Media Release

Roche's IPATential150 study evaluating ipatasertib in combination with abiraterone and prednisone/prednisolone met one of its co-primary endpoints

- **Phase III IPATential150 study evaluating ipatasertib in combination with abiraterone and prednisone/prednisolone compared to current standard-of-care (abiraterone and prednisone/prednisolone alone) plus placebo met its co-primary endpoint of radiographic progression free survival (rPFS) in patients with PTEN loss tumours**

Basel, 19 June 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III IPATential150 study met its co-primary endpoint of radiographic progression-free survival (rPFS) in patients with metastatic castration-resistant prostate cancer (mCRPC) and whose tumours had PTEN loss. In this patient group, ipatasertib in combination with abiraterone and prednisone/prednisolone provided a statistically significant reduction in the risk of disease worsening or death, compared to current standard of care (abiraterone and prednisone/prednisolone) plus placebo. The other co-primary endpoint of rPFS in the overall study population (ITT) was not met. The safety profile for the combination of ipatasertib and abiraterone was consistent with previous analyses and known risks. The results of the IPATential150 study will be presented at an upcoming medical meeting.

While initial data are encouraging, overall survival benefit and additional secondary endpoints are not yet mature. The trial will continue until the next planned analysis and data will be shared with health authorities.

"Prostate cancer remains a leading cause of death in men worldwide and patients with metastatic castration-resistant prostate cancer can be difficult to treat," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "The early results of the IPATential150 study are encouraging in our ongoing mission to develop new treatment options for people with advanced prostate cancer."

Ipatasertib is an oral, highly specific, investigational medicine designed to target and bind to all three isoforms of AKT (protein kinase B), which blocks the PI3K/AKT signalling pathway – a key driver of cancer cell growth and proliferation in prostate cancer.[1,2] The PI3K/AKT pathway has also been implicated in resistance to anti-androgen therapy as androgen receptor (AR) inhibition is associated with an increase in AKT pathway activation.[2,3] Functional loss of the tumour suppressor protein PTEN within the tumour, seen in approximately 40-60% of mCRPC patients, results in hyperactivation of the PI3K/AKT pathway and is associated with adverse outcomes such as increased tumour grade and stage, earlier biochemical recurrence after radical prostatectomy, metastasis, prostate-cancer-specific death, and androgen-independent progression.[4,5]

Roche's clinical development programme for ipatasertib focuses on tumours that are frequently found to have activation of the PI3K/AKT pathway. In addition to prostate cancer, ipatasertib is being studied in certain types of breast cancer including triple-negative breast cancer (TNBC) and hormone-receptor positive (HR+), HER2- negative breast cancer. Results are anticipated later in 2020.

About the IPATential150 study[6]
IPATential150 is a double-blind, placebo-controlled, randomised phase III study assessing ipatasertib in combination with abiraterone and prednisone/prednisolone, compared to placebo plus abiraterone and prednisone/prednisolone, in adult male patients with asymptomatic or mildly symptomatic, previously untreated mCRPC.

The co-primary endpoints of the study are investigator-determined rPFS in the overall study population, as well as a subpopulation whose tumours have PTEN loss, as assessed by immunohistochemistry (Ventana assay). PFS in the study is defined as the time from date of randomisation to the first occurrence of disease progression or death from any cause, whichever occurs earlier. Secondary endpoints include overall survival, safety, time to pain progression, time to initiation of cytotoxic chemotherapy and time to function deterioration.

About ipatasertib
Ipatasertib is an oral, highly specific, investigational medicine designed to target and bind to all three isoforms of AKT, which blocks the PI3K/AKT signalling pathway and may prevent cancer cell growth and survival.[1,2]

Ipatasertib is being studied in tumours that are frequently found to have activation of the PI3K/AKT pathway, including breast and prostate cancers. Clinical studies are ongoing to evaluate the efficacy and safety of ipatasertib and the opportunity it may provide to address significant unmet needs for patients with these diseases.

Ipatasertib was discovered at Genentech in partnership with Array BioPharma Inc. (acquired by Pfizer Inc. on July 30, 2019).

About metastatic castration-resistant prostate cancer (mCRPC)
Prostate cancer is the second most frequent cancer and the fifth leading cause of death in men.[7] Metastatic prostate cancer refers to prostate cancer that has spread beyond the prostate to other parts of the body (metastasised).[8] Although most men are cured with treatment of localised disease, recurrent or newly diagnosed metastatic disease is associated with significant morbidity and mortality.[9,10,11]

Primary treatment of advanced prostate cancer is androgen deprivation therapy (ADT); however, up to one-third of patients will progress despite reduction in serum testosterone levels to castrate levels (<50 ng/dL), either through surgical or medical castration.[12,13] Castration-resistant prostate cancer (CRPC) is defined by disease progression, as measured by prostate specific antigen (PSA) or radiographic measures, despite adequate suppression of serum testosterone levels.[14,15] Despite the current availability of life-extending therapies for mCRPC, the majority of men will die of their disease: the median life expectancy in this population is less than three years.[16,17]

Prostate cancer growth and survival is driven by abnormal AR signalling. In CRPC, cell growth and proliferation is also commonly driven by activation of the PI3K/AKT signalling pathway.[1,2] In particular, functional loss of the tumour suppressor protein PTEN within the tumour, seen in approximately 40-60% of

people with mCRPC, results in hyperactivation of the PI3K/AKT pathway.[4] PTEN loss is associated with adverse outcomes such as increased tumour grade and stage, earlier biochemical recurrence after radical prostatectomy, metastasis, prostate-cancer-specific death, and androgen-independent progression.[5] The PI3K/AKT pathway has also been implicated in resistance to anti-androgen therapy as AR inhibition is associated with an increase in AKT pathway activation, suggesting that the tumour compensates for the loss of one pathway with another.[2,3]

About Roche in prostate cancer
For more than 50 years, Roche has been developing medicines with the goal of redefining treatment in oncology. Our research and development aim is to provide effective cancer therapies through the discovery and development of novel therapeutics that target the specific molecular pathways associated with cancer. Roche is expanding into additional areas of unmet need, working to find innovative solutions for diseases such as prostate cancer, the most prevalent cancer in men and fifth leading cause of cancer-related male death worldwide.[5] Roche is committed to research into genitourinary cancers, including bladder and renal cancers, and to providing life extending treatment options for these patients.

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. More than 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 eleventh consecutive year, Roche has been recognised as one of the most sustainable companies 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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