June 14, 2024

Rigel Announces Five Presentations at the EHA2024 Hybrid Congress

- *Oral presentation highlighting final five-year 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*
- *New data shows clinically meaningful effect of olutasidenib in patients with mIDH1 AML secondary to MPN and as bridge-to-transplant treatment in patients with R/R mIDH1 AML*

SOUTH SAN FRANCISCO, Calif., June 14, 2024 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced one oral and four poster presentations at the European Hematology Association (EHA) 2024 Hybrid Congress in Madrid, Spain being held June 13-16, 2024, and online. The oral presentation includes 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 oral presentation will be given by Dr. Jorge E. Cortes, Director, Georgia Cancer Center, Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer, and Phase 2 trial investigator, who will present an overview of the five-year study results, including transfusion independence, overall survival and patients R/R to prior venetoclax. In May, Dr. Cortes was published in the *Expert Review of Hematology* outlining the drug profile and summarizing key safety and efficacy data for olutasidenib, including in patients previously treated with venetoclax or ivosidenib.

"Olutasidenib offers patients with R/R mIDH1 AML a treatment option with rapid and durable responses, and a well-characterized and manageable safety profile. Furthermore, a post-hoc analysis of patients previously treated with venetoclax regimens demonstrated consistent durable responses, supporting the clinical benefit of olutasidenib in R/R mIDH1 AML," stated Dr. Cortes.

The company's poster presentations include data on the safety and efficacy of olutasidenib treatment in multiple subgroups, including elderly patients, patients who had previously failed venetoclax treatment and as a bridge to allogeneic hematopoietic stem cell transplantation (HSCT) in patients with R/R mIDH1 AML. In addition, data from olutasidenib treatment in patients with mIDH1 AML secondary to myeloproliferative neoplasms (MPN) will be presented.

"The collective data being presented at EHA support REZLIDHIA's strong efficacy and durability of response in several mIDH1 AML patient populations," said Raul Rodriguez, Rigel's president and CEO. "Additionally, we are excited about the compelling data in patients with mIDH1 AML secondary to MPN, supporting a role for REZLIDHIA in the treatment of this population which has no standardized treatment options and where patients have historically had poor responses to available treatments."

Oral Presentation

Saturday, June 15, 17:30 to 17:45 CEST
Abstract #: S144
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: IFEMA Madrid Recinto Ferial (Halls of the Fairgrounds), Hall Dali 1

- 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.

Poster Presentations

Friday, June 14, 18:00 to 19:00 CEST
Abstract #: P605
Title: Olutasidenib Demonstrates Clinical Activity in Mutated IDH1 Acute Myeloid Leukemia (AML) Secondary to Myeloproliferative Neoplasms (MPN)
Presenter: Stéphane de Botton, M.D., Ph.D.
Location: IFEMA Madrid Recinto Ferial (Halls of the Fairgrounds), Hall 7

- Olutasidenib was well tolerated in patients with post-MPN mIDH1 AML, supporting a role for olutasidenib based therapy in mIDH1 AML secondary to MPN.
- Of the 15 patients in the Phase 2 study of olutasidenib who had prior history of MPNs that transformed into AML, five had newly diagnosed AML and 10 had R/R AML.
- Six patients (40%) achieved CR with a median duration of response of 15.6 months. Two additional patients had a complete response with incomplete hematologic recovery (CRi), and one patient had morphologic leukemia free state (MLFS) giving a composite complete response (CRc) in 53% and an overall response rate (ORR) of

60%. Median overall survival was 13.8 months.
- Olutasidenib-based therapy may serve as a bridge to allogeneic stem cell transplantation.

Friday, June 14, 18:00 to 19:00 CEST
Abstract #: P614
Title: Response to Olutasidenib in Patients with Acute Myeloid Leukemia (AML) Following Venetoclax Failure
Presenter: Jorge E. Cortes, M.D.
Location: IFEMA Madrid Recinto Ferial (Halls of the Fairgrounds), Hall 7

- Olutasidenib induced complete remissions in patients with mIDH1 AML who were R/R to prior venetoclax-based regimens from the Phase 2 pivotal cohort.
- The ORR in the 18 patients was 50%, including CR in six patients (33%), CR/CRh in seven patients (39%), and CRc in nine patients (50%).
- In the 16 R/R patients, ORR was 44%, including CR/CRh in five patients (31%). Median time to CR/CRh was 2.1 months. Kaplan–Meier (KM) estimate of CR/CRh duration ≥18 months was 75%.
- Two patients in the maintenance cohort had CRi at baseline; both achieved a CR, lasting 15.7 months and ongoing at 31.3+ months. Although only a small number of patients receiving maintenance therapy were included in this analysis, the data show that maintenance of a CR and even improvement of response from CRi to CR is possible with olutasidenib.
- The demonstrated activity is clinically meaningful and reveals a therapeutic advance in the treatment of this poor-prognosis patient population with R/R mIDH1 AML.

Friday, June 14, 18:00 to 19:00 CEST
Abstract #: P611
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: IFEMA Madrid Recinto Ferial (Halls of the Fairgrounds), Hall 7

- 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 25.3 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.

Friday, June 14, 18:00 to 19:00 CEST
Abstract #: P1373
Title: Olutasidenib as Bridge-to-Transplant Treatment in Patients with Relapsed/Refractory mIDH1 Acute Myeloid Leukemia (AML)
Presenter: Stéphane de Botton, M.D., Ph.D.

Location: IFEMA Madrid Recinto Ferial (Halls of the Fairgrounds), Hall 7

- Olutasidenib helped achieve remission in patients with mIDH1 R/R AML and served as a bridging strategy towards potentially curative allogeneic transplantation in a substantial subset of these previously ineligible patients.
- 153 patients with mIDH1 R/R AML received olutasidenib monotherapy, and 16 patients (11%) proceeded to allogeneic HSCT. Of the 16 patients, eight patients (50%) were refractory to prior therapy, three patients (19%) had prior HSCT, and 15 patients (94%) had prior intensive chemotherapy (IC), 50% of whom were IC-refractory.
- Of the 16 patients proceeding to transplant, 12 patients (75%) achieved CR/CRh prior to proceeding to transplant, including 11 patients (69%) with CR, and all 16 patients were alive at 100 days. Median survival from start of olutasidenib treatment has not been reached. Overall survival probability was 83% at 12 months and 50% at 18 months.

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.[1]

Relapsed AML affects about half of all patients who, following treatment and remission, experience a return of leukemia cells in the bone marrow.[2] 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.[3] 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 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. 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
2. 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
3. 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, that olutasidenib may provide a meaningful approach to the treatment of heavily pretreated R/R mIDH1 AML patients including those receiving prior venetoclax treatment, the use of olutasidenib in treating elderly patients with R/R mIDH1 AML, the use of olutasidenib treatment in patients with mIDH1 AML secondary to myeloproliferative neoplasms (MPN), and the use of olutasidenib as bridge-to-transplant treatment in patients with *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 "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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