



NEWS RELEASE

Updated Data from CIRCULATE-Japan Presented at ESMO 2023 Reinforces Signatera's Prognostic and Predictive Value in Analysis of 2,500+ Colorectal Cancer Patients

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Builds on published evidence with twice as many patients and disease-free survival data extended to 24 months

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced updated data from the GALAXY arm of the CIRCULATE-Japan trial further showcasing the ability of the Signatera™ molecular residual disease (MRD) test to help identify patients with resectable colorectal cancer (CRC) who are at an increased risk of recurrence and predict who are most likely to benefit from adjuvant chemotherapy.

In a presentation today at the 2023 European Society for Medical Oncology (ESMO) Congress in Madrid, Natera and its collaborators shared an expanded GALAXY analysis that builds on results **published in January 2023** in Nature Medicine. With 2,625 CRC patients and disease free survival (DFS) assessment at 24 months, this analysis includes more than twice the number of patients and significantly longer follow-up than the previously published 18-month findings.

Key highlights include:

- Circulating tumor DNA (ctDNA) negative patients continued to show exceptional DFS regardless of adjuvant chemotherapy (ACT) treatment.
 - No significant difference in DFS at 24 months was observed for ctDNA negative patients receiving ACT compared to those with no ACT (88.3% DFS v. 89.9%, p-value 0.156).



- Lack of absolute risk reduction between the two groups further improves on the previously published analysis.
- The presence of post-surgical ctDNA was the most significant prognostic factor for disease recurrence and was predictive of chemotherapy benefit.
 - ctDNA positive patients receiving ACT had significantly higher DFS at 24 months compared to those with no ACT (38.6% DFS v. 16.1%, p-value <0.01).
 - Patients with ctDNA positive results had significantly lower DFS at 24 months than ctDNA negative patients (31% v. 89%, p-value <0.01).
 - In a multivariate analysis, ctDNA status continued to be the most prognostic factor for cancer recurrence (HR 10.44).
- Early ctDNA dynamics were predictive of recurrence.
 - Changes in ctDNA status at 3 months post-surgery were significantly associated with DFS at 24 months.

“The latest data from one of the largest prospective studies of MRD testing in colorectal cancer provides further evidence that Signatera can help clinicians determine which patients are most likely to benefit from adjuvant chemotherapy, while also showing that postoperative ctDNA status is a highly prognostic factor for cancer recurrence,” said the study’s principal investigator, Takayuki Yoshino, M.D., of the National Cancer Center Hospital East, Kashiwa, Chiba, Japan. “With a larger cohort of patients and longer-term follow up, this updated analysis builds upon previously published findings and shows how ctDNA can play a critical role in monitoring disease progression and guiding adjuvant treatment.”

Additional randomized, phase III studies designed to evaluate Signatera MRD-guided adjuvant strategies in CRC are also underway as part of the CIRCULATE-Japan platform. These include the randomized ALTAIR trial, which aims to establish the utility of ACT escalation as well as treatment on molecular recurrence in the MRD-positive population; and the VEGA trial, which is analyzing de-escalation of ACT in the MRD-negative population.

“With these updated findings from GALAXY, the upcoming analyses from the VEGA and ALTAIR trials, and other anticipated read-outs from key studies in our pipeline, Natera continues to demonstrate leadership in data generation from a broad clinical roadmap in colorectal cancer,” said Minetta Liu, M.D., chief medical officer of oncology at Natera. “We are extremely pleased to continue the collaboration with our international partners, including NCC East in Japan, in building clinical evidence to transform disease management for patients with cancer.”

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 is covered by Medicare for patients with colorectal cancer, breast cancer (stage IIb and higher) and muscle invasive bladder cancer, as well as for immunotherapy monitoring of any solid tumor. Signatera has been clinically validated across multiple cancer types and indications, with published evidence in more than 50 peer-reviewed papers.

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 150 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.

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