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Caris Life Sciences to Showcase Research Highlighting the Clinical Value of Comprehensive Molecular Profiling at the 2024 San Antonio Breast Cancer Symposium

In collaboration with leading cancer centers, research results to be presented from seven studies across multiple breast cancer types, including male breast cancer, demonstrate Caris' impact on precision medicine

IRVING, Texas, December 3, 2024 – [Caris Life Sciences](#)® (Caris), a leading next-generation AI TechBio company and precision medicine pioneer, today announced that the company and collaborators from leading cancer centers, including those within the [Caris Precision Oncology Alliance™](#) (Caris POA), will collectively present seven studies across a range of breast cancer types, including male breast cancer, at the San Antonio Breast Cancer Symposium (SABCS) from December 10-13, 2024 (Booth #1217). The research highlights the capability of Caris' extensive multimodal database to uncover new cancer insights, which may significantly influence a patient's diagnosis, prognosis, treatment plan and therapeutic response.

"The research being presented at this year's San Antonio Breast Cancer Symposium is a testament to Caris' continued commitment to data-driven molecular innovation and the power of our ever-expanding network of collaborators to answer some of today's pressing questions in precision oncology," said Caris EVP and Chief Medical Officer [George W. Sledge, Jr., MD](#). "More than half of the studies presented focus on male breast cancer, an often-overlooked form of breast cancer. The findings underscore the critical role of comprehensive profiling in cancer care and the power of large clinico-genomic datasets to enable the identification of new biomarkers with clinical implications across diverse tumor types, including rare cancers."

"Our comprehensive molecular profiling coupled with rich clinical data is enabling Caris to help clinicians make the best treatment choices, researchers to discover novel cancer biology, and the biopharmaceutical industry to develop the next breakthrough medicines," said Caris President [David Spetzler, MS, PhD, MBA](#). "Our vast real-world evidence from over 748,000 cases, including over 550,000 with matched molecular data and outcomes, enables our team and research collaborators to better understand the biological hallmarks of cancers and how they impact clinical outcomes, paving the way for personalized therapies and improved patient outcomes."

Spotlight Poster Presentations include:

- A Caris study titled "**Molecular and Immune Landscape of Metaplastic Triple Negative Breast Cancer Compared with Invasive Ductal Triple Negative Breast Cancer**" (Presentation #PS17-02) will be featured in Concurrent Poster Spotlight Session 17, named "Early Triple Negative Breast Cancer," on Thursday, December 12, from 5:30 – 6:30 p.m. CST in the Stars at Night Ballroom 1-2. The study was performed in collaboration with [Caris Precision Oncology Alliance™](#) (Caris POA) members Dana-Farber Cancer Institute, Norris Comprehensive Cancer Center,

Legorreta Cancer Center at Brown University and Yale School of Medicine, as well as the Mayo Clinic.

In the featured study, the molecular and immunological landscapes of metaplastic triple-negative breast cancer (M-TNBC) were investigated using [Caris' Next-Generation Sequencing \(NGS\) technology](#). The results indicate that M-TNBC is associated with an aggressive disease biology, with differential molecular and immune features compared to invasive ductal TNBC. A better understanding of these differences may help inform disease outcomes, provide a rationale for tailored therapeutic approaches and guide the design of future treatments for M-TNBC, a rare and aggressive form of breast cancer.

- A Caris study titled **“Mechanisms of Resistance to Trastuzumab Deruxtecan in Breast Cancer Elucidated by Multi-omic Molecular Profiling” (Presentation #PS13-09)** will be featured during Concurrent Poster Spotlight Session 13, named “Molecular Determinants of Therapeutic Response and Resistance - Spotlight on CDK 4/6i and ADCs” on Friday, December 13 from 7:00 – 8:30 a.m. CST in the Stars at Night Ballroom 1-2. Caris EVP and Chief Medical Officer George W. Sledge Jr., MD will present results of the study conducted by Caris scientists.

In this study, whole transcriptome sequencing (WTS), immunohistochemistry and real-world clinical data were analyzed for more than 2,000 Trastuzumab Deruxtecan (T-DXd)-treated breast cancer samples. This multi-omic approach revealed a clinically relevant mechanism of resistance to T-DXd, a drug widely used in the treatment of metastatic HER-2 low and HER2-positive breast cancer. In T-DXd-treated patients, clinical outcome was a function of trastuzumab target expression and expression of *ABCC1*, the gene encoding the multidrug resistance protein-1 (MRP1). These results increase our understanding of how T-DXd resistance develops and may help oncologists tailor treatment plans for breast cancer patients accordingly.

