REZLIDHIA™ (olutasidenib) Capsules U.S. FDA Approval Call

December 1, 2022

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1955 ("PSLRA") relating to, among other things, the development and commercialization of olutasidenib; the potential of REZLIDHIA to address patient and stakeholder needs; and the growth of our hematology-oncology business.

Any statements contained in this presentation that are not statements of historical fact may be deemed to be forward-looking statements and as such are intended to be covered by the safe harbor for "forward-looking statements" provided by the PSLRA. Words such as "potential", "may", "expects", and similar expressions are intended to identify these forward-looking statements. These forward-looking statements are based on Rigel's current expectations and information available to Rigel on the date of this presentation. 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 REZLIDHIA; risks that the FDA, European Medicines Agency or other regulatory authorities may make adverse decisions regarding olutasidenib; risks that our clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; 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, manufacture and commercialize our product candidates; market competition; and those other risks detailed from time to time in Rigel's reports filed with the Securities and Exchange Commission, including the Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 and subsequent filings. Rigel does not undertake any obligation to update forward-looking statements 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.

Agenda

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REZLIDHIA™ Approval
Raul Rodriguez,
President and CEO

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Clinical Overview
Wolfgang Dummer, M.D., Ph.D.
Chief Medical Officer

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A Clinical Perspective
Jorge E. Cortes, M.D.
Director, Georgia Cancer Center at the University of Augusta
Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer

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U.S. Launch Readiness
Dave Santos
Chief Commercial Officer

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Q&A and Closing Remarks

REZLIDHIA™
(olutasidenib) 150 mg capsules

REZLIDHIA™ (olutasidenib) 150 mg capsules

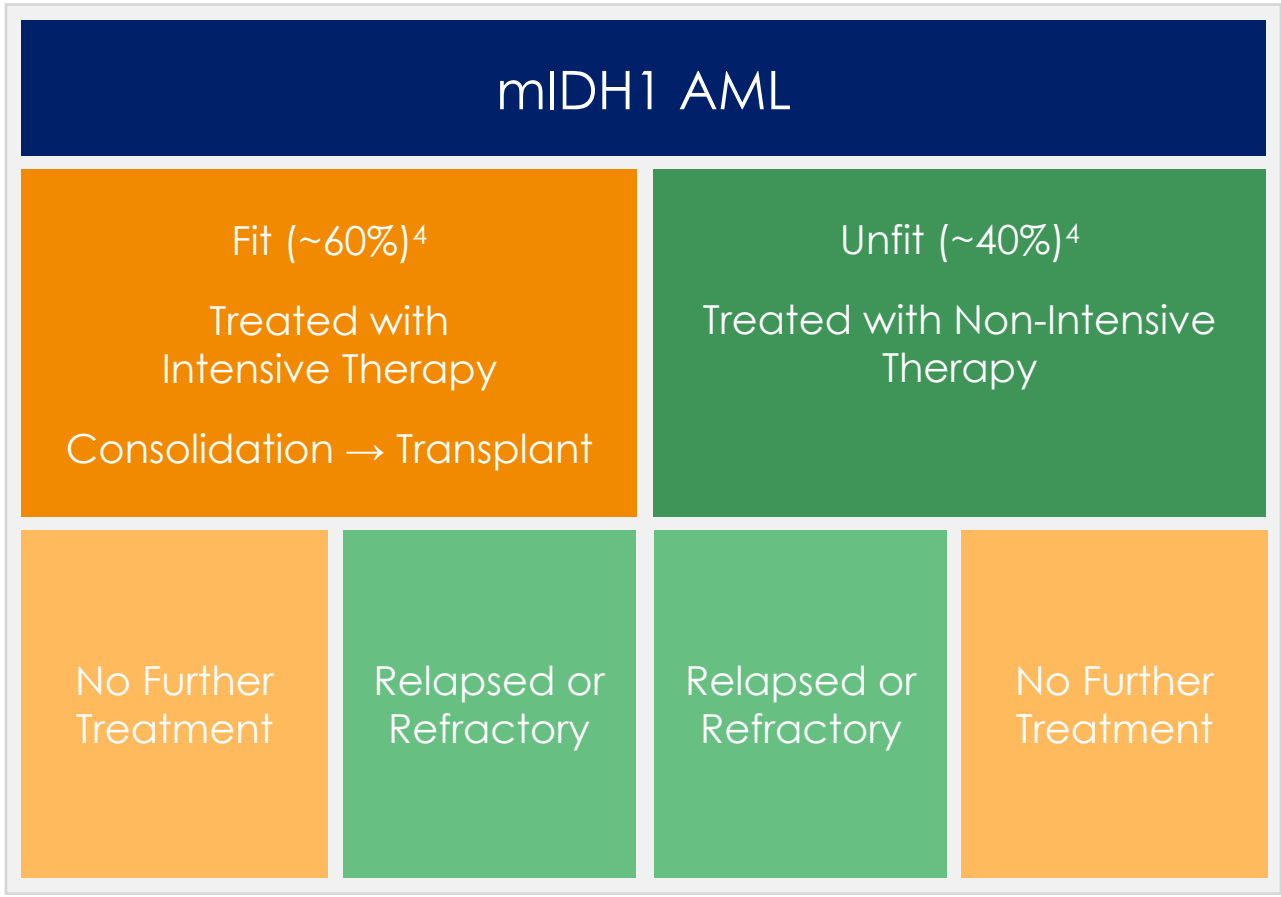
APPROVED IN THE U.S.

