

Basel, 8 September 2017

## **Roche announces progress in biomarker science in cancer immunotherapy at the European Society for Medical Oncology Congress**

- **First data on new blood-based assay for measuring tumour mutational burden**
- **Two prospective studies underway to assess the potential of tumour mutational burden to predict response to certain cancer immunotherapies**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the first data on a novel blood-based assay, co-developed with Foundation Medicine (NASDAQ: FMI), will be presented during the European Society for Medical Oncology (ESMO) Congress from 8-12 September 2017 in Madrid, Spain.<sup>1</sup> These data have been generated as part of a broad, ongoing effort to advance the personalisation of cancer immunotherapy by delivering treatment options tailored to the specific immune biology associated with a person's tumour. In pursuit of this goal, Roche is currently developing 20 cancer immunotherapy medicines across 9 types of cancer and in more than 50 combinations with other medicines.<sup>2</sup> Roche is committed to advancing the science of cancer immunotherapy and exploring multiple biomarker approaches including PD-L1 immunohistochemistry, tumour gene expression, RNA sequencing and tumour mutational burden (TMB).<sup>2</sup>

New data presented at ESMO demonstrates for the first time that a blood-based TMB test (bTMB) can measure TMB with a high degree of precision and accuracy.<sup>1</sup> TMB is a quantitative clinical marker that measures the number of mutations within a tumour genome. TMB has been found to be an indicator of likelihood of progression-free survival (PFS) benefit from immunotherapies when used alone (monotherapy) in patients with non-small cell lung cancer (NSCLC).<sup>3, 4</sup> Until now, TMB could only be measured using a tumour biopsy. By using this blood-based testing approach, it may be possible to extend TMB testing to more patients, including those who are unable to undergo an invasive tumour biopsy, or where tissue is unavailable or of insufficient size to evaluate.

“Pursuing next generation biomarker development is a critical component of our cancer immunotherapy strategy,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Biomarkers will not only improve our understanding of immune biology but will ultimately help match our therapies and combinations to the people most likely to benefit. This blood-based TMB assay is one example of how we and our partners are advancing the science toward personalisation of cancer therapy.”

The bTMB biomarker study being presented at ESMO was conducted using 794 plasma samples from the pivotal phase II POPLAR and phase III OAK Tecentriq® studies. The purpose of the analysis was to collect initial, retrospective evidence of an association between bTMB and Tecentriq activity. These early data will inform ongoing and future prospective research to better understand the role of both TMB and bTMB as it relates to treatment with cancer immunotherapy.<sup>1</sup>

Two prospective studies in patients receiving first-line treatment for NSCLC are underway, which aim to clinically evaluate and prospectively validate our novel blood-based diagnostic assay and assess the efficacy and safety Tecentriq and/or Alecensa® (alectinib) for patients with NSCLC.<sup>5</sup>

- The B-FIRST study is a single-arm study evaluating the safety and efficacy of Tecentriq in first-line NSCLC and will evaluate the association between bTMB and efficacy in biomarker-unselected patients through prospective collection of blood samples that will be retrospectively tested.<sup>5</sup>
- BFAST is a phase II/III global, multicentre, open-label, umbrella trial designed to evaluate the safety and efficacy of Tecentriq or Alecensa in patients with unresectable, advanced or metastatic NSCLC. Treatment selection of Tecentriq or Alecensa is based on the presence of a positive bTMB score or oncogenic somatic mutations, respectively.<sup>5</sup>

Tecentriq is currently approved in the United States for certain types of lung and bladder cancers regardless of PD-L1 expression levels. Beyond cancer immunotherapy, Roche has an extensive oncology pipeline with ongoing studies in collaboration with Foundation Medicine for molecules such as the oral AKT inhibitor ipatasertib, Alecensa, and Avastin®.<sup>2</sup>

## Overview of Roche bTMB presentations at ESMO 2017

Abstract title	Abstract number
Blood-based biomarkers for cancer immunotherapy: Tumour mutational burden in blood (bTMB) is associated with improved atezolizumab (atezo) efficacy in 2L+ NSCLC	Abstract #1295O (oral) Friday, 8 September, 4.00pm – 5.30pm CET
Blood first line ready screening trial (B-FIRST) and blood first assay screening trial (BFAST) enable clinical development of novel blood-based biomarker assays for tumour mutational burden (TMB) and somatic mutations in 1L advanced or metastatic NSCLC.	Abstract #1383TiP (poster), Saturday, 9 September, 1.15pm – 2.15pm CET
Analytic validation of a next generation sequencing assay to identify tumour mutational burden from blood (bTMB) to support investigation of an anti-PD-L1 agent, atezolizumab, in a first line non-small cell lung cancer trial (BFAST)	Abstract #102P (poster) Monday, 11 September, 1.15pm – 2.15pm CET

### About the retrospective POPLAR and OAK analyses

The bTMB assay was used to analyse a total of 794 plasma samples from the phase II POPLAR and phase III OAK clinical trials and found that patients with NSCLC and high bTMB experienced longer progression-free survival when treated with Tecentriq.

POPLAR is a multi-centre, international, randomised, open-label, controlled phase II study, that evaluated the safety and efficacy of Tecentriq compared to docetaxel in patients with locally advanced or metastatic NSCLC who progressed during or following a platinum-containing regimen, regardless of PD-L1 expression. OAK is a global, multi-centre, randomised, open-label, controlled phase III study that evaluated the efficacy and safety of Tecentriq compared with docetaxel. In these retrospective analyses, plasma samples from OAK and POPLAR were analysed with the blood-based TMB assay to correlate bTMB with Tecentriq clinical activity.

The biomarker evaluable population (BEP) included 211 patients in POPLAR (ITT population=287) and 583 patients in OAK (excludes patients with known EGFR/ALK mutations; ITT=850), with blood samples available for targeted genomic sequencing.

### **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. The Roche cancer immunotherapy research and development programme comprises more than 20 investigational candidates, 11 of which are in clinical trials.

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 that provide the greatest number of people with a chance for transformative benefit. PCI encompasses the search for reliable biomarkers that correlates with clinical benefit either as a monotherapy or in combination, and across a broad range of cancers.

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](#).

### **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 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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](http://www.roche.com).

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## References

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<sup>1</sup> Gandara DR, et al. Blood-Based Biomarkers for Cancer Immunotherapy: Tumor Mutational Burden in Blood (bTMB) is Associated With Improved Atezolizumab (atezo) Efficacy in 2L+ NSCLC (POPLAR and OAK). Presented at ESMO Congress; 2017 September 8-12; Madrid, Spain. Abstract #1295O.

<sup>2</sup> F. Hoffman-La Roche Ltd. data on file.

<sup>3</sup> Rizvi NA, et al. *Science*. 2015;348(6230): 124-128.

<sup>4</sup> Patel PS and Kurzrock R. *Mol Cancer Ther*. 2015;14(4): 847-856.

<sup>5</sup> Mok T, et al. Blood First-Line Ready Screening Trial (B-FIRST) and Blood First Assay Screening Trial (BFAST) enable clinical development of novel blood-based biomarker assays for tumor mutational burden (TMB) and somatic mutations in 1L advanced or metastatic NSCLC. Presented at ESMO Congress; 2017 September 8-12; Madrid, Spain. Abstract #1383TiP.