Additional Presentations Reveal Potential Impact of Comprehensive Molecular Profiling

Poster and abstract summaries highlighting the Caris research presented at SABCS 2024 will be available onsite at Caris' Booth #1217. The full abstracts will be available on the [Caris website](#) at the event's conclusion.

- **Molecular landscape of HR+/HER2- male breast cancer (MaBC) compared with female breast cancer (FeBC) (Presentation Number: P1-01-16)**
This study aimed to identify the molecular and immune differences between HR+/HER2- male and female breast cancer. NGS-based analysis of more than 8,200 breast cancer samples indicated that HR+/HER2- male breast cancer has a distinct mutational and immunological profile compared to its female counterpart. These findings suggest important differences in tumor biology between men and women with HR+/HER2- breast cancer. A better understanding of these differences may help in the design of future clinical trials and the development of treatments for men with HR+/HER2- breast cancer.
- **Spliceosome Mutations (Smut) in Metastatic Breast Cancer (MBC): An Analysis of a Decentralized Clinical Trial and Large Clinical-Genomic Dataset (Presentation Number: P1-01-20)**
In this study, spliceosome mutations were analyzed in metastatic breast cancer (MBC) using data from the PRISMM (Patient Response to Immunotherapy using Spliceosome Mutational

Markers) trial and Caris' large clinical-genomic dataset. This analysis found that patients with spliceosome mutations do not have significant responses to immunotherapy. HR+/HER2- MBC had the highest frequency of spliceosome mutations and was associated with genomic aberrations of endocrine resistance, an immune-cold phenotype, and worse overall survival. These findings underscore the importance of molecular profiling in patients with MBC.

- **Prognostic implications of oncogenetic pathway alterations in advanced male breast cancer (Presentation Number: P1-05-21)**

Male breast cancer has a distinct molecular and immune landscape compared to female breast cancer, but the prognostic implications of these differences have previously been unclear. In this study, 17,759 breast tumors were tested using WES and WTS to assess the effect of gene alterations on male breast cancer-related survival. Results showed that select genomic alterations have different prognostic significance in male and female breast cancer, suggesting that breast cancer in men may have a unique trajectory that differs from female breast cancer. Further investigation of sex-defined differences in breast cancer may help tailor future therapeutic strategies.

- **Comprehensive characterization of androgen receptor in male breast cancer (Presentation Number: P1-03-22)**

While the estrogen receptor (ER) is well-studied in breast cancer, the role of the androgen receptor (AR) is less understood, particularly in male patients. This study aimed to characterize the molecular and immunological features associated with *AR* gene expression in male breast cancer. Comprehensive molecular profiling revealed that specific genomic alterations and immune markers are associated with *AR* expression. Further investigations of these features may assist in clinical trial design for men with breast cancer.

- **Molecular and immunological characterization of HER2-low, HER2 ultra-low, and HER2-null male breast cancer (Presentation Number: P3-01-25)**

This final study aimed to determine whether there are differences in molecular and immunological features between HER2-low, HER2-ultra-low and HER2-null/negative breast cancer in males. Generally, these three HER2 subtypes in men shared genomic features, suggesting that their disease biology may be similar across the spectrum of what historically has been considered HER2-negative disease. Differences were noted, however, between these HER2 subtypes in their tumor immune microenvironments and warrant further investigation. These findings expand our current understanding of the HER2 spectrum in male breast cancer.

The Caris POA includes 96 cancer centers, academic institutions, research consortia and healthcare systems, including 47 NCI-designated cancer centers, who collaborate to advance precision oncology and biomarker-driven research. Caris and POA members work together to establish and optimize standards of care for molecular testing through innovative research focused on predictive and prognostic markers that improve the clinical outcomes for cancer patients.

About Caris Life Sciences

Caris Life Sciences® (Caris) is a leading next-generation AI TechBio company and precision medicine pioneer that is actively developing and delivering innovative solutions to revolutionize healthcare and improve the human condition. Through comprehensive molecular profiling (Whole Exome and Whole Transcriptome Sequencing) and the application of advanced AI and machine learning algorithms, Caris has created the large-scale, multimodal database and computing capability needed to analyze and unravel the molecular complexity of disease. This convergence of sequencing power, big data and AI technologies provides an unmatched platform to deliver the next generation of precision medicine tools 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, and we value our employees as much as we do our patients of every creed, color, sex, sexual orientation and religion. 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., Europe, Asia and other international markets. To learn more, please visit CarisLifeSciences.com.

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Caris Life Sciences Media:

Corporate Communications

214.294.5606