Revolution Medicines and Amgen Partner on Phase 1b Study to Evaluate Combination of RMC-4630 and AMG 510

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Study to Evaluate Combination of Investigational SHP2 and KRASG12C Inhibitors in Patients with KRASG12C Mutant Advanced Solid Tumors

REDWOOD CITY, Calif., Nov. 4, 2019 /PRNewswire/ -- Revolution Medicines, Inc., a clinical-stage oncology company focused on developing targeted therapies to inhibit elusive frontier targets within notorious cancer pathways, today announced an agreement with Amgen to evaluate the combination of RMC-4630, the company's investigational SHP2 inhibitor, and AMG 510, Amgen's investigational $KRAS^{G12C}$ inhibitor. Amgen will conduct a Phase 1b clinical trial evaluating the safety, tolerability, pharmacokinetics, and efficacy of AMG 510 in combination with RMC-4630 in subjects with advanced solid tumors harboring the $KRAS^{G12C}$ mutation. Revolution Medicines will provide Amgen with clinical supply of RMC-4630 for the planned study.

RMC-4630 and AMG 510 are selective investigational inhibitors of oncogenic targets at distinct positions within the RAS signaling cascade that are frequently exploited by human cancers. RMC-4630 is a potent and orally bioavailable small molecule that is designed to selectively inhibit the activity of SHP2, an upstream cellular protein that plays a key role in modulating cell growth by transmitting signals from receptor tyrosine kinases to RAS. RMC-4630 and SHP2 are the focus of an exclusive global research, development and commercialization agreement with Sanofi. AMG 510 is designed to selectively and irreversibly target the $KRAS^{G12C}$ protein, an oncogenic RAS mutant at the core of the RAS signaling cascade.

Preclinical and clinical research has shown that cancers caused by $KRAS^{G12C}$ and other RAS pathway mutations exhibit "oncogene addiction," in which tumor cells are highly dependent on RAS pathway signaling to survive. Such tumors can develop adaptive resistance by hijacking cell signaling circuitry to circumvent pathway inhibitors and restore RAS signaling. The planned clinical Phase 1b study is the first step in evaluating whether inhibition of the RAS pathway at two nodes simultaneously through the combination of RMC-4630 and AMG 510 increases the depth or durability of clinical benefit for patients with tumors bearing $KRAS^{G12C}$.

"We and our partner Sanofi are committed to a clinical strategy that includes exploring in-pathway combinations including RMC-4630 to optimize treatment options for patients with RAS-dependent tumors. This collaboration with Amgen, a clinical pioneer in the field, provides another opportunity to leverage RMC-4630," said Mark A. Goldsmith, M.D., Ph.D., president and chief executive officer of Revolution Medicines. "Our development program for RMC-4630 currently includes an ongoing Phase 1 monotherapy trial, an ongoing Phase 1b/2 study evaluating a combination with cobimetinib, a MEK inhibitor, and a planned Phase 1b trial evaluating a combination with AMG 510, the leading investigational $KRAS^{G12C}$ inhibitor."

About RMC-4630 and Sanofi Collaboration

RMC-4630 is currently being evaluated in a Phase 1 monotherapy clinical trial (RMC-4630-01) for a range of tumor types featuring specific, molecularly-defined oncogenic mutations, as well as a Phase 1b/2 study (RMC-4630-02) in combination with cobimetinib in patients with relapsed/refractory solid tumors displaying specific genomic mutations. The RMC-4630 program is the focus of an exclusive global research, development and commercialization agreement with Sanofi, under which Revolution Medicines received a $50 million upfront payment, and Sanofi agreed to reimburse the Revolution Medicines for substantially all research and all development costs for the joint SHP2 program. Sanofi received an exclusive worldwide license for global commercialization of any approved products targeting SHP2, subject to a U.S. co-promote right for Revolution Medicines. The companies have agreed to enter into a 50/50 profit and loss share arrangement in the U.S., and Revolution Medicines is entitled to receive tiered royalties on annual net sales ranging from high single digit to mid-teen percentages on sales in other markets. Revolution Medicines could also receive more than $500 million in development and regulatory milestone payments.

About Revolution Medicines, Inc.

Revolution Medicines is a clinical-stage oncology company focused on developing novel targeted therapies to inhibit elusive high-value frontier cancer targets within notorious growth and survival pathways, with particular emphasis on RAS and mTOR signaling pathways. The company possesses sophisticated structure-based drug discovery capabilities built upon deep chemical biology and cancer pharmacology know-how and innovative, proprietary technologies that enable the creation of small molecules tailored to unconventional binding sites.

The company's pipeline includes RMC-4630, a clinical-stage drug candidate that is designed to selectively inhibit the activity of SHP2. Additionally, the company is developing a broad portfolio of inhibitors of other key frontier oncology targets within the notorious RAS pathway, as well as the related mTOR signaling cascade. These include inhibitors of multiple mutant RAS proteins and SOS1, as well as RMC-5552, a development candidate within our 4EBP1/mTORC1 program currently in IND-enabling studies.

For more information, please visit: www.revmed.com

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