



NEWS RELEASE

# Natera and Alliance for Clinical Trials in Oncology Announce Activation of Alliance A032103 (MODERN): A Randomized, Phase II/III Adjuvant Trial in Urothelial Cancer

4/1/2024

First of its kind study in muscle-invasive urothelial cancer, with both escalation and de-escalation arms

Approximately 1,000 patients will be enrolled at more than 300 sites

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA testing, and the Alliance for Clinical Trials in Oncology, which is part of the National Clinical Trials Network (NCTN) funded by the National Cancer Institute (NCI), part of National Institutes of Health, today announced the launch of Alliance A032103 (**MODERN**), a randomized, phase II/III, biomarker-integrated trial. Alliance A032103 (MODERN) will utilize Signatera™, Natera's personalized and tumor-informed molecular residual disease (MRD) test, to help guide personalized treatment based on molecular status in patients diagnosed with muscle-invasive urothelial cancer (MIUC) after radical cystectomy.

Urothelial cancer is the most common urinary cancer diagnosed in the United States, and approximately 35,000 patients per year are diagnosed with localized and locally advanced urothelial cancer.<sup>1</sup> Approximately 50% of patients treated with cystectomy will develop metastatic recurrence within 2-3 years.<sup>2,3</sup>

In the Alliance A032103 (MODERN) trial, approximately 1,000 patients will be enrolled at more than 300 sites in North America. Patients will be divided into two cohorts based on an initial assessment of MRD status. Patients who are Signatera MRD-positive will have treatment randomized to either nivolumab, a PD-1 antibody, or escalation with



nivolumab, a PD-1 antibody plus relatlimab, a LAG-3 antibody; LAG-3 and PD-1 are distinct inhibitory immune checkpoints. Patients who are Signatera MRD-negative will be randomized to either nivolumab, a standard of care therapy, or de-escalation to surveillance, with the surveilled patients receiving treatment only upon future conversion to MRD-positive status based on serial testing.

This trial was made possible by results of the pivotal CheckMate 274 trial,<sup>4</sup> which established the safety and efficacy of adjuvant nivolumab in MIUC, and is now the only FDA-approved therapy in this disease setting.<sup>5</sup> Additionally, data published in the journal Nature in 2021 from the IMvigor010 trial showed that 63% of patients with MIUC tested Signatera MRD-negative after surgery, and those patients received no significant benefit from adjuvant immunotherapy (atezolizumab) versus observation.<sup>6</sup>

“The MODERN trial represents a step towards precision medicine in bladder cancer treatment,” said Matthew Galsky, MD, professor of medicine (hematology and medical oncology), director of genitourinary medical oncology, co-director of the Center of Excellence for Bladder Cancer and associate director for translational research at the Tisch Cancer Institute. “By using Signatera to measure residual cancer after surgery, the Alliance A032103 (MODERN) trial may ultimately help to tailor the use of immunotherapy after surgery and optimize the care of individual patients.”

“MODERN, like the CIRCULATE clinical trials in colorectal cancer, is a pivotal study that examines how Signatera-guided escalation and de-escalation pathways can potentially improve patient outcomes,” said Minetta Liu, MD, chief medical officer of oncology at Natera. “We are grateful to collaborate with the Alliance on this important study.”

## 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, ovarian cancer 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](http://www.natera.com).

## About Alliance for Clinical Trials in Oncology

The Alliance for Clinical Trials in Oncology develops and conducts clinical trials with promising new cancer therapies, and utilizes the best science to develop optimal treatment and prevention strategies for cancer, as well as research methods to alleviate side effects of cancer and cancer treatments. The Alliance is part of the National Clinical Trials Network (NCTN) funded by the National Cancer Institute (NCI) and serves as a research base for the NCI Community Research Oncology Program (NCORP). The Alliance comprises nearly 10,000 cancer specialists at hospitals, medical centers, and community clinics across the United States and Canada. To learn more, visit [www.AllianceforClinicalTrialsinOncology.org](http://www.AllianceforClinicalTrialsinOncology.org).

## Forward-Looking Statements (Natera)

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](http://www.natera.com/investors) and [www.sec.gov](http://www.sec.gov).

## References

1. Source: Kantar Health (Cerner Enviza) estimate.
2. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol*. 2001;19(3):666-75.
3. Tian J, Sun J, Fu G, et al. Population-based outcome of muscle-invasive bladder cancer following radical cystectomy: who can benefit from adjuvant chemotherapy? *Transl Androl Urol*. 2021;10(1):356-373.
4. Bajorin D, Witjes JA, Gschwend JE, et al. Adjuvant atezolizumab versus observation in muscle-invasive urothelial

- carcinoma (IMvigor010): a multicentre, open-label, randomised, phase 3 trial. N Engl J Med. 2021;384(22):2102-2114.
5. Nivolumab Package Insert. [https://packageinserts.bms.com/pi/pi\\_opdivo.pdf](https://packageinserts.bms.com/pi/pi_opdivo.pdf)
  6. Powles T, Assaf ZJ, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. Nature. 2021;595(7867):432-437.

Investor Relations: Mike Brophy, CFO, Natera, Inc., 510-826-2350, [investor@natera.com](mailto:investor@natera.com)

Media: Lesley Bogdanow, VP of Corporate Communications, Natera, Inc., [pr@natera.com](mailto:pr@natera.com)

Source: Natera, Inc.