NEWS RELEASE

# Natera Announces Publication of Prospective, Multi-Site CIRCULATE Study in Nature Medicine Demonstrating Signatera's Ability to Predict Chemotherapy Benefit in Colorectal Cancer

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New predictive data evaluates patient outcomes up to 24.8 months post-surgery, confirms findings presented at ASCO GI 2022

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced the publication of a **new study** in Nature Medicine, which demonstrates the ability of the SignateraTM molecular residual disease (MRD) test to identify patients with stage II-IV colorectal cancer (CRC) who are at an increased risk of recurrence and predict who is likely to benefit from adjuvant chemotherapy (ACT). With this study, data supporting the clinical validity and utility of Signatera has now been published in 40 peer-reviewed publications.

The paper describes results from the GALAXY arm of the ongoing CIRCULATE-Japan trial, which is one of the largest and most comprehensive prospective studies of MRD testing in resectable CRC. The data builds on results previously presented at the 2022 ASCO Gastrointestinal Cancers Symposium (ASCO GI), now with median clinical follow-up extended to 16.74 months and DFS assessment at 18 months.

In the study, 1,039 patients with stage II-IV resectable CRC were monitored prospectively using the Signatera MRD test. Key takeaways include:

- Post-surgical MRD status was predictive of chemotherapy benefit.

    - Patients who were MRD-positive four weeks after surgery (18%) derived significant benefit from ACT (adjusted HR 6.59, p-value <0.001).
    - MRD-negative patients (82%) did not see a significant benefit from ACT (p-value <0.167).

- Post-surgical MRD status was the most significant prognostic risk factor for recurrence, in a multivariate analysis that accounted for all clinicopathological risk factors currently used for prognostication (HR 10.82, p-value <0.001).
- Pre-surgical detection rate of 95.9% in patients with pathologic stage II-III disease and 93.1% in patients with stage II-IV disease.
- Signatera dynamics are indicative of treatment response. Among the MRD-positive patients who were treated with ACT, those with ctDNA clearance had superior DFS compared to those without ctDNA clearance (adjusted HR 11, p-value <0.0001).

“Until now, oncologists did not have adequate tools to determine which colorectal cancer patients are likely to benefit from adjuvant systemic therapy,” said the study’s principal investigator, Dr. Takayuki Yoshino, of the National Cancer Center Hospital East, Kashiwa, Chiba, Japan. “This study provides strong evidence that Signatera MRD-positive patients will benefit significantly from adjuvant therapy, while MRD-negative patients may be safely observed, regardless of clinical or pathological stage.”

“This is a practice-changing study for the colorectal cancer community, demonstrating the predictive power of Signatera in the adjuvant setting,” said Minetta Liu, M.D., chief medical officer of oncology at Natera. “We are proud to partner with the CIRCULATE consortium and look forward to making Signatera accessible to all colorectal cancer patients in the U.S., Japan and worldwide.”

## 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 include quotes of management and represent Natera's expectations as of the date of this press release. Natera disclaims any obligation to update these 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 payors. 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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