Revolution Medicines Announces U.S. FDA Breakthrough Therapy Designation for RASONQUE™ (daraxonrasib) in Combination with Chemotherapy for First Line Metastatic Pancreatic Cancer

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- Company receives third Breakthrough Therapy Designation for RASONQUE and fifth across its portfolio of RAS(ON) inhibitors, further highlighting its differentiated strategy for developing innovative medicines for patients with RAS-addicted cancers

REDWOOD CITY, Calif., Sept. 14, 2026 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a global, commercial-stage oncology company dedicated to discovering, developing and delivering innovative medicines for patients with RAS-addicted cancers, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to RASONQUE (daraxonrasib), the company's RAS(ON) multi-selective inhibitor, for treatment-naïve metastatic pancreatic adenocarcinoma (PDAC) in combination with gemcitabine and nab-paclitaxel (GnP), a multiagent chemotherapy regimen widely used in treating patients with PDAC. RASONQUE was recently approved by the U.S. FDA for the treatment of adult patients with metastatic PDAC who have received at least one prior systemic therapy or who are not candidates for multiagent systemic therapy.

The Breakthrough Therapy Designation is based on data from patients with treatment-naïve RAS mutant metastatic PDAC who received RASONQUE in combination with GnP in the open-label, multicenter Phase 1/2 RMC-GI-102 trial. In this cohort, RASONQUE in combination with GnP showed encouraging preliminary antitumor activity and a manageable safety profile that was consistent with the known safety profiles previously observed for both RASONQUE and GnP. These data informed the design of RASolute 303, the ongoing global Phase 3 trial evaluating RASONQUE as monotherapy and in combination with GnP versus GnP alone in patients with previously untreated metastatic PDAC, independent of tumor RAS genotype. The use of RASONQUE in combination with chemotherapy for treatment-naïve metastatic PDAC remains investigational with safety and efficacy not yet established.

"This Breakthrough Therapy Designation underscores the significant unmet need among patients with previously untreated metastatic pancreatic adenocarcinoma and recognizes the importance of advancing new treatment options earlier in their treatment journey," said Alan Sandler, M.D., chief development officer of Revolution Medicines. "RASONQUE monotherapy demonstrated compelling clinical benefit in the RASolute 302 trial, leading to FDA approval for patients with previously treated metastatic pancreatic adenocarcinoma or those who are not candidates for multiagent systemic therapy. Data from the RMC-GI-102 study have now shown the therapeutic potential of RASONQUE in combination with GnP, a commonly used multiagent systemic therapy, in treatment-naïve patients. Together with our other ongoing studies, these findings reflect our deep commitment to advancing a broad RAS(ON) approach for patients with some of the most difficult-to-treat cancers."

Breakthrough Therapy Designation is intended to expedite the development and review of potential new medicines designed to treat serious conditions and address significant unmet medical needs. Pursuant to FDA guidelines, the medicine needs to have shown preliminary clinical evidence that demonstrates substantial improvement on a clinically significant endpoint over available medicines.

About Pancreatic Adenocarcinoma (PDAC)
Pancreatic adenocarcinoma, or PDAC, is the most common form of pancreatic cancer and among the most challenging malignancies. Approximately 55,000 people are diagnosed with PDAC in the U.S. each year, and more than 50,000 die from the disease with current standard of care.[1,2] Because early-stage pancreatic cancer often causes few or no symptoms, approximately 80% of patients are diagnosed after the disease has spread, when treatment options are more limited. For patients with metastatic PDAC, the five-year relative survival rate is approximately 3% in the U.S.[3,4]

About RASONQUE™ (daraxonrasib)
RASONQUE (daraxonrasib) is an oral, RAS(ON) multi-selective, noncovalent, tri-complex inhibitor (TCI), approved by the U.S. FDA for the treatment of adult patients with metastatic pancreatic adenocarcinoma (PDAC) who have received at least one prior systemic therapy or who are not candidates for multiagent systemic therapy.[5] RASONQUE is being investigated through a global Phase 3 registrational program in patients with PDAC and metastatic RAS mutant non-small cell lung cancer (NSCLC). Outside the U.S., RASONQUE is an investigational agent that has not been approved by any regulatory authority.

U.S. FDA APPROVED INDICATION
RASONQUE is indicated for the treatment of adult patients with metastatic pancreatic adenocarcinoma who have received at least one prior systemic therapy or who are not candidates for multiagent systemic therapy.

IMPORTANT SAFETY INFORMATION FOR U.S. APPROVED INDICATION
RASONQUE is associated with the following **Warnings and Precautions**: Dermatologic and Soft Tissue Toxicity, Stomatitis and Oral Disorders, Diarrhea, Gastrointestinal Perforation, Interstitial Lung Disease (ILD)/Pneumonitis, and Embryo-Fetal Toxicity.

WARNINGS AND PRECAUTIONS

Dermatologic and Soft Tissue Toxicity
RASONQUE can cause dermatologic toxicity, which may be severe. Clinical manifestations included, but were not limited to, rash, pruritus, paronychia, dry skin, and skin fissures. In clinical trials of patients with pancreatic adenocarcinoma, dermatologic toxicity occurred in 86% of patients treated with RASONQUE, of which 10% were Grade 3.

Monitor patients who develop dermatologic or soft tissue toxicities while receiving RASONQUE. Initiate prophylactic measures (e.g., topical corticosteroids, emollient creams, sunscreen, oral antibiotics) prior to the first dose of RASONQUE to reduce the risk of moderate to severe dermatologic reactions. Advise patients to limit sun exposure while taking RASONQUE. Initiate supportive measures (e.g., oral corticosteroids) as clinically indicated, and consider dermatologic consultation. Withhold, reduce the dose, or permanently discontinue RASONQUE based on severity.

