



Caris Life Sciences' Real-World Data Uncovers Metastatic Breast Cancer Patient Responses and Resistance to Trastuzumab Deruxtecan

January 28, 2026

IRVING, Texas, Jan. 28, 2026 /PRNewswire/ -- [Caris Life Sciences®](#) (NASDAQ: CAI), a leading, patient-centric, next-generation AI TechBio company and precision medicine pioneer, has published a study in Nature's [npj Breast Cancer](#) journal titled, "Mechanisms of Resistance to Trastuzumab Deruxtecan in Breast Cancer Elucidated by Multiomic Molecular Profiling." Utilizing large-scale real-world clinico-genomic data and Caris's comprehensive multiomic profiling, Caris scientists uncovered clinically relevant mechanisms of resistance to trastuzumab deruxtecan (T-DXd) in metastatic breast cancer. This study explains why patient responses vary and reveals how resistance can evolve over time.

This study addresses a critical gap in understanding why responses to T-DXd, an antibody–drug conjugate approved by the FDA for HER2-positive and HER2-low metastatic breast cancer, vary widely since resistance to T-DXd is common. By combining large-scale, real-world clinical outcomes with Caris's comprehensive molecular profiling, including whole exome sequencing (WES) and whole transcriptome sequencing (WTS), the study enables a population-level analysis of resistance pathways across DNA, RNA and protein expression.

"In this large real-world analysis, clinical outcomes allowed Caris to pinpoint molecular features linked to treatment-specific survival," said [George W. Sledge, Jr., MD](#), Caris EVP and Chief Medical Officer. "Post-treatment molecular shifts further reveal biologically plausible routes to acquired resistance, underscoring that RNA-level and multiomic profiling can provide actionable insights beyond standard HER2 classification to better stratify patients and inform therapies."

The study analyzed 2,799 T-DXd-treated breast cancer patients and found that WTS identified ERBB2 (HER2) and ABCC1 as the strongest transcriptomic predictors of T-DXd-specific overall survival. Higher ERBB2 expression correlated with improved outcomes, while higher ABCC1 correlated with poorer outcomes, independent of HER2 category.

ABCC1 further stratified outcomes within HER2-defined subgroups, indicating predictive value beyond standard HER2 testing and post-treatment samples showed increased ABCC1 expression alongside enrichment of mutations in ERBB2, NFE2L2, KEAP1 and TOP1. Consistent with acquired resistance mechanisms. Preclinical models supported a functional, context-dependent role for ABCC1-mediated drug efflux in T-DXd resistance.

"This study demonstrates how population-scale, multiomic real-world data can drive high impact translational discoveries, reinforcing the value proposition for patients and equipping biopharma with actionable insights into resistance biology to guide next-generation drug development," said [David Spetzler, MS, PhD, MBA](#), Caris President.

About Caris Life Sciences

Caris Life Sciences® (Caris) is a leading, patient-centric, next-generation AI TechBio company and precision medicine pioneer that is actively developing and commercializing innovative solutions to transform healthcare. Through comprehensive molecular profiling (Whole Exome and Whole Transcriptome Sequencing) and the application of advanced AI and machine learning algorithms at scale, Caris has created the large-scale, multimodal clinico-genomic database and computing capability needed to analyze and further unravel the molecular complexity of disease. This convergence of next-generation sequencing, AI and machine learning technologies, and high-performance computing provides a differentiated platform to develop the latest generation of advanced precision medicine diagnostic solutions for early detection, diagnosis, monitoring, therapy selection and drug development.

Caris was founded with a vision to realize the potential of precision medicine in order to improve the human condition. Headquartered in Irving, Texas, Caris has offices in Phoenix, New York, Cambridge (MA), Tokyo, Japan and Basel, Switzerland. Caris or its distributor partners provide services in the U.S. and other international markets.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the federal securities laws. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding our business, solutions, plans, objectives, goals, industry trends, financial outlook and guidance. In some cases forward-looking statements can be identified by words such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "potential," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or similar expressions.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in these forward-looking statements are reasonable based on information currently available to us, we cannot guarantee

that the future results, discoveries, levels of activity, performance or events and circumstances reflected in forward-looking statements will be achieved or occur. Forward-looking statements involve known and unknown risks and uncertainties, some of which are beyond our control. Risks and uncertainties that could cause our actual results to differ materially from those indicated or implied by the forward-looking statements in this press release include, among other things: developments in the precision medicine industry; our future financial performance, results of operations or other operational results or metrics; development, analytical and clinical validation, timing and performance of future solutions by us and our competitors; commercial market acceptance for our solutions, including acceptance of preventive as well as diagnostic testing paradigms, and our ability to meet resulting demand; the rapidly evolving competitive environment in which we operate; third-party payer reimbursement and coverage decisions related to our solutions; risks related to data management, storage, and processing capabilities and our ability to integrate and deploy artificial intelligence and advanced data analytics technologies; our ability to protect and enhance our intellectual property; regulatory requirements, decisions or approvals (including the timing and conditions thereof) related to our solutions; reliance on third-party suppliers; risks related to data security, patient privacy, and compliance with healthcare data protection regulations as well as potential cybersecurity threats to our data platforms; our compliance with laws and regulations; the outcome of government investigations and litigation; risks related to our indebtedness; and our ability to hire and retain key personnel as well as risks, uncertainties, and other factors described in the section titled "Risk Factors" and elsewhere in our Quarterly Report on Form 10-Q filed on or about November 5, 2025, and in our other filings we make with the SEC from time to time. We undertake no obligation to update any forward-looking statements to reflect changes in events, circumstances or our beliefs after the date of this press release, except as required by law.

Caris Life Sciences Media:

Corporate Communications

CorpComm@CarisLS.com

214.294.5606

 View original content to download multimedia: <https://www.prnewswire.com/news-releases/caris-life-sciences-real-world-data-uncovers-metastatic-breast-cancer-patient-responses-and-resistance-to-trastuzumab-deruxtecan-302672228.html>

SOURCE Caris Life Sciences