Media & Investor Release

New data show Roche's Itovebi significantly extended survival in a certain type of HR-positive advanced breast cancer

- **The Itovebi™ (inavolisib)-based regimen reduced the risk of death by more than 30% in people with *PIK3CA*-mutated HR-positive, HER2-negative advanced breast cancer, compared with palbociclib and fulvestrant alone[1]**
- **The *PIK3CA* mutation is found in approximately 40% of HR-positive advanced breast cancers and is associated with a poor prognosis[2,3]**
- **New data are being presented in an oral session at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and published in the *New England Journal of Medicine*[1]**

Basel, 31 May 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive final results from the overall survival (OS) analysis of the phase III INAVO120 study. These data showed Itovebi™ (inavolisib), in combination with palbociclib (Ibrance®) and fulvestrant, reduced the risk of death by more than 30% compared with palbociclib and fulvestrant alone. This represents a statistically significant and clinically meaningful improvement in overall survival 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.[1] The results are being presented in an oral session at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in the *New England Journal of Medicine (NEJM).*[1]

"For the first time, a PI3K pathway-targeted drug has shown it can help people with this breast cancer subtype live longer," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Itovebi exemplifies our continued commitment to improve survival rates for people with this common *PIK3CA* mutation, for whom more effective treatment options are needed."

"The landmark data for the inavolisib-based regimen showed not only a doubling in progression-free survival, but importantly that it extended lives and gave people more time without chemotherapy," said Professor Nicholas Turner, Lead Study Author and Professor of Molecular Oncology at The Institute of Cancer Research, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, London, United Kingdom. "These results give us confidence that this regimen could become the new standard of care in the first-line setting, having demonstrated a substantial benefit on patient outcomes and quality of life."

The Itovebi-based regimen demonstrated a meaningful OS benefit compared with palbociclib and fulvestrant alone.[1] The median OS was 34.0 months (95% CI: 28.4–44.8) for people in the Itovebi arm, compared with 27.0 months (95% CI: 22.8–38.7) in the palbociclib and fulvestrant

arm (stratified hazard ratio [HR]=0.67; 95% CI: 0.48–0.94, p-value=0.0190 [boundary=0.0469]).[1] The benefit seen in delaying cancer progression was maintained in the updated analysis, with the Itovebi-based regimen showing a consistent improvement in median progression free survival of 17.2 months versus 7.3 months (stratified HR=0.42; 95% CI: 0.32-0.55) in the comparator arm.[1]

The Itovebi-based regimen also led to a statistically significant improvement in objective response rate (the percentage of patients whose signs of cancer completely disappear or their tumours shrink significantly after treatment) and ad-hoc exploratory analyses showed it substantially delayed time to chemotherapy by approximately two years (stratified HR=0.43; 95% CI: 0.30-0.60).[1] No new safety signals were observed at the time of the final OS analysis, with a low discontinuation due to adverse events supporting good tolerability.[1]

The Itovebi-based regimen is approved in the United States, Switzerland, Canada, Australia, United Arab Emirates and China. In May, it received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP), with a final decision regarding the approval expected from the European Commission in the near future. Data from the INAVO120 study are currently under review with other global health authorities.

Beyond INAVO120, Itovebi is currently being investigated in three company-sponsored phase III studies (INAVO121, INAVO122, INAVO123), all in *PIK3CA*-mutated, locally advanced or metastatic breast cancer in various combinations.[4-7] We are exploring additional studies in breast cancer and other tumour types with the hope of providing the benefit of this targeted therapy to more people with *PIK3CA* mutations.

About Itovebi ™ (inavolisib)

Itovebi is an oral, targeted treatment that has been shown to provide well-tolerated and durable disease control in people with *PIK3CA*-mutated, hormone receptor-positive, human epidermal growth factor receptor 2-negative, advanced breast cancer, who often have a poor prognosis and are in urgent need of new treatment options.[2,3,8] 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.[4]

The study included 325 patients, who were randomly assigned to either the investigational or control treatment arm.[4] 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.[4] Secondary endpoints include overall survival, objective response rate, and clinical benefit rate.[4]

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:[5-7]

- in combination with fulvestrant versus alpelisib plus fulvestrant in HR-positive/HER2-negative breast cancer post cyclin-dependent kinase 4/6 (CDK4/6) inhibitor 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 CDK4/6 inhibitor and letrozole versus placebo plus a CDK4/6 inhibitor and letrozole in the first-line setting in *PIK3CA*-mutated HR-positive/HER2-negative, endocrine-sensitive 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.[3]

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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Roche Global Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Nathalie Altermatt
Phone: +41 79 771 05 25

Simon Goldsborough
Phone: +44 797 32 72 915

Nina Mählitz
Phone: +41 79 327 54 74

Yvette Petillon
Phone: +41 79 961 92 50

Sileia Urech
Phone: +41 79 935 81 48

Lorena Corfas
Phone: +41 79 568 24 95

Karsten Kleine
Phone: +41 79 461 86 83

Kirti Pandey
Phone: +49 172 6367262

Dr Rebekka Schnell
Phone: +41 79 205 27 03

Roche Investor Relations

Dr Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com