

Q2 2024 Financial Results Presentation

August 6, 2024



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, expected commercial and financial results; Rigel's ability to earn and receive milestone payments; expectations related to the potential and market opportunity of REZLIDHIA® (olutasidenib) as therapeutics for relapsed or refractory acute myeloid leukemia (AML) and other conditions; the potential and market opportunity for GAVRETO® (pralsetinib) for the treatment of non-small cell lung cancer and advanced thyroid cancer; the regulatory approval and commercialization of fostamatinib or olutasidenib or pralsetinib 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 and collaboration/alliance efforts, including the progress of the Phase 1b clinical trial of R289 for the treatment of lower-risk myeloid dysplastic syndrome (MDS), the advancement of the Phase 2a clinical trial of R552 for the treatment of rheumatoid arthritis, and the development of olutasidenib as a therapy for a broad range of mIDH1+ cancers, including but not limited to AML, MDS, and glioma, and Rigel's partnering efforts and ability to achieve regulatory and commercial milestones and earn and receive milestone payments.

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. 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 Rigel's 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 or pralsetinib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib, olutasidenib or pralsetinib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib, olutasidenib or pralsetinib may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop, manufacture and commercialize Rigel's 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 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



Rigel Participants



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Executive Vice President & Chief Financial Officer







GAVRETO is the only once daily, oral, RET inhibitor approved for patients with metastatic NSCLC or thyroid cancer* with RET gene fusions

*Thyroid indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

RET, rearranged during transfection; NSCLC, non-small cell lung cancer. Please see Important Safety Information on slides 36 & 37. Please visit www.GAVRETO.com for Full Prescribing Information.



Growing Our Hematology and Oncology Business

Commercial Execution















RET fusion-positive NSCLC or TC

Development & Expansion

Development Programs¹

- Evaluate REZLIDHIA in a broad range of IDH1mutant cancers including AML, MDS and glioma
- Complete enrollment of R289, IRAK1/4 inhibitor, Phase 1b trial in lower-risk MDS

In-Licensing and Product Acquisition

 Identify new late-stage assets which leverage current capabilities and capacity

Financial Discipline





Commercial Portfolio



US Net Product Sales Growth





rigel



Grow Sales of TAVALISSE in ITP





Kinase inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (cITP) who have had an insufficient response to a previous treatment.

Select Important Safety Information

Adverse Reactions:

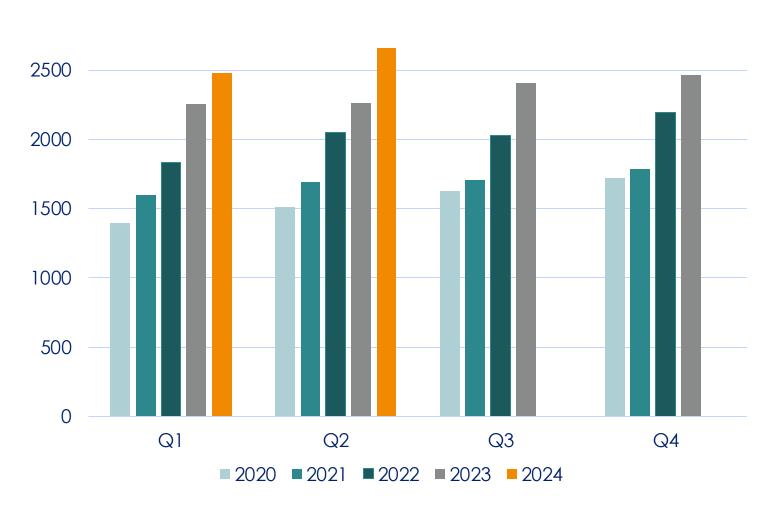
- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest 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.



