# Media & Investor Release

## FDA approves Roche's Itovebi, a targeted treatment for advanced hormone receptor-positive, HER2-negative breast cancer with a *PIK3CA* mutation

- **Approval is based on Phase III INAVO120 results, showing the Itovebi™ (inavolisib)-based regimen more than doubled progression-free survival compared with palbociclib and fulvestrant alone in the first-line setting[1]**
- **This approval helps address an urgent unmet need in breast cancer for people with a *PIK3CA* mutation, one of the most commonly mutated genes in HR-positive disease, associated with poor prognosis[2,3]**
- **Itovebi is Roche's first targeted therapy approved for people with HR-positive disease, the most prevalent breast cancer subtype, marking an important step in our ambition to continue bringing innovative medicines to more people with breast cancer[4,5]**

Basel, 11 October 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the United States Food and Drug Administration (FDA) approved Itovebi™ (inavolisib), in combination with palbociclib (Ibrance®) and fulvestrant, for the treatment of adults with endocrine-resistant, *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy. The *PIK3CA* mutation is found in approximately 40% of HR-positive metastatic breast cancers.[2]

"The PI3K pathway plays a pivotal role in disease progression and has been challenging to target," said Komal Jhaveri, M.D., section head for the endocrine therapy research portfolio and clinical director of the early drug development service at Memorial Sloan Kettering Cancer Center, and one of the principal investigators of the INAVO120 study. "The Itovebi-based regimen more than doubled progression-free survival and maintained a manageable safety and tolerability profile, adding a new standard in how *PIK3CA*-mutated breast cancers are treated."

"With the approval of this Itovebi-based regimen, we continue our long-standing track record of cancer therapeutic discovery by offering an important new first-line option for people living with HR-positive breast cancer with a *PIK3CA* mutation," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Despite the high prevalence of *PIK3CA* mutations in this setting, treatment options have thus far remained limited, which makes today's approval all the more significant."

F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland
Group Communications
Roche Group Media Relations
Phone +41 61 688 88 88
www.roche.com

This approval is based on results of the pivotal Phase III INAVO120 study, 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<0.0001) in the first-line setting, demonstrating a statistically significant and clinically meaningful benefit.[1] Overall survival (OS) data were immature at the time of primary analysis, but a clear positive trend was observed (stratified HR=0.64, 95% CI: 0.43-0.97, p=0.0338 [boundary of 0.0098]).[1] Follow-up for OS is continuing to the next analysis.

"We are thrilled by the approval of the Itovebi-based regimen, which is a huge step forward for advanced breast cancer patients with a *PIK3CA* mutation," said Jean Sachs, CEO of Living Beyond Breast Cancer. "It remains critical that all patients have access to early, comprehensive biomarker testing so they can better understand what treatment options may be most beneficial for them and their tumour type."

The Itovebi-based regimen was granted FDA Priority Review and Breakthrough Therapy Designation in May 2024 based on the INAVO120 study results.[6,7] Data from INAVO120 are also being used for filing submissions to other global health authorities, including the European Medicines Agency. Itovebi will be available in the US in the coming weeks. Early, comprehensive biomarker testing with an FDA-approved test, such as Foundation Medicine's FoundationOne®Liquid CDx, can help identify people with HR-positive, HER2-negative breast cancer with a *PIK3CA* mutation.

Itovebi is currently being investigated in various combinations across three company-sponsored Phase III clinical studies (INAVO120, INAVO121, INAVO122) in *PIK3CA*-mutated locally advanced or metastatic breast cancer.[8-10] We continue to evaluate opportunities to expand our clinical development programme to address patient unmet needs in various tumour types across oncology.

## 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.[8]

The study included 325 patients, who were randomly assigned to either the investigational or control treatment arm.[8] 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.[8] Secondary endpoints include overall survival, objective response rate, and clinical benefit rate.[8]

Beyond INAVO120, Itovebi is currently being investigated in two additional company-sponsored Phase III clinical studies in *PIK3CA*-mutated locally advanced or metastatic breast cancer in various combinations:[9,10]

- in combination with fulvestrant versus alpelisib plus fulvestrant in HR-positive/HER2-negative breast cancer post cyclin-dependent kinase 4/6 inhibitor and endocrine combination therapy (INAVO121; NCT05646862), and
- 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).

