



NEWS RELEASE

Alliance Foundation Trials and Natera Announce AFT-70 NAVIGATE: a Global, Randomized, Phase III Trial Evaluating Genentech's Oral Selective Estrogen Receptor Degradar (SERD) with Signatera™ MRD-Guided CDK4/6 Inhibitor Therapy in Breast Cancer

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Trial will use Natera's ultrasensitive MRD test, Signatera Genome with Phased and Structural Variants, paired with giredestrant monotherapy, Genentech's investigational oral SERD, aiming to spare patients unnecessary CDK4/6 inhibitor exposure and associated toxicities

BOSTON & AUSTIN, Texas--(BUSINESS WIRE)-- Alliance Foundation Trials, LLC (AFT), a national leader in conducting innovative, practice-changing cancer clinical trials, and Natera, Inc. (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced the launch of AFT-70 NAVIGATE, a randomized phase III trial evaluating a novel molecular residual disease (MRD)-guided treatment strategy for patients with intermediate and high-risk ER-positive/HER2-negative early breast cancer. The trial is sponsored and led by AFT, with collaboration and co-funding from Natera and Genentech, a member of the Roche Group.

AFT-70 NAVIGATE is designed to test whether patients can maintain excellent outcomes while more selectively using CDK4/6 inhibitors, rather than exposing all patients to prolonged combination therapy. The strategy pairs giredestrant, an investigational highly active next-generation oral selective estrogen receptor degrader (SERD), with longitudinal Signatera Genome MRD monitoring, to identify patients who may benefit from treatment escalation with a CDK4/6 inhibitor.

Giredestrant was selected as the endocrine therapy backbone for the investigational arm based on results from the phase III lidERA trial, which showed giredestrant achieved a statistically significant and clinically meaningful improvement in invasive disease-free survival compared with standard endocrine monotherapy in patients with ER-positive/HER2-negative early breast cancer. These findings support the potential for giredestrant to provide an endocrine therapy backbone on which an MRD-guided treatment strategy can be built.

Signatera was selected as the MRD test for this trial based on its extensive clinical evidence in ER-positive, HER2-negative early breast cancer, including from the AFT-05 PALLAS and MonarchE trials, and because of its new ultrasensitive Genome-based technology with Phased and Structural Variants reporting analytical sensitivity below 1 ppm (parts per million).

AFT expects to enroll more than 2,000 patients with stage II-III ER-positive/HER2-negative breast cancer who are eligible for endocrine therapy at approximately 200 sites across the U.S. and internationally. Patients with no detectable MRD by Signatera after completing standard-of-care treatment, including surgery, radiotherapy, and chemotherapy when indicated, will be randomly assigned to one of two approaches: (1) a control arm receiving standard-of-care endocrine therapy plus upfront CDK4/6 inhibition; or (2) an investigational arm receiving giredestrant monotherapy, with CDK4/6 inhibition added only if Signatera becomes positive. The primary endpoint is non-inferiority in 4-year distant recurrence-free survival.

“This collaboration brings together leading expertise in breast cancer research, clinical care, and molecular testing to address an important question for patients: How can we make treatment more precise while avoiding unnecessary toxicity?” said Evanthia Galanis, M.D., D.Sc., president of Alliance Foundation Trials, LLC. “By using MRD technology to guide treatment decisions, this trial has the potential to transform care for eligible breast cancer patients and individualize treatment intensity.”

“We know that patients with ER-positive, HER2-negative breast cancer do not all face the same risk of recurrence, yet adjuvant treatment decisions are still largely based on clinical and pathological features measured at diagnosis,” said Komal Jhaveri, M.D., FACP, FASCO study chair, breast medical oncologist and early drug development specialist at Memorial Sloan Kettering Cancer Center. “The AFT-70 NAVIGATE trial combines two important advances: an endocrine therapy backbone with giredestrant and longitudinal MRD testing with Signatera that can provide a dynamic measure of recurrence risk. The trial will determine whether MRD-guided monitoring can distinguish patients most likely to benefit from adding a CDK4/6 inhibitor from those in whom it can be safely omitted. It’s an important step forward using biology—not just baseline risk—to guide adjuvant therapy.”

“More treatment is not always better treatment,” said Gaorav Gupta, M.D., Ph.D., study co-chair, breast radiation oncologist, and co-leader of the Breast Cancer Research Program at UNC Lineberger Comprehensive Cancer Center. “CDK4/6 inhibitors can be an important part of care for some patients, but they can also add side effects,

monitoring, and treatment burden. If highly sensitive blood-based MRD testing can identify patients who can safely defer additional therapy, we may be able to spare many patients from the burdens of more treatment while maintaining excellent cancer control. That is the promise we hope to explore through this study.”

“Natera and AFT have a longstanding partnership and shared commitment to cutting-edge trials across many cancer types,” said Minetta Liu, M.D., chief medical officer, oncology and early cancer detection, Natera. “AFT-70 NAVIGATE creates enormous potential to enhance treatment options for patients with intermediate and high-risk, hormone receptor positive breast cancer.”

About Alliance Foundation Trials, LLC (AFT)

Alliance Foundation Trials, LCC, is a research organization that develops and conducts cancer clinical trials, working closely with the Alliance for Clinical Trials in Oncology scientific investigators, institutional member network, research partners, and non-NCI funding organizations. AFT seeks to fulfill the vision of the Alliance for Clinical Trials in Oncology to reduce the impact of cancer on people by uniting a broad community of scientists and clinicians from many disciplines committed to discovering, validating, and disseminating effective strategies for the prevention and treatment of cancer. AFT’s current studies are supported by industry collaborators and the Patient Outcomes Research Institute (PCORI). To learn more, visit AllianceFoundationTrials.org.

About Natera

Natera is a global leader in cell-free DNA and precision medicine, dedicated to oncology, women’s health, and organ health. We aim to make personalized genetic testing and diagnostics part of the standard-of-care to protect health and inform earlier, more targeted interventions that help lead to longer, healthier lives. Natera’s tests are supported by more than 400 peer-reviewed publications that demonstrate excellent performance. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas, and San Carlos, California, and through Foresight Diagnostics, its subsidiary, operates an ISO 27001-certified and CAP-accredited laboratory certified under CLIA in Boulder, Colorado. For more information, visit www.natera.com.

Forward-Looking Statements (for Natera)

All statements other than statements of historical facts contained in this press release are forward-looking statements and are not a representation that Natera’s plans, estimates, or expectations will be achieved. These forward-looking statements represent Natera’s expectations as of the date of this press release, and Natera disclaims any obligation to update the forward-looking statements. These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual results to differ materially, including with

respect to our or our partners' efforts to develop and commercialize new product offerings, whether the results of clinical or other studies will support the use of our product offerings, the impact of results of such studies, our expectations of the reliability, accuracy, and performance of our tests, or of the benefits of our tests and product offerings to patients, providers, and payers. Additional risks and uncertainties are discussed in greater detail in "Risk Factors" in Natera's recent filings on Forms 10-K and 10-Q, and in other filings Natera makes with the SEC from time to time. These documents are available at www.natera.com/investors and www.sec.gov.

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