November 5, 2024

Rigel Announces Six Poster Presentations at the 66th American Society of Hematology Annual Meeting and Exposition

- *Initial data from the ongoing Phase 1b study evaluating R289, a dual IRAK1/4 inhibitor, in LR-MDS*
- *Additional data for REZLIDHIA® (olutasidenib) in patients with mIDH1 AML and MDS*

SOUTH SAN FRANCISCO, Calif., Nov. 5, 2024 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced upcoming presentations of six posters highlighting data from their commercial and clinical-stage hematology-oncology portfolio at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition being held December 7-10, 2024, in San Diego, California and virtually.

Rigel's presentations will include data from the ongoing Phase 1b dose escalation/expansion study evaluating R289[1], a potent and selective dual inhibitor of IRAK1 and IRAK4, in patients with lower-risk myelodysplastic syndrome (LR-MDS) who are relapsed or refractory (R/R) to prior therapies; REZLIDHIA® (olutasidenib) for the treatment of R/R mutated isocitrate dehydrogenase-1 (m*IDH1*) acute myeloid leukemia (AML); and TAVALISSE® (fostamatinib disodium hexahydrate) for the treatment of chronic immune thrombocytopenia (ITP).

"We look forward to the presentation of posters at ASH from across our product portfolio. We are very encouraged by the preliminary safety and efficacy data from our ongoing Phase 1b study of R289 in lower risk MDS. R289 was generally well tolerated and demonstrated responses in heavily pretreated LR-MDS patients, a population with a critical unmet need," said Raul Rodriguez, Rigel's president and CEO. "In addition, data from olutasidenib will be presented that adds to the growing body of evidence showing the benefits of its use in patients with m*IDH1* AML."

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

Abstract #: 4595
Title: R289, a Dual IRAK 1/4 Inhibitor, in Patients with Relapsed/Refractory (R/R) Lower-Risk Myelodysplastic Syndrome (LR-MDS): Initial Results from a Phase 1b Study
Presenter: Guillermo Garcia-Manero, M.D.
Time: Monday, December 9, 2024, 6:00pm to 8:00pm PT

- Initial data from the dose escalation phase using a July 15, 2024 data cutoff date indicate that R289 was generally well tolerated in a heavily pretreated LR-MDS patient population (median number of prior therapies was 4; 79% had received an hypomethylating agent), the majority of whom were high transfusion burden (received ≥8 units red blood cells in 16 weeks prior to enrollment) at study entry.
- Fourteen of 19 patients were evaluable for efficacy (received ≥1 dose of study drug with ≥1 efficacy assessment). Per International Working Group (IWG) 2018, RBC-transfusion independence (RBC-TI)/hematologic improvement (HI-E) occurred in 36% of patients receiving R289 doses ≥500 mg QD, with a median duration of RBC-TI of 29 weeks (range 12.4-35.9 weeks). RBC-TI >24 weeks was achieved in 2 high transfusion burden patients following 3 and 5 prior therapies, including a hypomethylating agent.
- Updated data as of October 25, 2024 data cutoff will be presented during the poster session.

Abstract #: 1514
Title: Time to Response and Overall Survival in Patients with m*IDH1* Relapsed/Refractory Acute Myeloid Leukemia Treated with Olutasidenib
Presenter: Stéphane de Botton, M.D., Ph.D.
Time: Saturday, December 7, 2024, 5:30pm to 7:30pm PT

- Results show that while some patients with m*IDH1* R/R AML achieve response to olutasidenib very quickly, within 1-2 months of treatment, other patients responded after 6 months of treatment for complete remission (CR) plus CR with partial hematologic recovery (CRh) and up to 10 months for overall response.
- These results support the prescribing information that suggests treating for at least 6 months to allow time for clinical response in patients without disease progression or unacceptable toxicity.
- A Cox regression model showed no significant association between time to response and overall survival in the overall responders and those with a CR/CRh response.

Abstract #: 2886
Title: Combination of Olutasidenib and Azacitidine Induces Durable Complete Remissions in m*IDH1* Acute Myeloid Leukemia: A Multicohort Open-Label Phase 1/2 Trial
Presenter: Jorge E. Cortes, M.D.
Time: Sunday, December 8, 2024, 6:00pm to 8:00pm PT

- Olutasidenib plus azacitidine induced high response rates and durable remissions with a tolerable side effect profile in patients with R/R m*IDH1* AML, in the first reported analysis of a combination therapy with an mIDH1 inhibitor and a hypomethylating agent focused on the R/R AML setting.
- CR/CRh was achieved in 31% (21/67) of patients and median duration of CR/CRh was 15 months.