REZLIDHIA is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.

Please see Important Safety Information on Slide 22,
including Boxed WARNING regarding differentiation syndrome

mIDH1 Relapsed/Refractory AML Background

- AML is an aggressive, highly complex malignancy typically diagnosed in older adults[1]
- AML will be diagnosed in over 20K patients and result in nearly 11.5K deaths in 2022[2]
- IDH1 mutations are found in 6-9%[3] of AML
- IDH1 patients are well-identified, and have limited options for treatment, particularly in relapsed/refractory (R/R) disease
- A significant unmet need exists for targeted treatments for mIDH1 R/R AML that are well-tolerated and efficacious



[1]Leukemia & Lymphoma Society, Facts About Acute Myeloid Leukemia (AML), December 2019 [2] American Cancer Society, Key Statistics for Acute Myeloid Leukemia (AML), 2022
[3]NCCN Clinical Practice Guidelines in Oncology, Acute Myeloid Leukemia. Version 2.2022 – June 14, 2022. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1411.
[4]Rigel HCP Quantitative Market Research, 2022 (Data on File)

REZLIDHIA Phase 2 Clinical Trial: Study Design[1]

REZLIDHIA™ (olutasidenib) 150 mg capsules

Monotherapy

REZLIDHIA[2] 150 mg BID

Cohort 1: R/R AML (N=153)

Cohort 2: AML in CR/CRi but MRD positive

Cohort 3: R/R AML/MDS treated previously with IDH1 inhibitor therapy AND standard treatments are contraindicated

Cohort 7: TN AML for whom standard treatments are contraindicated

Combination Therapy

REZLIDHIA[2] 150 mg BID + AZA[3]

Cohort 4: R/R AML/MDS naïve to prior HMA and IDH1 inhibitor therapy

Cohort 5: R/R AML/MDS inadequately responded to or progressed on prior HMA

Cohort 6: R/R AML/MDS treated previously with IDH1 inhibitor monotherapy as last prior therapy

Cohort 8: TN AML candidates for AZA as first-line treatment

Primary Endpoint:

CR+CRh rate

Key Secondary Endpoints:

- ORR, DOR, Transfusion independence, OS
- Safety

Cohort 1: All adults, median age 71 (32-87) years, 73% had intermediate AML cytogenetic risk. Most (75%) had ≥1 co-occurring mutations. Most (97%) had prior induction therapy and a median 2 (1-7) prior treatments (all naïve to m1DHI-inhibitor).

[1]NCT02719574; [2]REZLIDHIA PO given daily over continuous 28-day cycles; [3]AZA IV or SC given daily on Days 1–7 of each 28-day cycle.
Patients received first dose ≥6 months prior to data cutoff of June 18, 2021. Source: Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 7006-7006 DOI: 10.1200/JCO.2021.39.15_suppl.7006

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REZLIDHIA Phase 2 Clinical Trial: Efficacy Results

