November 3, 2025

Rigel Announces One Oral and Four Poster Presentations at the 67th American Society of Hematology Annual Meeting and Exposition

- *Oral presentation to feature updated data from the ongoing Phase 1b study evaluating R289, Rigel's dual IRAK1/4 inhibitor, in patients with relapsed or refractory lower-risk MDS*
- *Four poster presentations will exhibit new REZLIDHIA® (olutasidenib) data in patients with R/R mIDH1 AML*

SOUTH SAN FRANCISCO, Calif., Nov. 3, 2025 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced that data from the ongoing Phase 1b study of R289[1], a potent and selective inhibitor of dual interleukin receptor-associated kinases 1 and 4 (IRAK1/4), in patients with lower-risk myelodysplastic syndrome (MDS) who are relapsed or refractory (R/R) to prior therapies will be presented in an oral session at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition on Sunday, December 7, 2025. In addition, the ASH Annual Meeting will feature four poster presentations with data for REZLIDHIA® (olutasidenib) for the treatment of R/R mutated isocitrate dehydrogenase-1 (m*IDH1*) acute myeloid leukemia (AML). The ASH Annual Meeting is being held December 6-9, 2025, in Orlando, Florida and virtually.

"We are very pleased to have the opportunity to highlight our hematology and oncology portfolio at ASH this year," said Lisa Rojkjaer, M.D, Rigel's chief medical officer. "In particular, we are delighted that updated results from our Phase 1b study in patients with relapsed or refractory lower-risk MDS have been accepted for oral presentation. Despite the availability of approved agents, there remains an unmet need for additional therapies to treat patients with transfusion dependent lower-risk MDS, and we look forward to advancing the dose expansion phase of the study to completion."

ASH Annual Meeting abstracts may be accessed online at www.hematology.org. Details of the oral and poster presentations, which will be available in the poster hall and via the virtual event platform, are as follows:

Oral Presentation

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.

- As of the data cutoff date (July 15, 2025), 33 patients were enrolled in the dose escalation part of the study. Patients had a median age of 75 with a median of 3 prior therapies and 61% were high transfusion burden at baseline.
- Patients received R289 at doses ranging from 250 mg QD (once daily) to 500 mg BID (twice daily). For the 500 mg BID dose group, five patients were not yet evaluable (<16 weeks follow up) for determination of hematologic responses and one patient withdrew consent.
- R289 was generally well tolerated across all dose groups, with the most frequent treatment emergent adverse events (≥20%) being diarrhea (28.1%), constipation/fatigue (25% each), and creatinine/alanine aminotransferase (ALT) increased (21.9% each), the majority being Grade 1/2. One (1) dose limiting toxicity (DLT) (Grade 4 aspartate aminotransferase (AST) increase/Grade 3 ALT increase) was reported in the 750 mg dose group.
- For evaluable transfusion dependent patients (≥16 weeks follow up) at dose levels of at least 500 mg QD and higher, 4/13 patients (31%) achieved durable red blood cell transfusion independence (RBC-TI) for >8 weeks (500 mg QD [1/3], 750 mg QD [2/5], 500/250 mg QD [1/5]). Duration of RBC-TI was >16 weeks in 3 patients, >24 weeks in 2 patients, and >12 months in 1 patient. The median time to onset of RBC-TI was 2.2 months and the median duration of RBC-TI was 24.3 weeks.
- All responding patients had R835 plasma concentrations similar to those at which ≥50% LPS-induced inhibition of cytokine release was observed in healthy volunteers, indicating a potential threshold for dose response (≥500 mg QD).
- Updated data as of an October 28, 2025, data cutoff will be presented during the oral presentation.

Poster Presentations

Saturday, December 6, 2025, 5:30pm to 7:30pm ET
Publication #: 1659
Title: Clinical Characteristics and Response in Olutasidenib-Treated Relapsed/Refractory m*IDH1* Acute Myeloid Leukemia (AML) Patients With Stable Disease Following Two Treatment Cycles
Presenter: Justin M. Watts, M.D.

