Revolution Medicines Announces Dosing of First Patient in Phase 1/1b Clinical Study of RMC-5552 in Patients with Advanced Solid Tumors

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First-in-Class Bi-steric mTORC1 Inhibitor Advances into Clinical Development

Newly Issued U.S. Patent Further Strengthens RMC-5552 IP Portfolio

REDWOOD CITY, Calif., April 21, 2021 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage precision oncology company focused on developing targeted therapies to inhibit frontier targets in RAS-addicted cancers, today announced dosing of the first patient in a multicenter Phase 1/1b clinical trial evaluating RMC-5552, the company's investigational first-in-class bi-steric mTORC1 inhibitor as a monotherapy. The trial is an open-label dose-escalation and dose-expansion study designed to evaluate the safety, tolerability, preliminary efficacy and pharmacokinetics of RMC-5552 in patients with advanced relapsed/refractory solid tumors. Results from this study will inform Revolution Medicines' identification of the maximum tolerated dose (MTD) and selection of recommended Phase 2 dose and schedule (RP2DS) for further evaluation of the compound.

RMC-5552 is a potent and selective inhibitor of mTORC1 that is being developed as an anticancer therapeutic for patients with solid tumors that have hyperactivation of the mTOR pathway, including certain RAS-addicted cancers. The compound is designed to inhibit mTORC1 and preserve the natural tumor suppressive activity of 4EBP1, without the undesired inhibition of mTORC2. RMC-5552 has demonstrated antitumor activity in a wide variety of preclinical models. Revolution Medicines has also reported *in vivo* data demonstrating that RMC-5552 may increase antitumor activity in combination with $KRAS^{G12C}$ inhibitors in lung and colon cancers harboring KRAS mutations and co-mutations in the mTOR signaling pathway that can cause resistance to single agent RAS inhibition.

"The initiation of the RMC-5552 clinical program is the first step in the evaluation of our first-in-class, bi-steric mTORC1 inhibitor as a RAS Companion Inhibitor for the treatment of tumors driven by co-occurring RAS mutations and genomic activation of the mTORC1 pathway, which account for a significant proportion of RAS-addicted cancers," said Steve Kelsey, M.D., president, research and development at Revolution Medicines. "These co-occurring mutations may contribute to resistance to single-agent RAS inhibitors, and the potential to add RMC-5552 to RAS-directed therapies aligns nicely with our strategy of developing rational, biomarker-driven drug combinations that can achieve maximum clinical benefit in patients with RAS-driven cancers. We also look forward to evaluating RMC-5552 in selected indications where mTORC1 is activated independently of RAS."

New Patent Issuance for RMC-5552 and Related Compounds

In additional news regarding the RMC-5552 program, Revolution Medicines today announced that the United States Patent and Trademark Office has issued U.S. Patent No. 10,980,889. This patent provides, in part, composition of matter protection for RMC-5552, as well as related compounds in the company's proprietary series of selective mTORC1 inhibitors.

About mTORC1

The mTOR Complex 1 (mTORC1) is a central node within the mTOR signaling pathway and a critical regulator of metabolism, growth and proliferation in cancer cells. Oncogenic mutations of genes upstream of mTOR, including PI3 kinase, PTEN, and STK11, can drive abnormal activation of mTORC1 and subsequent inactivation of the tumor suppressor 4EBP1. Selective inhibition of mTORC1 to reactivate 4EBP1 is a potential therapeutic strategy for patients with tumors bearing such mutations. These mutations are often co-occurring with RAS mutations in RAS-addicted tumors and combinations of mTORC1 and RAS-targeted inhibitors may be of particular benefit in this context.

About Revolution Medicines, Inc.

Revolution Medicines is a clinical-stage precision oncology company focused on developing novel targeted therapies to inhibit high-value frontier targets in RAS-addicted cancers. 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 R&D pipeline comprises RAS(ON) Inhibitors designed to suppress diverse oncogenic variants of RAS proteins, and RAS Companion Inhibitors for use in combination treatment strategies. RAS(ON) Inhibitors in development include RMC-6291 and RMC-6236, and a pipeline of research compounds targeting additional RAS variants. RAS Companion Inhibitors in development include RMC-4630, RMC-5552, and RMC-5845.

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 the tolerability and potential efficacy of Revolution Medicines' clinical candidates, including RMC-5552; the outcome of the company's clinical trials, including the Phase 1/1b study of RMC-5552; identification of the MTD and selection of a RP2DS for RMC-5552; the strategy of developing drug combinations that can achieve maximum clinical benefit; and Revolution Medicines' plans to evaluate RMC-5552 in selected indications where mTORC1 is activated independently of RAS. 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 the company's 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, the company's ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of the company's 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 2, 2021, 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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