FOR IMMEDIATE RELEASE

Caris Life Sciences Showcases Data Demonstrating the Clinical Value of Clonal Hematopoiesis Identification and Subtraction in Liquid Biopsy to Improve the Accuracy of Treatment Recommendations

Caris Assure™ detected clonal hematopoiesis (CH) mutations in ~40% of cases and demonstrated that CH identification and correction is vital for accurate therapy selection for cancer patients

IRVING, Texas, November 25, 2024 – Caris Life Sciences® (Caris), a leading next-generation AI TechBio company and precision medicine pioneer, today announced the presentation of data highlighting the clinical value of subtracting clonal hematopoiesis (CH) mutations from liquid biopsy profiling results to avoid incorrect treatment recommendations. Caris generated the findings, in collaboration with leading cancer centers, including those within the Caris Precision Oncology Alliance™ (Caris POA), and presented the data on November 23, 2024, at the International Society for Liquid Biopsy (ISLB) 6th Annual Congress. The study's results demonstrate the power of the Caris Assure™ assay to identify somatic tumor, incidental CH and incidental germline variants by sequencing both the plasma and buffy coat in a single whole exome and whole transcriptome next-generation sequencing assay.

"As we age, we accumulate somatic CH mutations in our blood that can lead to clinical false positives in blood-based molecular profiling tests, complicating treatment decisions," said George W. Sledge, Jr., MD, EVP and Chief Medical Officer of Caris. "Accurately determining which variants are coming directly from the tumor, versus which are germline or CH, is critical to patient care. This enables oncologists to treat the tumor rather than treating mutations from other sources, lessening the possibility of recommending a treatment that is not appropriate, and potentially harmful, for the patient."

According to a joint consensus recommendation from the Association for Molecular Pathology (AMP) and College of American Pathologists (CAP), laboratories should interpret variants identified in genes associated with CH cautiously and consider matched white blood cell sequencing with ctDNA testing to avoid falsely identifying CH variants as somatic mutations derived from the tumor.[1]

In the study presented at ISLB, 11,914 patients with advanced cancer across 48 tumor types were analyzed using the Caris Assure blood assay to characterize the plasma circulating cell-free DNA variants as either tumor or CH in origin. Nearly four out of ten (39.5%) patients had at least one pathogenic or likely pathogenic CH variant among reportable clinical genes. This prevalence increased with age, ranging from 17% for patients aged 65-69 to 50% for those over 80 years. If only plasma is analyzed, these mutations can be interpreted as tumor-derived and lead to improper therapy selection.

High CH rates were notably detected in the DNA repair genes that, when mutated, are prescriptive for PARP inhibitors in cancers including breast, female genital tract, ovarian, pancreatic, prostate, and endometrial cancer. Most notably, 79.9% of *BRCA2* variants were of CH origin, meaning that nearly eight out of every ten mutations detected were not from the tumor itself and, therefore, not relevant to

therapeutic decision-making. High CH rates were also seen for *CHEK2* (79.4%), *BRCA1* (68.5%) and *ATM* (41.9%). By excluding CH, Caris Assure provides higher confidence for therapy selection than plasma-only biopsies.

"By sequencing DNA from both the buffy coat and plasma, Caris Assure uniquely and accurately identifies clonal hematopoiesis in a way that is not possible when sequencing plasma alone," said Caris President David Spetzler, MS, PhD, MBA. "To our knowledge, Caris Assure is the only commercially available blood-based profiling assay that is accounting for clonal hematopoiesis mutations instead of using ineffective algorithmic approximations, which provides doctors and patients with more accurate treatment recommendations to fight their disease."

The study was performed in collaboration with members of the Caris POA, which includes 96 cancer centers, academic institutions, research consortia and healthcare systems, including 47 NCI-designated cancer centers, collaborating 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 can improve 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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1. Lockwood, Christina M et al. "Recommendations for Cell-Free DNA Assay Validations: A Joint Consensus Recommendation of the Association for Molecular Pathology and College of American Pathologists." The Journal of molecular diagnostics: JMD vol. 25,12 (2023): 876-897.

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