- In the pivotal cohort of the Phase 2 registrational study, of 147 patients with R/R m*IDH1* AML who received olutasidenib, 36 (24%) patients maintained stable disease (SD) after 2 cycles of treatment. Treatment duration ranged from 2.6 to 51.1 months. In these 36 patients, the subsequent response rate was 33% (n=12), including 6 (17%) complete remission (CR), 2 (6%) CR with partial hematologic recovery (CRh), 1 (3%)

CR with incomplete recovery, 1 (3%) morphologic leukemia-free state, and 2 (6%) partial remission.
- Median time to best response from the start of treatment was 3.7 months (range: 2.8-5.7). 8 patients (22%) remained in SD and 16 (44%) had subsequent disease progression on study.
- In the 12 late responders, median duration of response (DOR), duration of CR/CRh, and duration of CR were 9.9 months, 17.3 months, and not reached, respectively. Additionally, of the late responders who were transfusion dependent for platelets (n=6) or red blood cells (n=9) at baseline, 5 (83%) and 8 (89%), respectively, became transfusion independent.
- Patients who achieved any late response had a longer median treatment duration (10.1 months) than non-responders. Median overall survival (OS) for late responders was 23.9 months and 32.7 months for those with CR/CRh.
- Patients with SD after 2 cycles of olutasidenib may experience meaningful clinical benefit with continued treatment, as one-third of these patients subsequently achieved a late response, resulting in a lower risk of death compared to patients with no later response. These findings suggest that early SD may not predict treatment failure and support continuing olutasidenib for at least 6 cycles or until disease progression.

Sunday, December 7, 2025, 6:00pm to 8:00pm ET
Publication #: 4616
Title: Assessment of Real-World Treatment Patterns and Outcomes of Olutasidenib in Patients with Mutated Isocitrate Dehydrogenase 1 Acute Myeloid Leukemia Previously Treated with Venetoclax Using Electronic Health Record Data
Presenter: Catherine Lai, M.D., MPH

- This retrospective cohort study analyzed data from Loopback Analytics' electronic health records data in the U.S. until September 2024, incorporating structured clinical data and abstracted data from physician notes. Fourteen olutasidenib-treated patients in the Loopback database met inclusion criteria for the study.
- The overall response rate (ORR) was 50% (7/14) and the composite complete remission (CRc) rate was 36% (5/14). Among patients who achieved any response, 86% (6/7) received venetoclax immediately prior to olutasidenib.
- Median OS from olutasidenib initiation in the full cohort was 12.2 months, with the proportion of patients surviving 6, 9, and 12 months estimated to be 88%, 70%, and 53%, respectively.
- In this real-world cohort, despite the small sample size, 50% of patients responded to post-venetoclax olutasidenib, consistent with the clinical efficacy observed in the pivotal Phase 2 trial. These findings support the use of olutasidenib as a viable therapeutic option in post-venetoclax treatment settings.

Publication #: 3439
Title: Analysis of Hematologic Improvement (HI) by Time to Response in Relapsed/Refractory Acute Myeloid Leukemia (AML) Patients Treated with Olutasidenib
Presenter: Shira N. Dinner, M.D

- In the pivotal cohort of the Phase 2 registrational study (n=147), increases in hemoglobin were seen early in the course of treatment and levels continued to increase over 12 cycles. Similarly, platelet counts increased and blast percentages

decreased over the course of treatment.

- A total of 71 patients (48%) achieved an overall response; 47 patients (32%) achieved CR and 51 (35%) achieved CR/CRh. Among CR/CRh responders, 28 (55%) achieved a response in <2 months, 17 (33%) from 2 to 4 months, and 6 (12%) at >4 months.
- Patients with a longer time to response tended to have lower baseline platelet counts and higher bone marrow blast percentages compared with earlier responders, suggesting lower hematopoietic reserve and greater disease burden.
- In 37 patients (25%) who had a best response of SD, several showed improvement in platelets and hemoglobin levels by end of treatment. 7 of 21 (33%) patients with prior platelet transfusion dependence became independent and 7 of 23 (30%) with prior red blood cell transfusion dependence became independent.
- This report highlights the hematological responses to olutasidenib in these patients with R/R m*IDH1* AML and suggests that continuing olutasidenib treatment beyond 2 cycles may offer hematologic benefits, even in the absence of an early clinical response.

