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Rigel Announces Publication of Final ARROW Clinical Trial Data on GAVRETO® (pralsetinib) in Patients with RET+ NSCLC in the Journal of Clinical Oncology

Pralsetinib induced robust and durable responses with a manageable safety profile, reinforcing the benefits of selective RET inhibitors in treating RET fusion-positive NSCLC

SOUTH SAN FRANCISCO, Calif., March 31, 2026 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced publication of the final data from the Phase 1/2 ARROW study evaluating pralsetinib for the treatment of metastatic rearranged during transfection (*RET*) fusion-positive non-small cell lung cancer (NSCLC) in the*Journal of Clinical Oncology*. The final data includes an additional 42 months of follow-up from previously published data. Pralsetinib is the only once daily, oral RET-inhibitor therapy that is designed to selectively target *RET* in metastatic NSCLC and advanced or metastatic thyroid carcinoma.

"The final data from the ARROW study shows robust and durable responses with a manageable safety profile in patients with RET fusion-positive NSCLC, emphasizing the importance of early biomarker testing and suggesting that pralsetinib may be a valuable tool in the treatment armamentarium," said Justin F. Gainor, M.D., Phase 1/2 trial investigator and Director of the Center for Thoracic Cancers at Mass General Brigham Cancer Institute. "In addition, the responses observed in the subset of patients with measurable CNS metastases at baseline further expand the potential clinical value of pralsetinib in everyday practice."

"The results published in the*Journal of Clinical Oncology* demonstrate the positive impact pralsetinib can have for patients with *RET* fusion-positive NSCLC," said Lisa Rojkjaer, M.D, Rigel's chief medical officer. "These longer-term data further support pralsetinib's role as a first-line treatment option for *RET* fusion-positive NSCLC patients."

Additional key points from the paper include:

- Consistent with previous reports from the ARROW study NSCLC cohort, pralsetinib was generally well tolerated with a manageable toxicity profile. Three treatment-related

deaths occurred in treatment-naive patients in Asia (pneumonia, n=2; interstitial lung disease and rhabdomyolysis, n=1 each), no new safety signals were observed and no hypersensitivity reactions were reported in patients receiving prior immunotherapies.
- Among patients with measurable disease (n=259), the overall response rate (ORR) was 70%, including 7% complete responses and 63% partial responses.
- ORR was 78% among treatment-naïve patients and 63% among patients receiving prior platinum-based chemotherapy.
- At final data lock, median treatment duration was 15.0 months.
- Median overall survival (OS) was 44.3 months in the overall measurable disease patient population, 50.1 months in treatment-naïve patients, and 39.7 months in prior-platinum patients, with median follow-ups of 47.6, 43.7, and 49.7 months, respectively. Longer median OS in the overall measurable disease patient population was seen in patients treated in the United States (62.4 months) vs. Asia (44.5 months) or Europe (29.6 months).
- Median overall progression-free survival (PFS) was 13.1 months in the overall measurable disease patient population, but was longer in patients in the United States (25.9 months) vs. Asia (12.6 months) or Europe (12.8 months).
- ORR remained high in subgroups bearing the RET fusion partners KI5FB and CCDC6 among both treatment-naive and prior platinum-based chemotherapy patients. Among all patients, median duration of response (DOR) was longer in patients with CCDC6 (47.9 months) vs. KIF5B (13.1 months).
- Fifteen patients had measurable central nervous system (CNS) metastases at baseline. The intracranial response rate (CNS ORR) among these patients was 53%. In the 11 response-evaluable patients with CNS metastases, CNS ORR was 73%.

The publication, titled "Final Efficacy and Safety Data From the Phase 1/2 ARROW Study of Pralsetinib in Patients With Advanced RET Fusion-Positive Non-Small Cell Lung Cancer (NSCLC)," was published online and can be found here.

About NSCLC

It is estimated that over 229,000 adults in the U.S. will be diagnosed with lung cancer in 2026. Lung cancer is the leading cause of cancer death in the U.S., with non-small cell lung cancer (NSCLC) being the most common type accounting for 77% of all lung cancer diagnoses.[1] *RET* fusions are implicated in approximately 1-2% of patients with NSCLC.[2]

About GAVRETO® (pralsetinib)

INDICATIONS

GAVRETO (pralsetinib) is indicated for the treatment of:

- Adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA-approved test
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*

*This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS, INCLUDING OPPPORTUNISTIC INFECTIONS
GAVRETO may increase the risk for serious infections, including bacterial, fungal, viral and opportunistic infections, which can lead to hospitalization or death. Withhold, reduce the dose or permanently discontinue GAVRETO based on severity.

