FOR IMMEDIATE RELEASE

Caris Life Sciences’ Molecular Intelligence Platform Identifies Patients with MSI-High (or Mismatch Repair Deficient) Solid Tumors More Likely to Respond to Immunotherapy

Results Published in Science Demonstrate Molecular Profile of Tumor Cells Rather than Tumor Origin Can Drive Therapeutic Strategy

IRVING, Texas, June 8, 2017 – Caris Life Sciences®, a leading innovator in molecular science focused on fulfilling the promise of precision medicine, today highlighted an article published in *Science* containing data on microsatellite instability (MSI) status and mismatch repair (MMR)-deficient tumors on a wide range of tumor types using Caris Molecular Intelligence®, the company’s comprehensive genomic profiling plus (CGP+) molecular testing service. The primary objective of this study was to estimate the efficacy of the immunotherapy drug pembrolizumab in patients with MSI-High or MMR-deficient cancers regardless of tumor origin, an indication recently added to the drug’s label by the Food and Drug Administration (FDA). The study, entitled “Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade,” was published on June 8, 2017 in *Science* First Release online (doi:10.1126/science.aan6733).

The thesis underlying immunotherapy for cancer is that the immune system maintains the capacity to initiate an immune response against tumor cells if the immune system is appropriately activated to attack them. This approach has been successfully demonstrated with therapeutics that block PD-L1 (ex: pembrolizumab and nivolumab), a PD-1 receptor ligand found on the surface of tumor cells which, when overexpressed, down-regulates or suppresses the immune system’s response. Blocking the receptor enables the immune system to recognize tumor cells and kill them. Tumor cells emerge from genetic mutations and thus they manufacture proteins that can be recognized as neoantigens (antigens not found on normal cells) that can activate the immune system. Tumors with MSI-H or MMR deficient cancers produce a very large number of mutations, and thus neoantigens, and would be good therapeutic targets for checkpoint inhibitors.

“In the past, anti-neoplastic agents were developed based on the site of origin, such as breast, prostate or lung,” said David Spetzler, M.S., Ph.D., M.B.A., President and Chief Scientific Officer of Caris Life Sciences and co-author on the paper. “With our increased knowledge, both of the genetic alterations that drive and sustain tumorigenesis, as well as the down-regulation of the immune system that enables tumors to escape an immune response, we are better positioned than ever to attack cancers based on their molecular profiles and to develop a treatment plan that is tailored to each patient, regardless of tumor origin. The results of this clinical trial demonstrate that this is truly the case. This now opens a
new approach to therapy that is exemplified by the recent FDA approval of pembrolizumab for MSI-High or mismatch repair deficient solid tumors – the first cancer therapy approved for use based on a biomarker, regardless of tumor type, and the same population evaluated in this study.”

The clinical trial evaluated the efficacy of pembrolizumab in advanced MSI-High or MMR-deficient patients. Eighty-six patients, with 12 different tumor types were enrolled. The objective response rate was 53% and the complete response rate was 21%, demonstrating durable responses with pembrolizumab regardless of tumor origin. The investigators concluded that patients with a large number of neoantigens in MMR-deficient cancers made them sensitive to checkpoint inhibition. Researchers also included Caris Molecular Intelligence prevalence data for MSI-High or MMR-deficient tumors. Using next-generation sequencing (NGS) across 24 tumor types, Caris Molecular Intelligence identified patients with MSI-High solid tumors by evaluating more than 7,000 microsatellite regions across approximately 2,200 cases. Patients were considered MSI-High if they had at least 43 altered microsatellite regions, which was determined by comparing NGS results to traditional polymerase chain reaction (PCR) analysis. The Caris NGS platform performed at 95.8% sensitivity and 99.4% specificity.

“The results of this study, along with the FDA approval of pembrolizumab for MSI-High or mismatch repair deficient solid tumors, marks a turning point where precision medicine is now becoming standard of care for all solid tumor patients,” said John Marshall, M.D., Chief Medical Officer of Caris Life Sciences. Dr. Marshall is also the Associate Director for Clinical Care for the Georgetown Lombardi Comprehensive Cancer Center and the Chief of the Division of Hematology-Oncology at MedStar Georgetown University Hospital in Washington, D.C. “The Caris CGP+ tumor profiling platform enables more patients to get MSI results because it does not require normal tissue like the PCR assay, therefore making it optimally positioned to assist clinicians in accurately identifying MSI-High patients so that they receive appropriate therapy. In addition, CGP+ assists innovative biopharmaceutical companies and other healthcare organizations develop the next personalized cancer treatments.”

The study was a multi-institution clinical trial conducted by academic, medical, government and commercial organizations including Johns Hopkins, Stanford University, Providence Cancer Center, University of Pittsburgh, National Cancer Institute, Ohio State University, West Virginia University Cancer Institute, Memorial Sloan Kettering Cancer Center, Merck & Company, with funding in part by The Lustgarten Foundation for Pancreatic Cancer Research.

About Caris Life Sciences®
Caris Life Sciences® is a leading innovator in molecular science focused on fulfilling the promise of precision medicine through quality and innovation. Caris Molecular Intelligence®, the company’s Comprehensive Genomic Profiling Plus (CGP+) molecular testing service and the world’s leading immunotherapy diagnostic expert, assesses DNA, RNA and proteins, including microsatellite instability (MSI), total mutational load (TML) and PD-L1, to reveal a molecular blueprint to guide more precise and personalized treatment decisions. The ADAPT Biotargeting System™, the company’s revolutionary and unbiased profiling platform, is currently being utilized for drug target identification, therapeutic discovery and development, fixed tissue-based companion diagnostics, blood-based cancer screening and biomarker identification. Headquartered in Irving, Texas, Caris Life Sciences offers services throughout the U.S., Europe and other international markets. To learn more, please visit www.CarisLifeSciences.com.

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