New England Journal of Medicine Publishes Phase 1/2 Clinical Data on Revolution Medicines' RASONQUE™ (daraxonrasib) in Metastatic Non-Small Cell Lung Cancer

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- Results support the clinical rationale for RASolve 301, an ongoing Phase 3 trial in RAS mutant metastatic non-small cell lung cancer

REDWOOD CITY, Calif., Sept. 02, 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 New England Journal of Medicine* (NEJM) has published a report describing data from the Phase 1/2 clinical trial evaluating RASONQUE (daraxonrasib), an oral, RAS(ON) multi-selective inhibitor, in patients with previously treated advanced RAS mutant non-small cell lung cancer (NSCLC).

"RAS mutations are among the most common oncogenic drivers in lung cancer, occurring in approximately 30 percent of cases. Targeted RAS inhibition has demonstrated clinical benefit in patients with RAS G12C non-small cell lung cancer following initial treatment with chemotherapy and immunotherapy, but there are no targeted therapies for patients with other RAS tumor mutations. The rates of objective response, disease control and survival observed in patients treated with RASONQUE in this Phase 1/2 study support the ongoing global, randomized pivotal RASolve 301 trial evaluating RASONQUE in previously treated RAS mutant non-small lung cancer. Together with the recent FDA approval of RASONQUE in metastatic pancreatic cancer, the data reported in the NEJM publication provide additional clinical validation of our broad RAS(ON) multi-selective and mutant-selective approach across major RAS-driven cancers," said Alan Sandler, M.D., chief development officer of Revolution Medicines.

The results published in NEJM are based on the Phase 1/2 RMC-6236-001 trial (NCT05379985), with a July 21, 2025 data cut off. The trial evaluated the safety and efficacy of once-daily doses of RASONQUE 300 mg or less in 136 patients with second-line or later NSCLC with tumors carrying diverse RAS mutations other than RAS G12C, and whose disease had progressed following, or who were intolerant to, platinum-based chemotherapy and anti-PD-(L)1 therapy.

RASONQUE demonstrated dose-dependent antitumor activity and exhibited a manageable safety profile in the Phase 1/2 trial. Within the 160 mg to 220 mg dose group, a subgroup of 38 docetaxel-naïve patients had previously received first- or second-line platinum-based chemotherapy and anti-PD-(L)1 therapy. In this subgroup, the confirmed objective response rate was 42% (95% confidence interval [CI], 26%-59%) and a disease control rate of 89% (95% CI, 75%-97%). The median progression-free survival was 8.3 months (95% CI: 4.0-12.5) and median overall survival was 16.0 months (95% CI, 9.5-not estimable). At these dose levels, Grade 3 treatment-related adverse events (TRAEs) occurred in 25% of patients, most commonly rash (8%) and diarrhea (3%). No Grade 4 or Grade 5 TRAEs were reported within this dose range.

The results from this Phase 1/2 trial informed the design and initiation of RASolve 301 (NCT06881784), the company's ongoing global, randomized, open-label Phase 3 trial evaluating RASONQUE compared with docetaxel in patients with previously treated, locally advanced or metastatic RAS mutant NSCLC. RASONQUE is an investigational agent for the treatment of RAS mutant NSCLC.

About Non-Small Cell Lung Cancer and RAS Mutations

Non-small cell lung cancer (NSCLC) accounts for 80%-85% of all lung cancers, with more than 229,000 people diagnosed in the U.S. each year.[1,2] Despite treatment advancements, NSCLC remains a leading cause of cancer-related mortality worldwide, primarily due to its late-stage diagnosis and limited response to conventional therapies. RAS mutations are among the most common oncogenic drivers in NSCLC, occurring in approximately 30% of cases.[3]

About RASONQUE™(daraxonrasib)

RASONQUE is an oral, RAS(ON) multi-selective, noncovalent, tri-complex inhibitor, 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.

RASONQUE 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. It works by suppressing RAS signaling through inhibition of the interaction between both wild-type and mutant RAS(ON) proteins and their downstream effectors.

RASONQUE is being advanced through a global Phase 3 registrational program in patients with PDAC and metastatic RAS mutant 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)
- 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; RASONQUE becoming a standard of care; treatment practices for pancreatic cancer; 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 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 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.

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[1] American Cancer Society. What Is Lung Cancer. Available at: https://www.cancer.org/cancer/types/lung-cancer/about/what-is.html. Accessed August 2026.

[2] American Cancer Society. Key Statistics for Lung Cancer. Available at: https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html. Accessed August 2026.

[3] Reita D, Pabst L., Pencreach E, et al. Direct Targeting KRAS Mutation in Non-Small Cell Lung Cancer: Focus on Resistance. Cancers (Basel). 2022; 14(15):1321. doi: 10.3390/cancers14051321.