REZLIDHIA™ (olutasidenib) 150 mg capsules

Endpoint	Phase 2 Cohort 1 N=147
CR+CRh[1,2] n (%)	**51 (35)**
95% CI	(27, 43)
Median time to CR or CRh (months)	**1.9**
Range	(0.9 to 5.6)
Median duration of CR+CRh[3] (months)	**25.9**
95% CI	(13.5, NR)
CR[1] n (%)	**47 (32)**
95% CI	(25, 40)
Median duration of CR[3] (months)	**28.1**
95% CI	(13.8, NR)
CRh[1] n (%)	**4 (2.7)**
95% CI	(0.7, 6.8)
Observed duration of CRh[3] (months)	**1.8, 5.6, 13.5, 28.5+**

CI: confidence interval; NR = not reached [1] CR (complete remission) was defined as <5% blasts in the bone marrow, no blasts with Auer rods, no extramedullary disease, and full recovery of peripheral blood counts (platelets >100,000/microliter and absolute neutrophil counts [ANC] >1,000/microliter); CRh (complete remission with partial hematologic recovery) was defined as <5% blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/microliter and ANC >500/microliter). [2] CR+CRh rate was consistent across all baseline demographic and baseline disease characteristic subgroups with the exception of IDH1 R132H mutation (CR+CRh 17%). [3] Duration of response is defined as the time from the date of the first response to the date of the relapse or death. Patients who did not relapse were censored at the date of last response assessment. + indicates censored observation.

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REZLIDHIA Phase 2 Clinical Trial: Safety - Adverse Reactions (≥10%)

REZLIDHIA™ (olutasidenib) 150 mg capsules

Body System Adverse Reaction	Olutasidenib 150 mg BID (N=153) All Grades (%)	 Grade 3 or 4 (%)
Gastrointestinal Disorders		
Nausea	38	0
Constipation	26	0
Mucositis[2]	23	3
Diarrhea	20	1
Abdominal pain[1]	18	1
Vomiting	17	1
General Disorders and Administration Site Conditions		
Fatigue/malaise[1]	36	3
Pyrexia	24	1
Edema[1]	18	3
Blood System and Lymphatic Disorders		
Leukocytosis	25	9
Differentiation syndrome*,[4]	16	8

Body System Adverse Reaction	Olutasidenib 150 mg BID (N=153) All Grades (%)	 Grade 3 or 4 (%)
Musculoskeletal and Connective Tissue Disorders		
Arthralgia[3]	28	3
Respiratory, Thoracic and Mediastinal Disorders		
Dyspnea*,[5]	24	5
Cough[1]	17	1
Skin and Subcutaneous Tissue Disorders		
Rash[1]	24	1
Investigations		
Transaminitis[6]	20	12
Metabolism and Nutrition Disorders		
Decreased appetite	16	2
Nervous System Disorders		
Headache	13	0
Vascular Disorders		
Hypertension[1]	10	5

* Includes fatal adverse reaction. [1] Includes multiple similar adverse reaction terms. [2] Mucositis includes gingival hypertrophy, gingivitis, gingivitis ulcerative, oral disorder, colitis, mouth ulceration, stomatitis, tongue ulceration, oral pain, oropharyngeal pain, pharyngitis, proctalgia, and colitis ischemic. [3] Arthralgia grouped term includes arthralgia, bone pain, back pain, neck pain, pain in extremity, arthritis, joint effusion, joint range of motion decreased, and joint swelling. [4] Symptoms of differentiation syndrome in patients treated with REZLIDHIA included leukocytosis, dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, fever, edema, pyrexia, and weight gain. [5] Dyspnea grouped term includes acute respiratory distress syndrome, dyspnea, dyspnea exertional, hypoxia, oxygen saturation decreased, respiratory distress, respiratory failure. [6] Transaminitis grouped term includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, hypertransaminasemia, liver function test abnormal, liver function test increased, transaminases increased, hepatitis acute, and blood alkaline phosphatase increased.

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REZLIDHIA Phase 2 Clinical Trial: Safety cont'd

Differentiation syndrome and hepatic effects were AEs of special interest:

- Differentiation syndrome occurred in 16% of patients, with 8% grade ≥3; most cases were generally successfully managed with dose interruptions and supportive treatments with steroids, diuretics or hydroxyurea
    - Incidence rate of differentiation syndrome for REZLIDHIA was comparable to that reported for FDA approved IDH1 and IDH2 inhibitors in similar patient populations
- Hepatotoxicity (presenting as increases in liver function tests) occurred in 23% of patients, with 13% grade ≥3; most cases were manageable with dose modifications. Many were successfully rechallenged

