Revolution Medicines Announces Dosing of First Patient in Phase 1b Combination Study of RMC-4630 and AMG 510

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Study Evaluates Combination Treatment with Investigational SHP2 and KRAS^{G12C} Inhibitors in Patients with KRAS^{G12C} Mutant Solid Tumors

REDWOOD CITY, Calif., June 09, 2020 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company focused on developing targeted therapies to inhibit frontier cancer targets, today announced dosing of the first patient in a Phase 1b clinical trial evaluating the combination of RMC-4630, the company's investigational SHP2 inhibitor, and AMG 510, Amgen's investigational KRAS ^{G12C} inhibitor. The trial, which is being sponsored and conducted by Amgen with clinical supply of RMC-4630 provided by Revolution Medicines, is an open-label, dose-escalation and dose-expansion study evaluating the safety, tolerability, pharmacokinetics, and efficacy of the combination of RMC-4630 and AMG 510 in patients with advanced solid tumors harboring the KRAS^{G12C} mutation.

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 central role in modulating cell survival and growth by transmitting signals from receptor tyrosine kinases to RAS. AMG 510 is a first-in-class investigational oral therapy 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 RAS pathway mutations exhibit "oncogene addiction," in which tumor cells become highly dependent on signaling through the RAS pathway to survive. Suppressing KRAS^{G12C} activity, either directly with AMG 510 or indirectly by inhibiting SHP2 with RMC-4630, has shown anti-tumor activity against non-small cell lung tumors harboring KRAS^{G12C} in early clinical trials. In addition, adaptive resistance to inhibition of RAS signaling is common. SHP2 is an upstream RAS pathway node that often plays a key role in adaptive resistance, and inhibiting SHP2 with RMC-4630 has been shown preclinically to suppress adaptive resistance to KRAS^{G12C} inhibitors.

"Our strategy is to advance a broad clinical program to assess the therapeutic potential of RMC-4630 in both monotherapy and multiple combination treatment regimens. With our recent demonstration of encouraging monotherapy activity for RMC-4630 against KRAS^{G12C} lung cancers, it is compelling to pair this investigational drug with KRAS^{G12C} inhibitors such as AMG 510," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "This collaborative trial sponsored by Amgen, a leader in the field, will help test our hypothesis that RMC-4630 may be useful as the backbone of targeted therapy combinations for the treatment of various RAS-dependent tumors."

"RMC-4630 and AMG 510 have each demonstrated activity in early-stage clinical trials in patients with KRAS ^{G12C} tumors," stated Steve Kelsey, M.D., president, research and development at Revolution Medicines. "Initiation of this trial is an important step in the evaluation of this combination and its potential to treat RAS-dependent cancers by simultaneously inhibiting the activity of different oncogenic targets within the RAS signaling cascade."

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, a Phase 1b/2 study (RMC-4630-02) in combination with cobimetinib in patients with relapsed/refractory solid tumors displaying specific genomic mutations, and in the recently initiated Amgen-sponsored Phase 1b study in combination with AMG 510 in patients with advanced solid tumors harboring the KRAS^{G12C} mutation.

The SHP2 inhibitor program, including RMC-4630, is the focus of an exclusive global research, development and commercialization agreement with Sanofi.

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 and the related mTOR signaling cascade. These include inhibitors of multiple mutant RAS proteins and SOS1, as well as RMC-5552, a development candidate within the company's 4EBP1/mTORC1 program currently in IND-enabling studies.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statements in this press release that are not historical facts may be considered "forward-looking statements," including without limitation statements regarding Revolution Medicines' development plans and timelines, including without limitation the planned clinical study of RMC-4630 in combination with an investigational KRAS^{G12C} inhibitor, AMG 510, the potential anti-tumor mechanisms for SHP2 inhibitors, Revolution Medicines' goal of assessing the therapeutic potential of RMC-4630 as monotherapy or in combination treatment regimens to treat RAS pathway cancer, and the potential benefits of, and markets for, Revolution Medicines' product candidates. Forward-looking statements are typically, but not always, identified by the use of words such as "may," "will," "would," "believe," "intend," "plan," "anticipate," "estimate," "expect," and other similar terminology indicating

future results. Such forward-looking statements are subject to substantial risks and uncertainties that could cause our development programs, future results, performance or achievements to differ materially from those anticipated in the forward-looking statements. Such risks and uncertainties include without limitation risks and uncertainties inherent in the drug development process, including Revolution Medicines' programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, Revolution Medicines' ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of Revolution Medicines' capital resouces to fund operations, reliance on third parties for manufacturing and development efforts, changes in the competitive landscape and the effects on our business of the worldwide COVID-19 pandemic. For a further description of the risks and uncertainties that could cause actual results to differ from those anticipated in these forward-looking statements, as well as risks relating to the business of Revolution Medicines in general, see Revolution Medicines' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 14, 2020, and its future periodic reports to be filed with the Securities and Exchange Commission. Except as required by law, Revolution Medicines undertakes no obligation to update any forward-looking statements to reflect new information, events or circumstances, or to reflect the occurrence of unanticipated events.

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