NEWS RELEASE

Signatera Data From I-SPY 2 Trial to Be Presented at ESMO Breast Annual Congress

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Demonstrates Signatera's ability to predict long-term outcomes in early-stage, high-risk breast cancers

Several datasets will be presented, highlighting Natera's leadership in breast cancer MRD

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, will present multiple datasets in breast cancer together with its collaborators at the 2025 ESMO Breast Cancer Annual Congress in Munich, Germany, taking place from May 14-17, 2025.

Results from the I-SPY 2 clinical trial, sponsored and operated by Quantum Leap Healthcare Collaborative, will be shared in a mini-oral presentation on May 16, 2025. The report includes data from 712 patients with early-stage, high-risk breast cancer, and it evaluates the association of distant recurrence free survival (DRFS) with ctDNA concentration at diagnosis, before receiving neoadjuvant systemic therapy and curative-intent surgery. Key highlights include:

- Signatera positive patients at diagnosis had 3x higher risk of recurrence than Signatera negative patients (HR 3.1, p< 0.001%), though the risk can be significantly reduced based on response to subsequent therapy.
- Patients who were Signatera negative at diagnosis had extremely good outcomes.
- Among patients who were Signatera positive at diagnosis, higher ctDNA quantities at the time of diagnosis were significantly correlated with a higher risk of recurrence. However, effective treatment can affect ctDNA levels as well as pathologic response status, both of which further refine risk of recurrence. This is the first time that pre-treatment absolute ctDNA quantity has been shown to correlate with clinical outcomes in breast

cancer.

- Among all clinicopathologic risk factors available at diagnosis, a multivariate analysis identified Signatera status as the most significant factor in predicting DRFS, regardless of disease subtype ($p<0.001$). DRFS prediction can be further refined by integrating additional variables before, during, and after treatment, including ctDNA dynamics.

“The I-SPY 2 trial is uncovering insights that may allow us to tailor treatment plans for breast cancer patients based on their individual genomic profiles and better identify patients who may be more likely to experience adverse outcomes,” said Laura Esserman, M.D., MBA, and Laura van ‘t Veer, Ph.D., professors at the University of California, San Francisco, and principal investigators of the I-SPY 2 study. “Our hope is that these findings will encourage future interventional trials in breast cancer, specifically in the neoadjuvant setting.”

“Signatera was able to predict excellent clinical outcomes in a high risk population at the time of diagnosis,” said Angel Rodriguez, M.D., medical director, oncology at Natera. “This may give rise to new protocols, evaluating whether some patients can avoid chemotherapy or other intensive treatments, if they test Signatera-negative at diagnosis.”

Natera will present an additional three abstracts at the ESMO Breast conference, highlighting real-world evidence and genomic landscaping from its multi-modal database of de-identified clinical and genomic data in over 200,000 early- and late-stage cancer patients.

Full list of Natera’s ESMO Breast presentations:

May 16, 9:40 AM CT | FPN 5MO

Presenter: Mark Magbanua, Ph.D., UCSF Helen Diller Family Comprehensive Cancer Center
Pretreatment Circulating Tumor (ct)DNA Predicts Metastatic Recurrence in Patients (pts) With High-Risk Early Breast Cancer (eBC) Enrolled in the I-SPY 2 Trial

May 15, 12:00 PM CT | FPN 115P

Presenter: Chu-Ling Yu, Merck
Real-World Testing Patterns of Circulating Tumor DNA (ctDNA) in Early-Stage Triple-Negative Breast Cancer (TNBC): a U.S. Nationwide Database Study

May 15, 12:00 PM CT | FPN 12P

Presenter: Melinda Telli, M.D., Stanford University School of Medicine
Real-world experience of longitudinal circulating tumor (ct)DNA monitoring in patients (pts) with early-stage triple-negative breast cancer (TNBC)

May 15, 12:00 PM CT | FPN 412TiP

Presenter: Thibault De La Motte Rouge, M.D., Ph.D., Comprehensive Cancer Centre Eugène Marquis (Rennes, France)

HEROES: De-escalation of medical therapies in HER2-positive metastatic breast cancer in long-term persistent response and minimal residual disease undetectable in circulating tumor DNA

May 15, 12:00 PM CT | FPN 37P

Presenter: Marla Lipsyc-Sharf, M.D., UCLA Health

Genetic Ancestry and Tumor Mutations Influence Circulating Tumor DNA (ctDNA) Detection Rates in Breast Cancer: A Large Real-World Study

May 15, 12:00 PM CT | FPN 93P

Presenter: Yara Abdou, M.D., UNC School of Medicine

Assessment of antibody-drug conjugate utilization in patients with breast cancer undergoing circulating tumor DNA testing

About Signatera

Signatera is a personalized, tumor-informed, molecular residual disease test for patients previously diagnosed with cancer. Custom-built for each individual, Signatera uses circulating tumor DNA to detect and quantify cancer left in the body, identify recurrence earlier than standard of care tools, and help optimize treatment decisions. The test is available for clinical and research use and has coverage by Medicare across a broad range of indications. Signatera has been clinically validated across multiple cancer types and indications, with published evidence in more than 100 peer-reviewed papers.

About Natera

Natera™ is a global leader in cell-free DNA and genetic testing, 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 250 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. For more information, visit **www.natera.com**.

Forward-Looking Statements

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 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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