REZLIDHIA Phase 2 Clinical Trial – Summary

REZLIDHIA™ (olutasidenib) 150 mg capsules

- CR+CRh rate of 35%, with a median duration of response of 25.9 months
- 92% of CR+CRh responders were CR, with a median duration of response of 28.1 months
- Transfusion independence was achieved in all subgroups
- REZLIDHIA has a well characterized safety profile with no cardiac events leading to discontinuation

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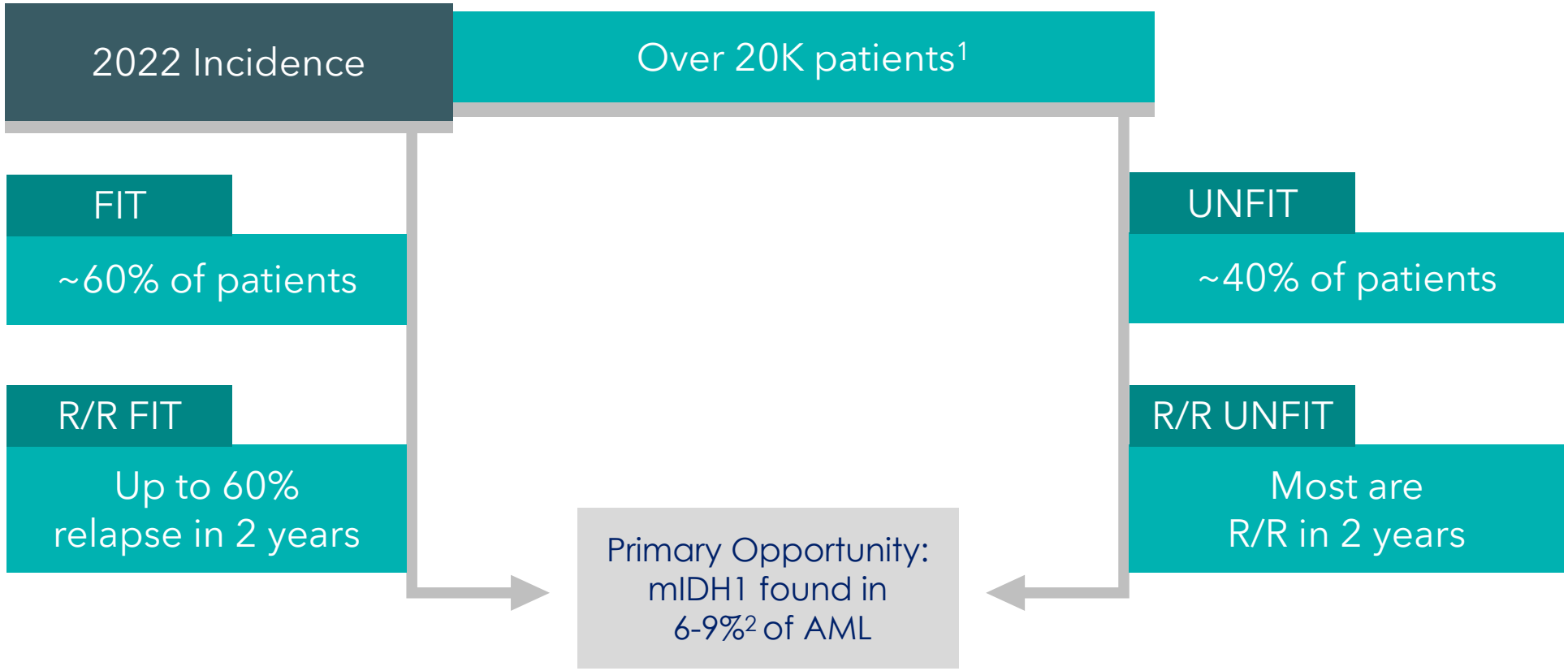
A Clinical Perspective

JORGE E. CORTES, M.D.

Director, Georgia Cancer Center at the University of Augusta, Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer and Phase 2 Trial Investigator

Expanding our Commercial Hem/Onc Portfolio with REZLIDHIA

mIDH1 R/R AML Market Overview



Near-term opportunity to impact the lives of ~1,000 IDH1 positive AML patients each year

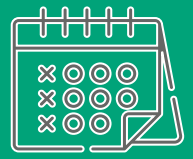
Rigel Market Research Q3, 2022. [1]American Cancer Society, Key Statistics for Acute Myeloid Leukemia (AML), 2022. [2]NCCN Clinical Practice Guidelines in Oncology, Acute Myeloid Leukemia. Version 2.2022 – June 14, 2022. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1411.

