Revolution Medicines Reports Discovery that May Expand Range of Clinically Actionable Cancer Mutations

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Redwood City, CA –September 14, 2017 – REVOLUTION Medicines, Inc., a company focused on frontier cancer targets and drug discovery, today published a report entitled “Efficacy of SHP2 phosphatase inhibition in cancers with nucleotide-cycling oncogenic RAS, RAS-GTP dependent oncogenic BRAF and NF1 loss” based on original research led by scientists at the company and conducted in collaboration with researchers at the University of California, San Francisco School of Medicine.The paper was published in BioRxIV. This paper describes new studies of a cell growth signaling pathway that frequently is hyperactive in human cancers, known as the RAS-MAP kinase pathway, and the regulation of this pathway by the enzyme SHP2 (PTPN11). The research revealed an unexpected dependence of some cancer-causing forms of proteins in the RAS-MAP kinase pathway on the normal biochemical actions of SHP2. These functions can be disrupted by small molecule inhibitors of SHP2 designed by the company, thereby curtailing tumor growth. REVOLUTION Medicines is developing SHP2 inhibitor compounds as potential drugs for the treatment of patients with cancer.

In this work, investigators found that an inhibitor of SHP2 suppresses activation of key proteins in the RAS-MAP kinase pathway that drive cancer by amplifying normal growth signals rather than functioning as fully independent or autonomous drivers of cancer. Among these proteins are certain cancer-causing forms of KRAS, NF1 and BRAF, which are common in prevalent cancers such as non-small cell lung cancer. These oncoproteins behave semi-autonomously by requiring cues from SHP2 before initiating cancer-causing effects. These targets have been largely unreachable by conventional drug discovery, leaving a gap in cancer treatment. The present discovery informs a potential roadmap for using an inhibitor of SHP2 to treat patients with cancers containing clinically important cancer gene mutations that previously were not considered actionable.

“Inhibition of SHP2 may represent a new treatment option specifically for patients with certain forms of cancer caused by selected mutations in the RAS-MAP kinase pathway,” said Steve Kelsey, M.D., president of research and development at REVOLUTION Medicines. “We are proud to share this discovery and to continue advancing our program toward the clinic on behalf of patients with cancers that are poorly responsive to established cancer drugs.”

“The new findings highlight an innovative precision medicine framework for approaching genetically-defined cancer targets previously considered undruggable, in this case aimed at SHP2 as a regulator of cancer cell signaling,” said Mark A. Goldsmith, M.D., Ph.D., president and chief executive officer of REVOLUTION Medicines. “More broadly, this paradigm may expand the range of suitable drug targets and therapeutic strategies for other cancers caused by semi-autonomous genetic factors, including some tumor suppressors.”

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ABOUT REVOLUTION MEDICINES

The mission of REVOLUTION Medicines is to discover and develop new drugs directed toward frontier oncology targets for cancer patients. The company has a robust pipeline of R&D programs focused on frontier targets, including a second tyrosine phosphatase enzyme, SHP1 (PTPN6), a regulator of multiple arms of the immune response, and 4EBP1, a key regulator of oncogene translation in the PI3K/AKT/mTOR pathway. Headquartered in Redwood City, Calif. at the intersection of Silicon Valley and the birthplace of biotechnology, REVOLUTION Medicines is a private company financed by top-tier investors Third Rock Ventures and The Column Group. For more information, please visit www.revolutionmedicines.com.