Revolution Medicines Presents Promising Clinical Activity and Safety Data from Phase 1/1b Trial of RMC-6236

October 22, 2023

Investor Webcast to be held Sunday, October 22 at 12:30 p.m. Eastern Time

REDWOOD CITY, Calif., Oct. 22, 2023 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced promising anti-tumor and safety data for RMC-6236, its RAS^{MULTI}(ON) Inhibitor, in patients with previously treated non-small cell lung cancer (NSCLC) and pancreatic ductal adenocarcinoma (PDAC) across several dose levels and KRAS^{G12X} genotypes, including common KRAS-mutant genotypes G12D and G12V. These initial results were presented during a Proffered Paper session at the European Society for Medical Oncology (ESMO) Congress in Madrid, October 20-24, 2023.

"Today's presentation marks an important milestone in the clinical development of RMC-6236, an unprecedented, oral RAS ^{MULTI}(ON) Inhibitor with an innovative mechanism of action. The findings reinforce our belief that by inhibiting the (ON), or active, form of diverse RAS cancer drivers, RMC-6236 can lead to meaningful clinical responses in patients at dose levels that are generally well tolerated," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "These data also confirm that RMC-6236 can target multiple common RAS variants that cause cancer, supporting its ongoing development as monotherapy in patients with NSCLC or PDAC harboring RAS mutations. Further, RMC-6236 has a compelling profile for evaluation in combination treatment strategies with RMC-6291, our mutant-selective RAS^{G12C}(ON) Inhibitor, and with immunotherapy and other cancer drugs."

The RMC-6236-001 Phase 1/1b trial is a multicenter, open-label, dose-escalation and dose-expansion study designed to evaluate RMC-6236 as monotherapy in patients with advanced solid tumors harboring KRAS^{G12X} mutations. As of an October 12, 2023 data extraction, a total of 111 patients with NSCLC (n=46) or PDAC (n=65) were treated at dose levels administered once daily (QD) ranging from 80 mg to 400 mg. Common KRAS mutations in patients evaluated included G12D, G12V, G12R, G12A and G12S; patients with KRAS^{G12C} mutations were excluded from the study due to the availability of currently approved KRAS^{G12C}(OFF) inhibitors. All patients had previously been treated with standard of care appropriate for tumor type and stage. Patients with NSCLC had received a median of two prior lines of therapy (range 1–6) while patients with PDAC had received a median of three prior lines of therapy (range 1–7).

RMC-6236 demonstrated preliminary evidence of clinical activity and an acceptable safety profile that was generally well tolerated across the dose levels analyzed. Clinical activity was evaluated in patients who had received the first dose of RMC-6236 at least eight weeks prior to the data extraction date (n=86). Among the 40 efficacy evaluable NSCLC patients, the objective response rate was 38 percent, with one patient achieving a complete response (CR) as a best response and 14 patients achieving a partial response (PR) (including three unconfirmed PRs). The disease control rate (DCR) in this NSCLC population was 85 percent. Among the 46 efficacy evaluable PDAC patients, the objective response rate was 20 percent, with nine patients achieving a PR (including four unconfirmed PRs) as a best response. The DCR in this PDAC population was 87 percent. Confirmed objective responses included tumors harboring KRAS mutations G12D, G12V or G12R, and disease control was observed across all KRAS mutations, including G12A and G12S.

The most common treatment-related adverse events (TRAEs) were rash and GI-related toxicities that were primarily Grade 1 or 2 in severity. The reported Grade 3 TRAEs were rash (6%), stomatitis (2%), and diarrhea (1%). One previously reported Grade 4 TRAE occurred in a patient with PDAC at the 80 mg QD dose level who had a large intestine perforation at the site of an invasive tumor that reduced in size while on treatment, which resulted in treatment discontinuation. No safety signals were observed that indicated an elevated risk of hepatotoxicity, which has been reported for some KRAS^{G12C}(OFF) inhibitors.

"There is a high unmet need among patients living with KRAS-mutated NSCLC or PDAC, two aggressive cancer types for which current standard of care treatments are often inadequate," said Kathryn C. Arbour, M.D., thoracic oncologist at Memorial Sloan Kettering Cancer Center and a principal investigator for the RMC-6236-001 study. "It is quite encouraging to see this level of anti-tumor activity in previously treated patients by a generally well-tolerated investigational drug. We look forward to continuing the dose optimization portion of the Phase 1/1b study to inform future development and further our understanding of the effects of RMC-6236 on RAS-mutant cancers."

Investor Webcast
Revolution Medicines will host an investor webcast on Sunday, October 22, 2023 at 12:30 p.m. Eastern Time to discuss the data presented at both the 2023 AACR-NCI-EORTC Triple meeting and ESMO, in addition to other pipeline updates. To participate in the live webcast, participants may register in advance here: https://edge.media-server.com/mmc/p/eb8agxe6. A live webcast of the call will also be available on the Investors section of Revolution Medicines' website at https://ir.revmed.com/events-and-presentations. Following the live webcast, a replay will be available on the company's website for at least 14 days.

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}), RMC-6291 (KRAS^{G12C}) and RMC-9805 (KRAS^{G12D}) are currently in clinical development. Additional RAS(ON) Inhibitors in the company's pipeline include RMC-0708 (KRAS ^{Q61H}) and RMC-5127 (KRAS^{G12V}) which are currently in IND-enabling development, RMC-8839 (KRAS^{G13C}), and additional compounds targeting other 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; progression of clinical studies and findings from these studies, including the tolerability and potential efficacy of the company's candidates being studied; the potential advantages and effectiveness of the company's clinical and preclinical candidates, including its RAS(ON) Inhibitors; the validation of the company's platform; the

company’s goal of bringing therapies to cancer patients; and the company’s expectations regarding the potential market size and size of the potential patient populations for the company’s product candidates, if approved for commercial use. 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 global events and other macroeconomic conditions. 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 8, 2023, 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.

Investors & Media Contact: Erin Graves 650-779-0136 egraves@revmed.com