Abstract #: 4600
Title: Olutasidenib Alone or in Combination with Azacitidine in Patients with m*IDH1* Myelodysplastic Syndromes/Neoplasms: Final 5-Year Data
Presenter: Jorge E. Cortes, M.D.
Time: Monday, December 9, 2024, 6:00pm to 8:00pm PT

- Olutasidenib demonstrated encouraging response rates with durable remissions and an acceptable and manageable safety profile in patients with intermediate to very high-risk m*IDH1* MDS treated with olutasidenib monotherapy or in combination with azacitidine.
- In a sub analysis of the 19 efficacy evaluable patients, 79% (11/14) of patients responded to combination therapy and 40% (2/5) responded to monotherapy, which included both patients (2/2) using the approved dose of 150 mg BID olutasidenib.

Abstract #: 1525
Title: Effectiveness of Olutasidenib Versus Ivosidenib in Patients with Mutated Isocitrate Dehydrogenase 1 Acute Myeloid Leukemia Who Are Relapsed or Refractory to Venetoclax: The 2102-HEM-101 Trial Versus a US Electronic Health Record-Based External Control Arm
Presenter: Catherine E. Lai, M.D.
Time: Sunday, December 8, 2024, 6:00pm to 8:00pm PT

- This study provides the first evidence suggesting favorable effectiveness of olutasidenib versus ivosidenib in patients with m*IDH1* AML who were R/R to a venetoclax-based regimen.
- As with any real-world experience study, limitations include risk of unmeasured confounding and differential outcome reporting.

Abstract #: 5080
Title: Real-World Experience with Combination Therapy of Fostamatinib and Thrombopoetin Receptor Agonists (TPO-RAs) for Treatment of Immune Thrombocytopenia (ITP): Patient-Reported Outcomes
Presenter: Elizabeth Bowhay-Carnes, M.D.
Time: Monday, December 9, 2024, 6:00pm to 8:00pm PT

- This real-world study treating patients with fostamatinib and a thrombopoetin receptor agonist (TPO-RA) demonstrated that the combination led to a clinically meaningful response in a majority of patients with ITP.

ASH Publication

Abstract #: 7908
Title: Treatment Patterns and Outcomes of Olutasidenib in Patients with Relapsed/Refractory (R/R) mutated *IDH1* Acute Myeloid Leukemia (AML) in the Real World
Authors: Aaron Sheppard, Ph.D.; Lixia Wang, Ph.D.; Ravi Potluri, MBA; Eros Papademetriou, MA

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 20,800 new cases in the United States, most in adults, in 2024.[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] 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.[5] 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 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 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,
visit www.fda.gov/medwatch or call 1-800-FDA-1088 (800-332-1088).

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).

REZLIDHIA and TAVALISSE are registered trademarks 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. Accessed September 30, 2024. DOI: https://doi.org/10.3389/fonc.2016.00151
3. The American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML). Revised June 5, 2024. Accessed September 30, 2024:

https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html
4. Leukaemia Care. Relapse in Acute Myeloid Leukaemia (AML). Version 3. Reviewed October 2021. Accessed September 30, 2024: https://media.leukaemiacare.org.uk/wp-content/uploads/Relapse-in-Acute-Myeloid-Leukaemia-AML-Web-Version.pdf
5. Thol F, Schlenk RF, Heuser M, Ganser A. *How I treat refractory and early relapsed acute myeloid leukemia*. Blood (2015) 126 (3): 319-27. Accessed September 30, 2024. 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, clinical information regarding studies of Rigel's products, including; the progress of the Phase 1b clinical trial of R289 for the treatment of lower-risk myeloid dysplastic syndrome; olutasidenib as a treatment for mIDH1 Relapsed/Refractory Acute Myeloid Leukemia, use of olutasidenib with azacitidine, and use of olutasidenib versus ivosidenib; and, fostamatinib in combination with thrombopoetin receptor agonists for treatment of immune thrombocytopenia, and fostamatinib as early treatment of immune thrombocytopenia. 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", "look to", "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, olutasidenib and pralsetinib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib, pralsetinib or olutasidenib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib, pralsetinib 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, 2024 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
646.461.6387
david.rosen@argotpartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/rigel-announces-six-poster-presentations-at-the-66th-american-society-of-hematology-annual-meeting-and-exposition-302296599.html

SOURCE Rigel Pharmaceuticals, Inc.