



Revolution Medicines Presents Updated Data from RMC-6236 Monotherapy Study in Patients with Advanced Pancreatic Ductal Adenocarcinoma

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Encouraging progression-free survival and overall survival profile

Safety findings consistent with previously reported data, no new safety signals observed

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

REDWOOD CITY, Calif., Oct. 23, 2024 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced encouraging antitumor activity and safety/tolerability data for RMC-6236, its RAS(ON) multi-selective inhibitor, in patients with previously treated pancreatic ductal adenocarcinoma (PDAC). These updated results were presented during a late-breaking poster session at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, October 23-25, 2024.

"The maturing data reported today continue to solidify the compelling progression-free survival and overall survival for patients with pancreatic cancer treated with RMC-6236, our oral RAS(ON) multi-selective inhibitor, in the Phase 1 study," said Mark A. Goldsmith, M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. "These results support our ongoing Phase 3 registrational study, RASolute 302, and our belief that RMC-6236 monotherapy could potentially become an important therapeutic option for patients living with advanced or metastatic pancreatic cancer."

The RMC-6236-001 Phase 1/1b study 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 RAS mutations or wild-type RAS. As of the July 23, 2024 data cutoff date, a total of 127 patients previously treated for PDAC were treated with RMC-6236 at doses ranging from 160 mg to 300 mg once daily (QD).

RMC-6236 appeared to be generally well tolerated at dose levels ranging from 160 mg to 300 mg QD and showed an overall safety profile consistent with previously reported results. No new safety signals were observed. The most common treatment-related adverse events (TRAEs) were rash and GI-related toxicities that were primarily Grade 1 or 2 in severity. The most common reported Grade ≥ 3 TRAEs were rash (8%), stomatitis (3%), and diarrhea (2%). TRAEs leading to dose modification occurred in 35% of patients with no treatment discontinuations due to TRAE. The average dose intensity across doses ranging from 160 mg to 300 mg was 92%.

RMC-6236 demonstrated durable antitumor activity as evidenced by updated progression-free survival (PFS) and overall survival (OS) at daily doses ranging from 160 mg to 300 mg, as described below. Patients with PDAC harboring a KRAS G12X mutation in the second-line (2L) setting achieved a median PFS of 8.5 months (95% confidence interval (CI), 5.3 – 11.7 months) and a median OS of 14.5 months (95% CI, 8.8 – not-estimable (NE)). Patients with PDAC harboring any RAS mutation in the 2L setting achieved a median PFS of 7.6 months (95% CI, 5.9 – 11.1 months) and a median OS of 14.5 months (95% CI, 8.8 – NE). Landmark OS for these patients at 6 months was 89% and 91% in patients with PDAC harboring a KRAS G12X mutation and patients with PDAC harboring any RAS mutation, respectively. The objective response rate for patients with tumors harboring KRAS G12X mutations was 29% in the 2L group and 22% in the third-line and beyond (3L+) group. The disease control rate was 91% and 89% in these patients, respectively.

"Pancreatic cancer remains one of the highest unmet needs in medicine. It is the most RAS-mutated of all major cancers with more than 90% of patients having tumors that harbor a RAS mutation," said Brian M. Wolpin, M.D., M.P.H., professor of medicine at Harvard Medical School, and director of the Gastrointestinal Cancer Center and Robert T. & Judith B. Hale Chair in Pancreatic Cancer at Dana-Farber Cancer Institute, principal investigator for the RMC-6236-001 study and lead author of the ENA presentation. "To see the level of clinical activity at doses with manageable tolerability demonstrated in this Phase 1 study is very exciting, providing much needed hope for patients with this difficult to treat cancer."

Investor Webcast

Revolution Medicines will host an investor webcast on Friday, October 25, 2024 at 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 RMC-6236

RMC-6236 is an oral, direct RAS(ON) multi-selective inhibitor with the potential to help address a wide range of cancers driven by oncogenic RAS mutations. RMC-6236 suppresses RAS signaling by blocking the interaction of RAS(ON) with its downstream effectors. It does so across oncogenic RAS mutations G12X, G13X and Q61X, in major cancers including pancreatic ductal adenocarcinoma (PDAC), non-small cell lung cancer (NSCLC) and colorectal cancer (CRC).

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; and the company's belief that RMC-6236 could become a therapeutic option for pancreatic cancer 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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