 0.46, 0.68) in the ITT population. Due to the study design, pre-defined subgroup analyses and pre-defined PRO analyses were not assessed for statistical significance and are descriptive only.

"This is the second positive Phase III study that includes TECENTRIQ and Avastin as part of a treatment regimen, providing further evidence to support the potential of this unique combination," said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. "We are encouraged that initial treatment with TECENTRIQ and Avastin significantly reduced the risk of disease worsening or death in people with advanced kidney cancer, while also providing more time before disease symptoms interfere with day-to-day life compared with sunitinib, a current standard of care. We look forward to discussing these results with regulatory authorities worldwide."

The late-breaking IMmotion151 data will be presented at the 2018 Genitourinary Cancers Symposium on Saturday, February 10 at 13:00-14:00 Pacific Time (PT) (Abstract #578), and were highlighted as part of the conference's official press programme.

**About the IMmotion151 study**
IMmotion151 is a Phase III multicentre, randomised, open-label study to evaluate the efficacy and safety of TECENTRIQ and Avastin versus sunitinib in people with inoperable, locally advanced or metastatic renal cell carcinoma (RCC) who have not received prior systemic active or experimental therapy. It enrolled 915 people globally who were randomised 1:1 to receive TECENTRIQ and Avastin, or sunitinib alone.

People in the TECENTRIQ and Avastin arm received TECENTRIQ at a fixed dose of 1200 milligrams (mg) and Avastin at a dose of 15 milligrams per kilogram (mg/kg) via intravenous (IV) infusion every 3 weeks until loss of clinical benefit or unacceptable toxicity. People in the sunitinib arm received sunitinib 50 mg orally, once daily for 4 weeks followed by 2 weeks rest until loss of clinical benefit or unacceptable toxicity.
The co-primary endpoints were PFS, as determined by the investigator using Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) in people whose tumours expressed PD-L1 (expression ≥1 percent on immune cells [IC]), and OS in the overall study population (intention-to-treat, ITT). PD-L1 expression was prospectively assessed using an immunohistochemistry (IHC) test (SP142) developed by Roche Tissue Diagnostics. Secondary endpoints included OS in people whose tumours expressed PD-L1, PFS as determined by an Independent Review Facility (IRF) according to RECIST v1.1, investigator-assessed objective response rate (ORR) and median duration of response (mDOR), change from baseline in symptom interference and symptom severity as determined by M.D. Anderson Symptom Inventory (MDASI), and change from baseline in health-related quality of life as determined by European Quality of Life 5-Dimension (EQ-5D) Scores.

Stratification factors included the Memorial Sloan-Kettering Cancer Center (Motzer) prognostic scoring system, which predicts for OS based upon an individual’s baseline clinical and laboratory characteristics. Depending on the presence of one or several of five variables (risk factors), people are classified in one of the three risk groups: "Favourable" with 0 risk factors, "Intermediate" with 1-2 risk factors and "Poor" with ≥ 3 risk factors.

<table>
<thead>
<tr>
<th>Phase III IMmotion151 Study Results: Investigator Assessed</th>
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<tbody>
<tr>
<td>Population</td>
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<tr>
<td>Treatment Arm</td>
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<tr>
<td>PFS</td>
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<tr>
<td>mPFS (95% CI)</td>
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<tr>
<td>Stratified HR (95% CI)</td>
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<tr>
<td>ORR</td>
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<tr>
<td>ORR (95% CI)</td>
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<tr>
<td>mDOR</td>
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## Phase III IMmotion151 Study Results: IRF-Assessed

<table>
<thead>
<tr>
<th>Population</th>
<th>PD-L1+ (programmed death-ligand 1: Expression ≥1% on IC)</th>
<th>ITT (intent-to-treat)</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>n = 362</td>
<td>n = 915</td>
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<tr>
<th>PFS</th>
<th>Secondary</th>
<th>Secondary</th>
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<tbody>
<tr>
<td>mPFS</td>
<td>7.2 months (6.1, 11.1)</td>
<td>8.9 months (6.9, 12.5)</td>
</tr>
<tr>
<td>Stratified HR (95% CI)</td>
<td>0.93 (0.72, 1.21)</td>
<td>0.88 (0.74, 1.04)</td>
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### Initial observations from the co-primary endpoint of overall survival:

**Descriptive Only**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>TECENTRIQ &amp; Avastin</th>
<th>Sunitinib</th>
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<td>ITT (intent-to-treat)</td>
<td>n = 915</td>
</tr>
<tr>
<td>Median OS</td>
<td>Not reached</td>
<td>23.3 (21.3, NR)</td>
<td>Not reached</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.68 (0.46, 1.00)</td>
<td>0.81 (0.63, 1.03)</td>
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</tbody>
</table>

Event/patient ratio: PD-L1+, TECENTRIQ and Avastin, 25% and sunitinib, 35%; ITT, TECENTRIQ and Avastin, 27% and sunitinib, 31%. Assessed by investigator; minimum follow-up, 12 mo. Median of follow-up, 15 months.

NE, not estimable aData assessed by independent review facility

*Difference in IRF-assessed PFS HR driven by IC1/2/3 population (IRF-assessed PFS HR in IC0 was 0.84 compared to 0.93 for Investigator-assessed PFS in IC0) despite study participants being blinded to PD-L1 status. Totality of data support the Investigator assessment of PFS. Preparations for further analyses of IRF-assessed PFS are ongoing.

### About RCC

Kidney cancer remains one of the most common cancers in the world, accounting for over 140,000 deaths worldwide each year,¹ with renal cell carcinoma (RCC) accounting for approximately 90% of all cases.² Over 300,000 people are diagnosed with RCC every year and currently only about 1 in 10 people are alive beyond 5 years following diagnosis of metastatic disease.³
RCC occurs when abnormal cells develop in the tissue of the kidneys, specifically in the small tubes (also known as tubules) where our blood is filtered. Typically, RCC is a single tumour in one kidney but, in rare cases, there can be multiple tumours, which can occur in one or both kidneys.

Despite recent progress in the field of kidney cancer, treatment options for people with the disease remains limited.

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.

TECENTRIQ is already approved in the European Union, United States and more than 50 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) in RCC
Avastin (bevacizumab) is an anti-VEGF inhibitor. VEGF (vascular endothelial growth factor) is a protein that stimulates the formation and maintenance of blood vessels and has been shown to play a key role in the development of RCC.

RCC tumours are highly vascularised, meaning they have many blood vessels and also exhibit a high concentration of VEGF. There is, therefore a strong rationale for medicines such as Avastin that block the VEGF pathway. Avastin is the only currently available treatment for patients with mRCC that directly inhibits VEGF.
There is a strong scientific rationale to support further investigation of TECENTRIQ and Avastin in combination. The TECENTRIQ and Avastin regimen may enhance the potential of the immune system to combat first-line advanced NSCLC and mRCC. 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 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row 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. All trademarks used or mentioned in this release are protected by law.

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References