Natera and Genentech Initiate Phase III Trial Using Signatera™ as a Companion Diagnostic for Atezolizumab in Early-Stage Muscle-Invasive Bladder Cancer

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Signatera used to identify muscle-invasive urothelial carcinoma patients who are MRD-positive after surgery, for enrollment in IMvigor011 study evaluating adjuvant immunotherapy with atezolizumab

AUSTIN, Texas, March 10, 2021 /PRNewswire/ -- Natera, Inc. (NASDAQ: NTRA), a pioneer and global leader in cell-free DNA testing, today announced that the first patient has been screened in a new phase III clinical trial that uses its tumor-informed, personalized molecular residual disease (MRD) test, Signatera, as a companion diagnostic to identify muscle-invasive urothelial carcinoma (MIUC) patients eligible for investigational treatment with Genentech's, a member of the Roche group, cancer immunotherapy drug atezolizumab (Tecentriq)®.

The IMvigor011 study, sponsored by Genentech, is a global, randomized, placebo-controlled, phase III clinical trial to evaluate the safety and efficacy of adjuvant treatment with the PD-L1 inhibitor, atezolizumab, in patients with MIUC who are MRD-positive after surgery. Eligible patients will be screened with Signatera within the first 20 weeks after surgery, and the first approximately 500 patients who test MRD-positive will be enrolled and randomized to receive either atezolizumab or placebo for 12 cycles, or up to one year. The primary endpoint of the study will be disease-free survival.

"There is a strong unmet need in this population, as bladder cancer patients with residual disease post-surgery are known to be at the highest risk of recurrence," said Thomas Powles, M.D., Professor, Barts Cancer Institute, and Principal Investigator of the study. "The Signatera MRD test offers a personalized, real-time diagnostic to identify bladder cancer patients who need additional therapy and may benefit from adjuvant treatment with Tecentriq."

In an exploratory analysis from the phase III, randomized, controlled IMvigor010 trial, presented at the ESMO Immuno-Oncology conference in December 2020, the 37% of patients who tested MRD-positive with Signatera after surgery experienced significant benefit from adjuvant atezolizumab vs. observation (HR 0.59, p<0.001), while the 63% of patients who tested MRD-negative experienced zero treatment benefit. In an independent study of 68 patients with MIUC, published in the *Journal of Clinical Oncology* in 2019, Signatera detected relapse with 100% sensitivity and 98% specificity, reporting a median lead time of 96 days.[1]

"This partnership with Genentech marks a significant milestone for Natera and for the field of personalized medicine," said Solomon Moshkevich, Natera's General Manager of Oncology. "We look forward to a successful clinical trial, pairing atezolizumab with Signatera in an effort to bring highly effective treatment to the right set of patients at the earliest possible time."

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 clinical and research use, and in 2019, it was granted Breakthrough Device Designation by the FDA. 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. This maximizes accuracy for detecting the presence or absence of residual disease in a blood sample, even at levels down to a single tumor molecule in a tube of blood. Unlike a standard liquid biopsy, Signatera is not intended to match patients with any particular therapy; rather, it is intended to detect and quantify how much cancer is left in the body, to detect recurrence earlier and to help optimize treatment decisions. Signatera test performance has been clinically validated in multiple cancer types including colorectal, non-small cell lung, breast, and bladder cancers. Signatera has been developed and its performance characteristics determined by Natera, the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified.

About Natera

Natera is a pioneer and global leader in cell-free DNA testing from a simple blood draw. The mission of the company is to change the management of disease worldwide with a focus on women's health, oncology, and organ health. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas and San Carlos, California. It offers proprietary genetic testing services to inform obstetricians, transplant physicians, oncologists, and cancer researchers, including biopharmaceutical companies, and genetic laboratories through its cloud-based software platform. For more information, visit natera.com. Follow Natera on LinkedIn.

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 our efforts to develop and commercialize new product offerings, our ability to successfully increase demand for and grow revenues for our product offerings, whether the results of clinical or other studies will support the use of our product offerings, 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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References

1. Christensen E, Birkenkamp-Demtröder K, Sethi H, et al. Early detection of metastatic relapse and monitoring of therapeutic efficacy by ultra-deep sequencing of plasma cell-free DNA in patients with urothelial bladder carcinoma. *J Clin Oncol*. 2019;37(18):1547-1557.