December 15, 2022

Rigel Doses First Patient in Phase 1b Study of R289 for the Treatment of Lower-Risk Myelodysplastic Syndromes

R289 is an investigational, oral, inhibitor of interleukin receptor-associated kinases 1 and 4 (IRAK1/4), being studied as a potentially differentiated approach to treating lower-risk MDS

SOUTH SAN FRANCISCO, Calif., Dec. 15, 2022 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced it dosed the first patient in its Phase 1b study of R289, an IRAK1/4 dual inhibitor, in patients with lower-risk myelodysplastic syndromes (MDS) who are refractory or resistant to prior therapies.

"R289's dual inhibition of IRAK1 and IRAK4 has the potential to provide a more robust suppression of the pro-inflammatory environment that causes lower-risk MDS by blocking inflammatory cytokine production," said Wolfgang Dummer, M.D., Ph.D., Rigel's chief medical officer. "The initiation of our Phase 1b study demonstrates our continued ability and commitment to bringing innovative, investigational candidates for hematology-oncology indications into the clinic. We believe R289 may represent a promising new approach to treating patients with lower-risk MDS and look forward to investigating R289 further in this Phase 1b study."

Rigel's open-label, Phase 1b study of R289 is expected to enroll approximately 22 patients with lower-risk MDS who are refractory or resistant to prior therapies (NCT05308264). The primary objective of the study is safety, with secondary and exploratory objectives to assess preliminary efficacy and characterize the pharmacokinetic (PK) and pharmacodynamic (PD) profile of R289. The safety and efficacy data from this Phase 1b study, along with the safety and PK/PD data from the completed first-in-human (FIH) study in heathy volunteers, are intended to be used to determine the recommended Phase 2 dose for future clinical development of R289 targeting lower-risk MDS.

About R289[1]

R289 is a prodrug of R835[1], 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 small molecule drugs that significantly improve the lives of patients with hematologic disorders, cancer and rare immune diseases. Founded in 1996, Rigel is based in South San Francisco, California. For more information on Rigel, the Company's marketed product and pipeline of potential products, visit www.rigel.com.

1. R289 and R835 are investigational compounds 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.2016.0015

Forward-Looking Statements

This press release contains forward-looking statements relating to, among other things, that R289 may provide a meaningful approach to treatment of patients with lower-risk MDS, the enrollment of patients in the Phase 1b study of R289, and the use of the safety and efficacy data from the Phase 1b study of R289 in lower-risk MDS. 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 "plan", "potential", "may", "expect", "will", "believe", "intend" 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 regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions, 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 that the FDA, EMA 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, 2022 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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