October 8, 2025

Rigel Announces First Patient Enrolled in the Dose Expansion Phase of its Phase 1b Study of R289 in Patients with Lower-Risk MDS

Dose expansion phase will determine the recommended Phase 2 dose of R289 for patients with transfusion dependent R/R lower-risk MDS

SOUTH SAN FRANCISCO, Calif., Oct. 8, 2025 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced the first patient has been enrolled in the dose expansion phase of the ongoing Phase 1b study of R289[1] in patients with relapsed or refractory (R/R) lower-risk myelodysplastic syndrome (MDS). R289 is Rigel's potent and selective dual inhibitor of interleukin receptor-associated kinases 1 and 4 (IRAK1/4).

"Today marks an important step in the evaluation of R289 for the treatment of patients with transfusion dependent lower-risk MDS, a disease with a persistent unmet need despite the availability of approved agents. In the dose expansion phase of this study, patients with transfusion dependent R/R lower-risk MDS will be randomized to receive a 500 mg R289 dose either once or twice daily," said Lisa Rojkjaer, M.D., Rigel's chief medical officer. "The outcome of this phase of the study will be the selection of the recommended Phase 2 dose of R289 for future clinical studies. We remain grateful to our investigators for their continued support of our program."

Rigel's open-label, Phase 1b study of R289 is evaluating the safety, tolerability, pharmacokinetics and preliminary activity in patients with R/R lower-risk MDS (NCT05308264). Enrollment in the dose escalation phase of the study was completed in July 2025, and the company expects to share updated data from the study later this year. In the dose expansion phase of the study, up to 40 patients will be randomized into dose levels of 500 mg once daily or 500 mg twice daily to determine the recommended Phase 2 dose (RP2D) for future development of R289. In addition, once the RP2D has been determined, an exploratory cohort of erythropoiesis-stimulating agent (ESA) R/R, or ineligible, lower-risk MDS patients will be evaluated at the RP2D.

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 http://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 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, including the ability to share new trial data later this year. 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 June 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.

Contact for Investors & Media:
Investors:
Rigel Pharmaceuticals, Inc.
650.624.1232
ir@rigel.com

Media:
David Rosen
Argot Partners
646.461.6387
david.rosen@argotpartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/rigel-announces-first-patient-enrolled-in-the-dose-expansion-phase-of-its-phase-1b-study-of-r289-in-patients-with-lower-risk-mds-302577663.html

SOURCE Rigel Pharmaceuticals, Inc.