NEWS RELEASE

Prospective DEFINE-HT Study Demonstrates that Prospera™ Heart is Predictive of Clinical Outcomes and Outperforms Biopsy in Predicting Graft Dysfunction

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Prospera Heart with donor quantity score (DQS) demonstrates significant correlation with clinical outcomes

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and genetic testing, announced the results of its DEFINE-HT clinical trial in heart transplantation, which were shared today, April 29, 2025, in an oral presentation at the International Society for Heart and Lung Transplantation 45th Annual Meeting in Boston, MA.

DEFINE-HT is the first prospective, multicenter study in heart transplant recipients designed to assess whether elevated levels of donor-derived cell-free DNA (dd-cfDNA), as measured by Prospera Heart with DQS, are associated with adverse clinical outcomes. Following heart transplant, Prospera testing was performed concurrently with rejection surveillance monitoring, including endomyocardial biopsies (EMB), for up to one year.

Findings from the study, which included more than 1,100 dd-cfDNA samples, demonstrated that dd-cfDNA significantly correlated with adverse outcomes, a composite endpoint defined as the total number of treated rejections, graft dysfunctions, re-transplantations, and deaths at one year after heart transplant.

Key findings include:

- Patients with at least one elevated dd-cfDNA measurement were significantly more at risk for experiencing an

adverse event (HR: 2.56, p=0.0299).

- Elevated dd-cfDNA predicted graft dysfunction 3x more than biopsy.
- Prospera with DQS demonstrated a stronger correlation with clinical outcomes compared to donor fraction alone.

“The results of DEFINE-HT show that dd-cfDNA can predict clinical outcomes after heart transplantation, which can allow for improved and personalized patient management based on individual risk,” said Palak Shah, M.D., M.S., national principal investigator for DEFINE-HT, director of the Inova Cardiovascular Genomics Center, and medical director of mechanical circulatory support at Inova Fairfax Medical Campus. “Through vigorous research, we continue to drive innovative advancements in heart transplantation, finding less invasive approaches that lead to better patient outcomes.”

“In combination with a better understanding of the association of dd-cfDNA and clinical outcomes, DEFINE-HT underscores the utility of Prospera as a tool to help identify patients who may be at risk for adverse outcomes,” said Michael Olympios, M.D., medical director, heart transplant at Natera. “Importantly, the insights gained from this study suggest that Prospera has the potential to obviate invasive surveillance EMB, which will be investigated in an ongoing multi-center, randomized, comparative effectiveness study comparing dd-cfDNA and EMB surveillance (ACES-EMB).”

About Prospera

The Prospera™ test leverages Natera’s core single-nucleotide (SNP)-based massively multiplexed PCR (mmPCR) technology to identify allograft rejection non-invasively and with high precision and accuracy, without the need for prior donor or recipient genotyping. The test works by measuring the fraction of donor-derived cell-free DNA (dd-cfDNA) in the recipient’s blood. It may be used by physicians considering the diagnosis of active rejection, helping to rule in or out this condition when evaluating the need for diagnostic testing or the results of an invasive biopsy. The Prospera test has been clinically and analytically validated for performance regardless of donor relatedness, rejection type, and clinical presentation.

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 supported by more than 250 peer-reviewed publications that demonstrate excellent performance. 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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