NEWS RELEASE

Natera to Present over 25 Signatera™ Studies at 2025 ASCO Annual Meeting

2025-05-22

Studies include nearly 25,000 patients across multiple indications, showcasing the clinical impact of Signatera

- Breast: 8 accepted abstracts (4 oral presentations), including interim analysis from the randomized Signatera-guided interventional DARE trial; a large real-world study of metastatic treatment monitoring; and two readouts from the ISPY-2 trial
- Signatera Genome: Large-scale, pan-cancer performance of Signatera Genome assay
- GI, GU, Skin, Sarcoma: Significance of Signatera MRD and dynamics to predict recurrence, progression, and treatment response across multiple disease subtypes

AUSTIN, Texas--(BUSINESS WIRE)-- **Natera, Inc.** (NASDAQ: NTRA), a global leader in cell-free DNA and precision medicine, today announced that data from more than 25 Signatera studies will be presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place from May 30 - June 3, 2025 in Chicago, IL.

Together with its collaborators, Natera will showcase the clinical utility of Signatera across 10 different cancer types. This extraordinary breadth of data includes analyses of thousands of patients, demonstrating Natera's leadership in circulating tumor DNA (ctDNA) monitoring and molecular residual disease (MRD) assessment.

"The depth and breadth of Natera's research at ASCO is our most significant to date, with multiple impactful datasets in several histologies," said Alexey Aleshin, M.D., corporate chief medical officer and general manager of oncology at Natera. "The interim analysis from the DARE trial shows a possible first signal in a randomized setting that treating high-risk breast cancer patients based on Signatera results can impact clearance rates. We also look forward to sharing results on our ultra-sensitive Signatera Genome assay, along with numerous other

presentations underscoring our commitment to advance the way cancer is managed."

Highlights include:

- DARE Clinical Trial: Oral Presentation
    - DARE is a prospective, randomized study, launched in 2021, to investigate the utility of Signatera for guiding adjuvant endocrine therapy in 585 women with high-risk, estrogen receptor-positive, HER2-negative (ER+/HER2-) breast cancer. It assesses the novel concept of "treatment on molecular recurrence" (TOMR). Patients who were Signatera-positiveand imaging-negative were randomized into two arms: the standard-of-care (SOC) arm with endocrine therapy vs. the escalated arm with fulvestrant+palbociclib (CDK 4/6i). This interim analysis of 507 women and 2,208 plasma samples demonstrates the exceptional clinical performance of Signatera, and the early feasibility of both this treatment escalation approach and the TOMR trial strategy, including:
    - Strong test sensitivity and NPV: Among patients who remained persistently Signatera-negative during screening (>400 pts), 99% remained recurrence free with a median follow up of 27.4 months.
    - High randomization rate: Of patients who tested Signatera-positive, 73% were negative on imaging, and 93% were willing to be randomized.
    - 2x higher ctDNA clearance: Patients in Arm A had a 2x higher rate of ctDNA clearance at 3 months vs. Arm B.
- Signatera Monitoring in Metastatic Breast Cancer: Oral Presentation
    - This real-world analysis of over 600 metastatic breast cancer (mBC) patients across all disease subtypes and a wide range of therapeutic regimens (e.g., chemo, ADCs, CDK4/6) shows the utility of metastatic monitoring with Signatera:
    - Serial ctDNA testing done at an appropriate cadence (6 weeks) can inform treatment response and clinical decisions in metastatic breast cancer.
    - Signatera ctDNA dynamics were the strongest predictor of treatment benefit in a multivariate analysis, based on measuring time to next treatment (TTNT).
    - Nearly 75% of patients with favorable dynamics remained on the same treatment for over 4 months, including those receiving antibody drug conjugates (ADCs) where therapy response can be challenging to evaluate on imaging.
- Pan-Cancer Performance of Signatera Genome: Poster Presentation
    - Large-scale presentation of Signatera's Genome assay, analyzing more than 3,000 samples from over 300 patients across 5 major cancer types.
    - The study includes analysis of patients with breast cancer, colorectal cancer, non-small cell lung cancer, melanoma, and renal cell carcinoma.