## 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.[4,5] 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.[5,11,12] 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.[4,5]

## 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.



## References

[1] Jhaveri K, et al. Phase III study of inavolisib or placebo in combination with palbociclib and fulvestrant in patients with *PIK3CA*-mutant, hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer: INAVO120 primary analysis. Presented at San Antonio Breast Cancer Symposium, 2023 December 5-9; San Antonio, USA. Abstract #GS03-13.
[2] Fillbrunn M, et al. *PIK3CA* mutation status, progression and survival in advanced HR+/HER2- breast cancer: a meta-analysis of published clinical trials. BMC Cancer. 2022;22:1002.
[3] Anderson E, et al. A Systematic Review of the Prevalence and Diagnostic Workup of PIK3CA Mutations in HR+/HER2– Metastatic Breast Cancer. Int J Breast Cancer. 2020;2020:3759179.
[4] National Cancer Institute: Surveillance, Epidemiology and Ends Result Program. Cancer Stat Facts: Female Breast Cancer Subtypes [Internet; cited 2024 October]. Available from: https://seer.cancer.gov/statfacts/html/breast-subtypes.html.
[5] Lim E, et al. The natural history of hormone receptor-positive breast cancer. Oncology (Williston Park). 2012;26(8):688-94,696.
[6] Roche. FDA grants Priority Review to Roche's inavolisib for advanced hormone receptor-positive, HER2-negative breast cancer with a PIK3CA mutation [Internet; cited 2024 October]. Available from: https://www.roche.com/media/releases/med-cor-2024-05-29.
[7] Roche. FDA grants Breakthrough Therapy Designation to Roche's inavolisib for advanced hormone receptor-positive, HER2-negative breast cancer with a PIK3CA mutation [Internet; cited 2024 October]. Available from: https://www.roche.com/media/releases/med-cor-2024-05-21.
[8] ClinicalTrials.gov. A Study Evaluating the Efficacy and Safety of Inavolisib + Palbociclib + Fulvestrant vs Placebo + Palbociclib + Fulvestrant in Patients With *PIK3CA*-Mutant, Hormone Receptor-Positive, Her2-Negative,

Locally Advanced or Metastatic Breast Cancer (INAVO120) [Internet; cited 2024 October]. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT04191499.
[9] ClinicalTrials.gov. A Study Evaluating the Efficacy and Safety of Inavolisib Plus Fulvestrant Compared With Alpelisib Plus Fulvestrant in Participants With HR-Positive, HER2-Negative, *PIK3CA* Mutated, Locally Advanced or Metastatic Breast Cancer Post CDK4/6i and Endocrine Combination Therapy (INAVO121) [Internet; cited 2024 October]. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT05646862.
[10] ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of Inavolisib in Combination With Phesgo Versus Placebo in Combination With Phesgo in Participants With *PIK3CA*-Mutated HER2-Positive Locally Advanced or Metastatic Breast Cancer [Internet; cited 2024 October]. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT05894239.
[11] Tomas R and Barrios CH. Optimal management of hormone receptor positive metastatic breast cancer in 2016. Ther Adv Med Oncol. 2015;7(6):304-20.
[12] Galipeau N, et al. Understanding key symptoms, side effects, and impacts of HR+/HER- advanced breast cancer: qualitative study findings. J Patient-Rep Outcomes. 2019;3(1):10.

Dr. Jhaveri has financial interests related to Roche and Genentech.

**Roche Global Media Relations**
Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

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

**Sileia Urech**
Phone: +41 79 935 81 48

**Nathalie Altermatt**
Phone: +41 79 771 05 25

**Lorena Corfas**
Phone: +41 79 568 24 95

**Simon Goldsborough**
Phone: +44 797 32 72 915

**Karsten Kleine**
Phone: +41 79 461 86 83

**Nina Mählitz**
Phone: +41 79 327 54 74

**Kirti Pandey**
Phone: +49 172 6367262

**Yvette Petillon**
Phone: +41 79 961 92 50

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

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

## Investor Relations North America

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