R/R AML Market Research

Stakeholders continue to perceive significant unmet needs in IDH1+ R/R AML

HCPs continue to perceive a significant unmet need in AML, particularly in the R/R setting, for

efficacious targeted treatments



Patients continue to fear relapse, and would benefit from the peace of mind associated with therapies with

longer duration of response

HCPs and patients both continue to seek R/R AML therapies with a better

balance of efficacy and toxicity

Rigel Market Research
No head-to-head data comparing REZLIDHIA and other IDH1+ R/R AML therapies has been generated

REZLIDHIA Potential

REZLIDHIA™ (olutasidenib) 150 mg capsules

- ✓ Promising new treatment for R/R AML
- ✓ Targeted treatment across all IDH1 mutation subtypes
- ✓ Potential benefit in appropriate patients who have failed other therapies

- ✓ CR+CRh in 35% of patients (32% CR)
- ✓ DoR of 25.9 months in this patient group (28.1 months in CR patients)
- ✓ Positions REZLIDHIA favorably compared to other treatment options

- ✓ Strong efficacy across R/R setting
- ✓ Well characterized safety profile
- ✓ No requirement for cardiac monitoring

REZLIDHIA has the potential to address many patient and HCP needs

Please see Slides 22 & 23 for Important Safety Information. Please visit www.REZLIDHIA.com for Full prescribing information, including Boxed WARNING.

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Executing Commercial Launch – Key Priorities

Drive Awareness

Maximize Access

Optimize Experience

Sales | Marketing | Medical | Market Access

Leveraging Our Existing Commercial Infrastructure

REZLIDHIA™ (olutasidenib) 150 mg capsules

Tavalisse® (fostamatinib disodium hexahydrate) tablets

- **Two approved drugs** in hem/onc portfolio
- **Already calling on the majority of hematologists/oncologists in the U.S.**
- **Heme-onc tenured field team** covering 54 territories
- **Strategically experienced** business operations and marketing team
- **Customer focused Market Access team** that has the expertise to:
  - **Efficiently distribute** REZLIDHIA and TAVALISSE
  - Ensure patients have access to **coverage, reimbursement, and assistance**

64th Annual ASH Meeting and Exposition

American Society of Hematology
New Orleans, LA - Dec 10-13, 2022

- Important opportunity to increase awareness of Rigel and the Rigel pipeline, including TAVALISSE (fostamatinib) and REZLIDHIA (olutasidenib)
- First meeting to have multiple presentations on two heme/onc therapies
- Numerous customer engagements planned

Growing our Heme/Onc Business

REZLIDHIA™ (olutasidenib) 150 mg capsules

Commercial Launch of REZLIDHIA: Two approved products in hematology-oncology portfolio

REZLIDHIA highly complementary to our existing commercial infrastructure

REZLIDHIA international regulatory filings: Rigel retains the right to ex-US sub-licenses and is evaluating potential regulatory strategies ex-U.S.

Next Steps for REZLIDHIA: helping patients gain access in the U.S., bringing a potentially market-leading mIDH1 inhibitor to patients with R/R AML

Tavalisse® (fostamatinib disodium hexahydrate) tablets

Grow TAVALISSE Sales in ITP

Second approved product has the potential to broaden the reach of sales force by bringing two promising therapies to customer attention

Advance Key Development Programs

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Our sincere thanks to employees, patients, caregivers, investigators and our partner, Forma Therapeutics (a Novo Nordisk company)

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Q&A

Raul Rodriguez

President & Chief Executive Officer

Wolfgang Dummer, M.D., Ph.D.

Executive Vice President & Chief Medical Officer

Dave Santos

Executive Vice President & Chief Commercial Officer

Dean Schorno

Executive Vice President & Chief Financial Officer

Jorge E. Cortes, M.D.

Director, Georgia Cancer Center at the University of Augusta Cecil F. Whitaker Jr., GRA Eminent Scholar Chair in Cancer

About REZLIDHIA™ (olutasidenib)

INDICATION

REZLIDHIA is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible 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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hepatotoxicity

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.

Please see REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING