Revolution Medicines Presents Phase 1/2 Clinical Data for Zoldonrasib Combination Regimens in Patients with RAS G12D Metastatic Pancreatic Cancer at ESMO Gastrointestinal Cancers Congress 2026

July 2, 2026

REDWOOD CITY, Calif., July 02, 2026 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a late-stage clinical oncology company developing targeted therapies for patients with RAS-addicted cancers, today announced results from two Phase 1/2 clinical trials evaluating zoldonrasib, its oral RAS(ON) G12D-selective covalent inhibitor, in combination regimens for patients with RAS G12D metastatic pancreatic ductal adenocarcinoma (PDAC). The results, which will be presented today in a proffered paper session at the 2026 European Society for Medical Oncology (ESMO) Gastrointestinal Cancers Congress, include zoldonrasib in combination with standard of care chemotherapy in previously untreated patients and zoldonrasib in combination with daraxonrasib, the company's oral RAS(ON) multi-selective inhibitor, in previously treated patients.

"The Phase 3 RASolute 302 results provided clinical validation of RAS(ON) inhibition with daraxonrasib in second line metastatic pancreatic cancer and established a strong foundation for evaluating this therapeutic approach across additional RAS genotypes, treatment settings and combination strategies. The results presented at ESMO GI demonstrate compelling proof-of-concept for two zoldonrasib-based regimens in RAS G12D disease: combination with standard of care chemotherapy in previously untreated patients and a RAS(ON) inhibitor doublet with daraxonrasib in previously treated patients. Together, these findings are the foundation of two distinct Phase 3 strategies we are pursuing in previously untreated metastatic RAS G12D pancreatic cancer: the ongoing RASolute 305 trial evaluating zoldonrasib plus standard of care chemotherapy, and the planned RASolute 309 trial evaluating the combination of zoldonrasib plus daraxonrasib," said Alan Sandler, M.D., chief development officer of Revolution Medicines.

Safety and Efficacy of Zoldonrasib Plus Chemotherapy in Patients with First Line RAS G12D Metastatic Pancreatic Cancer (Abstract #340O)

RMC-GI-102 (NCT06445062) is an ongoing Phase 1/2 trial evaluating zoldonrasib 1200 mg once daily in combination with investigator's choice of standard of care chemotherapy in patients with previously untreated metastatic RAS G12D PDAC. Investigator's choice of chemotherapy includes modified FOLFIRINOX (mFFX) or gemcitabine plus nab-paclitaxel (GnP). As of the February 8, 2026 data cutoff, the trial enrolled 41 patients in the zoldonrasib plus mFFX arm and 40 patients in the zoldonrasib plus GnP arm.

Zoldonrasib demonstrated a manageable safety and tolerability profile in combination with standard chemotherapy. The safety profile of zoldonrasib in combination with chemotherapy was broadly consistent with the established profiles of each respective chemotherapy regimen. Grade 3 or greater treatment-related adverse events (TRAEs) occurred in 61% of patients who received the zoldonrasib plus mFFX and 80% of patients who received zoldonrasib plus GnP. The most common Grade 3 or greater TRAEs with zoldonrasib plus mFFX were decreased neutrophil count (37%), anemia (12%), and platelet count decreased (7%). The most common Grade 3 or greater TRAEs with zoldonrasib plus GnP were decreased neutrophil count (35%), anemia (28%), and fatigue (25%). No Grade 5 TRAEs were reported in either arm. The mean dose intensity was 86% with zoldonrasib plus mFFX and 90% with the zoldonrasib plus GnP.

In the trial, zoldonrasib with chemotherapy showed compelling antitumor activity, with an objective response rate (ORR) of 82% (95% confidence interval [CI]: 60, 95) and disease control rate (DCR) of 96% (95% CI: 77, 100) in the mFFX population, and an ORR of 61% (95% CI: 42, 78) and DCR of 90% (95% CI: 74, 98) in the GnP population.

These preliminary safety and clinical activity data support the ongoing RASolute 305 pivotal trial (NCT07621718), a global, randomized, double-blind placebo-controlled Phase 3 clinical trial evaluating zoldonrasib plus investigator's choice of standard of care chemotherapy compared with placebo plus investigator's choice of chemotherapy in patients with previously untreated metastatic RAS G12D PDAC.

Safety and Efficacy of Zoldonrasib Plus Daraxonrasib in Patients with Second Line-Plus RAS G12D Metastatic Pancreatic Cancer (Abstract #341O)

RMC-9805-001 (NCT06040541) is a Phase 1 trial evaluating zoldonrasib 1200 mg once daily plus daraxonrasib 300 mg once daily in advanced solid tumors with RAS G12D mutations. As of the February 9, 2026 data cutoff, 60 patients with RAS G12D metastatic PDAC who had previously received one or more prior lines of therapy were treated with the combination.

Zoldonrasib plus daraxonrasib demonstrated a manageable safety and tolerability profile that was broadly consistent with the established profile of daraxonrasib monotherapy. Grade 3 or greater TRAEs occurred in 35% of patients who received the combination. Among TRAEs occurring in 10% or more of all patients, the most common Grade 3 or greater events were rash (12%), anemia (10%), and stomatitis/mucositis (7%). Few patients discontinued due to TRAES; 2% discontinued zoldonrasib and 5% discontinued daraxonrasib. The mean dose intensity was 88% for zoldonrasib and 76% for daraxonrasib.

