November 2, 2023

Rigel Announces Poster Presentations at the 65th American Society of Hematology Annual Meeting and Exposition

-- Growing body of data on REZLIDHIA® (olutasidenib) *in mIDH1 relapsed or refractory (R/R) acute myeloid leukemia (AML) patients --*

-- New data on olutasidenib in patients with mIDH1 myelodysplastic syndromes/neoplasms (MDS) --

SOUTH SAN FRANCISCO, Calif., Nov. 2, 2023 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced the upcoming presentation of four posters highlighting data from their commercial and clinical-stage hematology-oncology portfolio at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition being held December 9-12, 2023, in San Diego, California and virtually.

"We are encouraged by the collective data supporting the potential use of REZLIDHIA in various *mIDH1* AML patient populations, including those that are relapsed or refractory to hematopoietic stem cell transplant, ivosidenib, or venetoclax. These data continue to indicate this treatment could meaningfully improve the lives of underserved patients living with *mIDH1* R/R AML," said Raul Rodriguez, Rigel's president and CEO. "We are also excited by the compelling data in patients with *mIDH1* MDS and look forward to evaluating this potential opportunity further. On top of the olutasidenib data, we are delighted to share other updates and data across our development portfolio, demonstrating our presence in the hematology-oncology space."

Details of the poster presentations and publication at the ASH Annual Meeting are as follows:

Poster Presentations

Abstract #: 2888
Title: Olutasidenib for the Treatment of mIDH1 Acute Myeloid Leukemia in Patients Relapsed or Refractory to Hematopoietic Stem Cell Transplant, Prior mIDH1 Inhibitor, or Venetoclax
Presenter: Jorge E. Cortes, M.D., Director, Georgia Cancer Center, Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer, and Phase 2 Trial Investigator

Session Name: 615. Acute Myeloid Leukemias: Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
Date: Sunday, December 10, 2023
Presentation Time: 6:00-8:00 PM PT
Location: San Diego Convention Center, Halls G-H

- *This poster reports post hoc analyses from the registrational Phase 1/2 trial of olutasidenib, a small molecule, oral, mutated-IDH1 (mIDH1) inhibitor approved for the treatment of relapsed/refractory (R/R) acute myeloid leukemia (AML), alone or in combination with azacitidine in a subset of patients with mIDH1 R/R AML or MDS that were R/R to previous hematopoietic stem cell transplant (HSCT), ivosidenib (IVO) or venetoclax (VEN).*
- *In the post-HSCT group (n=31), 19% of these patients had a complete response (CR), and 10% of patients had a CR with incomplete count recovery (CRi) resulting in a 29% composite complete remission (CRc) rate.*
- *In the post-IVO group (n=9), 22% achieved a response, all of which were CR.*
- *In the post-VEN group (n=20), response rates included CR in 30% of patients, CR with partial hematologic recovery (CRh) in 5%, and CRi in 10% resulting in a CRc of 45% and an ORR of 45%.*
- *The analyses suggests that olutasidenib alone or in combination with azacitidine may induce complete remissions in patients with mIDH1 AML or MDS that are R/R to VEN, IVO or even HSCT.*

Abstract #: 1872
Title: Olutasidenib Alone or in Combination with Azacitidine Induces Durable Complete Remissions in Patients with mIDH1 Myelodysplastic Syndromes/Neoplasms (MDS)
Presenter: Jorge E. Cortes, M.D., Director, Georgia Cancer Center, Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer, and Phase 2 Trial Investigator
Session Name: 637. Myelodysplastic Syndromes – Clinical and Epidemiological: Poster I
Date: Saturday, December 9, 2023
Presentation Time: 5:30-7:30 PM PT
Location: San Diego Convention Center, Halls G-H

- *This poster reports the results from a Phase 1/2 trial of olutasidenib alone or in combination with azacitidine in a subset of 22 patients with mIDH1 MDS.*
- *For the pooled Phase 1 and 2 data, 27% of patients achieved CR and 32% of patients achieved marrow CR with no partial remissions, generating a 59% overall response rate. The median time to response was 2.0 months and the median duration of response was not reached at 30.1+ months.*
- *All patients with MDS experienced at least 1 treatment-emergent adverse event (TEAE). The most frequent TEAEs in the study were nausea, constipation, vomiting, thrombocytopenia, neutropenia, diarrhea, and fatigue. Grade 3 TEAEs occurred in 19/22 (86%) patients, and Grade 4 TEAEs in 9/22 (41%). The most frequent Grade 3/4 TEAEs reported were cytopenias.*
- *Olutasidenib, both as monotherapy and in combination with azacitidine, induced durable remissions in patients with intermediate-, high-, or very high-risk MDS. Patients had varying treatment backgrounds, including treatment-naïve and up to four prior regimens. This treatment had a tolerable and manageable safety profile.*
- *These encouraging results, which warrant further investigation with a larger number of*

patients, showed that olutasidenib had clinically meaningful activity in patients with mIDH1 MDS.