TAVALISSE Q2 2024 Performance



Bottles Shipped to Patients and Clinics



\$26.4M Q2 2024 Net Product Sales

24% Growth vs. Q1 2024

25% Growth vs. Q2 2023

2,672 Bottles Shipped to Patients and Clinics in Q2 2024

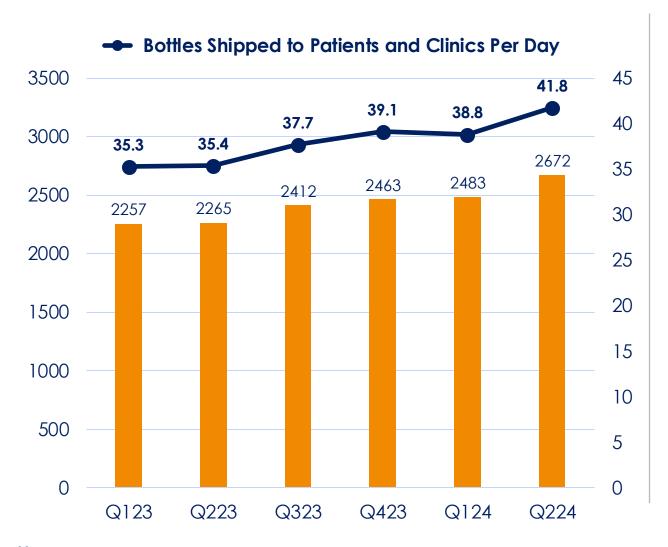
8% Growth vs. Q1 2024

18% Growth vs. Q2 2023



TAVALISSE Q2 2024 Sales Growth





Sales Growth Accelerated in Q2

- Growth of 3 bottles shipped per day over Q1 is the largest increase in 2 years
- Bottles shipped per day consistently increased throughout each month of Q2
- Continuous flow of new patient starts and carryover from refills driving stronger growth in 2024





Grow Sales of REZLIDHIA in mIDH1 R/R AML





APPROVED AND AVAILABLE IN THE U.S.

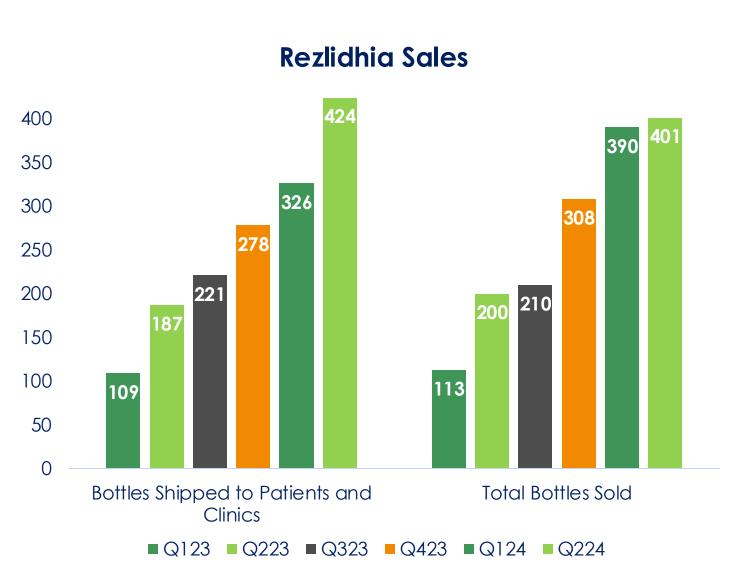
REZLIDHIA is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.

Please see Important Safety Information on slides 34 & 35, including Boxed WARNING regarding differentiation syndrome



REZLIDHIA Q2 2024 Performance





424 Bottles Shipped to Patients and Clinics in Q2 2024

30% vs. Q1 2024 127% vs. Q2 2023

\$5.2M Q2 2024 Net Product Sales

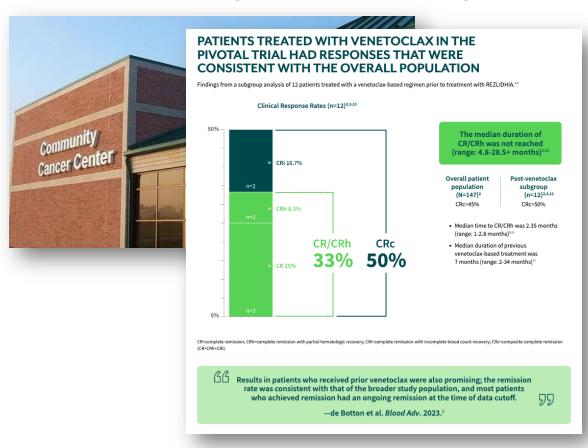
5% vs. Q1 2024 102% vs. Q2 2023



REZLIDHIA Q2 2024 Sales Growth



Growing Community Usage



Q2 2024 Growth Drivers

- Community volume represented nearly 25% of sales in Q2, representing strong growth vs. Q1
- Awareness and support continues to grow, as more clinicians are finding the post-venetoclax data clinically relevant
- Significant opportunity remains to improve adoption in relapsed/refractory mIDH1 AML





GAVRETO Transition Update





APPROVED IN THE U.S.

