NEWS RELEASE

Natera Announces Publication of Signatera™ Analysis from Randomized, Phase III CALGB (Alliance)/SWOG 80702 Study in Colorectal Cancer

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JAMA Oncology study highlights that Signatera-positive patients treated with celecoxib and conventional chemotherapy experienced a >40% reduction in risk of death, whereas Signatera-negative patients derived no significant benefit

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced the publication of findings from the randomized, phase III CALGB (Alliance)/SWOG 80702 study in **JAMA Oncology**. This publication builds on the initial presentation of results at the 2025 American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO GI) earlier this year.

CALGB (Alliance)/SWOG 80702 assessed the predictive value of postoperative personalized circulating tumor DNA (ctDNA) in patients with stage III colorectal cancer (CRC). The pre-specified post-hoc analysis included 940 patients with available post-surgical plasma samples, who were randomized to receive FOLFOX +/- celecoxib, a non-steroidal anti-inflammatory drug (NSAID). Key findings included:

- Adding celecoxib to conventional chemotherapy in Signatera-positive patients, after surgery reduced the risk of cancer recurrence and death by ~40%. Celecoxib improved disease-free survival (DFS) (adjusted HR=0.61, 95% CI 0.42-0.89; 3-year 41.0% vs. 22.6%) and overall survival (OS) (adjusted HR=0.62, 95% CI 0.40-0.96; 5-year: 61.6% vs. 39.9%) compared to placebo in Signatera-positive patients.
- Celecoxib benefit in Signatera-positive patients was independent of demographic, pathologic or molecular factors, including PIK3CA status, further defining a patient population who may benefit from the addition to

adjuvant treatment. Celecoxib improved DFS of Signatera-positive patients for both PIK3CA wild-type (adjusted HR=0.64, 95% CI 0.42-0.98) and PIK3CA altered (adjusted HR=0.19, 95% CI 0.06-0.58) tumors. No benefit was observed in Signatera-negative patients (PIK3CA wild-type adjusted HR=0.80, 95% CI 0.55-1.18; PIK3CA altered HR=0.85, 95% CI 0.33-2.24).

- New analysis showed statistical significance in the interaction between MRD status and treatment randomization. In 66% of patients with plasma and DNA samples that would pass minimum QC criteria for Signatera analysis in the CLIA lab, analysis showed an even stronger benefit for adjuvant celecoxib than in the overall cohort (adjusted HR=0.49); and it showed significance in the statistical interaction test comparing the effect of celecoxib vs. placebo between patients who were Signatera positive vs. negative. In Natera's standard lab practice, 99% of plasma and DNA samples meet QC criteria.

"For patients with detectable ctDNA after surgery, adding celecoxib to standard chemotherapy improved both DFS and OS," said Jonathan Nowak, M.D., Ph.D., Brigham and Women's Hospital, and corresponding author of the publication. "In addition to highlighting Signatera's predictive abilities in this setting, the publication also underscores its value as a prognostic marker for disease recurrence and survival."

"This publication marks another important milestone in colorectal cancer research, highlighting Signatera as a critical tool in disease management," said Adham Jurdi, M.D., senior medical director of GI oncology at Natera. "It further demonstrates Signatera's predictive utility in identifying, with great precision, patients with MRD who will likely benefit from celecoxib in addition to chemotherapy, regardless of their PIK3CA status."

About Natera

Natera™ is a global leader in cell-free DNA and precision medicine, 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 325 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, and through Foresight Diagnostics, its subsidiary, operates an ISO 27001-certified and CAP-accredited laboratory certified under CLIA in Boulder, Colorado. 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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