Roche presents positive results from pivotal study of investigational immunotherapy atezolizumab in specific type of advanced bladder cancer at 2015 European Cancer Congress

- Results show PD-L1 expression correlated with response to atezolizumab
- Data will be submitted to global health authorities, including the US Food and Drug Administration (FDA)

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced early results from a pivotal phase II study, IMvigor 210, of the investigational cancer immunotherapy atezolizumab (anti-PDL1; MPDL3280A) in people with locally advanced or metastatic urothelial carcinoma (mUC). The study showed that atezolizumab shrank tumours (objective response rate, ORR) in 27 percent of people with mUC whose disease had medium and high levels of PD-L1 expression and worsened after initial treatment. Ninety-two percent of people who responded to atezolizumab continued to respond when the results were assessed. Median duration of response was not yet reached. Adverse events were consistent with those observed in previous studies.

“These results may represent the first major treatment advancement in advanced bladder cancer in nearly 30 years,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. “We are encouraged that responses to atezolizumab were ongoing in the large majority of people when the study results were assessed.”

Roche is planning to submit these data to global health authorities and to the FDA under a Breakthrough Therapy Designation for the treatment of people whose metastatic bladder cancer expresses PD-L1. This designation is designed to expedite the development and review of medicines intended to treat serious diseases that may demonstrate substantial improvement over existing therapies.

About the IMvigor 210 study
These final results from cohort 2 of this study (minimum of 24 weeks’ follow-up) will be presented in an oral
Atezolizumab in patients (pts) with locally-advanced or metastatic urothelial carcinoma (mUC): Results from a pivotal multicenter phase II study (IMvigor 210).

IMvigor 210 is an open-label, multicentre, single-arm phase II study that evaluated the safety and efficacy of atezolizumab in people with locally advanced or mUC, regardless of PD-L1 expression. People in the study were enrolled into one of two cohorts. Cohort 1 consisted of people who had received no prior therapies for locally advanced or mUC, but who were ineligible for first-line cisplatin-based therapy; results for this cohort are not yet mature. Cohort 2, for which results were announced today, included people whose disease had progressed during or following previous treatment with a platinum-based chemotherapy regimen. People received a 1200-mg intravenous dose of atezolizumab on day one of 21-day cycles until progressive disease (Cohort 1) or loss of clinical benefit (Cohort 2).

The primary endpoint of the study was ORR. Secondary endpoints included duration of response (DoR), overall survival (OS), progression-free survival (PFS) and safety. People were selected by histology, prior lines of therapy and PD-L1 expression on tumour-infiltrating immune cells (IC), using an investigational immunohistochemistry (IHC) test that is being developed by Roche Diagnostics.

<table>
<thead>
<tr>
<th>IMvigor 210 cohort 2 study results</th>
<th>IC 2/3 (medium and high)</th>
<th>IC123 (any expression)</th>
<th>Intent-To-Treat (ITT; all patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Group measuring expression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Patients</td>
<td>100</td>
<td>208</td>
<td>311</td>
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<tr>
<td>Objective Response Rate* (Co-Primary Endpoints)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ORR ( IRF \text{ assessed ORR per RECIST v.1.1 (95% CI)} )</td>
<td>27% (19%, 37%)</td>
<td>18% (13%, 24%)</td>
<td>15% (11%, 20%)</td>
</tr>
<tr>
<td>( p )-value</td>
<td>( p&lt;0.0001 )</td>
<td>( p=0.0004 )</td>
<td>( p=0.0058 )</td>
</tr>
<tr>
<td>Investigator-assessed ORR per modified RECIST (95% CI)</td>
<td>26% (18%, 36%)</td>
<td>21% (15%, 27%)</td>
<td>18% (14%, 23%)</td>
</tr>
<tr>
<td>p-value</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
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<tr>
<td><strong>Median DoR (months)</strong> (95% CI)</td>
<td>Not reached (6.0, NE)</td>
<td></td>
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<tr>
<td><strong>Progression-Free Survival (IRF-Assessed; RECIST v1.1) (Secondary Endpoint)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Median PFS (months) (95% CI)</td>
<td>2.1 (2.1, 4.1)</td>
<td>2.1 (2.1, 2.1)</td>
<td>2.1 (2.1, 2.1)</td>
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<tr>
<td><strong>Overall Survival (Secondary Endpoint)</strong></td>
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<tr>
<td>Median OS (months) (95% CI)</td>
<td>NR (6.7, NE)</td>
<td>8.0 (6.7, NE)</td>
<td>7.9 (6.7, NE)</td>
</tr>
</tbody>
</table>