GAVRETO is indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer as detected by an FDA-approved test, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*

Please see Important Safety Information on slides 36 & 37



GAVRETO Transition Plan Implementation







Patient Services

- www.RigelONECARE.com and www.GAVRETOcopay.com active within 2 hours of the June 24, 2024 NDA transfer
- RigelONECARE successfully transferred majority of Patient Assistance Program and Copay Program patients

Customer Support

- www.GAVRETO.com and www.GAVRETO-hcp.com active within 2 hours of the NDA transfer
- Patient information, dosing and administration, distribution information, and copay assistance materials deployed to the field for implementation on the day of NDA transfer

Field Team Activation

- Field team trained and ready to deliver the GAVRETO availability message on the day of NDA transfer
- Prioritized list of Key Accounts and prescribers contacted within the first week of availability
- Identified additional patients and prescribers



GAVRETO Stocked and Now Shipping





Smooth Transition Under Way

- 3PL shipments to distributors began on June 27th
- Product stocked in Rigel distribution network on June 28th, ahead of July 1st target
- Distribution network began shipping GAVRETO bottles to patients and clinics on July 1st



GAVRETO Q2 2024 Sales





GAVRETO is available in 2 bottle sizes

- 60 count bottle
- 90 count bottle (1.5x 60 count bottle)
- Will report 60 count equivalent bottles

228 60 ct. eq. bottles sold in Q2

(initial stocking of Rigel distribution network)

\$1.9M

Q2 2024 Net Product Sales





Clinical Development Program Update



Hematology and Oncology Pipeline Expansion

Development Opportunities¹

Olutasidenib

 Broad range of IDH1-mutant cancers including AML, MDS and glioma

R289 IRAK1/4 Inhibitor

Lower-risk MDS (LR-MDS)

Fostamatinib

Investigator sponsored trials

Leverage Heme/Onc Capabilities

In-Licensing & Product Acquisition

- Differentiated asset(s) in hematology, oncology or related areas
- Late-stage programs
- Synergistic to current in-house capabilities and capacity



Strategic Alliance with MD Anderson Cancer Center to Advance Olutasidenib in AML and Other Cancers¹

 Rigel and The University of Texas MD Anderson Cancer Center will evaluate olutasidenib in combination with other agents to treat newly-diagnosed and relapsed/refractory patients with IDH1-mutated:



- Higher-risk MDS and advanced MPN
- The collaboration will also support the evaluation of olutasidenib as:
 - Monotherapy in IDH1-mutated CCUS & lower-risk MDS
 - Post-transplant maintenance therapy for IDH1-mutated hematologic malignancies

Rigel will provide \$15 million in time-based milestone payments and study material over the 5-year collaboration



Olutasidenib: Phase 1b/2 Triplet Therapy Trial in IDH1-mutated AML

Phase 1b/2 open-label, non-randomized clinical trial to evaluate the safety and efficacy of decitabine and venetoclax in combination with olutasidenib for mIDH1 AML (n=78)¹

Phase 1b: R/R mIDH1 AML/HR-MDS

Up to 3 dose levels (6 patients per dose level) will be evaluated with:

- Decitabine or decitabine/cedazuridine at approved doses, days 1-5
- Venetoclax 400-600 mg daily, days 1-14
- Olutasidenib 150 mg twice daily from C1D8

Key Objectives:

- Safety, tolerability and RP2D of IV/oral decitabine + venetoclax + olutasidenib
- PK

Phase 2: ND and R/R mIDH1 AML/HR-MDS

Arm A: Newly-diagnosed AML* (n=30)

* Patients not eligible for intensive chemotherapy

Arm B:
R/R AML, HR-MDS
(n=30)

RP2D

Key Objectives:

- Complete and composite remission rate (CR, CRh, CRi) and ORR
- Duration of response, EFS, OS
- MRD negativity



IDH1, isocitrate dehydrogenase-1; AML, acute myeloid leukemia: mIDH1, mutated IDH1; R/R, relapsed/refractory; HR-MDS, higher-risk myelodysplastic syndrome; RP2D, recommended Phase 2 dose; PK, pharmacokinetics; ND, newly-diagnosed; CR, complete response; CRh, CR with partial hematologic recovery; CRi, CR with incomplete recovery; ORR, overall response rate; EFS, event-free survival; OS, overall survival: MRD, minimal residual disease.

