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Caris Life Sciences Presents Data Demonstrating the Ability of ADAPT Biotargeting System to Identify Responders and Non-Responders in a Phase III Pancreatic Cancer Study

Leveraging ADAPT Biotargeting System would have significantly increased the probability of success

Data presented at the ESMO World Congress on Gastrointestinal Cancer 2018

IRVING, Tex., June 21, 2018 – Caris Life Sciences®, a leading innovator in molecular science focused on fulfilling the promise of precision medicine, today announced new data supporting the use of its proprietary ADAPT Biotargeting System™ to drive clinical trial success. Results show the assay built using the ADAPT platform was able to identify responders and non-responders from the unsuccessful MAESTRO Phase III clinical trial in advanced pancreatic cancer such that if the assay had been used to stratify patients, the study would have had a 98% probability of meeting the primary endpoint. These results were presented at the European Society for Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer 2018 (ESMO GI) in Barcelona, Spain, on June 21.

"Clinical studies that do not use biomarkers or use single biomarkers to identify potential drug responders are evaluating investigational drugs on molecularly heterogeneous populations. These studies can often result in failed clinical trials and limit patient access to potentially useful drugs," said W. Michael Korn, M.D., Chief Medical Officer at Caris Life Sciences. "However, with our ADAPT Biotargeting System, we are able to simultaneously identify multiple targets and develop a molecular signature tuned to those patients that will likely benefit from the therapy and those that will not. Specifically for this study, we set out to demonstrate that a clinical trial leveraging the ADAPT Biotargeting System would be more likely to succeed."

The MAESTRO Phase III clinical trial randomized patients with locally-advanced or metastatic pancreatic cancer to receive gemcitabine plus placebo or gemcitabine plus evofosfamide. The clinical trial failed to meet the primary endpoint of 33% improvement in median overall survival (OS). The hypothesis of the study presented at ESMO GI was that biomarker-based selection of patients for study accrual might have led to success. Caris' ADAPT Biotargeting System employs poly-ligand profiling to survey a vast array of potential biomarkers and create a molecular profile that can identify patients most likely to derive clinical benefit from a given therapeutic regimen. Biopsy samples from known responders and non-responders (n=20) in the study were used to train a library of more than one trillion oligodeoxynucleotides with aptameric-binding properties. The resulting trained library was then tested on specimens from a fully blinded cohort of 172 patients from the MAESTRO study (122 primary tumors and 49 metastatic tumors).

The original MAESTRO study demonstrated a median OS increase of 17.4% (p=0.053) for the combination arm compared to gemcitabine monotherapy. Based on the ADAPT assay results in the test cohort of 172 patients where tissue was available, 1,000 trial simulations were performed to model the assay impact for the 693 patients enrolled in the study by randomly assigning all patients to either study arm and generating Kaplan-Meier plots. This resulted in a predicted 37.6% median OS increase (p=0.006) for all patients and a predicted 54.9% increase in median OS (p<0.001) for patients whose specimens came from primary tumors. Aptamers from the trained library were used as affinity purification probes to isolate biomarkers from FFPE specimens. High-resolution mass spectrometry detected 20 proteins, 11 of which were previously associated with pancreatic cancer and six of which have been reported to play roles in gemcitabine resistance.

"This is the first time that our ADAPT Biotargeting System was applied to tumor samples from a clinical trial," commented David Spetzler, M.S., Ph.D., M.B.A., President and Chief Scientific Officer of Caris Life Sciences. "Our analysis suggests that if ADAPT had been used to enroll patients in the MAESTRO study, the probability of success would have been 98%. In addition, ADAPT was able to detect several proteins that could be explored as potential therapeutic targets. We anticipate that this study, along with work evaluating patient benefit of trastuzumab therapy in HER2+ breast cancer, will lead to additional collaborations with biopharmaceutical companies and ultimately to the prospective incorporation of ADAPT in cancer drug development."

Poster Presentation:
Thursday, June 21, 2018 – 10:00 a.m. CEST – CCIB Poster Hall
Poster session: 132
"Poly-Ligand Profiling differentiates pancreatic cancer patients according to treatment benefit from gemcitabine+placebo versus gemcitabine+evofosfamide and identifies candidate targets," presented by Valeriy Domenyuk
Collaborating Institutions: Arizona State University, Berry Consultants, Threshold Pharmaceuticals, University of Bonn

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, and the world's leading immunotherapy diagnostic expert. Caris Molecular Intelligence®, the company's Comprehensive Genomic Profiling Plus (CGP+) molecular testing service, assesses DNA, RNA and proteins, including microsatellite instability (MSI), tumor mutational burden (TMB) and PD-L1, to reveal a molecular blueprint to guide more precise and personalized treatment decisions. Caris' profiling services are routinely covered by third-party payors, including CMS for Medicare patients. 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, Asia and other international markets. To learn more, please visit www.CarisLifeSciences.com.

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