NEWS RELEASE

Natera Announces Enrollment of First Patients in SAGITTARIUS: a Randomized, Phase III Clinical Trial in Colon Cancer

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SAGITTARIUS is Natera's first interventional trial using SignateraTM to select patients for targeted therapy in early-stage colon cancer

Approximately 700-900 patients expected to be enrolled across more than 20 sites

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and genetic testing, today announced the enrollment of the first patients in the SAGITTARIUS clinical trial. Sponsored by The AIRC Institute of Molecular Oncology (IFOM-ETS) and funded by the European Union Horizon Europe Programme, SAGITTARIUS is a global, randomized, phase III clinical trial designed to evaluate the use of Signatera to guide personalized adjuvant treatment strategies for patients with colon cancer.

The study aims to enroll approximately 700-900 stage III and high-risk stage II colon cancer patients following surgical resection.

- Signatera-positive patients will be randomized to receive either genotype-guided therapy tailored to their individual tumor mutational profile or six months of standard chemotherapy. The trial’s investigational arm will explore the potential of administering immunotherapy or targeted agents approved for metastatic colon cancer earlier in the disease course to increase the proportion of patients cured with adjuvant therapy. This genomically-driven approach will focus on mismatch repair status, POLE, RAS/RAF mutation status, and HER2 amplification status.

- For Signatera-negative patients, the trial will compare physician choice treatments with options for de-escalation to observation or single-agent capecitabine for six months.

SAGITTARIUS includes collaborations with 9 partners in 5 countries in Europe, and a network of 26 clinical centers in Italy, Spain, and Germany.

“The enrollment of the first patients in SAGITTARIUS represents a significant milestone in a trial that has the potential to transform treatment approaches for colorectal cancer,” said Silvia Marsoni, MD, PhD, head of the precision oncology unit at IFOM ETS and scientific coordinator of the SAGITTARIUS Project.

“The trial aims to move beyond the traditional one-size-fits-all, post-surgical standard of care with chemotherapy by introducing a truly personalized treatment approach tailored to each patient,” said Adham Jurdi, MD, senior medical director of oncology at Natera. “Signatera-positive patients will receive adjuvant therapies matched to their specific mutational profiles. Additionally, we are optimistic that the study will generate evidence to support the de-escalation of chemotherapy for Signatera-negative patients.”

Clara Montagut, MD, PhD, head of the gastrointestinal cancer unit at Hospital del Mar in Barcelona, Spain, and principal investigator of the SAGITTARIUS clinical trial, further emphasized the study’s innovative goals, noting, “We aim to anticipate the use of therapies tailored to the molecular landscape of the patient’s tumor, including immunotherapy and targeted therapies with proven efficacy in the metastatic setting within the adjuvant treatment context. To our knowledge, SAGITTARIUS is currently the only trial pursuing this approach in the field of liquid biopsy research.”

About the SAGITTARIUS Horizon Europe project

The SAGITTARIUS clinical trial is part of a wider effort, the SAGITTARIUS project, funded by the European Union Horizon Europe Programme. The SAGITTARIUS project, which also includes health cost and quality of life research to comprehensively assess the full cost-effectiveness of interventional liquid biopsy, aims to pave the way for more effective, tailored treatments that enhance both outcomes and quality of life for colon cancer patients, while potentially lowering the cost impact on private and public health systems and reducing treatment disparities. The SAGITTARIUS project is a collaboration of 9 partners in Italy, Spain, Germany, Belgium and Estonia. For more information, visit **www.sagittarius-horizon.eu**.

About IFOM ETS

IFOM ETS - the AIRC Institute of Molecular Oncology is a leading cancer research institute based in Milan, Italy, with international outreach in Japan. The institute, supported by the AIRC Foundation for Cancer Research, is focused on the study of cancer formation and development at molecular level, with a strong emphasis on rapidly translating

research findings into clinical benefit for cancer patients. With the expertise in trial design and management of its Precision Oncology Unit, IFOM is the sponsor of the SAGITTARIUS clinical trial and the coordinator of the homonymous Horizon Europe project. For more information, visit **www.ifom.eu/en/**.

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 over 100 peer-reviewed papers.

About Natera

Natera™ is a global leader in cell-free DNA and genetic 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 250 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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