Revolution Medicines Shares New Clinical Results Supporting Initiation of RASolute 303, a Global Phase 3 Registrational Trial of Daraxonrasib in First Line Metastatic Pancreatic Ductal Adenocarcinoma

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Long-term follow-up data for daraxonrasib monotherapy in second line metastatic pancreatic ductal adenocarcinoma reinforces promising clinical activity and durability

Highly encouraging initial clinical results for daraxonrasib monotherapy and daraxonrasib plus chemotherapy in first line metastatic pancreatic ductal adenocarcinoma support planned initiation of three-arm Phase 3 trial in Q4 2025

Revolution Medicines to host webcast today at 5:00 p.m. Eastern Time

REDWOOD CITY, Calif., Sept. 10, 2025 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a late-stage clinical oncology company developing targeted therapies for patients with RAS-addicted cancers, today announced key clinical updates from its daraxonrasib Phase 1 clinical trials. The data, to be presented during an investor webcast today at 5:00 p.m. Eastern Time (ET), will focus on new daraxonrasib data in patients with metastatic pancreatic ductal adenocarcinoma (PDAC), including long-term follow-up data in second line patients and initial monotherapy and chemotherapy-combination data in first line patients.

“Patients living with pancreatic cancer have an urgent need for more effective and durable treatment options, and we are pursuing a bold vision to establish new global standards of care across treatment lines for this devastating disease,” said Mark A. Goldsmith M.D., Ph.D., chief executive officer and chairman of Revolution Medicines. “Daraxonrasib’s pioneering mechanism of action covering RAS cancer driver mutations broadly, and highly encouraging new clinical findings released today, together provide strong evidence of its potential to serve these patients. The promising clinical profile observed in investigational studies to date in both previously treated and treatment-naïve patients with pancreatic cancer compels initiation of our planned registrational study evaluating daraxonrasib as monotherapy and in combination with chemotherapy in the first line metastatic setting.”

Daraxonrasib Monotherapy: Long-term Follow-Up in 2L Metastatic PDAC
As of a June 30, 2025 cutoff date, patients with second line and beyond (2L+) metastatic PDAC treated with daraxonrasib 300 mg daily (QD) were evaluated for long-term follow-up on key safety and efficacy endpoints.

- **Safety**: In 2L+ patients with RAS mutant PDAC (n=83), daraxonrasib 300 mg QD was generally well tolerated with a safety profile consistent with previously reported data. No new safety signals were identified.
- **Efficacy**: Daraxonrasib at 300 mg QD demonstrated compelling antitumor activity and durability, with the following results for patients with second line (2L) RAS mutant PDAC with a RAS G12X mutation (n=26) or any RAS mutation (n=38), respectively:
  - The confirmed objective response rate (ORR) per RECIST v1.1 was 35% and 29%.
  - The disease control rate (DCR) was 92% and 95%.
  - The median progression-free survival (PFS) was 8.5 months (95% confidence interval (CI), 6.7 – 10.5) and 8.1 months (95% CI, 5.9 – 10.1).
  - The median overall survival (OS) was 13.1 (95% CI, 10.9 – NE) and 15.6 months (95% CI, 10.9 – NE).
  - Median follow-up was 16.7 months.
- RASolute 302, the ongoing Phase 3 registrational trial of daraxonrasib monotherapy as a 2L treatment for metastatic PDAC, remains on track to complete global enrollment this year to enable an expected data readout in 2026.

Daraxonrasib Monotherapy: Initial Results in 1L Metastatic PDAC
As of a July 28, 2025 cutoff date, patients with treatment-naïve RAS-mutant PDAC treated with daraxonrasib 300 mg QD monotherapy were evaluated on key safety and antitumor activity endpoints.

- **Safety**: In patients treated in this cohort (n=40), the safety profile observed for daraxonrasib monotherapy as a first line (1L) treatment was generally consistent with the reported safety findings for daraxonrasib in the 2L setting. The mean dose intensity was 85%.
- **Efficacy**: In patients who met the definition of 1L metastatic PDAC and had sufficient follow-up (n=38), the ORR was 47% and the DCR was 89%, with a median follow-up of 9.3 months. The majority of patients remained on study treatment as of the data cutoff date, and additional follow-up will be needed to determine the durability of clinical benefit.