- Signatera Performance in Post-Surgical Stage I-IIIb Melanoma: Poster Presentation
    - This study includes 197 patients and 1,681 plasma samples, tested for a median period of 2 years. This is one of the most comprehensive MRD/monitoring datasets thus far in early melanoma, demonstrating the ability of Signatera to identify patients who may benefit from escalated imaging or earlier treatment initiation.
    - Post-surgical Signatera-positivity was the most significant predictor of recurrence free survival (RFS).
    - In the surveillance setting, Signatera-positivity was predictive of shorter RFS (HR: 24.0, P < 0.001).

Full list of oral presentations at ASCO:

May 30, 2:45 PM CT | 3008 | Breast

Presenter: Silver Alkhafaji

Circulating tumor DNA (ctDNA) in patients with stage 2/3 HR+HER2-negative breast cancer (BC) treated with neoadjuvant endocrine therapy (NET) in the I-SPY2 endocrine optimization pilot (EOP) trial

June 1, 9:45 AM CT | 4503 | Genitourinary

Presenter: Thomas Powles, MBBS, MRCP, M.D.

Circulating tumor DNA (ctDNA) in patients with muscle-invasive bladder cancer (MIBC) who received perioperative durvalumab (D) in NIAGARA

June 1, 11:30 AM CT | 3518 | Gastrointestinal

Presenter: Aron Bercz, M.D.

Circulating Tumor DNA Provides an Early Response Assessment in Anal Squamous Cell Carcinoma Treated With Definitive Chemoradiation

June 1, 4:30 PM CT | 1010 | Breast

Presenter: Lajos Pusztai, M.D., DPhil

Circulating tumor (ct)DNA monitoring of ER+/HER2- high-risk breast cancer (BC) during adjuvant endocrine therapy (ET) (DARE)

June 1, 4:30 PM CT | 1011 | Breast

Presenter: Pedram Razavi, M.D., Ph.D.

Circulating tumor DNA (ctDNA) dynamics as a predictor of treatment response in metastatic breast cancer (mBC)

June 2, 3:00 PM CT | 504 | Breast

Presenter: Rita Mukhtar, M.D.

Predicting nodal burden after neoadjuvant chemotherapy (NAC) with circulating tumor (ct)DNA for surgical

planning: Results from the I-SPY2 trial

Full list of poster presentations at ASCO:

May 31, 9:00 AM CT | 11537 | Sarcoma

Presenter: Adie Victor, M.D., M.S.

Early on-treatment circulating tumor (ct)DNA dynamics in response to therapy in patients with sarcoma

May 31, 9:00 AM CT | 11531 | Sarcoma

Presenter: Maggie Zhou, M.D.

Early assessment of response to chemotherapy via ctDNA in soft tissue sarcoma

May 31, 9:00 AM CT | TPS3647 | Gastrointestinal

Presenter: Clara Montagut, M.D.

A precision medicine trial leveraging tissue and blood-based tumor genomics to optimize treatment in resected stage III and high-risk stage II colon cancer (CC) patients (pts): The SAGITTARIUS Trial.

May 31, 9:00 AM CT | 4067 | Gastrointestinal - FMI

Presenter: Michele Prisciandaro, M.D.

Tumor-informed liquid biopsy in predicting recurrence in patients with operable gastroesophageal adenocarcinoma: the LIQUID study

May 31, 9:00 AM CT | 4130 | Gastrointestinal

Presenter: Maen Abdelrahim, M.D.

Real-world analysis of ctDNA and other biomarkers in patients with curatively resected Stage I-III Biliary Tract Cancer

May 31, 9:00 AM CT | 3600 | Gastrointestinal

Presenter: Eiji Oki, Ph.D.

Impact of Perioperative Complications on ctDNA-based MRD Detection and Prognosis: Insights from the GALAXY Study

May 31, 9:00 AM CT | 3591 | Gastrointestinal

Presenter: Emerik Osterlund, M.D., Ph.D.

Biologic correlates of circulating tumor DNA (ctDNA) shedding in the INTERCEPT colorectal cancer (CRC) study

May 31, 9:00 AM CT | 3597 | Colorectal

Presenter: Midhun Malla, M.D., M.S.

ctDNA dynamics and targeted therapies associated with genetic mutations in patients with colorectal cancer

May 31, 9:00 AM CT | 4073 | Esophagogastric Gastric

Presenter: Reetu Mukherji, M.D.

