Media Release

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Roche's TECENTRIQ (atezolizumab) shows significant survival advantage compared to chemotherapy regardless of PD-L1 status in a specific type of lung cancer in Phase III study

- **TECENTRIQ provides survival benefit over chemotherapy, even in people with low or no observed levels of PD-L1 expression**
- **Data included overall survival results for squamous and non-squamous disease types**
- **Full results will be presented at European Society of Medical Oncology Presidential Symposium**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced data from the positive, pivotal Phase III OAK study of TECENTRIQ® (atezolizumab) at the European Society of Medical Oncology (ESMO) 2016 Annual Meeting in Copenhagen, Denmark. The study showed TECENTRIQ helped people live a median of 13.8 months, 4.2 months longer than those treated with docetaxel chemotherapy (median overall survival [mOS]: 13.8 vs 9.6months; HR=0.73, 95% CI: 0.62-0.87), regardless of their levels of programmed death-ligand 1 (PD-L1) expression. The OAK study evaluated people with NSCLC whose disease had progressed on or after treatment with one or more platinum-based chemotherapy (second-line and third-line. The study enrolled people regardless of their PD-L1 status and included both squamous and non-squamous disease types. Adverse events (AEs) were consistent with those observed in previous TECENTRIQ studies.

"TECENTRIQ is the first and only anti PD-L1 cancer immunotherapy to help patients with metastatic NSCLC live significantly longer than when treated with chemotherapy regardless of their PD-L1 expression level or their disease histology," said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "Even people whose disease had low or no observed PD-L1 expression still showed a significant benefit from the medicine."

The FDA granted Breakthrough Therapy Designation (BTD) for TECENTRIQ for the treatment of people with PD-L1 positive non-small cell lung cancer (NSCLC) whose disease has progressed during or after platinum-based chemotherapy (and appropriate targeted therapy for those with an EGFR mutation-positive or ALK-positive tumour). Roche's Biologics Licence Application (BLA) for NSCLC was granted Priority

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Review with an action date of 19 October 2016.

Roche has eight Phase III lung studies underway evaluating TECENTRIQ alone or in combination with other treatments in patients with early and advanced stages of lung cancer.

Full results from the OAK study will be presented in the Presidential Symposium in a presentation by Fabrice Barlesi, Assistance Publique Hôpitaux de Marseille, Marseille, France (abstract #LBA44) on Sunday, Oct. 9, 4:25 p.m. Central European Time (CET).

Primary analysis from OAK, a randomised phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC

About the OAK study

OAK is a global, multicentre, open-label, randomised, controlled Phase III study that evaluated the efficacy and safety of TECENTRIQ compared with docetaxel in 1,225 people with locally advanced or metastatic NSCLC whose disease had progressed following previous treatment with platinum-containing chemotherapy, with the primary analysis consisting of the first 850 randomised patients. Approximately one-quarter of patients had squamous disease (26 percent). Patients were randomised (1:1) to receive either TECENTRIQ administered intravenously at 1200 mg every 3 weeks or docetaxel administered intravenously at 75 mg/m2 every 3 weeks until unacceptable toxicity or disease progression. The co-primary endpoints were overall survival (OS) in all randomised patients (ITT population) and in a PD-L1-selected subgroup in the primary analysis population. A summary of the OAK results is included below.

Data Table

Overall survival results						
Study group	**ITT** *(the first 850 randomised patients)*		**TC 1/2/3 or IC 1/2/3** *(PD-L1 expression on ≥ 1% on TC or IC)*		**TC 0 or IC 0** *(PD-L1 expression of <1% on TC and IC)*	
Treatment arm *T=TECENTRIQ: D=Docetaxel*	**T**	**D**	**T**	**D**	**T**	**D**
N=	425	425	241	222	180	199
Median OS (months)	13.8	9.6	15.7	10.3	12.6	8.9
HR* (95% CI)	HR 0.73, 95% CI: 0.62 - 0.87		HR 0.74, 95% CI: 0.58 - 0.93;		HR 0.75, 95% CI: 0.59-0.96	
P value**	*P* = .0003		*P* = .0102		P=.0215	

Overall Survival by Histology				
Histology	**Non-squamous**		**Squamous**	
Treatment arm *T=TECENTRIQ: D=Docetaxel*	**T**	**D**	**T**	**D**
N=	313	315	112	110
Media OS (Months)	15.6	11.2	8.9	7.7
Unstratified HR (95% CI)	HR=0.73, 95% CI: 0.60–0.89		HR=0.73, 95% CI: 0.54–0.98	

Safety-evaluable population N=1187

- Adverse events (AEs) were consistent with those observed in previous studies of TECENTRIQ.
- Fewer people receiving TECENTRIQ experienced treatment-related Grade 3-4 AEs compared to docetaxel (15% vs 43%).
- AEs occurring more frequently (5% or more) for TECENTRIQ were musculoskeletal pain (11% for TECENTRIQ vs. 4% for docetaxel) and pruritus (8% for TECENTRIQ vs. 3% for docetaxel)
- There were no deaths related to TECENTRIQ and 1 related to docetaxel

The demographics and baseline characteristics were balanced between two arms. Patients had a median age of 64 year and 61% were male. 25% had 2 prior lines of therapies, and 18% never smoked Baseline ECOG performance status was 0 (37%) or 1 (63%). About 17% of people in the docetaxel arm received immunotherapy as the subsequent subsequent therapy.

*Unstratified for the TC0 and IC0 subgroup, stratified for others.

**Stratified log-rank p value.

About non-small cell lung cancer

Lung cancer is the leading cause of cancer death globally. Each year 1.59 million people die as a result of the disease; this translates into more than 4,350 deaths worldwide every day. 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.

About TECENTRIQ (atezolizumab)

TECENTRIQ is a monoclonal antibody designed to target and bind to a protein called PD-L1 (programmed death-ligand 1), which is expressed on tumour cells and tumour-infiltrating immune cells. PD-L1 interacts with PD-1 and B7.1, both found on the surface of T cells, causing inhibition of T cells. By blocking this interaction, TECENTRIQ may enable the activation of T cells, restoring their ability to effectively detect and attack tumour cells.

About personalised cancer immunotherapy (PCI)

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.

The aim of personalised cancer immunotherapy (PCI) is to provide patients and physicians with treatment options tailored to the specific immune biology associated with a person's individual tumour. The purpose is to inform treatment strategies which provide the greatest number of people with a chance for transformative benefit. In the case of TECENTRIQ, the goal of PD-L1 as a biomarker is to explore PD-L1 expression on tumour cells and tumour infiltrating immune cells and how that correlates with clinical benefit either as a monotherapy or in combination, and across a broad range of tumour types. The Roche PCI research and development programme comprises more than 20 investigational candidates, ten of which are in clinical trials.

PCI is an essential component of how Roche delivers on the broader commitment to personalised healthcare. 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.

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. 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.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. 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 cancer medicines. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry eight years in a row by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2015 employed more than 91,700 people worldwide. In 2015, Roche invested CHF 9.3 billion in R&D and posted sales of CHF 48.1 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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