Revolution Medicines Announces Publication of Scientific Paper Describing Anti-Tumor Immunity Induced by SHP2 Inhibitor in Preclinical Cancer Models

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Findings Support Plans to Expand Clinical Evaluation of RMC-4630, the Company's Investigational SHP2 Inhibitor, to Include Combination with Anti-PD-1 Drug

REDWOOD CITY, Calif., April 29, 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 the publication of an original scientific paper in *Cancer Research,* a journal of the American Association for Cancer Research, describing anti-tumor effects of a SHP2 inhibitor through modulation of key elements of the immune system in preclinical cancer models. These findings demonstrate that inhibition of SHP2, a cellular protein that plays a central role in cell survival and growth, 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.

Revolution Medicines is currently evaluating RMC-4630, its potent and orally bioavailable investigational small molecule designed to selectively inhibit the function of SHP2, in a multi-cohort Phase 1/2 clinical program in patients with advanced tumors. The company and its collaboration partner Sanofi intend to expand this clinical program to include a study evaluating a combination of RMC-4630 with an anti-PD-1 antibody.

It is well established that tumors often induce an immune-suppressive environment that allows cancer cells to remain shielded from anti-tumor immunity. In the published study, researchers at Revolution Medicines evaluated the impact of SHP2 inhibition on the tumor microenvironment in preclinical cancer models. Treatment with a SHP2 inhibitor was found to alter the tumor microenvironment by depleting a type of immune cells known as pro-tumorigenic macrophages, while increasing infiltration of the tumors by anti-tumor immune cells known as T cells. These changes in the immune response profile resulted in tumor growth inhibition in preclinical models. Furthermore, 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.

"This study elucidates a potentially important second anti-tumor mechanism for SHP2 inhibitors such as RMC-4630 through reversal of the immune-suppressive tumor microenvironment leading to a more effective immune response to the tumor," said Steve Kelsey, M.D., president of research and development at Revolution Medicines. "We believe the particularly deep tumor reduction we observed following treatment with inhibitors of both SHP2 and an immune checkpoint provides a strong rationale for our plan to conduct a clinical trial evaluating dual treatment with RMC-4630 and an anti-PD-1 antibody in patients with solid tumors."

The paper published in *Cancer Research* is titled, "Allosteric inhibition of SHP2 stimulates anti-tumor immunity by transforming the immunosuppressive environment," and can be accessed at: https://cancerres.aacrjournals.org/content/early/2020/04/28/0008-5472.CAN-19-3038

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. A planned combination study of RMC-4630 and the $KRAS^{G12C}$(OFF) inhibitor, AMG 510, to be sponsored by Amgen, has been announced previously.

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, 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 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 intention of Revolution Medicines and its collaboration partner Sanofi to expand the RMC-4630 clinical program to include a study evaluating a combination of RMC-4630 with an anti-PD-1 antibody, the potential anti-tumor mechanisms for SHP2 inhibitors, Revolution Medicines' goal of identifying and evaluating promising rational combination therapies featuring RMC-4630 to treat RAS pathway cancers and the potential benefits of 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 resources 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' Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 30, 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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