Collaboration with CONNECT to Advance Olutasidenib in Glioma¹

- Gliomas account for 29-35% of CNS tumors in children, adolescents and young adults; approximately 1/3 are high grade gliomas (HGG) (800-1000 new cases/year in US)²
- IDH1 mutations are found in up to 36% of HGGs in adolescents and young adults^{3,4,5}
- Safety and preliminary activity of single-agent olutasidenib in adult patients with relapsed/refractory high grade *IDH1*-mutant gliomas were recently reported⁶
- Olutasidenib will be included in CONNECT's TarGeT-D trial, a molecularly-guided Phase 2 umbrella clinical trial for HGG
- The Rigel-sponsored arm will evaluate a post-radiotherapy maintenance regimen of olutasidenib¹ in combination with temozolomide, followed by olutasidenib monotherapy, in newly-diagnosed adolescent and young adult patients (≤39 years) with IDH1 mutation positive HGG

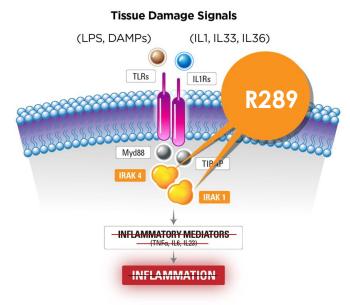
Rigel will provide funding up to \$3 million and study material over the 4-year collaboration



Targeting Inflammatory Pathways in MDS with R289, a Dual IRAK 1/4 Inhibitor¹

Dysregulation of immune/inflammatory signaling is associated with MDS

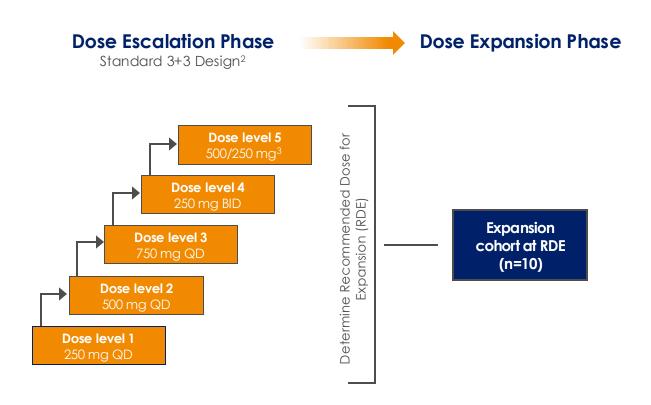
- Treatment options are limited for LR-MDS patients, especially for those with recurrent disease or who are refractory to prior lines of therapy
- IRAK 1 and 4 are key for downstream signaling of the IL-1R family and most TLRs, leading to a proinflammatory marrow environment and persistent cytopenias in patients with LR-MDS²
- Dual inhibition of IRAK1 & IRAK4 showed greater suppression of inflammatory cytokines vs an IRAK4-selective inhibitor in vitro³
- R835, a selective dual inhibitor of IRAK 1/4, markedly suppressed LPS induced cytokine release vs placebo in healthy volunteers⁴
- R289, an oral prodrug that is rapidly converted to R835 in the gut, is now being evaluated in a Phase 1b study in LR-MDS





R289¹: Phase 1b Trial in Relapsed/Refractory Lower-Risk MDS

Open-label, multicenter trial to evaluate the safety, tolerability, PK and preliminary activity of R289 in patients with LR-MDS (NCT05308264)



Primary Endpoints:

- Incidence of adverse events
- Incidence of dose-limiting toxicities

Secondary Endpoints:

- Transfusion independence
- Response rates
- Hematologic improvement
- PK
- PD

Preliminary data expected by end of 2024



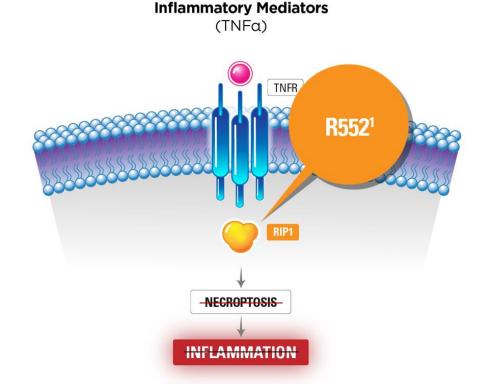
RIPK1 Inhibitor Programs in Immune and CNS Diseases with Partner Lilly

Immune Diseases

- R552, a potent and selective RIPK1 inhibitor, completed a Phase 1 study which demonstrated potential best-in-class status compared to competition
- Lilly initiated a Phase 2a clinical trial studying ocadusertib (previously R552 and LY3871801) in adult patients with moderately to severely active rheumatoid arthritis (RA)

CNS Diseases

- Selection of RIPK1 inhibitor candidates that cross the blood-brain barrier for CNS diseases is underway
- Lilly would lead clinical development of brain-penetrating RIPK1 inhibitors in CNS diseases





RIPK1 inhibitors play key role in TNF signaling and induction of pro-inflammatory necroptosis, which could support broad potential in RA, psoriasis and IBD, and with their experience, Lilly is the ideal partner.





