Revolution Medicines Presents Initial Data from RMC-9805 Monotherapy Study in Patients with Advanced Pancreatic Ductal Adenocarcinoma

October 25, 2024

First clinical results for RMC-9805, a RAS(ON) G12D-selective inhibitor, demonstrate encouraging tolerability and antitumor activity in patients with PDAC

Investor webcast to be held Friday, October 25 at 12:00 p.m. Eastern Time (ET)

REDWOOD CITY, Calif., Oct. 25, 2024 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced preliminary safety and antitumor data for RMC-9805, its RAS(ON) G12D-selective inhibitor, in patients with previously treated pancreatic ductal adenocarcinoma (PDAC). These initial results were presented during the late-breaking oral session at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Barcelona on October 25, 2024.

“We are pleased to report the first clinical data for RMC-9805, our novel, oral RAS(ON) G12D-selective covalent inhibitor, which demonstrate encouraging initial safety, tolerability and antitumor activity evidenced by tumor regressions,” said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. “While preliminary, these data bolster our belief that RMC-9805 has the potential to play a role in an emerging treatment paradigm for patients living with pancreatic cancer, both as monotherapy and in combinations. With today’s presentation, RMC-9805 becomes the third tri-complex compound from the Revolution Medicines pipeline to demonstrate clinical proof-of-concept, and it reaffirms our commitment to bringing novel RAS(ON) inhibitors to patients with RAS-addicted cancers.”

The RMC-9805-001 Phase 1/1b study is a multicenter, open-label, dose-escalation and dose-expansion study designed to evaluate RMC-9805 in patients with advanced solid tumors harboring a KRAS G12D mutation. As of the September 2, 2024 data cutoff date, 179 patients were treated with escalating doses of RMC-9805 (ranging from 150-1200 mg once daily (QD) and 300-600 mg twice daily (BID)). Study patients had received a median of two prior therapies (range 0-9) and all had previously been treated with standard of care.

As of the data cutoff date, RMC-9805 demonstrated an encouraging safety profile and was generally well tolerated across dose levels. For patients receiving 1200 mg of RMC-9805 daily (n = 99), the most common treatment-related adverse events (TRAEs) occurring in greater than 10% of patients were GI-related toxicities (nausea, diarrhea and vomiting) and rash that were primarily Grade 1 in severity and typically of limited duration. One Grade 3 TRAE of ALT elevation was reported, and no Grade 4 or 5 TRAEs were observed. Four patients (4%) experienced TRAEs that led to dose reduction and no patients discontinued treatment as a result of TRAEs. No dose limiting toxicities were observed and the maximum tolerated dose was not reached.

Preliminary efficacy was assessed in PDAC patients. At a candidate recommended Phase 2 dose of 1200 mg daily (20 patients at 1200 mg QD and 20 patients at 600 mg BID), patients who received a first dose of RMC-9805 at least 14 weeks prior to the data cutoff date achieved a 30% (n = 12) objective response rate (confirmed or pending), with a disease control rate of 80% (n = 32).

“Pancreatic cancer is the most RAS-addicted of all major cancers and the G12D variant is the most common RAS mutation in pancreatic cancer. No approved targeted therapies are available for these patients, making this an area of significant unmet need,” said David Hong, M.D. of MD Anderson Cancer Center, principal investigator and lead author for the RMC-9805-001 presentation. “This is a challenging disease, but we observed a promising level of antitumor activity at generally tolerable doses in this Phase 1 study."

Investor Webcast
Revolution Medicines will host an investor webcast on Friday, October 25, 2024 at 12:00 p.m. Eastern Time / 6:00 p.m. Central European Standard Time to discuss the RMC-6236 and RMC-9805 monotherapy data in PDAC presented at the EORTC-NCI-AACR (“Triple”) meeting. To participate in the live webcast, participants may register in advance here. A live webcast of the call will 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 Pancreatic Cancer and Pancreatic Ductal Adenocarcinoma
Pancreatic cancer is one of the most lethal malignancies, characterized by its typically late-stage diagnosis, resistance to standard chemotherapy, and high mortality rate. In the U.S., recent estimates indicate that in 2024, approximately 60,000 people will be diagnosed with pancreatic cancer, and about 50,000 people will die from this aggressive disease.

The most common form of pancreatic cancer, pancreatic ductal adenocarcinoma (PDAC) and its variants, accounts for approximately 92% of all pancreatic cancer cases. Due to the lack of early symptoms and detection methods, approximately 80% of patients are diagnosed with PDAC at an advanced or metastatic stage. It is the most RAS-addicted of all major cancers, and more than 90% of patients have tumors that harbor RAS mutations. Metastatic PDAC remains one of the most common causes of cancer-related deaths in the U.S., with a five-year survival rate of approximately 3%.

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. The company’s RAS(ON) inhibitors RMC-6236, a RAS(ON) multi-selective inhibitor, RMC-6291, a RAS(ON) G12C-selective inhibitor, and RMC-9805, a RAS(ON) G12D-selective inhibitor, are currently in clinical development. Additional development opportunities in the company’s pipeline focus on RAS(ON) mutant-selective inhibitors, including RMC-5127 (G12V), RMC-0708 (Q61H) and RMC-8839 (G13C), in addition to RAS companion inhibitors RMC-4630 and RMC-5552.

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 progression of clinical studies and findings from these studies, including the safety, tolerability and antitumor activity of the company’s candidates being studied and the durability of these results; dosing and enrollment in the company’s clinical trials; the company’s belief that RMC-9805

could play a role in treatment options for pancreatic cancer patients; the company's beliefs regarding demonstration of clinical proof-of-concept; and the company's plans to bring RAS(ON) inhibitors to patients. 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' current stage of development, the process of designing and conducting preclinical and clinical trials, risks that the results of prior clinical trials may not be predictive of future clinical trials, clinical efficacy, or other future results, 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 global events, such as international conflicts or global pandemics. 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 (the "SEC") on August 7, 2024, and its future periodic reports to be filed with the SEC. 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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