BillionToOne's Northstar Response® Is a Stronger Predictor of Immunotherapy Outcomes Than Standard-of-Care Imaging for Cancer Patients in Peer-Reviewed Study

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Tissue-free ctDNA monitoring was the dominant independent predictor of survival across 12 tumor types and two prospective cohorts

MENLO PARK, Calif., June 29, 2026 /PRNewswire/ -- BillionToOne, Inc. (Nasdaq: BLLN), a next-generation molecular diagnostics company with a mission to create powerful and accurate tests that are accessible to all, today announced the publication of *Longitudinal Methylated ctDNA Increases Predict Immunotherapy Progression Across Solid Tumors*, a peer-reviewed study demonstrating that Northstar Response® was a stronger predictor of survival than standard-of-care imaging in patients with advanced solid tumors receiving immunotherapy or immunotherapy combination therapy, and that the addition of molecular monitoring to imaging provided greater predictive power than imaging alone. The findings were reproduced in an independent prospective validation cohort, with consistent results across tumor types and treatment regimens.

Conducted in collaboration with the Allegheny Health Network Cancer Institute, the study enrolled 142 patients across two independent cohorts spanning 12 solid tumor types. In a multivariate analysis incorporating both Northstar Response and blinded central radiographic review using RECIST criteria, molecular progression emerged as the dominant independent predictor of survival (**hazard ratio 5.3**), substantially outweighing radiographic progression. The strongest predictive performance came from pairing Northstar Response with imaging: patients whose disease progressed on both molecular and imaging assessment had the poorest outcomes of all (**hazard ratio 13.8 at the landmark assessment**; **19.7 with continued longitudinal monitoring**), and the combined molecular-plus-imaging approach achieved the highest predictive discrimination of any method evaluated.

Northstar Response also helped resolve a particularly challenging clinical dilemma in oncology: patients whose imaging show "stable disease" and thus have findings that cannot reliably be distinguished between early treatment benefit and failure. Among these patients, molecular progression identified those at substantially higher risk and conveyed prognostic information that imaging alone could not provide.

On average, Northstar Response identified cancer progression **a median of 62 days** before clinicoradiographic progression, representing a potentially actionable window for oncologists to reassess surveillance or treatment strategy before conventional methods signal failure. The assay achieves this through simple serial blood draws collected throughout treatment that integrate into routine oncology practice.

"The lead time advantage here is reflective of real-world patient treatment situations and the rhythm of typical oncology practices — by using Response, a physician has information two treatment cycles earlier than they would when using imaging alone," said Ali Zaidi, MD, *Professor of Surgery and Medicine at Drexel University College of Medicine; Medical Director of Aerodigestive Research at Allegheny Cancer Institute, Allegheny Health Network.* "That window has real implications for how we manage patients."

The study also found that 1 in 4 patients exhibited a molecular rebound pattern (an early favorable decrease signal followed by a subsequent rise) that suggests a single ctDNA assessment could misclassify patients as responding when the likelihood of treatment failure remains high. Only through serial sampling across multiple cycles were the investigators able to fully capture this kinetic shift, underscoring an important limitation of single-timepoint monitoring approaches for patients receiving immunotherapy.

"For patients with advanced cancer on immunotherapy, the clinical question that matters most isn't whether treatment is working at week four — it's whether it's still working over time," said Dr. Zaidi. "These data show that serial molecular monitoring can answer that question earlier, and more independently, than imaging alone."

The Northstar Response assay uses proprietary single-molecule next-generation sequencing (smNGS) platform with Quantitative Counting Template ™ (QCT ™) technology to quantify tumor-specific methylation from a simple blood draw, enabling treatment response monitoring across multiple solid tumor types. Northstar Response complements Northstar Select®, BillionToOne's liquid biopsy for therapy selection in cancer patients. Together, the assays support clinicians from treatment selection through ongoing response monitoring without dependence on tumor tissue.

"Therapy selection and treatment monitoring are two of the most important decisions in oncology," said Allen Chen, MD, Vice President of Oncology Clinical Development and Medical Affairs at BillionToOne. "Through simple blood draws, Northstar Select and Northstar Response provide clinicians with complementary molecular tools that allow for truly personalized cancer care to guide patients throughout their treatment journey."

