Media & Investor Release

Roche's Itovebi demonstrated statistically significant and clinically meaningful overall survival benefit in a certain type of HR-positive advanced breast cancer

- **Updated overall survival (OS) results - a key secondary endpoint - reinforce the significant benefit of the Itovebi™ (inavolisib)-based regimen for patients with advanced *PIK3CA*-mutated, HR-positive, HER2-negative breast cancer in the first-line setting**
- **Primary analysis showed the Itovebi-based regimen reached statistical significance, more than doubling progression-free survival in this patient population**[1]
- **Full OS results from the phase III INAVO120 study will be presented at an upcoming medical meeting**

Basel, 28 January 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline results from the overall survival (OS) analysis of the phase III INAVO120 study investigating Itovebi™ (inavolisib) in combination with palbociclib (Ibrance®) and fulvestrant for people with *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, endocrine-resistant, locally advanced or metastatic breast cancer. The study met its key secondary endpoint, showing a statistically significant and clinically meaningful OS benefit with the Itovebi-based regimen compared with palbociclib and fulvestrant alone.

"The INAVO120 overall survival results show that the Itovebi-based regimen not only delayed disease progression, but also helped people with advanced HR-positive, *PIK3CA*-mutated breast cancer live longer," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These findings underscore our ambition to improve survival rates for people with breast cancer. The Itovebi-based regimen has the potential to become the new standard of care for these patients."

These OS results build upon the previously reported primary analysis, which showed that the Itovebi-based regimen reduced the risk of disease worsening or death by 57% compared with palbociclib and fulvestrant alone (15.0 months vs. 7.3 months; hazard ratio [HR]=0.43, 95% CI: 0.32-0.59, p<0.001) in the first-line setting.[1] OS data were immature at the time of primary analysis, but a clear positive trend was observed at that time (stratified HR=0.64, 95% CI: 0.43-0.97, p=0.0338 (boundary of 0.0098)).[1] No new safety signals were observed since the previous analysis. The full results from the OS analysis will be presented at an upcoming medical meeting.

The U.S. Food and Drug Administration (FDA) approved the Itovebi-based regimen in October 2024 for the treatment of adults with endocrine-resistant, *PIK3CA*-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.[2] Data from INAVO120, recently published in the *New England Journal of Medicine*, are also being reviewed by other global health authorities, including the European Medicines Agency.

Itovebi is currently being investigated in four company-sponsored phase III clinical studies (INAVO120, INAVO121, INAVO122, INAVO123) in *PIK3CA*-mutated locally advanced or metastatic breast cancer in various combinations.[3-6] We are exploring additional studies in breast cancer and other tumour types with the hope of bringing the benefit of this targeted therapy to more people with *PIK3CA*-mutated cancer and addressing patient unmet needs.

About Itovebi ™ (inavolisib)

Itovebi is an oral, targeted treatment with best-in-class potential that could provide well-tolerated, durable disease control and potentially improved outcomes for people with *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, who often have a poor prognosis and are in urgent need of new treatment options.[1,7,8] Itovebi has been designed to help minimise the overall burden and toxicity of treatment and is differentiated from other PI3K inhibitors due to its high potency and specificity for the PI3K alpha isoform versus other isoforms, and unique mechanism of action that facilitates the degradation of mutated PI3K alpha.[9,10]

About the INAVO120 study

The INAVO120 study [NCT04191499] is a phase III, randomised, double-blind, placebo-controlled study evaluating the efficacy and safety of Itovebi™ (inavolisib) in combination with palbociclib and fulvestrant versus placebo plus palbociclib and fulvestrant in people with *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer whose disease progressed during treatment or within 12 months of completing adjuvant endocrine therapy and who have not received prior systemic therapy for metastatic disease.[3]

The study included 325 patients, who were randomly assigned to either the investigational or control treatment arm.[3] The primary endpoint is progression-free survival, as assessed by investigators, defined as the time from randomisation in the clinical trial to the time when the disease progresses, or a patient dies from any cause.[3] Secondary endpoints include overall survival, objective response rate, and clinical benefit rate.[3]

Beyond INAVO120, Itovebi is currently being investigated in three additional company-sponsored phase III clinical studies in *PIK3CA*-mutated locally advanced or metastatic breast cancer in various combinations:[4,5,6]

- in combination with fulvestrant versus alpelisib plus fulvestrant in HR-positive/HER2-negative breast cancer post cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) and endocrine combination therapy (INAVO121; NCT05646862).
- in combination with pertuzumab plus trastuzumab for subcutaneous injection (SC) versus pertuzumab plus trastuzumab for SC and optional physician's choice of endocrine therapy as a maintenance treatment in HER2-positive disease (INAVO122; NCT05894239).
- in combination with CDK4/6i and letrozole versus placebo plus a CDK4/6i and letrozole in the first-line setting in endocrine-sensitive, *PIK3CA*-mutated HR-positive/HER2-negative breast cancer (INAVO123; NCT06790693).

About hormone receptor (HR)-positive breast cancer

HR-positive breast cancer is the most prevalent type of all breast cancers, accounting for approximately 70% of cases.[11,12] A defining feature of HR-positive breast cancer is that its tumour cells have receptors that attach to one or both hormones – oestrogen or progesterone – which can contribute to tumour growth. People diagnosed with HR-positive metastatic breast cancer often face the risk of disease progression and treatment side effects, creating a need for additional treatment options.[12-14] The PI3K signalling pathway is commonly dysregulated in HR-positive breast cancer, often due to activating *PIK3CA* mutations, which have been identified as a potential mechanism of intrinsic resistance to standard of care endocrine therapy in combination with cyclin-dependent kinase 4/6 inhibitors.[8]

About Roche in breast cancer

Roche has been advancing breast cancer research for more than 30 years with the goal of helping as many people with the disease as possible. Our medicines, along with companion diagnostic tests, have contributed to bringing breakthrough outcomes in human epidermal growth factor 2-positive and triple-negative breast cancers. As our understanding of breast cancer biology rapidly improves, we are working to identify new biomarkers and approaches to treatment for other subtypes of the disease, including oestrogen receptor-positive breast cancer, which is a form of hormone receptor-positive breast cancer, the most prevalent type of all breast cancers.[11,12]

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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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