Monday, December 8, 2025, 6:00pm ET to 8:00pm ET
Publication #: 5213
Title: Olutasidenib Monotherapy in Patients With m*IDH1* Acute Myeloid Leukemia Who Received Prior Intensive Chemotherapy
Presenter: Jay Yang, M.D.

- In the pivotal cohort of the Phase 2 registrational study (n=147), in patients with prior intensive chemotherapy (IC), the ORR was 50% with 35/105 (33%) achieving CR and 38/105 (36%) achieving CR/CRh. Median DOR was 15.5 months, with median duration of CR not reached and CR/CRh of 17.6 months.
- After a median follow up of 37.3 months, the median OS was 12.5 months. In comparison, in the 38 patients who received prior non-intensive therapy the ORR was 42%; 9/38 achieved CR and 10/38 achieved CR/CRh. The median DOR in this group was 16.2 months, with a median duration of CR and CR/CRh of 28.1 months and 29.0 months, respectively.
- Among this cohort of patients with R/R m*IDH1* AML who had received prior IC, treatment with olutasidenib monotherapy produced clinically meaningful response rates that closely align with those observed in the overall population, with durable responses and acceptable tolerability.

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 AML

Acute myeloid leukemia (AML) is a rapidly progressing cancer of the blood and bone marrow that affects myeloid cells, which normally develop into various types of mature blood cells. AML occurs primarily in adults and accounts for about 1 percent of all adult cancers. The

American Cancer Society estimates that there will be about 22,010 new cases in the United States, most in adults, in 2025.[3]

Relapsed AML affects about half of all patients who, following treatment and remission, experience a return of leukemia cells in the bone marrow.[4,5] Refractory AML, which affects between 10 and 40 percent of newly diagnosed patients, occurs when a patient fails to achieve remission even after intensive treatment.[6] Quality of life declines for patients with each successive line of treatment for AML, and well-tolerated treatments in relapsed or refractory disease remain an unmet need.

About REZLIDHIA®

INDICATION

REZLIDHIA is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME
Differentiation syndrome, which can be fatal, can occur with REZLIDHIA treatment. Symptoms may include dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, hypotension, fever, and weight gain. If differentiation syndrome is suspected, withhold REZLIDHIA and initiate treatment with corticosteroids and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome

REZLIDHIA can cause differentiation syndrome. In the clinical trial of REZLIDHIA in patients with relapsed or refractory AML, differentiation syndrome occurred in 16% of patients, with grade 3 or 4 differentiation syndrome occurring in 8% of patients treated, and fatalities in 1% of patients. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal. Symptoms of differentiation syndrome in patients treated with REZLIDHIA included leukocytosis, dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, fever, edema, pyrexia, and weight gain. Of the 25 patients who experienced differentiation syndrome, 19 (76%) recovered after treatment or after dose interruption of REZLIDHIA. Differentiation syndrome occurred as early as 1 day and up to 18 months after REZLIDHIA initiation and has been observed with or without concomitant leukocytosis.

If differentiation syndrome is suspected, temporarily withhold REZLIDHIA and initiate systemic corticosteroids (e.g., dexamethasone 10 mg IV every 12 hours) for a minimum of 3 days and until resolution of signs and symptoms. If concomitant leukocytosis is observed, initiate treatment with hydroxyurea, as clinically indicated. Taper corticosteroids and hydroxyurea after resolution of symptoms. Differentiation syndrome may recur with premature discontinuation of corticosteroids and/or hydroxyurea treatment. Institute supportive measures and hemodynamic monitoring until improvement; withhold dose of REZLIDHIA and consider dose reduction based on recurrence.