WARNINGS AND PRECAUTIONS

- **Serious Infections, Including Opportunistic Infections:** GAVRETO may increase the risk for serious infections, including fatal and opportunistic infections. In the AcceleRET-Lung trial, infections occurred in 72% of patients who received GAVRETO, including 18% with Grade 3 and 3.7% with Grade 4 and 7% with fatal outcomes. Among the patients who received chemotherapy/immunotherapy, infections occurred in 52%, including 10% with Grade 3. Infections in the GAVRETO arm included pneumonia, urinary tract infection, opportunistic infections (such as pneumocystis jirovecii pneumonia and fungal infections) and others. Monitor patients for signs and symptoms of infection and treat appropriately. Withhold, reduce the dose, or permanently discontinue GAVRETO based on severity.
- **Interstitial Lung Disease (ILD)/Pneumonitis:** Severe, life-threatening, and fatal ILD/pneumonitis can occur in patients treated with GAVRETO. Pneumonitis occurred in 12% of patients who received GAVRETO, including 3.3% with Grade 3-4, and 0.2% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.
- **Hypertension:** Occurred in 35% of patients, including Grade 3 hypertension in 18% of patients. Overall, 8% had their dose interrupted and 4.8% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.
- **Hepatotoxicity:** Serious hepatic adverse reactions occurred in 1.5% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 49% of patients, including Grade 3 or 4 in 7% and increased alanine aminotransferase (ALT) occurred in 37% of patients, including Grade 3 or 4 in 4.8%. The median time to first onset for increased AST was 15 days (range: 5 days to 2.5 years) and increased ALT was 24 days (range: 7 days to 3.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.
- **Hemorrhagic Events:** Serious, including fatal, hemorrhagic events can occur with GAVRETO. Grade ≥3 events occurred in 4.1% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.
- **Tumor Lysis Syndrome (TLS):** Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or

dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

- **Risk of Impaired Wound Healing:** Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.
- **Embryo-Fetal Toxicity:** Based on findings from animal studies and its mechanism of action, GAVRETO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the last dose.

ADVERSE REACTIONS

- Common adverse reactions (≥25%) were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough. Common Grade 3/4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased leukocytes, decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased calcium (corrected), decreased platelets, increased alkaline phosphatase, increased potassium, decreased potassium, and increased bilirubin.

DRUG INTERACTIONS

- **Avoid coadministration of GAVRETO with strong or moderate CYP3A inhibitors, P-gp inhibitors, or combined P-gp and strong or moderate CYP3A inhibitors.** If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with strong or moderate CYP3A inducers. If coadministration cannot be avoided, increase the GAVRETO dose.

Lactation: Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the last dose.

Pediatric Use: Monitor open growth plates in adolescent patients. Consider interrupting or discontinuing GAVRETO if abnormalities occur.

Click here **for Important Safety Information and Full Prescribing Information, including Boxed WARNING.**

To report side effects of prescription drugs to the FDA,
visit www.fda.gov/medwatch or call 1-800-FDA-1088 (800-332-1088).

About Rigel

Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) is a biotechnology company dedicated to discovering, developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. Founded in 1996, Rigel is based in South San Francisco, California. For more information on Rigel, the Company's marketed products and pipeline of potential products, visit www.rigel.com.

1. The American Cancer Society. Key Statistics for Lung Cancer. Revised January 13, 2026. Accessed March 27, 2026: https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html
2. Kato, S. et al. RET Aberrations in Diverse Cancers: Next-Generation Sequencing of 4,871 Patients. Clin Cancer Res. 2017;23(8):1988-1997 doi: 10.1158/1078-0432.CCR-16-1679

Forward-Looking Statements

This press release contains forward-looking statements relating to, among other things, the potential for the referenced clinical trial or trial results to strengthen our commercial portfolio, GAVRETO's success in treating RET fusion-positive NSCLC, and its role as a first-line treatment option for RET+ NSCLC patients. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements can be identified by words such as "anticipates", "plan", "outlook", "potential", "may", "look to", "expects", "will", "initial", "promising", and similar expressions in reference to future periods. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Rigel's current beliefs, expectations, and assumptions and hence they inherently involve significant risks, uncertainties and changes in circumstances that are difficult to predict and many of which are outside of our control. Therefore, you should not rely on any of these forward-looking statements. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the commercialization and marketing of pralsetinib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding pralsetinib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that pralsetinib may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop Rigel's product candidates; market competition; as well as other risks detailed from time to time in Rigel's reports filed with the Securities and Exchange Commission, including its most recent Annual Report on Form 10-K, and subsequent filings, including Quarterly Reports on Form 10-Q. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. Rigel does not undertake any obligation to update forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise, and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein, except as required by law.

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