Daraxonrasib plus Gemcitabine nab-Paclitaxel (GnP) Combination: Initial Results in 1L Metastatic PDAC

The combination of daraxonrasib plus chemotherapy is designed to sustain continuous suppression of RAS signaling by maintaining sufficient dose intensity for daraxonrasib, to leverage the antitumor contribution of chemotherapy and to achieve a safety profile that is competitive against standard chemotherapy.

For the combination, the company selected daraxonrasib 200 mg QD plus the standard dose of GnP given on a Days 1 and 15 schedule.

As of a July 28, 2025 data cutoff date, patients with 1L metastatic PDAC treated with the combination of daraxonrasib plus GnP were evaluated on key safety and antitumor activity endpoints.

- **Safety**: In patients with RAS mutations (n=40), daraxonrasib plus GnP was generally well tolerated. The safety profile

observed for the combination regimen was consistent with the sum of the known safety findings of each respective agent, and no new safety signals emerged. The mean dose intensity was 81%.

- **Efficacy**: In patients who had sufficient follow-up (n=31), the ORR was 55% and the DCR was 90%, with a median follow-up of 6.9 months. The majority of patients remained on study treatment as of the data cutoff date, and additional follow-up will be needed to determine the durability of clinical benefit.

These encouraging clinical results support the company's plans to initiate RASolute 303, a global, randomized Phase 3 trial in patients with 1L metastatic PDAC, in the fourth quarter of 2025. The three-arm trial will evaluate daraxonrasib monotherapy and the combination of daraxonrasib plus GnP, each compared to a control arm with GnP treatment.

Investor Webcast

Revolution Medicines management will host an investor webcast today, September 10, at 5:00 p.m. ET (2:00 p.m. PT) to discuss these updates. To participate in the live webcast, participants may register at https://edge.media-server.com/mmc/p/sd9ugkvf. A live webcast of the call will be available on the 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 approximately 60,000 people will be diagnosed annually with pancreatic cancer[1], 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[2]. 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 commonly RAS-addicted of all major cancers, and more than 90% of patients have tumors that harbor RAS mutations[3]. 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%[4].

About Daraxonrasib
Daraxonrasib (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. Daraxonrasib suppresses RAS signaling by blocking the interaction of RAS(ON) with its downstream effectors. It does so by targeting oncogenic RAS mutations G12X, G13X and Q61X that are common drivers of 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 late-stage clinical oncology company developing novel targeted therapies for patients with 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 daraxonrasib (RMC-6236), a RAS(ON) multi-selective inhibitor; elironrasib (RMC-6291), a RAS(ON) G12C-selective inhibitor; and zoldonrasib (RMC-9805), a RAS(ON) G12D-selective inhibitor, are currently in clinical development. The company anticipates that RMC-5127, a RAS(ON) G12V-selective inhibitor, will be its next RAS(ON) inhibitor to enter clinical development. Additional development opportunities in the company's pipeline focus on RAS(ON) mutant-selective inhibitors, including RMC-0708 (Q61H) and RMC-8839 (G13C). For more information, please visit www.revmed.com and follow us on LinkedIn.

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, including the expected timing and plans for enrollment completion and data readouts; the potential for any of the company's investigational products, including daraxonrasib, to become a new global standard of care for patients with pancreatic cancer and address their urgent need for more effective and durable treatment options; expected findings from the company's clinical studies, including the safety, tolerability and antitumor activity of the company's candidates being studied and the durability of these results; expected timing and design of the company's planned clinical trials, including the company's plans for RASolute 303; the company's development plans including its expectation that RMC-5127 will be its next RAS(ON) inhibitor to enter clinical development; and the ability of the company to bring its clinical candidates to patients. Forward-looking statements are typically, but not always, identified by the use of words such as "will," "believe," "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 6, 2025, 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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[1] Siegel RL, et al. *CA Cancer J Clin.* 2024;74:12-49.

[2] Hallbrook CJ, et al. *Cell.* 2023;186:1729-1754.

[3] Lee JK, Sivakumar S, Schrock AB, et al. Comprehensive pan-cancer genomic landscape of KRAS altered cancers and real-world outcomes in solid tumors. *NPJ Precis Oncol.* 2022;6(1);91. Doi:10.1038/s41698-022-00334-z.

[4] American Cancer Society. Survival Rates for Pancreatic Cancer. Available at: https://www.cancer.org/cancer/types/pancreatic-cancer/detection-

diagnosis-staging/survival-rates.html. Accessed June 2025.