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Caris Life Sciences to Present Research at the 2024 ASCO Genitourinary Cancers Symposium

In collaboration with leading cancer centers, research results to be presented from eight studies across four tumor types, demonstrating Caris' impact on precision medicine

IRVING, Texas, January 23, 2024 – Caris Life Sciences® (Caris), the 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 using molecular science and AI, today announced that the company and collaborators within the Caris Precision Oncology Alliance™ (POA) will collectively present eight studies across four tumor types at the 2024 American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium, January 25-27, 2024 in San Francisco. The findings demonstrate the continued and expanded capabilities of Caris' comprehensive multi-modal database to enable novel insights into cancer that could have profound effects on a patient's diagnosis, prognosis, care plan and response to treatment.

"These presentations illustrate how our physicians, scientists and collaborators in the POA are leveraging real-world clinical evidence from over 593,000 lifetime clinical cases, including over 482,000 with matched molecular data and outcomes, in Caris' unique AI-driven platform to deepen our understanding of cancer and to develop the next breakthrough medicines," said Chadi Nabhan, MD, MBA, FACP, Chairman of the Caris Precision Oncology Alliance. "Caris molecular profiling enables deep exploration of the genetic and immune landscapes of cancer, providing insights into which signaling pathways explain the pathobiology of disease and leading to more precise targeted therapy. That's a major focus of the wide array of research Caris and our POA collaborators will proudly present at this year's ASCO GU."

Oral Abstract:

- A Caris study entitled **"Differences in genomic, transcriptomic, and immune landscape of prostate cancer (PCa) based on site of metastasis (mets)"** will be presented by Dr. Umang Swami from the Huntsman Cancer Institute on Thursday, January 25 at 4:20 p.m. PST during Rapid Oral Abstract Session A on Prostate Cancer in the Level 3 Ballroom. The research is a collaboration with the Huntsman Cancer Institute at the University of Utah and other POA members.

  Compared to primary PCa, both visceral (liver and lung) and non-visceral (lymph node and bone) metastases had higher Androgen Receptor (AR) and interferon γ signaling, upregulation of the E2F, G2M checkpoints and MYC target pathways, and were significantly less enriched in macrophage M2, NK, and regulatory T cells. Visceral metastases also had higher neuroendocrine (NEPC) scores and were less enriched for B cells and neutrophils. These data on the molecular and immunologic mechanisms of metastatic tropism in advanced PCa may facilitate future drug development.

Additional Presentations Reveal Potential Impact of Comprehensive Molecular Profiling
Caris will present additional data from studies demonstrating the critical role of comprehensive molecular profiling in the treatment of genitourinary cancers. Poster and abstract summaries highlighting this research will be available onsite at Caris' booth (#8). The full abstracts will be available through Caris' website beginning on January 23.

- **Survival outcomes in patients (pts) with prostatic cancer (PCa) based on pathologically confirmed sites of metastasis (January 25; Poster C7, Abstract 72)**
  Examination of 6,069 PCa specimens in Caris' CODEai multi-modal database showed that metastasis to the liver was associated with overall survival significantly shorter than metastasis to the lung, arguing against combining them into the single category of visceral metastases as a stratification factor in randomized clinical trials.

- **Correlation of PIM kinases with tumor immune microenvironment and clinical presentation of metastatic hormone-sensitive prostate cancer (January 25; Poster J19, Abstract 211)**
  In a study of 44 patients with treatment-naive metastatic hormone-sensitive prostate cancer (mHSPC), there was a strong association of high expression of PIM kinases with increased MAPK activation score, T cell inflamed score, inflammatory, PSA, AR, MHC class I and MHC class II gene expression, and differential immune cell infiltration. However, this did not significantly translate to a worse clinical presentation of mHSPC. A better understanding of these differences with additional research may provide a rationale for tailored therapeutic approaches for PIM-expressing mHSPC.

- **The influence of the germline *HSD3B1* adrenal-permissive variant (c.1100 C) on somatic alteration landscape, transcriptome, and immune-cell infiltration in prostate cancer (January 25; Poster K3, Abstract 215)**
  In a study of 5,421 prostate cancer biopsies from the Caris Life Sciences database, the homozygous adrenal-permissive HSD3B1 variant (c.1100 C) was characterized by elevated AR signaling and MAPK activation and a unique immune-cell regulatory landscape, with higher B7-H3 expression, increased intratumoral dendritic cells and decreased immunosuppressive neutrophils, suggesting that B7-H3–targeted therapies might be effective against this class of cancer.

- **The opposing effects of Class 1B and Class 2 *FOXA1* mutations in prostate cancer (January 25; Poster K4, Abstract 216)**
  Alterations in the FOXA1 transcription factor are present in 16% of prostate cancers (PCa), but different alterations exhibit divergent molecular and clinical profiles. In a study of more than 4,000 primary and metastatic PCa samples, missense mutations in the Wing2 region of FOXA1 (a.a. 248-269) had better response to androgen deprivation therapy (ADT), whereas mutations in a.a. R219, a highly conserved DNA contact residue, were associated with a neuroendocrine phenotype and showed poor survival with ADT.

- **Canonical Wnt signaling pathway (WSP) alterations in metastatic prostate cancer (January 25; Poster K9, Abstract 221)**
  In a study of 4,150 total PCa samples, 722 with aberrant canonical Wnt signaling (WSP-act), WSP-act tumors had pronounced upregulation of ROR1 gene expression and augmented levels of M2 macrophages, suggesting that ROR1 may contribute to immune evasion in WSP-act mPCa.

- **Comprehensive analysis of targetable alterations in urachal cancer by NGS (January 26; Poster K7, Abstract 663)**
  In a comprehensive characterization the molecular and immune landscape of urachal cancer (UrC), UrC tumors rarely harbored predictive markers of response to immunotherapy, suggesting limited efficacy in this patient population. However, the recurrence of MAPK alterations and associated pathway activation in UrC warrants further investigation of MAPK-targeted therapies in prospective clinical trials.

- **IL-6 and PIM1 expression in renal cell carcinoma (January 27; Poster K11, Abstract 470)**
  Based on the hypothesis that an IL-6/JAK/STAT pathway regulates the expression of PIM1 in renal cell carcinoma (RCC) as in pancreatic and breast cancer, the transcriptomes of RCC samples in the Caris multi-modal database were analyzed, showing that PIM1 expression was significantly increased in metastatic relative to primary RCC. IL-6 expression was up to 6.5-fold higher in RCC patients with PIM1 overexpression. Outcomes data showed that PIM1 overexpression was associated with decreased overall survival for RCC patients independent of treatment received. Since multiple FDA-approved agents are available that target this pathway, further investigation is warranted to determine the efficacy of these agents in pre-clinical models and clinical trials of RCC.

The POA includes 90 cancer centers, academic institutions, research consortia and healthcare systems, including 42 NCI-designated cancer centers, collaborating to advance precision oncology and biomarker-driven research. 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 the 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 using molecular science and AI. 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, multi-modal 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.

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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