NEWS RELEASE

New Publication Demonstrates Utility of Natera's Signatera™ Test in Melanoma

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Real-world findings from >550 plasma samples highlight prognostic and predictive value of Signatera for adjuvant decision-making and immunotherapy monitoring

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, today announced a new study published in Cancer showing the prognostic and predictive utility of Natera's personalized and tumor-informed molecular residual disease (MRD) test, Signatera, to inform adjuvant treatment decisions and monitor for recurrence and therapy response in patients with stages III-IV melanoma. The full study can be found **here**.

This study analyzed 555 prospectively collected plasma samples from 69 patients with stages III-IV melanoma, analyzed in three cohorts. Key takeaways include:

- Cohort A: Resectable stage III patients receiving immunotherapy or observation in the adjuvant setting:
  MRD positivity post-resection was associated with significantly shorter distant metastasis-free survival (HR=10.77; p=0.01), and identified patients most likely to benefit from adjuvant therapy. Signatera detected recurrence with an average lead time of 3 months over standard imaging.
- Cohort B: Unresectable stage III/IV patients receiving immunotherapy:
  An increase in ctDNA levels 3-11 weeks after starting immune checkpoint inhibitor therapy was associated with significantly shorter progression-free survival (HR=22; p=0.006). All patients with increasing ctDNA experienced disease progression (4/4), while all patients with decreasing ctDNA achieved complete or partial response (15/15). In two patients, Signatera also correctly differentiated between true progression vs. pseudo-

progression.

- Cohort C: Stage III/IV patients in surveillance after completion of immunotherapy:
  100% (7/7) of patients who were ctDNA-negative during surveillance remained progression-free until the last follow up (median 14.67 months), while all ctDNA-positive patients (3/3) experienced disease progression.

“ctDNA is emerging as a potential biomarker for informing adjuvant treatment decisions and assessing treatment response in metastatic disease in real-time,” said Zeynep Eroglu, M.D., medical oncologist in the department of cutaneous oncology at Moffitt Cancer Center and lead author of the study. “Our study shows the potential for a personalized, tumor-informed ctDNA assay to help with making informed and timely treatment decisions for patients with advanced melanoma across treatment settings. We hope that this will be explored further in prospective clinical trials.”

This new study builds upon prior literature supporting the validity and utility of Signatera for pan-cancer immunotherapy monitoring,1 which was the basis for Medicare’s **local coverage determination** issued in 2021. Although the use of immune checkpoint inhibitors has led to significant improvements in overall survival rates for patients with advanced melanoma,2-6 response can be difficult to assess and treatment related toxicity remains a problem. Current guidelines recommend periodic imaging and clinical assessment to determine therapeutic efficacy;7 however, imaging-based surveillance has limitations. This illustrates the unmet need for diagnostic tools, like Signatera, to help predict immunotherapy benefit in the adjuvant and metastatic settings and to identify patients early who have resistance to therapy.

“This collaborative analysis of real-world data supports the prognostic and predictive value of Signatera in the clinical management of melanoma patients after surgery, and those receiving an immune checkpoint inhibitor,” said Minetta Liu, M.D., chief medical officer of oncology at Natera. “It is critical to balance treatment-related benefit with toxicity, and ctDNA assessment by Signatera provides a means by which to predict and evaluate benefit from immunotherapy in melanoma, the deadliest of all skin cancers.”

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 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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