Stomatitis and Oral Disorders
RASONQUE can cause stomatitis, including mouth ulcers and oral mucositis. In clinical trials of patients with pancreatic adenocarcinoma, stomatitis occurred in 57% of patients, of which 9% were Grade 3.

Monitor patients for signs and symptoms of stomatitis while receiving RASONQUE. Initiate a steroid-containing mouthwash for treatment of stomatitis and administer other topical treatments (e.g., chlorhexidine mouthwash, 2% lidocaine viscous) as clinically indicated. Withhold, reduce the dose, or permanently discontinue RASONQUE based on severity.

Diarrhea
RASONQUE can cause diarrhea. In clinical trials of patients with pancreatic adenocarcinoma, diarrhea occurred in 63% of patients, of which 6% were Grade 3.
If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Withhold, reduce the dose, or permanently discontinue RASONQUE based on severity.

Gastrointestinal Perforation
RASONQUE can cause gastrointestinal perforation. In clinical trials of patients with pancreatic adenocarcinoma, gastrointestinal perforation occurred in 0.9% of patients treated with RASONQUE, of which 0.5% were Grade 3, one event was Grade 4, and one event was fatal.

Monitor patients for gastrointestinal perforation. Withhold RASONQUE if gastrointestinal perforation is suspected. Reduce the dose or permanently discontinue RASONQUE if no other potential causes of gastrointestinal perforation are identified.

Interstitial Lung Disease (ILD)/Pneumonitis
RASONQUE can cause interstitial lung disease or pneumonitis. In clinical trials of patients with pancreatic adenocarcinoma, ILD/pneumonitis occurred in 2.4% of patients treated with RASONQUE, of which 0.9% were Grade 3, and one event was fatal.

Monitor patients for new or worsening pulmonary symptoms. Withhold RASONQUE if ILD/pneumonitis is suspected. Reduce the dose or permanently discontinue RASONQUE if no other potential causes of ILD/pneumonitis are identified.

Embryo-Fetal Toxicity
Based on findings in animals, RASONQUE can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with RASONQUE and for 1 week after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with RASONQUE and for 1 week after the last dose.

ADVERSE REACTIONS
Serious adverse reactions occurred in 30% of patients treated with RASONQUE. Serious adverse reactions occurring in ≥ 2% of patients treated with RASONQUE were diarrhea (3.7%), pyrexia (3.3%), sepsis (2.9%), fatigue (2.1%), and hemorrhage (2.1%).

Adverse reactions leading to permanent discontinuation of RASONQUE occurred in 2.9% of patients, including two patients who discontinued due to rash (0.8%).

The most common (≥ 20%) adverse reactions in patients treated with RASONQUE were rash, diarrhea, stomatitis, nausea, fatigue, vomiting, abdominal pain, edema, decreased appetite, and hemorrhage.

DRUG INTERACTIONS

- Strong CYP3A Inhibitors with P-gp Inhibition: Avoid concomitant use.
- Strong CYP3A Inhibitors without P-gp Inhibition: Reduce RASONQUE dosage.
- Moderate CYP3A Inhibitors with or without P-gp Inhibition: Reduce RASONQUE dosage.
- P-gp Inhibitors: Reduce RASONQUE dosage.
- Cyclosporine A: Avoid concomitant use.
- Strong CYP3A Inducers: Avoid concomitant use. Increase RASONQUE dosage if concomitant use cannot be avoided.
- Moderate CYP3A Inducers: Increase RASONQUE dosage.
- P-gp Substrates: Take at least 4 hours apart from RASONQUE.

PROPHYLACTIC MEASURES
When initiating RASONQUE and throughout treatment, prophylactic and concomitant medications are recommended to reduce the risk of dermatologic reactions:

- administer a topical corticosteroid (applied to the face and chest) and emollient creams;
- advise patients to limit sun exposure and use broad-spectrum sunscreen (SPF 30 or higher); and
- consider prophylactic oral antibiotics (e.g., doxycycline or minocycline).

Please see U.S. Full Prescribing Information for RASONQUE

About Revolution Medicines, Inc.
Revolution Medicines is a global, commercial-stage oncology company dedicated to discovering, developing and delivering innovative medicines for patients with RAS-addicted cancers. Leveraging its differentiated RAS(ON) tri-complex inhibitor platform, the company is advancing a broad, integrated portfolio of oral RAS(ON) inhibitors designed to directly target the active, cancer-driving state of RAS. Founded on rigorous scientific inquiry and a willingness to challenge long-held assumptions, Revolution Medicines is committed to changing the trajectory of disease for patients with RAS-addicted cancers worldwide. For more information, visit www.revmed.com and follow Revolution Medicines on LinkedIn, X (Twitter) and Instagram.

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 broad potential of RAS(ON) inhibition; treatment practices; the company's regulatory interactions and the potential for Breakthrough Therapy Designation to expedite the development and review of new medicines; reactions to RASONQUE; and progression of clinical studies and findings from these studies, including the tolerability, safety, and potential efficacy of the company's candidates being studied.

Forward-looking statements are typically, but not always, identified by the use of words such as "aims," "anticipate," "believe," "estimate," "expect," "plan," "potential," "project," "up to," "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 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 5, 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.

Revolution Medicines Media & Investor Contacts

Media
media@revmed.com

Investors
investors@revmed.com

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