May 23, 2024

Rigel Announces Presentations at the Upcoming 2024 ASCO Annual Meeting and EHA2024 Hybrid Congress

- *Oral presentation of final five-year results from the registrational Phase 2 trial in R/R mIDH1 AML patients reinforces REZLIDHIA® (olutasidenib) efficacy in heavily pretreated patients, including those receiving prior venetoclax*
- *Other key posters further support the efficacy of REZLIDHIA® (olutasidenib) in elderly, transplant-eligible, and post-MPN patients with AML*

SOUTH SAN FRANCISCO, Calif., May 23, 2024 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced upcoming presentations from their commercial and clinical-stage hematology and oncology portfolio at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting and European Hematology Association (EHA) 2024 Hybrid Congress. The ASCO Annual Meeting is being held online and in person in Chicago, Illinois from May 31 to June 4, 2024. The EHA2024 Congress is being held online and in person in Madrid, Spain from June 13 to June 16, 2024.

Rigel's presentations will include data for REZLIDHIA® (olutasidenib), for the treatment of mutated isocitrate dehydrogenase-1 (mIDH1) acute myeloid leukemia (AML), and TAVALISSE® (fostamatinib), for the treatment of chronic immune thrombocytopenia (ITP), along with an overview of the ongoing Phase 1b trial evaluating R289[1], a potent and selective inhibitor of IRAK1 and IRAK4, in patients with lower-risk myelodysplastic syndrome (LR-MDS) who are refractory or resistant to prior therapies.

"We are excited to present new data on REZLIDHIA that adds to the growing body of evidence supporting its efficacy and safety in patients with mIDH1 AML, including difficult to treat patient populations. The five-year data from the registrational Phase 2 trial continue to demonstrate that REZLIDHIA induces rapid and durable responses. In addition, new analyses support the benefit it may provide to elderly patients," said Raul Rodriguez, Rigel's president and CEO. "The collective data to be presented at ASCO and EHA underscore the strength and compelling science of our hematology and oncology portfolio."

Highlights from the robust REZLIDHIA (olutasidenib) data published include:

- 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 relapsed or refractory (R/R) to prior venetoclax. The safety profile was consistent with what was previously reported.
- Olutasidenib was generally well tolerated in elderly patients with R/R mIDH1 AML and induced durable remissions. 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.
- Olutasidenib was effective in achieving 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.
- Olutasidenib was well tolerated in a subset of patients with post-myeloproliferative neoplasms (MPN) mIDH1 AML, a patient population often associated with poor responses to available therapies.

Data from the TAVALISSE (fostamatinib) observational study provides greater insight into use in the real-world setting:

- In the study, fostamatinib demonstrated efficacy and safety as second-line therapy for ITP. Fostamatinib allowed successful tapering and discontinuation of corticosteroids while maintaining platelet counts above 50,000/µL.

ASCO Annual Meeting abstracts may be accessed online via https://www.asco.org/abstracts. Details of the poster presentations and publications are as follows:

ASCO Poster Presentations

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.

Abstract #: 6527
Title: Safety and Efficacy of Olutasidenib Treatment in Elderly Patients with Relapsed/Refractory m*IDH1* Acute Myeloid Leukemia
Presenter: Stéphane de Botton, M.D., Ph.D.

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.

ASCO Publications

Abstract #: e18516
Title: Patients with Relapsed/Refractory m*IDH1* AML Who Proceeded to Transplant After Olutasidenib Treatment
Authors: Stéphane de Botton, M.D., Ph.D.; Justin M Watts, M.D.; Brian A Jonas, M.D., Ph.D.; Mwe Mwe Chao, M.D.; Jorge Cortes, M.D.

Abstract #: e23289
Title: Real-World Experience with Fostamatinib in Patients with Immune Thrombocytopenia: Results of an Observational Study (FORTE)
Authors: Ruchika Goel, M.D., MPH; Waqas Azhar, M.D.; Robert P. Numerof, Ph.D.; Donna Chow, MS; Bhavesh Shah, M.D.

EHA2024 Congress abstracts may be accessed online via theEHA Library. Details of the poster presentations and publications are as follows:

EHA 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.

EHA 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.

Abstract #: P614
Title: Response to Olutasidenib in Patients with Acute Myeloid Leukemia (AML) Following Venetoclax Failure
Presenter: Jorge E. Cortes, M.D.

Abstract #: P611
Title: Safety and Efficacy of Olutasidenib Treatment in Elderly Patients with Relapsed/Refractory m*IDH1* Acute Myeloid Leukemia
Presenter: Stéphane de Botton, M.D., Ph.D.

Abstract #: P1373
Title: Olutasidenib as Bridge-to-Transplant Treatment in Patients with Relapsed/Refractory m*IDH1* Acute Myeloid Leukemia (AML)
Presenter: Stéphane de Botton, M.D., Ph.D.

EHA Publications

Abstract #: PB3344
Title: Real-World Experience with Fostamatinib in Patients with Immune Thrombocytopenia: Results of an Observational Study (FORTE)
Authors: Ruchika Goel, M.D., MPH; Drew Provan, M.D.; Francois Di Trapani, Pharm.D.

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 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 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 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. 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.
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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, 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, transplant-eligible, and post-MPN patients with AML, and the use of fostamatinib as a second-line therapy for 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 "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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