NEWS RELEASE

Natera Announces DECIPHER: A Phase II, Single-Arm Adjuvant Trial in Gastroesophageal Cancer

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First-of-its-kind study in gastroesophageal adenocarcinoma using Signatera to guide treatment and assess the efficacy of a novel HER2-directed adjuvant treatment

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA (cfDNA) and genetic testing, today announced a new gastroesophageal cancer trial, DECIPHER, that will utilize the company's personalized and tumor-informed molecular residual disease (MRD) test, Signatera™, to guide patient selection and assess the rate of MRD clearance in patients being treated for gastroesophageal cancer.

DECIPHER (Developing ctDNA Guided Adjuvant Therapy for Gastroesophageal Cancer) is a single-arm, open-label phase II trial, and the first trial to evaluate the efficacy of a HER2-directed antibody-drug conjugate in gastroesophageal adenocarcinoma (EGC) patients in the adjuvant setting. The study plans to enroll 25 patients from more than 10 sites across the United Kingdom. Patients who are Signatera-positive following neoadjuvant chemotherapy and surgery will forgo standard-of-care adjuvant chemotherapy and receive the investigational therapy for a maximum of eight cycles. Signatera will be used to measure MRD-positivity following surgery and serially thereafter, with MRD clearance serving as the primary endpoint.

"With an adaptive approach aimed at eliminating MRD, DECIPHER is designed to offer patients a second chance at a cure when they have not responded to standard of care therapies," said Dr. Elizabeth Smyth, M.D., consultant in medical oncology at Oxford University Hospitals NHS Foundation Trust l and chief investigator of the trial. "Signatera's personalized, tumor-informed approach, which has demonstrated high sensitivity across several different cancer types including EGC, will be a key component of this study."

This launch of DECIPHER follows data from the PLAGAST study presented last month at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. The data showed that EGC patients who were Signatera-positive following neoadjuvant FLOT (fluorouracil, leucovorin, oxaliplatin and docetaxel) chemotherapy and surgical resection were at an extremely high risk of disease progression by 12 months, despite standard of care adjuvant treatment, and had a 24-month overall survival rate of zero.1

Gastroesophageal cancer is a common global cancer that has sustained a nearly 2.5-fold increase in incidence over the last two decades.1 Patients with early-stage disease are typically treated with neoadjuvant chemotherapy, followed by surgery and adjuvant chemotherapy. Despite this aggressive and multimodal approach, treatment is curative in less than 50 percent of patients.2

“We are pleased to work with leading investigators in the UK on the first interventional trial for Signatera in gastroesophageal cancer,” said Adham Jurdi, M.D., senior medical director of oncology at Natera. “With DECIPHER, we aim to demonstrate how the pairing of Signatera with innovative therapies can potentially enable new personalized treatment options and ultimately improve outcomes for EGC patients.”

DECIPHER will be featured today, June 27, 2024, in a poster at the European Society for Medical Oncology Gastrointestinal Cancers (ESMO GI) Congress 2024 in Munich, Germany. The poster is entitled, “A single arm phase II trial of trastuzumab deruxtecan in patients with gastro-oesophageal adenocarcinoma cancer who are ctDNA and HER2 positive: DECIPHER”.

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 60 peer-reviewed papers.

About Natera

NateraTM 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 200 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, or our expectations 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**.

References

1. Zannan et. al. Longitudinal circulating tumor DNA (ctDNA) analysis during treatment (Tx) of locally advanced resectable (LAR) gastric or gastroesophageal junction(G/GEJ) adenocarcinoma (ADENOCA): the PLAGAST prospective biomarker study. 2024 ASCO Annual Meeting. Poster #4028
2. **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9148370/**

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