NEWS RELEASE

New MRD Publication in Unresectable Stage I-III Lung Cancer Demonstrates Signatera's Ability to Risk Stratify and Detect Progression Early

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Test performance showed 82% pre-treatment detection, with 100% longitudinal sensitivity and 100% longitudinal specificity to disease progression

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced a new study published in Frontiers in Oncology demonstrating the ability of Natera's personalized and tumor-informed molecular residual disease (MRD) test, Signatera™, to detect progression early, with high sensitivity and specificity, and risk stratify patients with unresectable stage I-III non-small cell lung cancer (NSCLC) treated with definitive radiotherapy. The full study can be found **here**.

Worldwide, lung cancer is the second most commonly diagnosed cancer. NSCLC is the most common type of lung cancer in the U.S., accounting for 81% of all lung cancer diagnoses.1 For early-stage NSCLC patients, 36% are inoperable and primarily managed with curative-intent radiotherapy, with or without chemotherapy;2 however, despite the treatment, 46% of patients still experience disease progression.3,4 Accurate risk assessment can identify patients who might derive benefit from additional treatment after radiotherapy, versus patients with more favorable outcomes who could be spared the unnecessary treatment toxicity. In addition, there is a need for sensitive and specific biomarkers to support early detection of progression before the onset of disease-related symptoms, at a time when therapy might provide greater clinical benefit.

This prospective study investigated the association of circulating tumor DNA (ctDNA) status with progression in patients with unresectable stage I-III NSCLC who underwent definitive nonsurgical treatment. A total of 70 serial

plasma samples from 17 NSCLC patients were monitored before, during, and after conventional radiation with or without concurrent systemic therapy and adjuvant durvalumab for a median of 26 months.

Key findings include:

- Pre-treatment ctDNA detection rate was 82% (14/17) and varied based on histology and stage.
- In the longitudinal setting, all patients with clinical progression had at least one ctDNA-positive result (9/9; 100% sensitivity), and all progression-free patients were persistently ctDNA-negative after completing radiation with or without chemotherapy (8/8; 100% specificity).
- ctDNA detection demonstrated an average lead time of 5.4 months over clinical progression.
- ctDNA status after radiotherapy (single time point: HR=24.2; p=0.004), as well as during adjuvant systemic therapy and/or surveillance (longitudinally; p<0.0001), was highly predictive of disease progression.
- In a multivariate analysis, ctDNA detection at the first post-radiation time point was the only significant prognostic factor associated with progression-free survival (HR: 13.4; p=0.02).

“This study shows that longitudinal ctDNA monitoring can be a highly sensitive and specific approach to predicting disease progression, enabling more customized treatment strategies for patients with unresectable NSCLC,” said Minetta Liu, MD, chief medical officer of oncology at Natera. “All patients in the study cohort who developed clinical progression had detectable ctDNA, demonstrating the potential of Signatera to identify those at a high risk of relapse who are likely to benefit from systemic therapy. These promising findings add to the growing body of evidence supporting the potential for Signatera to enhance the quality of care for patients with non-small cell lung cancer.”

This study builds on previous Signatera data across early- and late-stage NSCLC. This includes the EMPower Lung-1 trial presented at the 2023 ASCO annual meeting, which demonstrated the ability of ctDNA to monitor response to immunotherapy and predict clinical outcomes in advanced NSCLC patients,5 as well as real-world data presented at the AATS 2023 annual meeting supporting the use of Signatera to detect progression early in resected, early-stage NSCLC patients.6 This recent work builds upon the 2017 TRACERx Nature publication that first reported Signatera’s ability to detect relapse early with high sensitivity and specificity in patients with early-stage NSCLC.7

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 four 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 help identify recurrence earlier and optimize treatment decisions. The test has not been cleared or approved by the US Food and Drug Administration (FDA).

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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