Exome analysis of over 5000 esophagogastric cancers

June 1, 9:00 AM CT | 9574 | Merkel Cell Carcinoma

Presenter: Joshua Elbridge Chan

Comparison of surveillance circulating tumor DNA and merkel polyomavirus antibody titer for detection of merkel cell carcinoma recurrence

June 1, 9:00 AM CT | 9571 | Melanoma

Presenter: George Ansstas, M.D.

Longitudinal ctDNA monitoring for post-surgical molecular residual disease in patients with stage I-IIIb melanoma

June 1, 9:00 AM CT | 9523 | Melanoma

Presenter: Caroline Burkey

Circulating tumor DNA (ctDNA) dynamics during anti-PD-1 based therapy to predict clinical outcomes in advanced stage melanoma: A multicenter retrospective study.

June 1, 9:00 AM CT | 9584 | Melanoma

Presenter: Vincent The-Luc Ma

Sensitivity of circulating tumor DNA (ctDNA) for disease recurrence or relapse in melanoma patients

June 1, 9:00 AM CT | 5563 | Gynecological

Presenter: Jung-Yun Lee, M.D., Ph.D.

ctDNA monitoring in participants with ovarian cancer treated with neoadjuvant pembrolizumab (pembro) plus chemotherapy (chemo) with or without the anti–immunoglobulin-like transcript 4 (ILT4) monoclonal antibody MK-4830

June 2, 9:00 AM CT | 4565 | Genitourinary

Presenter: Adanma Ayanambakkam, M.D.

Association of Tumor-Informed ctDNA-based Molecular Residual Disease (MRD) with Clinical Outcomes for Upper Tract Urothelial Cancer (UTUC)

June 2, 9:00 AM CT | 4602 | Genitourinary

Presenter: Ilana Epstein

Correlation of circulating tumor DNA (ctDNA) dynamics with clinical response in muscle-invasive bladder cancer (MIBC) patients (pts) undergoing trimodality therapy (TMT)

June 2, 9:00 AM CT | 4560 | Genitourinary

Presenter: Kevin R. Reyes, BS

Circulating tumor DNA (ctDNA) monitoring in patients (pts) with advanced urothelial carcinoma (aUC) treated with Enfortumab Vedotin +/- Pembrolizumab (EVP)

June 2, 9:00 AM CT | TPS620 | Breast

Presenter: Michail Ignatiadis, M.D., Ph.D.

EORTC-2129-BCG: Elacestrant for treating ER+/HER2- breast cancer patients with ctDNA relapse (TREAT ctDNA)

June 2, 9:00 AM CT | 581 | Breast

Presenter: Julia Foldi, M.D., Ph.D.

Serial circulating tumor DNA (ctDNA) monitoring in early-stage, HR+/HER2-, invasive lobular carcinoma (ILC) of the breast and impact on clinical outcomes

June 2, 9:00 AM CT | 560 | Breast

Presenter: Marla Lipsyc-Sharf, M.D.

Cadence of circulating tumor DNA (ctDNA) testing for molecular surveillance in early-stage breast cancer (eBC)

June 2, 9:00 AM CT | 612 | Breast

Presenter: Mei Wei, M.D.

I-SPY2 endocrine optimization pilot (EOP): Neoadjuvant lasofoxifene (Laso) in molecularly selected patients with hormone receptor positive (HR+)/HER2 negative (HER2-) stage 2/3 breast cancer (BC)

June 2, 1:30 PM CT | 3142 | Pancancer

Presenter: Mridula George, M.D.

Clinical performance of Signatera Genome assay in a cohort of patients (pts) with solid tumors

June 2, 1:30 PM CT | 3048 | Gastrointestinal

Presenter: John Paul Y.C. Shen, M.D.

Development of a methylation-based, tissue-free test for the detection of molecular residual disease by circulating tumor DNA

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 has coverage by Medicare across a broad range of indications. Signatera has been clinically validated across multiple cancer types and indications, with published evidence in more than 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 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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Source: Natera, Inc.