December 7, 2025

Rigel Presents Updated Data from the Ongoing Phase 1b Study Evaluating R289 in Patients with Lower-Risk MDS at the 67th ASH Annual Meeting and Exposition

- *R289 continues to be generally well tolerated and at doses of ≥500 mg QD preliminary efficacy was observed in elderly, heavily pre-treated lower-risk MDS patients*
- *RBC-TI was achieved by 33% (6/18) of evaluable transfusion dependent patients receiving R289 doses ≥500 mg QD, including 40% (2/5) in the 500 mg BID dose group*

SOUTH SAN FRANCISCO, Calif., Dec. 7, 2025 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced updated data from its ongoing Phase 1b study evaluating R289[1], an oral prodrug of R835, a potent and selective dual inhibitor of interleukin receptor-associated kinases 1 and 4 (IRAK1/4), in patients with relapsed or refractory (R/R) lower-risk myelodysplastic syndrome (MDS). The data are being presented today in an oral session by Dr. Guillermo Garcia-Manero at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition being held December 6-9, in Orlando, Florida and virtually.

"New therapies are needed for patients with transfusion dependent lower-risk MDS. We're pleased to share these updated study results, which underscore the potential of R289 to become a treatment option for these patients," said Lisa Rojkjaer, M.D., Rigel's chief medical officer. "We look forward to concluding the dose expansion phase of the study and anticipate selection of the recommended Phase 2 dose for future clinical studies in the second half of 2026."

Rigel's open-label Phase 1b study of R289 is evaluating the safety, tolerability, pharmacokinetics and preliminary efficacy in patients with R/R lower-risk MDS (NCT05308264). Enrollment in the dose escalation phase of the study was completed in July 2025. In October 2025, the first patient was dosed in the dose expansion phase where up to 40 patients will be randomized to either 500 mg once or twice daily to determine the recommended Phase 2 dose for future clinical trials.

Key highlights from the updated data as of October 28, 2025, include:

- 33 patients were enrolled, representing a difficult-to-treat population. The median age

was 75. The median number of prior therapies was 3 (range: 1-8); 76% (25) of patients had received luspatercept, 73% (24) had received an erythropoiesis stimulating agent (ESA), 67% (22) had received an hypomethylating agent (HMA) and 6% (2) had received imetelstat. 61% (20) of patients were high transfusion burden (HTB) at baseline. 67% (22) of patients were ring sideroblast (RS) negative.

- Median duration of treatment was 5.5 months (range: 0.9 - 27.7 months). R289 was generally well tolerated across all dose groups in this heavily pre-treated lower-risk MDS patient population, the majority of whom were HTB at baseline. The most common Grade 1/2 treatment-emergent adverse events (TEAEs) (in ≥18% of patients) were diarrhea (n=10, 30%), constipation and fatigue (each n=9, 27%), and creatinine increased and cough (each n=7, 21%). The most frequent Grade 3/4 TEAEs were anemia (n=6, 18%), neutrophil count decreased and pneumonia (each n=5, 15%), and alanine aminotransferase (ALT) increased and aspartate aminotransferase (AST) increased (each n=3, 9%). One (1) dose limiting toxicity (DLT) (Grade 4 AST increased/Grade 3 ALT increased) was reported in the 750 mg dose group.
- For evaluable transfusion dependent (TD) patients (≥16 weeks follow up) at dose levels of at least 500 mg QD and higher, 6/18 (33%) patients achieved durable red blood cell transfusion independence (RBC-TI) of >8 weeks [500 mg QD (1/3), 750 mg QD (2/5), 500/250 mg QD (1/5), 500 mg BID (2/5)]. Duration of RBC-TI was >16 weeks in 4 patients and >24 weeks in 3 patients. The median time to onset of RBC-TI was 1.9 months and the median duration of RBC-TI was 22.9 weeks. Peak hemoglobin increases of 2.9 to 6.1 g/dL compared to baseline occurred in patients achieving RBC-TI.
- Of the 6 patients achieving RBC-TI, 5 had received an HMA.
- At doses ≥500 mg QD, steady state R835 plasma concentrations reached or exceeded those associated with 50-90% inhibition of lipopolysaccharide (LPS)-induced cytokine release previously observed in healthy volunteers.

Oral presentation details are as follows:

Sunday, December 7, 2025, 9:45am to 10:00am ET
Publication #: 489
Session Name: 637. Myelodysplastic Syndromes: Clinical and Epidemiological: Moving the Needle Through Novel Approaches in MDS and CMML
Presentation Title: An Update of Safety and Efficacy Results from a Phase 1b Study of R289, a Dual IRAK 1/4 Inhibitor, in Patients with Relapsed/Refractory (R/R) Lower Risk Myelodysplastic Syndrome (LR-MDS)
Presenter: Guillermo Garcia-Manero, M.D.

R289 was previously granted Orphan Drug designation for the treatment of myelodysplastic syndromes and granted Fast Track designation for the treatment of previously-treated transfusion dependent lower-risk MDS by the FDA.

About R289
R289 is a prodrug of R835, an IRAK1/4 dual inhibitor, which has been shown in preclinical studies to block inflammatory cytokine production in response to toll-like receptor (TLR) and interleukin-1 receptor (IL-1R) family signaling. TLRs and IL-1Rs play a critical role in the innate immune response and dysregulation of these pathways can lead to various inflammatory conditions. Chronic stimulation of both these receptor systems is thought to

cause the pro-inflammatory environment in the bone marrow responsible for persistent cytopenias in lower-risk MDS patients.[2]

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. R289 is an investigational compound not approved by the FDA.
2. Sallman DA et al. *Unraveling the Pathogenesis of MDS: The NLRP3 Inflammasome and Pyroptosis Drive the MDS Phenotype*. Front Oncol. June 16, 2016. doi: https://doi.org/10.3389/fonc.2016.00151

Forward Looking Statements

This press release contains forward-looking statements relating to, among other things, the potential outcomes of the dose escalation and expansion phase of the ongoing Phase 1b study of R289, the potential benefits of R289 as a therapeutic for MDS and lower-risk MDS, the existence of patients with an unmet medical need for such therapy, and Rigel's ability to further develop its clinical stage product candidates. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements and as such are intended to be covered by the safe harbor for "forward-looking statements" provided by the PSLRA. Forward-looking statements can be identified by words such as "plan", "potential", "may", "look to", "expects", "outcome", "will" 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 Rigel's 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, the risks and uncertainties of clinical trials and drug development; risks and uncertainties associated with the commercialization and marketing of R289; risks that the FDA or other regulatory authorities may make adverse decisions regarding R289; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that R289 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2025 and subsequent filings. 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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