Abstract #: 3247
Title: Phase 1b Trial of IRAK 1/4 Inhibition for Low-Risk Myelodysplastic Syndrome Refractory/Resistant to Prior Therapies: A Trial In Progress
Presenter: Guillermo Garcia-Manero, M.D., The University of Texas MD Anderson Cancer Center, Department of Leukemia, Houston, TX
Session Name: 637. Myelodysplastic Syndromes – Clinical and Epidemiological: Poster II
Date: Sunday, December 10, 2023
Presentation Time: 6:00-8:00 PM PT
Location: San Diego Convention Center, Halls G-H

- *This trial in progress poster provides an overview of the study design of the ongoing Phase 1b trial evaluating R289[1], a potent and selective inhibitor of IRAK1 and IRAK4 kinases, in patients with low-risk myelodysplastic syndrome (LR-MDS) relapsed or refractory to prior therapies. The inhibition of IRAK1/4 is a potential target for the treatment of LR-MDS by decreasing inflammation and cell death within the bone marrow, allowing for restoration of hematopoiesis.*

Abstract #: 2578
Title: Long-Term Treatment with Fostamatinib in Japanese Patients with Primary Immune Thrombocytopenia: An Open-Label Extension Study Following a Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group Study
Session Name: 311. Disorders of Platelet Number or Function: Clinical and Epidemiological: Poster II
Date: Sunday, December 10, 2023
Presentation Time: 6:00-8:00 PM PT
Location: San Diego Convention Center, Halls G-H

- *This poster highlights the long-term efficacy and safety of fostamatinib in Japanese patients with primary immune thrombocytopenia (ITP), along with the feasibility of glucocorticoid reduction/discontinuation during fostamatinib treatment and a lack of bleeding events after abrupt discontinuation of fostamatinib. These results support the use of fostamatinib as a second-line treatment in patients with primary ITP.*

The conference abstracts can be accessed here.

To learn more about Rigel Pharmaceuticals and their clinical and commercial hematology/oncology portfolio visit Booth #2805 during ASH 2023.

About ITP
In patients with ITP (immune thrombocytopenia), the immune system attacks and destroys the body's own blood platelets, which play an active role in blood clotting and healing. Common symptoms of ITP are excessive bruising and bleeding. People suffering with chronic ITP may live with an increased risk of severe bleeding events that can result in serious medical complications or even death. Current therapies for ITP include steroids, blood platelet production boosters (TPO-RAs), and splenectomy. However, not all patients respond to existing therapies. As a result, there remains a significant medical need for additional treatment options for patients with ITP.

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 20,380 new cases, most in adults, in 2023.[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 registered trademark of Rigel Pharmaceuticals, Inc.

About TAVALISSE®

Indication

TAVALISSE (fostamatinib disodium hexahydrate) tablets is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

Important Safety Information

Warnings and Precautions

- Hypertension can occur with TAVALISSE treatment. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects. Monitor blood pressure every 2 weeks until stable, then monthly, and adjust or initiate antihypertensive therapy for blood pressure control maintenance during therapy. If increased blood pressure persists, TAVALISSE interruption, reduction, or discontinuation may be required.
- Elevated liver function tests (LFTs), mainly ALT and AST, can occur with TAVALISSE. Monitor LFTs monthly during treatment. If ALT or AST increase to ≥3 x upper limit of normal, manage hepatotoxicity using TAVALISSE interruption, reduction, or discontinuation.
- Diarrhea occurred in 31% of patients and severe diarrhea occurred in 1% of patients treated with TAVALISSE. Monitor patients for the development of diarrhea and manage using supportive care measures early after the onset of symptoms. If diarrhea becomes severe (≥Grade 3), interrupt, reduce dose or discontinue TAVALISSE.
- Neutropenia occurred in 6% of patients treated with TAVALISSE; febrile neutropenia occurred in 1% of patients. Monitor the ANC monthly and for infection during treatment. Manage toxicity with TAVALISSE interruption, reduction, or discontinuation.
- TAVALISSE can cause fetal harm when administered to pregnant women. Advise pregnant women the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose. Verify pregnancy status prior to initiating TAVALISSE. It is unknown if TAVALISSE or its metabolite is present in human milk. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during TAVALISSE treatment and for at least 1 month after the last dose.

Drug Interactions

- Concomitant use of TAVALISSE with strong CYP3A4 inhibitors increases exposure to the major active metabolite of TAVALISSE (R406), which may increase the risk of adverse reactions. Monitor for toxicities that may require a reduction in TAVALISSE dose.
- It is not recommended to use TAVALISSE with strong CYP3A4 inducers, as concomitant use reduces exposure to R406.
- Concomitant use of TAVALISSE may increase concentrations of some CYP3A4 substrate drugs and may require a dose reduction of the CYP3A4 substrate drug.
- Concomitant use of TAVALISSE may increase concentrations of BCRP substrate

drugs (eg, rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (eg, digoxin), which may require a dose reduction of the BCRP and P-gp substrate drug.

Adverse Reactions

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from FIT-1 and FIT-2 included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia.

Please see www.TAVALISSEUSPI.com **for full Prescribing Information.**

To report side effects of prescription drugs to the FDA, visitwww.fda.gov/medwatch **or call 1-800-FDA-1088 (800-332-1088).**

TAVALISSE 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. The American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Revised January 12, 2023. Accessed Feb. 15, 2023: 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 15, 2023: 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

Forward Looking Statements

This press release contains forward-looking statements relating to, among other things, the potential and market opportunity of olutasidenib as therapeutics for R/R AML and other conditions, the potential and market opportunity of fostamatinib as therapeutics for ITP and other conditions, the commercialization of fostamatinib or olutasidenib in the U.S. and international markets, and Rigel's ability to further develop its clinical stage and early-stage product candidates and Rigel's partnering effort, including the progress of Phase 1b clinical trial of R289 for the treatment of lower-risk myeloid dysplastic syndrome, and an open-label extension study of fostamatinib for long-term treatment of Japanese patients with primary ITP. 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 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 fostamatinib or olutasidenib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib or olutasidenib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib or 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 June 30, 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.

Contact for Investors & Media:

Investors:
Rigel Pharmaceuticals, Inc.
650.624.1232
ir@rigel.com

Media:
David Rosen
Argot Partners
212.600.1902
david.rosen@argotpartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/rigel-announces-poster-presentations-at-the-65th-american-society-of-hematology-annual-meeting-and-exposition-301975946.html

SOURCE Rigel Pharmaceuticals, Inc.