Revolution Medicines Doses First Patient in Phase 1/1b Clinical Trial of RMC-6291, Company's First Mutant-Selective RAS(ON) Inhibitor

September 22, 2022

$KRAS^{G12C}$(ON) Inhibitor with highly differentiated mechanism of action being evaluated in patients with cancers harboring $KRAS^{G12C}$ mutation

RMC-6291 is first mutant-selective RAS(ON) Inhibitor to enter clinic, following closely behind company's RAS ^{MULTI}(ON) Inhibitor, RMC-6236

REDWOOD CITY, Calif., Sept. 22, 2022 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced the first patient was dosed in its Phase 1/1b monotherapy clinical trial of RMC-6291, an oral, selective, covalent $KRAS^{G12C}$(ON) Inhibitor designed to treat patients with cancers driven by the $KRAS^{G12C}$ mutation. RMC-6291, which exhibits a potential best-in-class preclinical profile, is the first drug candidate from the company's pipeline of mutant-selective RAS(ON) Inhibitors to enter the clinic. Last quarter, Revolution Medicines initiated clinical development of RMC-6236, its oral RAS^{MULTI}(ON) Inhibitor designed to treat patients with cancers driven by a variety of RAS mutations.

The Phase 1/1b trial (NCT05462717) sponsored by Revolution Medicines is a multicenter, open-label, dose-escalation and dose-expansion study of RMC-6291 in patients with advanced solid tumors harboring the $KRAS^{G12C}$ mutation. The primary objectives of the study are to evaluate safety and tolerability and to inform the recommended Phase 2 dose and schedule (RP2DS) for the compound.

"RMC-6291 is an exciting first drug candidate from our collection of oral, mutant-selective RAS(ON) Inhibitors to advance into clinical development, and we expect learnings from this trial will also inform advancement of our pipeline of innovative compounds. The next mutant-selective RAS(ON) inhibitor we plan to advance into the clinic is RMC-9805, an oral and covalent inhibitor of $KRAS^{G12D}$, the most common mutant RAS driver of human cancers," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "The mutant-selective approach exemplified by RMC-6291, RMC-9805 and other assets in our pipeline differs from the profile of RMC-6236, which entered clinical evaluation recently and is designed to inhibit many RAS variants rather than a single RAS mutation. We believe that these complementary approaches, used in monotherapy and/or combination treatment regimens, will provide a powerful set of tools for countering the complex processes that cause and sustain a wide range of RAS-addicted cancers."

About Revolution Medicines, Inc.
Revolution Medicines is a clinical-stage oncology company developing novel targeted therapies for RAS-addicted cancers. 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. The company's RAS(ON) Inhibitors RMC-6236 (RAS^{MULTI}) and RMC-6291($KRAS^{G12C}$) are in clinical development. Additional RAS(ON) Inhibitors in development include RMC-9805 ($KRAS^{G12D}$) and RMC-8839 ($KRAS^{G13C}$), and a pipeline of research compounds targeting additional RAS variants. RAS Companion Inhibitors in clinical development include RMC-4630 (SHP2) and RMC-5552 (mTORC1/4EBP1).

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 company's development plans and timelines and its ability to advance its portfolio and R&D pipeline, including its RAS(ON) inhibitors; dosing and enrollment in the company's clinical trials and the tolerability, potential efficacy and utility of the company's candidates being studied; and the ability of the company's planned complementary treatment approaches to counter the processes that cause and sustain RAS-addicted cancers. 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 the company's 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 the company's 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 August 9, 2022, 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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