NEWS RELEASE

Natera to Present New Data from the CIRCULATE-Japan and BESPOKE CRC Studies at ASCO GI 2024 Supporting Signatera's Clinical Utility in CRC

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Oral presentations include updated 24-month DFS analysis from GALAXY and first interim analysis from BESPOKE CRC

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced that new data on its personalized and tumor-informed molecular residual disease (MRD) test, Signatera™, will be presented at the American Society of Clinical Oncology's 2024 Gastrointestinal Cancers Symposium (ASCO GI), taking place January 18 – 20, 2024 in San Francisco, California.

Natera and its collaborators will present 11 abstracts that feature new Signatera data across various GI indications, including two oral presentations. An updated analysis from the previously published **GALAXY study**, the observational arm of the prospective CIRCULATE-Japan trial, will be presented in an oral presentation at the symposium and is also featured in ASCO GI's **press program**. GALAXY is one of the largest and most comprehensive prospective studies of MRD testing in resectable colorectal cancer (CRC).

Additionally, the first read-out from the Natera-sponsored BESPOKE CRC study will be presented in a rapid oral presentation. BESPOKE CRC is the first large, prospective, US-based study in resectable CRC, with over 130 participating sites.

Highlights from the abstracts selected for oral presentation include:

Abstract ID: 6 | Oral Abstract Session C | CRC | Presenter: Hiroki Yukami, MD

Circulating tumor DNA (ctDNA) dynamics in CRC patients (pts) with MRD: Updated analysis from GALAXY study in CIRCULATE-JAPAN

This latest analysis from GALAXY included close to 3,000 stage I-IV CRC patients. Key findings include:

- ctDNA dynamics at the six-month time point post-surgery showed that patients who remained ctDNA-positive were >6 times more likely to recur compared to those who cleared their ctDNA.
- ctDNA-positive patients with sustained clearance in subsequent time points as a result of adjuvant chemotherapy (ACT) had remarkably better outcomes compared to those with transient ctDNA clearance (24-month DFS rate; 90.1% vs 2.3%) or no clearance (24-month DFS rate; 90.1% vs 2%).
- In ctDNA-positive patients treated with ACT, a >50% decrease in ctDNA MTM/mL levels at six months, including those with complete clearances, was associated with better DFS than a <50% decrease or increase (24-month DFS rate; 51.1% vs 29%).

Abstract ID: 9 | Rapid Oral Abstract Session C | CRC | Presenter: Pashtoon Kasi, MD, MS

ctDNA for informing adjuvant chemotherapy (ACT) in stage II/III CRC: Interim analysis of BESPOKE CRC study

This analysis included 689 patients with stage II/III resectable CRC. Key findings include:

- Within the ctDNA-positive cohort, patients receiving ACT had significantly longer DFS compared to those in the observation group (24-month DFS rate; 42.4% vs 12.5%). No benefit of ACT was observed in ctDNA-negative patients.
- ctDNA monitoring allowed for oligometastases-directed therapy in 40% of patients who recurred.
- A separate poster on the BESPOKE CRC study (abstract ID: 54) found that in 400+ patients surveyed, ≥92% valued the information received from their Signatera results or would use Signatera to guide their clinical care. In addition, 73% reported that Signatera results reduced anxiety about cancer recurrence.

“These latest findings from the landmark CIRCULATE trial underscore Signatera’s ability to identify patients who may be more likely to benefit from adjuvant chemotherapy, showing the value of personalized MRD testing to guide treatment decisions in CRC and potentially spare patients from unnecessary toxicity,” said Hiroki Yukami, MD, from the Cancer Chemotherapy Center, Osaka Medical and Pharmaceutical University, and lead study author of the GALAXY study. “We are encouraged by the widespread attention and recognition this presentation has received from the oncology community, and are optimistic that the GALAXY study, along with the ALTAIR escalation and VEGA de-escalation arms of CIRCULATE, will fundamentally change the way CRC is treated.”

“We are pleased to share new data from the Japanese-based GALAXY and US-based BESPOKE CRC studies, which further demonstrate the prognostic and predictive power of longitudinal testing with Signatera in resectable

colorectal cancer," said Minetta C. Liu, MD, chief medical officer of oncology at Natera. "These two prospective clinical trials provide strong evidence supporting the clinical utility of Signatera to inform adjuvant chemotherapy decisions and facilitate surveillance for cancer recurrence."

Below are the additional Natera poster presentations at ASCO GI:

- Abstract ID: 54 | CRC | Presenter: Pashtoon Kasi, MD, MS
  Patient-reported outcomes from the BESPOKE CRC study
- Abstract ID: 27 | CRC | Presenter: Giulia Maddalena, MD
  INTERCEPT Program of ctDNA Testing for MRD in CRC: Results from a Prospective Clinical Cohort
- Abstract ID: 183 | CRC | Presenter: Hidekazu Oyoshi
  Prediction of postoperative recurrence by integrating preoperative ctDNA levels and tumor metastasis volume in pts with CRC with resectable lung or liver metastasis
- Abstract ID: 528 | Bile Duct Cancer | Presenter: Woo Jin Choi, MD, PhD
  The role of pre-operative ctDNA in resectable intrahepatic cholangiocarcinoma
- Abstract ID: 212 | Rectal Cancer | Presenter: Sakti Chakrabarti, MD
  Prognostic value of ctDNA testing in rectal cancer pts after neoadjuvant therapy (NAT) and surgery
- Abstract ID: 23 | CRC | Presenter: Masaaki Miyo, MD, PhD
  Association of ctDNA MRD detection with lymph node metastasis after local excision of pathological T1 CRC: First results from DENEB, a CIRCULATE-Japan GALAXY substudy
- Abstract ID: 196 | CRC | Presenter: Andrew Pellatt, MD
  Redefining The Prognostic Significance of RAS and BRAF V600E Mutations on Disease Free Survival in CRC Pts in the Era of ct-DNA Defined MRD: Results from the MD Anderson INTERCEPT Program
- Abstract ID: 695 | Pancreatic Cancer | Presenter: Ujwal Yanala, MD
  Utility of ctDNA for the detection of MRD after curative-intent therapy for pts with localized pancreatic adenocarcinoma (PDAC): A single institution series and meta-analysis
- Abstract ID: 214 | CRC | Presenter: Nikolas Naleid, MD
  Surveillance of Resected Metastatic Colorectal Cancer Utilizing Circulating DNA

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 180 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**.

Investor Relations: Mike Brophy, CFO, Natera, Inc., 510-826-2350, **investor@natera.com**
Media: Lesley Bogdanow, VP of Corporate Communications, Natera, Inc., **pr@natera.com**

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