February 2, 2023

Rigel Announces Publication of REZLIDHIA™ (olutasidenib) Phase 2 Clinical Results in Blood Advances

- *REZLIDHIA induced durable remissions in adult patients with mIDH1 R/R AML*

SOUTH SAN FRANCISCO, Calif., Feb. 2, 2023 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced a peer-reviewed publication of data in *Blood Advances*, which summarizes clinical results from the Phase 2 registrational study of REZLIDHIA™ (olutasidenib), a potent, selective, oral, small-molecule inhibitor of mutant isocitrate dehydrogenase 1 (mIDH1)[1], in patients with mIDH1 relapsed or refractory acute myeloid leukemia (R/R AML). The published data demonstrate that REZLIDHIA induced durable remissions and transfusion independence with a well-characterized safety profile. The observed efficacy is clinically meaningful and represents a therapeutic advance in this poor prognosis patient population with limited treatment options.

The pivotal cohort of the Phase 2 registrational study enrolled 153 adult patients with mIDH1 R/R AML who received REZLIDHIA monotherapy 150 mg twice daily orally. The efficacy evaluable population included 147 patients with centrally confirmed mIDH1. The primary endpoint was a composite of complete remission (CR) plus complete remission with partial hematologic recovery (CRh). CRh is defined as less than 5% blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/microliter and absolute neutrophil count >500/microliter).

Key findings from the trial are summarized below:

- REZLIDHIA demonstrated a 35% (51/147) CR+CRh rate in mIDH1 R/R AML patients. Of the patients who achieved the primary endpoint of CR+CRh, 92% (47/51) were CR. Most patients who achieved CR or CRh responded early, with a median time to response of 1.9 months. The overall response rate was 48% (71/147). Response rates were similar in patients who had and who had not received prior venetoclax.
- In patients treated with REZLIDHIA, the median duration of CR+CRh was 25.9 months and the median duration of CR was 28.1 months. The median duration of overall response was 11.7 months.
- Median overall survival (OS) was 11.6 months in the overall population of 153 patients. In patients who achieved CR+CRh, median OS was not reached and the estimated 18-month survival was 78%.

- Conversion to transfusion independence (TI), another recognized indicator of clinical benefit, was achieved in 34% of patients receiving REZLIDHIA that had been classified as dependent on RBC and/or platelet transfusions at baseline. TI was observed in patients in all response groups.
- REZLIDHIA was well characterized with an adverse event profile largely representative of symptoms or conditions experienced by patients with AML undergoing treatment. Investigators observed differentiation syndrome in 14% of patients that was manageable in most cases with dose interruption and corticosteroids. The most common adverse events were gastrointestinal and hematologic in nature, and most cases were manageable with dose interruptions or modifications.

The paper, titled "Olutasidenib (FT-2102) induces durable complete remissions in patients with relapsed or refractory *IDH1*-mutated AML," was published online in *Blood Advances* on February 1, 2023. A link to the publication can be found here.

"REZLIDHIA demonstrated both a high rate of response and an extended median duration of complete response of 28.1 months, which is more than a year longer than what is reported with the standard of care," said Jorge E. Cortes, M.D., Director, Georgia Cancer Center, Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer, and Phase 2 trial investigator. "In addition to these impressive efficacy results that could differentiate REZLIDHIA from other available therapies, I am encouraged by the safety profile. These collective data support REZLIDHIA as a therapeutic advance in this poor prognosis patient population."

"The published data adds to our robust body of evidence reinforcing REZLIDHIA as a differentiated and potentially market-leading therapy for mIDH1 R/R AML patients," said Raul Rodriguez, Rigel's president and CEO. "With the recent approval of REZLIDHIA in the U.S., we believe our therapy will be an important new treatment option for this underserved patient population with a high unmet medical need. We are encouraged by this compelling data, particularly the durability of response, and look forward to providing REZLIDHIA to mIDH1 R/R AML patients"

On December 1, 2022, the U.S. Food and Drug Administration (FDA) approved REZLIDHIA (olutasidenib) capsules for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. REZLIDHIA became commercially available in the U.S. on December 22, 2022. REZLIDHIA was added to the latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for acute myeloid leukemia (AML) on January 13, 2023, and is now a recommended targeted therapy for adult patients with R/R AML with isocitrate dehydrogenase-1 (IDH1) mutation.

On November 10, 2022, Rigel announced the publication of data in *The Lancet Haematology* summarizing the Phase 1 results of the Phase 1/2 study of olutasidenib. The press release regarding this publication can be found here.

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 in the United States alone, there will be about 20,050 new cases, most in adults, in 2022.[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 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 trademark of Rigel Pharmaceuticals, Inc.

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 products and pipeline of potential products, visit www.rigel.com.

1. 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
2. The American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Revised January 12, 2022. Accessed Aug. 1, 2022 at https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html
3. Leukaemia Care. (2019). Relapse in Acute Myeloid Leukaemia (AML). Version 3. Reviewed October 2021. Accessed Dec 2, 2021 at 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

Rigel Forward Looking Statements

This press release contains forward-looking statements relating to, among other things, that olutasidenib may provide a meaningful benefit to people with relapsed or refractory acute myeloid leukemia, our ability to commercialize olutasidenib in the U.S. and identify potential partners outside of the U.S., and our expectations related to the potential and market opportunity of olutasidenib as therapeutics for R/R AML and other conditions. 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", "expects", "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 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 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 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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