About BillionToOne

Headquartered in Menlo Park, California, BillionToOne is a next-generation molecular diagnostics company with a mission to create powerful and accurate tests that are accessible to all. The company's patented Quantitative Counting Templates ™ (QCT ™) molecular counting platform is the only multiplex technology that can accurately count DNA molecules at the single-molecule level. For more information, visit www.billiontoone.com.

About Northstar Select®

Northstar Select, BillionToOne's highly sensitive comprehensive genomic profiling (CGP) liquid biopsy assay, demonstrated superior performance in detecting more clinically actionable alterations in circulating tumor DNA (ctDNA) compared to other liquid biopsy tests on the market. In a prospective head-to-head comparison study which included 182 patients with more than 17 solid tumor types, Northstar Select detected 51% more clinically actionable or pathogenic single nucleotide variant (SNV)/Indels and 109% more copy number variants (CNVs) than the aggregated results from available comparators, with 45% fewer null reports.[2]

About Northstar Response®

Northstar Response is BillionToOne's tissue-free, methylation-based ctDNA assay purpose-built for treatment response monitoring in patients with cancer. Powered by the company's patented QCT ™ molecular counting platform — the only multiplex technology capable of counting DNA molecules

at the single-molecule level — Northstar Response quantifies tumor burden through serial blood draws with no dependence on tumor tissue at any stage of the patient journey.

Disclaimer

Northstar Select and Northstar Response may produce false-positive or false-negative results. Test results are not a guarantee of the presence or absence of disease or treatment response and should not be used as the sole basis for medical decision-making. Results should be interpreted in conjunction with the patient's clinical presentation, radiographic findings, and other diagnostic information. Northstar Response is intended to complement, not replace, standard clinical and radiographic assessment of disease status. Northstar Select and Northstar Response are laboratory-developed tests (LDTs) performed in a CLIA-certified and CAP-accredited laboratory. These tests have not been cleared or approved by the U.S. Food and Drug Administration (FDA). Test performance may vary based on factors including cancer type, disease burden, treatment, and specimen characteristics.

Forward-Looking Statements

This press release contains certain forward-looking statements within the meaning of federal securities laws. These forward-looking statements generally are identified by the words "believe," "project," "expect," "anticipate," "estimate," "intend," "strategy," "future," "opportunity," "plan," "may," "should," "will," "would," "will be," "will continue," "will likely result," and similar expressions. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. Forward-looking statements in this press release include, but are not limited to, statements regarding the clinical performance and utility of Northstar Response. These statements are based on management's current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from these statements due to a number of factors, some of which are beyond BillionToOne's control. These and additional risks and uncertainties could affect BillionToOne's financial and operating results and cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. These risks and uncertainties include, but are not limited to, those discussed under the captions "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operation" and elsewhere in BillionToOne's most recently filed Quarterly Report on Form 10-Q, its Annual Report on Form 10-K, and other filings the company makes with the Securities and Exchange Commission from time to time. The forward-looking statements in this press release are based on information available to BillionToOne as of the date hereof, and BillionToOne disclaims any obligation to update any forward-looking statements provided to reflect any change in its expectations or any change in events, conditions, or circumstances on which any such statement is based, except as required by law. These forward-looking statements should not be relied upon as representing BillionToOne's views as of any date subsequent to the date of this press release.

1. Anees et al. Longitudinal Methylated ctDNA Increases Predict Immunotherapy Progression Across Solid Tumors, The Journal of Liquid Biopsy, https://doi.org/10.1016/ j.jlb.2026.100477

2. Bower, X., Wignall, J., Varga, M. G., et al. Validation of a liquid biopsy assay with increased sensitivity for clinical comprehensive genomic profiling. The Journal of Liquid Biopsy. https://doi.org/10.1016/j.jlb.2025.100322. Head-to-head improvement % determined when compared to comparator products in the aggregate. Actual percentages may vary depending on the individual comparator liquid biopsy test.

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