**Safety (n=311)**

- Adverse events were consistent with those observed in previous studies and there were no treatment-related deaths.
- Fifteen percent of people experienced Grade 3-4 treatment related AEs and 4% of people experienced a Grade 3-4, immune related AE.
- The most common Grade 3-4 treatment related AE’s were fatigue (2%), decreased appetite, fever (pyrexia), pain (arthralgia), shortness of breath (dyspnea), anemia, enzymes in the blood (ALT increase), inflammation of the lung wall (pneumonitis), hypertension and hypotension (all 1%).

*ORR was assessed by central review (RECIST v1.1) and by investigators using modified RECIST (co-primary endpoints); IC: tumor-infiltrating immune cell; CI: confidence interval; NR: not reached; NE: not estimable; DoR: duration of response

In addition to IMvigor 210, Roche has an ongoing randomised phase III study, IMvigor 211, comparing atezolizumab with standard-of-care chemotherapy in people who have mUC that worsened after initial treatment. All studies include the evaluation of a companion test developed by Roche Diagnostics to determine PD-L1 status.

**About metastatic urothelial cancer**

Metastatic urothelial cancer is associated with a poor prognosis and limited treatment options. It is a disease that has seen no major advancements for nearly 30 years. Urothelial cancer is the ninth most common cancer worldwide, with 430,000 new cases diagnosed in 2012, and it results in approximately 145,000 deaths globally each year. Men are three times more likely to suffer from urothelial cancer compared with women, and it is also three times more common in developed countries than in less developed countries.

**About atezolizumab**

Atezolizumab (anti-PDL1; MPDL3280A) is an investigational monoclonal antibody designed to interfere
with a protein called PD-L1. Atezolizumab is designed to target PD-L1 expressed on tumour cells and
tumour-infiltrating immune cells, preventing it from binding to PD-1 and B7.1 on the surface of T cells. By
inhibiting PD-L1, atezolizumab may enable the activation of T cells.

All studies of atezolizumab include the evaluation of an investigational IHC test that uses the antibody SP142
to measure PD-L1 expression on both tumour cells and tumour-infiltrating immune cells. The goal of PD-L1
as a biomarker is to identify those people most likely to benefit when treated with atezolizumab alone, and to
determine which people may benefit most from a combination of atezolizumab and another medicine. There
are 11 ongoing or planned phase III studies of atezolizumab across certain kinds of lung, kidney, breast and
bladder cancer.

About Roche in personalised cancer immunotherapy
For more than 30 years, Roche has been developing medicines with the goal to redefine treatment in
oncology. Today, we’re investing more than ever to bring personalised cancer immunotherapy (PCI) to
people with cancer. The goal of PCI is to provide each person with a treatment tailored to harness his or her
own immune system to fight cancer. Roche is studying more than 20 investigational medicines, seven of
which are in clinical trials. In every study we are evaluating biomarkers to identify which people may be
appropriate candidates for our medicines.

About Roche
Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in
pharmaceuticals and diagnostics. Roche is the world’s largest biotechnology company, with truly differentiated
medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world
leader in in vitro diagnostics and tissue-based cancer diagnostics, and a front runner in diabetes management.
Roche’s personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible
improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making
important contributions to global health for more than a century. Twenty-nine medicines developed by Roche are
included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics,
antimalarials and chemotherapy.

In 2014 the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss Francs in R&D and posted
sales of 47.5 billion Swiss Francs. 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
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www.roche.com/research_and_development/what_we_are_working_on/oncology.htm

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