Hepatotoxicity

REZLIDHIA can cause hepatotoxicity, presenting as increased alanine aminotransferase

(ALT), increased aspartate aminotransferase (AST), increased blood alkaline phosphatase, and/or elevated bilirubin. Of 153 patients with relapsed or refractory AML who received REZLIDHIA, hepatotoxicity occurred in 23% of patients; 13% experienced grade 3 or 4 hepatotoxicity. One patient treated with REZLIDHIA in combination with azacitidine in the clinical trial, a combination for which REZLIDHIA is not indicated, died from complications of drug-induced liver injury. The median time to onset of hepatotoxicity in patients with relapsed or refractory AML treated with REZLIDHIA was 1.2 months (range: 1 day to 17.5 months) after REZLIDHIA initiation, and the median time to resolution was 12 days (range: 1 day to 17 months). The most common hepatotoxicities were elevations of ALT, AST, blood alkaline phosphatase, and blood bilirubin.

Monitor patients frequently for clinical symptoms of hepatic dysfunction such as fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Obtain baseline liver function tests prior to initiation of REZLIDHIA, at least once weekly for the first two months, once every other week for the third month, once in the fourth month, and once every other month for the duration of therapy. If hepatic dysfunction occurs, withhold, reduce, or permanently discontinue REZLIDHIA based on recurrence/severity.

ADVERSE REACTIONS
The most common (≥20%) adverse reactions, including laboratory abnormalities, were aspartate aminotransferase increased, alanine aminotransferase increased, potassium decreased, sodium decreased, alkaline phosphatase increased, nausea, creatinine increased, fatigue/malaise, arthralgia, constipation, lymphocytes increased, bilirubin increased, leukocytosis, uric acid increased, dyspnea, pyrexia, rash, lipase increased, mucositis, diarrhea and transaminitis.

DRUG INTERACTIONS

- Avoid concomitant use of REZLIDHIA with strong or moderate CYP3A inducers.
- Avoid concomitant use of REZLIDHIA with sensitive CYP3A substrates unless otherwise instructed in the substrates prescribing information. If concomitant use is unavoidable, monitor patients for loss of therapeutic effect of these drugs.

LACTATION
Advise women not to breastfeed during treatment with REZLIDHIA and for 2 weeks after the last dose.

GERIATRIC USE
No overall differences in effectiveness were observed between patients 65 years and older and younger patients. Compared to patients younger than 65 years of age, an increase in incidence of hepatotoxicity and hypertension was observed in patients ≥65 years of age.

HEPATIC IMPAIRMENT
In patients with mild or moderate hepatic impairment, closely monitor for increased probability of differentiation syndrome.

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).

REZLIDHIA is a registered trademark of Rigel Pharmaceuticals, Inc.

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
3. The American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Revised March 4, 2025. Accessed March 31, 2025: https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html
4. Patel, A, et al. *Outcomes of Patients With Acute Myeloid Leukemia Who Relapse After 5 Years of Complete Remission*. 2021 Sep 7;28(7):811-814. doi: https://doi.org/10.3727/096504020X15965357399750
5. Thol F, Ganser, A. *Treatment of Relapsed Acute Myeloid Leukemia*. Curr. Treat. Options on Oncol. (2020) 21: 66. doi: https://doi.org/10.1007/s11864-020-00765-5
6. Thol F, Schlenk RF, Heuser M, Ganser A. *How I treat refractory and early relapsed acute myeloid leukemia*. Blood (2015) 126 (3): 319-27. doi: https://doi.org/10.1182/blood-2014-10-551911

Forward-Looking Statements

This press release contains forward-looking statements relating to, among other things, the potential for the referenced clinical trials or trial results to strengthen our commercial portfolio, R289's efficacy in R/R lower-risk MDS, and REZLIDHIA's efficacy in R/R mIDH1 AML. 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 olutasidenib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding olutasidenib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that olutasidenib 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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