Revolution Medicines Reports Progress Across Pipeline of Targeted Therapeutics for RAS-Addicted Cancers in Presentation at 40th Annual J.P. Morgan Healthcare Conference

January 11, 2022

RAS(ON) Inhibitor Pipeline Expands with Advancement of Two New Drug Candidates; Development-Stage Portfolio Covers RAS Drivers of Majority of RAS-Addicted Cancers

First Patient Dosed in Global Phase 2 Clinical Trial Evaluating Combination of RMC-4630 and Lumakras ™ (sotorasib) in Patients with Advanced Non-Small Cell Lung Cancer

Preliminary Evidence of Clinical Activity of mTORC1-Selective Inhibitor, RMC-5552, Obtained in Ongoing Phase 1/1b Monotherapy Study

REDWOOD CITY, Calif., Jan. 11, 2022 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing novel targeted therapies for RAS-addicted cancers, today reported progress across its pipeline of targeted therapeutics spanning its RAS(ON) Inhibitor and RAS Companion Inhibitor portfolios. These updates were announced in a corporate presentation delivered by Mark A. Goldsmith, M.D., Ph.D., the company's chief executive officer and chairman, at the 40 th Annual J.P. Morgan Healthcare Conference.

RAS(ON) Inhibitors

As a centerpiece of this presentation, Dr. Goldsmith provided updates on the company's expanding portfolio of innovative RAS(ON) Inhibitors. The company is on track to file investigational new drug (IND) applications in the first half of 2022 for its two most advanced RAS(ON) Inhibitors, RMC-6236 (RAS^{MULTI}) and RMC-6291 ($KRAS^{G12C}$), both of which have shown attractive preclinical profiles including strong anti-tumor activity.

Dr. Goldsmith also introduced two new mutant-selective RAS(ON) Inhibitors that Revolution Medicines has advanced into IND-enabling development. RMC-9805 is an oral, mutant-selective, covalent inhibitor of $KRAS^{G12D}$, which is the primary tumor driver in more than 50,000 new patients with colorectal, pancreatic or lung cancer annually in the United States. Evaluation in preclinical *in vivo* cancer models has demonstrated best-in-class potential for RMC-9805, and the company aims to file an IND application in the first half of 2023.

RMC-8839 is an oral, mutant-selective, covalent inhibitor of $KRAS^{G13C}$. Revolution Medicines believes that RMC-8839 is the first compound to directly target $KRAS^{G13C}$, an important therapeutic target primarily for lung and select colorectal cancer patients who are not currently served by any targeted RAS drug. This first-in-class development candidate has demonstrated strong anti-tumor responses in *in vivo* cancer models and the company aims to file an IND application in the second half of 2023.

In addition to its four development-stage RAS(ON) Inhibitors, the company disclosed that it has ongoing discovery programs pursuing additional mutant-selective compounds for various cancer mutations at RAS hotspots G12, G13 and Q61, with the goal of nominating a fifth development candidate in the second half of 2022.

RAS Companion Inhibitors

Dr. Goldsmith also provided updates on the company's class-leading, clinical-stage RAS Companion Inhibitors: RMC-4630, the company's investigational SHP2 inhibitor, and RMC-5552, the company's potent, selective inhibitor of mTORC1.

The first patient has been dosed in RMC-4630-03, a global, multicenter, open-label Phase 2 study evaluating the efficacy, safety, tolerability, and pharmacokinetics of RMC-4630 in combination with Lumakras ™ (sotorasib), Amgen's $KRAS^{G12C}$ inhibitor, in subjects with advanced non-small cell lung cancer. Revolution Medicines is sponsoring the RMC-4630-03 study under its global partnership with Sanofi and conducting the trial in collaboration with Amgen, which is supplying sotorasib to study sites globally. The study's first patient was enrolled and dosed at Sarah Cannon Research Institute in Nashville, Tennessee, by study investigator Melissa Johnson, M.D., Director of the Lung Cancer Research Program.

The company also reported initial findings from the ongoing dose escalation portion of its Phase 1/1b clinical trial of RMC-5552, including preliminary evidence of clinical activity against advanced tumors with mutations associated with hyperactive mTORC1 signaling. To date, all four efficacy evaluable patients treated with 6 mg per week have experienced disease control, including one patient exhibiting a confirmed partial response with a 63% reduction from baseline and the other three with stable disease. A strategic priority is to evaluate RMC-5552 in combination with RAS(ON) Inhibitors in patients carrying both RAS and mTOR pathway mutations, representing approximately 30,000 new patients per year in the United States.

"We begin 2022 with strong momentum in our efforts to serve critical unmet medical needs for patients with diverse RAS-addicted cancers," said Dr. Goldsmith. "We now have four development-stage RAS(ON) Inhibitors with compelling preclinical profiles, the first two of which are expected to enter the clinic this year and the other two advancing toward IND filings in 2023. In addition, both of our clinical-stage RAS Companion Inhibitors have now shown encouraging initial single agent clinical activity and are continuing in monotherapy and/or combination treatment studies. Our cohesive portfolio of development-stage assets is designed to inhibit the cancer drivers of all major RAS-addicted forms of human lung, colorectal and pancreatic cancer, and we remain optimistic that the era of targeted treatment for patients with these cancers is within reach."

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. RAS(ON) Inhibitors in development include RMC-6236 (RAS^{MULTI}), RMC-6291($KRAS^{G12C}$), 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).

Lumakras ™ (sotorasib) is a trademark of Amgen, 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 the company's development plans and timelines and its ability to advance its portfolio and R&D pipeline; dosing and enrollment in the company's clinical trials and the tolerability and potential efficacy of the company's candidates being studied; planned IND applications for RMC-6236, RMC-6291, RMC-9805 and RMC-8839; the potential of RMC-9805 to be best-in-class; the company's goal of nominating a new development candidate from its discovery programs; the company's aim to complete single agent dose escalation in the Phase 1/1b clinical trial of RMC-5552; the company's optimism that the era of targeted treatment for patients with RAS-addicted forms of human lung, colorectal and pancreatic cancer is within reach. 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' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 10, 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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