NEWS RELEASE

Natera Announces New Publication from I-SPY2 Trial Reinforcing Clinical Utility of Signatera™ for Breast Cancer Patients in the Neoadjuvant Setting

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Study with 283 patients, >1,000 plasma samples, and longest follow-up exceeding 5 years demonstrates how ctDNA monitoring can help inform treatment decisions in HR+/HER2- and TNBC patients

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced the publication of a new paper1 in Cancer Cell from the I-SPY2 trial, highlighting the prognostic and predictive utility of Natera's personalized and tumor-informed, molecular residual disease (MRD) test, Signatera, in locally advanced breast cancer patients receiving neoadjuvant chemotherapy (NAC, treatment before surgery).

Up to 50% of newly diagnosed breast cancer patients receive NAC.2 While patients with locally advanced breast cancer can benefit from NAC, response rates tend to be lower among HER2-negative breast cancers, which represent the majority of cases. Such patients are therefore in need of a reliable biomarker predictive of treatment benefit. This study focused on evaluating circulating tumor DNA (ctDNA) dynamics during NAC as a tool to assess response and predict patient outcomes, with the hypothesis that treatment protocols may be tailored to optimize efficacy and reduce exposure to the toxicity of ineffective therapies.

The publication reports on an expanded cohort of 283 patients and 1,024 plasma samples from the I-SPY2 study. Plasma samples were collected at four time points: pretreatment (T0), 3 weeks after initiation of treatment (T1), 12 weeks between paclitaxel-based and anthracycline (AC) NAC regimens (T2), and after NAC before surgery (T3).

Key findings include:

- ctDNA-positivity before, during, and after NAC was significantly associated with inferior distant recurrence-free survival (DRFS) in both subtypes (p=0.02 to p<0.0001); and in the 9% of TNBC patients who tested ctDNA-negative pretreatment, zero DRFS events were observed with a median follow-up of 3.12 years.
- Early ctDNA clearance at 3 weeks of NAC was a significant predictor of response, as determined by pathologic complete response (pCR) or residual cancer burden (RCB) in TNBC (p=0.0002).
- ctDNA-negativity after NAC was significantly associated with improved DRFS, even in patients with extensive residual cancer burden at surgery (p<0.0001), indicating that ctDNA status may be more prognostic than pCR status.

“Neoadjuvant chemotherapy is a powerful tool to optimize treatment of breast cancer. As we introduce new therapies, we need optimal tools to predict complete response,” said Laura Esserman, MD, MBA, and Laura van ‘t Veer, PhD, professors at the University of California, San Francisco, and co-authors of the paper. “This latest publication from the ISPY-2 study builds upon our previous findings that tumor-informed ctDNA monitoring has the potential to improve the prediction of response to NAC, and with more data, may allow non-invasive assays to replace core biopsies."

“I-SPY2 provides compelling evidence to support the role of ctDNA in predicting the likelihood of benefit from neoadjuvant chemotherapy for HER2-negative breast cancer,” said Minetta Liu, MD, chief medical officer of oncology at Natera. “The data support the use of Signatera to improve risk stratification and potentially guide escalation or de-escalation of systemic therapy in the neoadjuvant treatment setting.”

About Signatera

Signatera is a custom-built circulating tumor DNA (ctDNA) test for treatment monitoring and molecular residual disease (MRD) assessment in patients previously diagnosed with cancer. The test is available for both clinical and research use, and has been granted three Breakthrough Device Designations by the FDA for multiple cancer types and indications. The Signatera test is personalized and tumor-informed, providing each individual with a customized blood test tailored to fit the unique signature of clonal mutations found in that individual’s tumor. Signatera is intended to detect and quantify cancer left in the body, at levels down to a single tumor molecule in a tube of blood, to identify recurrence earlier and to help optimize treatment decisions.

About Natera

Natera™ is a global leader in cell-free DNA 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 validated by more than 100 peer-reviewed publications that demonstrate high accuracy. 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**.

References

1. Magbanua MJM, Swigart LB, Ahmed Z, et al. Clinical significance and biology of circulating tumor DNA in high-risk early-stage HER2-negative breast cancer receiving neoadjuvant chemotherapy. Cancer Cell. 2023.
2. Riedel F, Hoffmann AS, Moderow M, et al. Time trends of neoadjuvant chemotherapy for early breast cancer. Int J Cancer. 2020;147(11):3049–3058.

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