Revolution Medicines Announces Dosing of First Patient in Clinical Study of RMC-4630 (SAR442720) Combined with PD-1 Inhibitor

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Combination of Investigational SHP2 Inhibitor and Anti-PD-1 Antibody to be Evaluated in Patients with Solid Tumors

REDWOOD CITY, Calif., June 22, 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 multicenter Phase 1 clinical trial evaluating the combination of RMC-4630 (SAR442720), the company's investigational SHP2 inhibitor, and pembrolizumab (Keytruda ®), an anti-PD-1 antibody. The trial, which is being sponsored and conducted by the company's collaboration partner Sanofi, is an open-label, safety, preliminary efficacy and pharmacokinetics study in participants with advanced malignancies. This will include patients with non-small cell lung cancer (NSCLC) who have progressed on or after platinum-based chemotherapy, and patients with colorectal cancer who have progressed on or after standard of care therapy.

RMC-4630 (SAR442720) 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. Pembrolizumab, a humanized antibody used in cancer immunotherapy, is designed to selectively inhibit the activity of PD-1, a key immune checkpoint that can prevent the immune system from targeting and killing cancer cells. Pembrolizumab is an approved standard of care for the treatment of NSCLC, including lung cancers harboring RAS pathway mutations.

The company's recently published research in the journal *Cancer Research* described the anti-tumor effects of a SHP2 inhibitor such as RMC-4630 (SAR442720) through modulation of key elements of the immune system in preclinical cancer models. These findings demonstrated that inhibition of SHP2 may exert therapeutic anti-tumor effects by modulating multiple arms of the immune response to the tumor in addition to reducing oncogenic signaling within tumor cells themselves. Importantly, these data indicate that these two mechanisms may be additive in their anti-tumor impact. Additionally, company findings from the same preclinical study showed that when the SHP2 inhibitor was combined with an immune checkpoint inhibitor (anti-PD-1), deep and durable tumor growth inhibition was observed, with complete tumor regressions and sustained immunological memory in some mice.

"We have previously shown, in a preliminary report, that RMC-4630 (SAR442720) has activity against NSCLC bearing mutant RAS. There is also a compelling collection of data suggesting that the simultaneous inhibition of SHP2 and PD-1 may drive enhanced anti-tumor activity through potentially complementary mechanisms of action," said Steve Kelsey, M.D., president, research and development at Revolution Medicines. "Overall, this scientific foundation, and the possibility of combining two agents with activity in RAS-driven tumors, serves as a strong rationale for the clinical trial evaluating the combination of RMC-4630 (SAR442720) and pembrolizumab in patients with solid tumors, including NSCLC, and we look forward to the study results."

"We believe that SHP2's key roles within both the RAS signaling pathway and the immune response to tumors support the potential for RMC-4630 (SAR442720) to serve as the backbone of targeted therapy combinations for the treatment of various RAS-dependent tumors," stated Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "With these compelling findings, we are committed to evaluating broadly the combination of RMC-4630 (SAR442720) with inhibitors of other key oncogenic targets within the RAS signaling pathway and with other anti-cancer approaches such as immune checkpoint inhibitors, including anti-PD-1 antibodies."

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, a Phase 1b study (CodeBreaK 101) in combination with AMG 510 in patients with advanced solid tumors harboring the $KRAS^{G12C}$ mutation, and a Phase 1 study in combination with pembrozilumab in patients with advanced malignancies.

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.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

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 a PD-1 inhibitor, pembrolizumab, the potential anti-tumor mechanisms for SHP2 inhibitors, including potential enhanced anti-tumor activity when combined with an immune checkpoint inhibitor, Revolution Medicines' goal of evaluating broadly the combination of RMC-4630 with inhibitors of other

oncogenic targets within the RAS signaling pathway and with other anti-cancer approaches, 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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