Media Release

Roche's Tecentriq in combination with Abraxane improves outcomes as an initial treatment for people with PD-L1-positive metastatic triple-negative breast cancer

- **Tecentriq combination first immunotherapy regimen to demonstrate positive Phase III results in breast cancer**
- **Tecentriq and *nab*-paclitaxel significantly reduced the risk of disease worsening or death in both the intention-to-treat and PD-L1-positive populations**
- **Clinically meaningful overall survival improvement in the PD-L1-positive population at this interim analysis**
- **Data are being presented at the European Society for Medical Oncology (ESMO) 2018 Congress, featured in the press programme and simultaneously published in the *New England Journal of Medicine* on 20 October 2018**

Basel, 20 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the Phase III IMpassion130 study of Tecentriq® (atezolizumab) plus chemotherapy (Abraxane® [albumin-bound paclitaxel; *nab*-paclitaxel]) for the initial (first-line) treatment of unresectable locally advanced or metastatic triple-negative breast cancer (TNBC). The Tecentriq and chemotherapy combination significantly reduced the risk of disease worsening or death (progression-free survival; PFS) compared with chemotherapy alone in all randomised patients (intention-to-treat [ITT]) (median PFS=7.2 vs. 5.5 months; hazard ratio [HR]=0.80, 95% CI: 0.69-0.92, p=0.0025) and the PD-L1-positive population (median PFS=7.5 vs. 5.0 months; HR=0.62, 95% CI: 0.49-0.78, p<0.0001), a subgroup determined by PD-L1 biomarker testing. At this interim analysis, statistical significance was not met for overall survival (OS) in the ITT population (median OS=21.3 vs 17.6 months; HR=0.84, 95% CI: 0.69-1.02, p=0.0840), but showed a clinically meaningful 9.5-month OS improvement in the PD-L1-positive population (median OS=25.0 vs 15.5 months; HR=0.62, 95% CI: 0.45-0.86). Due to the hierarchical statistical design, results in the PD-L1-positive population were not formally tested. Follow-up will continue until the next planned analysis. Safety in the Tecentriq plus *nab*-paclitaxel arm appeared consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination.

"These important results in people with metastatic triple-negative breast cancer whose disease expresses the PD-L1 protein are highly encouraging and represent a significant step forward in the treatment of this challenging disease," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We have shared the IMpassion130 results with global health authorities with the hope of bringing this Tecentriq combination to people with PD-L1-positive, metastatic triple-negative breast cancer as soon as possible."

These data are being presented today at the European Society for Medical Oncology (ESMO) 2018 Congress Presidential Symposium at 16:30 – 16.45 pm CEST (abstract LBA1_PR) and will also be featured in the official ESMO press programme at 08:15 –09:00 am CEST. These results will simultaneously be published in the *New England Journal of Medicine*.

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Currently, Roche has seven ongoing Phase III studies investigating Tecentriq in TNBC, including early and advanced stages of the disease.

About the IMpassion130 study

The IMpassion130 study is a Phase III, multicentre, randomised, double-blind study evaluating the efficacy, safety, and pharmacokinetics of Tecentriq plus *nab*-paclitaxel compared with placebo plus *nab*-paclitaxel in people with unresectable locally advanced or metastatic TNBC who have not received prior systemic therapy for metastatic breast cancer (mBC). The study enrolled 902 people who were randomised equally (1:1).
The co-primary endpoints are PFS per investigator assessment (RECIST 1.1) and OS. PFS and OS were assessed in all randomised patients (ITT) and in the PD-L1-positive population. Secondary endpoints include objective response rate (ORR), duration of response and time to deterioration in Global Health Status/Health-Related Quality of Life.

A summary of the key study results is included below:

	PD-L1-positive population (programmed death-ligand 1 expression ≥1% on IC)		**ITT population (intention-to-treat)**	
	Tecentriq + *nab*-paclitaxel n=185	**Placebo + *nab*-paclitaxel n=184**	**Tecentriq + *nab*-paclitaxel n=451**	**Placebo + *nab*-paclitaxel n=451**
Number of patients	369 (40.9%)		902	
PFS (co-primary endpoint)				
Median (months) (95% CI)	7.5 (6.7, 9.2)	5.0 (3.8, 5.6)	7.2 (5.6, 7.5)	5.5 (5.3, 5.6)
Stratified HR (95% CI)	0.62 (0.49,0.78)		0.80 (0.69,0.92)	
Stratified p-value	<0.0001		0.0025	
OS (co-primary endpoint)				
Median (months) (95% CI)	25.0 (22.6, NE)	15.5 (13.1, 19.4)	21.3 (17.3, 23.4)	17.6 (15.9, 20.0)
Stratified HR (95% CI)	0.62 (0.45,0.86)		0.84 (0.69,1.02)	
Stratified p-value	Results were not formally tested		0.0840	
ORR (secondary endpoint)				
Responders	59%	43%	56%	46%
95% CI	51%, 66%	35%, 50%	51%, 61%	41%, 51%
Stratified p-value	0.0016 Not significant (α=0.001)		0.0021 Not significant (α=0.001)	

Adverse events
The nature and incidence of severe adverse events (SAEs) and Grade 3-4 adverse events (AEs) were consistent with the known safety profile of the individual study drugs or the underlying disease. • SAEs were reported in 23% of people receiving Tecentriq plus *nab*-paclitaxel compared to 18% of people receiving chemotherapy alone. SAEs occurring in 1% or more of people receiving Tecentriq plus *nab*-paclitaxel were pneumonia (2%), urinary tract infection (1%), difficulty breathing (dyspnea, 1%) and fever (pyrexia, 1%). • Grade 3-4 AEs were reported in 49% of people receiving Tecentriq plus *nab*-paclitaxel compared to 42% of people receiving chemotherapy alone. The most common Grade 3-4 AEs in people receiving Tecentriq plus *nab*-paclitaxel were an abnormal low count of a certain type of white blood cell (neutropenia, 8%); decreased neutrophil count (5%); numbness, tingling or pain in the hands or feet (peripheral neuropathy, 6%); fatigue (4%); and decrease in red blood cells (anaemia, 3%). Peripheral neuropathy was the only Grade 3-4 AE reported with a 2% or higher incidence in people receiving Tecentriq plus *nab*-paclitaxel compared to people receiving chemotherapy alone (6% vs. 3%).

About triple-negative breast cancer

Breast cancer is the most common cancer among women with more than 2 million diagnosed worldwide each year.[1] TNBC represents approximately 15% of all breast cancers and is more common in women under the age of 50, compared with other forms of breast cancer.[2; 3] It is defined by the lack of expression and/or amplification of the targetable receptors for oestrogen, progesterone and HER2 amplification.[4;5] Patients with metastatic TNBC generally experience rapid progression and shorter OS compared to other subtypes of breast cancer.[6]

About Tecentriq

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 80 countries for people with previously treated metastatic non-small cell lung cancer (NSCLC) and for certain types of untreated or previously treated metastatic urothelial carcinoma (mUC).

Abraxane is a registered trademark of Abraxis Bioscience, LLC, a wholly owned subsidiary of Celgene Corporation.

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.

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