June 3, 2024

Rigel Highlights New Data in Three Poster Presentations at the 2024 ASCO Annual Meeting

- *Long-term efficacy data from the registrational Phase 2 trial of REZLIDHIA® (olutasidenib) in heavily pretreated patients with R/R mIDH1 AML, including those receiving prior venetoclax*
- *Data from a subgroup analyses of elderly R/R mIDH1 AML patients treated with olutasidenib shows consistent CR/CRh results*
- *Overview of the Phase 1b trial of R289 in patients with lower-risk MDS*

SOUTH SAN FRANCISCO, Calif., June 3, 2024 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced the presentation of three posters at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL today and online. Presentations include five-year results from the pivotal cohort of the registrational Phase 2 trial of REZLIDHIA® (olutasidenib) for the treatment of relapsed or refractory (R/R) mutated isocitrate dehydrogenase-1 (mIDH1) acute myeloid leukemia (AML), the safety and efficacy of olutasidenib treatment in a subgroup analyses of elderly patients with R/R mIDH1 AML, and an overview of the ongoing Phase 1b trial of R289[1], a potent and selective inhibitor of IRAK1 and IRAK4, in patients with lower-risk myelodysplastic syndrome (LR-MDS).

"Our presentations at ASCO build on the strength of REZLIDHIA's data, reinforcing its important role in the R/R mIDH1 AML treatment landscape. REZLIDHIA continues to demonstrate durable responses and was well tolerated, even in difficult to treat and elderly patients with mIDH1 AML who have more safety concerns," said Raul Rodriguez, Rigel's president and CEO. "In addition, we are sharing an overview of the ongoing Phase 1b trial of R289 in lower-risk MDS, an area of high unmet need. We believe R289 could potentially provide a new treatment option to patients who have failed other agents."

Monday, June 3, 2024, 9:00am to 12:00pm CT
Abstract #: 6528
Title: Olutasidenib for Mutated IDH1 Acute Myeloid Leukemia: Final Five-Year Results from the Phase 2 Pivotal Cohort
Presenter: Jorge E. Cortes, M.D.
Location: McCormick Place South, Exhibit Hall A

- An additional two years of data, beyond the results that led to FDA approval of olutasidenib, further demonstrates the durable responses observed with olutasidenib in heavily pretreated patients with mIDH1 AML, including those R/R to prior venetoclax. The safety profile was consistent with what was previously reported.
- Of 147 efficacy evaluable patients, complete remission (CR) or CR with partial hematologic recovery (CRh) was achieved in 35%. The median time to CR/CRh was 1.9 months and median duration of CR/CRh was 25.3 months, with maximum duration ongoing at 54.6 months. Overall response rate was 48%, with median duration 15.5 months and maximum duration ongoing at 54.6 months. Median overall survival was 11.6 months.
- Transfusion independence (for ≥56 days) from red blood cells was achieved in 34 patients (39%) who were dependent at baseline and from platelets was achieved in 28 patients (41%) who were dependent at baseline.
- In the 12 patients that were R/R to prior venetoclax, 33% achieved a CR/CRh; median duration of CR/CRh was not reached (ongoing at 50.6 months), and median overall survival was 16.2 months.

Monday, June 3, 2024, 9:00am to 12:00pm CT
Abstract #: 6527
Title: Safety and Efficacy of Olutasidenib Treatment in Elderly Patients with Relapsed/Refractory mIDH1 Acute Myeloid Leukemia
Presenter: Stéphane de Botton, M.D., Ph.D.
Location: McCormick Place South, Exhibit Hall A

- Olutasidenib was generally well tolerated in elderly patients with R/R mIDH1 AML and induced durable remissions, consistent with the population in the pivotal cohort of the Phase 2 registrational trial. Despite the challenges of treating elderly patients who had already failed prior AML treatment, the results suggest that elderly patients can benefit from therapy with olutasidenib.
- In this subgroup analyses of the registrational Phase 2 trial of olutasidenib in 45 participants aged 75 and older with R/R mIDH1 AML, 31% of patients achieved CR/CRh; median time to CR/CRh was 1.5 months, and median duration of CR/CRh was 25.9 months.
- Of the five elderly patients who were R/R to prior venetoclax, four patients (80%) achieved an overall response, including two patients (40%) with CR/CRh.

Monday, June 3, 2024, 9:00am to 12:00pm CT
Abstract #: TPS6591
Title: Phase 1b Trial of IRAK 1/4 Inhibition for Lower-Risk Myelodysplastic Syndrome Refractory/Resistant to Prior Therapies: A Trial in Progress
Presenter: Guillermo Garcia-Manero, M.D.
Location: McCormick Place South, Exhibit Hall A

- An overview of the study design of the ongoing Phase 1b trial evaluating R289 in patients with LR-MDS will be presented. The primary endpoint for this trial is safety with key secondary endpoints including preliminary efficacy and evaluation of pharmacokinetic properties.
- Enrollment in dose levels 1 (250 mg QD), 2 (500 mg QD), and 3 (750 mg QD) has been completed. Two additional dose levels with twice daily dosing have been added (250

mg BID and 500/250 mg) and the trial is actively recruiting.

To learn more about Rigel and the company's clinical and commercial hematology and oncology portfolio, visit Booth #11059 during ASCO.

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 20,800 new cases in the United States, most in adults, in 2024.[2]

Relapsed AML affects about half of all patients who, following treatment and remission, experience a return of leukemia cells in the bone marrow.[3] 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.[4] 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 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.[5]

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 Full Prescribing Information, including Boxed WARNING.**

To report side effects of prescription drugs to the FDA, visitwww.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. de Botton S, et al. Olutasidenib (FT-2102) induces durable complete remissions in patients with relapsed or refractory IDH1-mutated AML. *Blood Advances*. February 1, 2023.
   doi: https://doi.org/10.1182/bloodadvances.2022009411
   The American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Revised January 17, 2024. Accessed Feb. 19, 2024: https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html
3. Leukaemia Care. Relapse in Acute Myeloid Leukaemia (AML). Version 3. Reviewed October 2021. Accessed Feb 19, 2024: https://media.leukaemiacare.org.uk/wp-content/uploads/Relapse-in-Acute-Myeloid-Leukaemia-AML-Web-Version.pdf
4. 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
5. 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,the use of olutasidenib in the treatment of R/R mIDH1 AML patients including those receiving prior venetoclax treatment, the use of olutasidenib in treating elderly patients, and an overview of a Phase 1b trial of R289 in patientswith lower-risk myelodysplastic

syndrome. 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 "may", "potential", "look forward", "believe", "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 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 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 Annual Report on Form 10-K for the year ended December 31, 2023 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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