The zoldonrasib plus daraxonrasib combination demonstrated compelling antitumor activity in patients with previously treated metastatic PDAC. In the second line cohort (2L) (N=30), the ORR was 50% (95% CI: 31–69) and DCR was 97% (95% CI: 83–100). Median progression-free survival (PFS) in the 2L cohort was 9.6 months (95% CI: 7.1–NE), with a 6-month PFS rate of 71%. Median overall survival (OS) in the 2L cohort was not yet estimable, with a 6-month OS rate of 89%. In the third line and beyond (3L+) cohort (N=30), the ORR was 47% (95% CI: 28–66) and DCR was 90% (95% CI: 74–98). Median PFS in the 3L+ cohort was 7.6 months (95% CI: 4.6–10.5), with a 6-month PFS rate of 59%. Median OS in the 3L+ cohort was 10.5 months (95% CI: 6.7–NE), with a 6-month OS rate of 82%.

These safety and clinical activity data support the planned pivotal global, Phase 3 RASolute 309 clinical trial of zoldonrasib plus daraxonrasib versus GnP in patients with previously untreated RAS G12D metastatic PDAC.

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. Pancreatic ductal adenocarcinoma, or PDAC, is the most common form of pancreatic cancer. Due to the lack of early symptoms and effective detection methods, approximately 80% of patients are diagnosed with advanced or metastatic disease. PDAC is the most commonly RAS-driven malignancy of all major cancers, with more than 90% of patients having tumors that harbor RAS mutations.[1] RAS G12D is the most prevalent RAS mutation subtype in PDAC, occurring in 40% of patients, and has been associated with poorer outcomes than RAS wild-type disease

and certain other RAS-mutant subgroups.[1-4]

About Zoldonrasib
Zoldonrasib is an investigational, oral RAS(ON) G12D-selective covalent tri-complex inhibitor. RAS G12D is the most prevalent RAS mutation, accounting for 29% of all RAS cancers.[1] Across tumor types, approximately 61,000 new patients with RAS G12D cancers are estimated each year in the U.S., and no targeted therapy is currently approved for these patients.[5] Zoldonrasib is currently being evaluated as a monotherapy and in combination with other therapies, including with Revolution Medicines' RAS(ON) multi-selective inhibitor daraxonrasib (RMC-6236), as well as standard of care regimens in lung and gastrointestinal cancers.

About Daraxonrasib
Daraxonrasib is an investigational, oral RAS(ON) multi-selective, non-covalent tri-complex inhibitor. The U.S. Food and Drug Administration (FDA) granted daraxonrasib Breakthrough Therapy Designation and Orphan Drug Designation for the treatment of patients with previously treated metastatic pancreatic ductal adenocarcinoma (PDAC) harboring G12 mutations. In addition, daraxonrasib was selected for the FDA Commissioner's National Priority Voucher pilot program, which is intended to accelerate the development and review of therapies aligned with U.S. national health priorities.

Daraxonrasib is designed to target cancers driven by a broad range of common RAS genotypes, including PDAC, non-small cell lung cancer (NSCLC), and colorectal cancer. Daraxonrasib is being advanced through a global Phase 3 registrational program comprising four trials, including the completed RASolute 302 trial and three additional trials in patients with PDAC and metastatic RAS mutant NSCLC.

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; zoldonrasib (RMC-9805), a RAS(ON) G12D-selective inhibitor; and RMC-5127, a RAS(ON) G12V-selective inhibitor, are currently in 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 our development strategy, including in RAS G12D pancreatic cancer; the potential of our product candidates for RAS(ON) inhibition, including in pancreatic cancer; the ability of daraxonrasib or zoldonrasib to improve patient outcomes; planned and ongoing clinical studies; and potential efficacy of the company's product candidates being studied.

Forward-looking statements are typically, but not always, identified by the use of words such as "anticipate," "estimate," "plan," "potential," "proof-of-concept," "pursuing," "will" 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' development stages, 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 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' Annual Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on May 6, 2026, 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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References

[1] 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

[2] Yousef, A., Yousef, M., Chowdhury, S. et al. Impact of KRAS mutations and co-mutations on clinical outcomes in pancreatic ductal adenocarcinoma. *NPJ Precis Oncol*. 2024;8:27. https://doi.org/10.1038/s41698-024-00505-0

[3] Qian ZR, Rubinson DA, Nowak JA, et al. Association of Alterations in Main Driver Genes With Outcomes of Patients With Resected Pancreatic Ductal Adenocarcinoma. *JAMA Oncol*. 2018;4(3):e173420. doi:10.1001/jamaoncol.2017.3420

[4] Norton C, Shaw MS, Rubnitz Z, et al. *KRAS* Mutation Status and Treatment Outcomes in Patients With Metastatic Pancreatic Adenocarcinoma. *JAMA Netw Open*. 2025;8(1):e2453588. doi:10.1001/jamanetworkopen.2024.53588

[5] Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022 and scaled to estimated patient numbers using cancer incidence from ACS Cancer Facts and Figures 2023.