Financials



Q2 2024 Financial Highlights

Q2 2024 Net Product Sales:

• TAVALISSE: \$26.4M

• REZLIDHIA: \$5.2M

• GAVRETO: \$1.9M

Q2 2024 Total Bottles Shipped:

• TAVALISSE: 2,722

• REZLIDHIA: 401

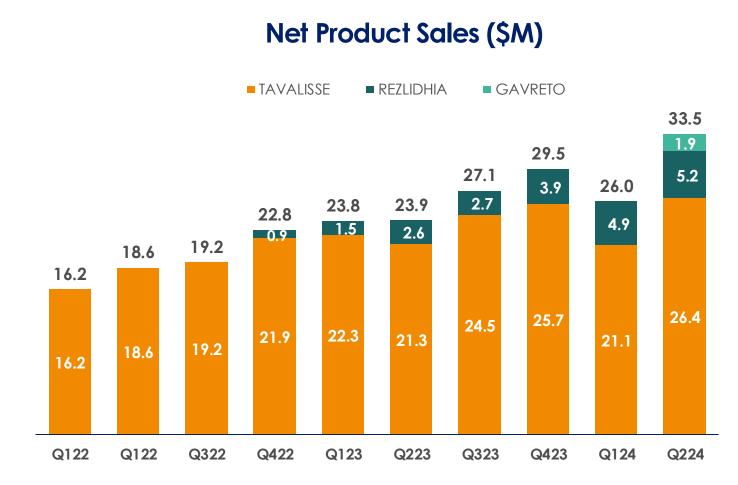
• GAVRETO1: 228

Q2 2024 Bottles Shipped to Patients and Clinics²:

• TAVALISSE: 2,672

• REZLIDHIA: 424

GAVRETO¹: n/a





Q2 2024 Financial Results

(In thousands, except for per share amounts)

		Three Months Ended June 30,			
	-	2024		2023	
Revenues				_	
Net Product Sales	\$	33,450	\$	23,881	
Contract revenues from collaborations		3,391		2,005	
Government contract		-		1,000	
Total revenues		36,841		26,886	
Costs and expenses:					
Cost of product sales		2,807		1,075	
Research and development		5,540		4,772	
Selling, general and administrative		28,047		26,306	
Total costs and expenses		36,394		32,153	
Income (loss) from operations		447		(5,267)	
Interest income		552		529	
Interest expense		(2,029)		(1,862)	
Net loss	\$	(1,030)	\$	(6,600)	
Net loss per share, basic and diluted ¹	\$	(0.06)	\$	(0.38)	
Weighted average shares used in computing net loss per share, basic and diluted ¹		17,549		17,356	
Dadio alla allotoa					

Q2 2024 Highlights

- Contract revenues from collaborations of \$3.4M included:
 - Kissei \$2.2M
 - Grifols \$1.1M
 - Medison \$0.1M
- Cash, cash equivalents and shortterm investments as of June 30, 2024 totaled \$49.1 million, compared to \$49.6 million as of March 31, 2024, and \$56.9 million as of December 31, 2023



2024 Value Drivers









Grow Product Sales for TAVALISSE, REZLIDHIA and GAVRETO

- Continue to broaden product awareness and adoption
- Identify ex-US collaboration(s) for olutasidenib

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Identify In-License and Product Acquisition Opportunities

Pursue late-stage assets which leverage current capabilities & capacity

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Advance Development Programs¹

- Enroll and generate preliminary data for R289 Phase 1b study in lower-risk MDS
- Initiate clinical trials for olutasidenib in AML, MDS, glioma and other opportunities
- Evaluate additional clinical development opportunities for olutasidenib and R289



Continue Financial Discipline



TAVALISSE® (fostamatinib disodium hexahydrate) Tablets

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 https://www.tavalisse.com/ for full Prescribing Information

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



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., dexamet hasone 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 (Cont.)

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, alan ine 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.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



Please see https://www.REZLIDHIA.com/ for full Prescribing Information, including Boxed WARNING.



About GAVRETO® (pralsetinib)

INDICATIONS

GAVRETO (pralsetinib) is indicated for the treatment of:

- Adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA-approved test
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*

*This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

- Interstitial Lung Disease (ILD)/Pneumonitis: Severe, life-threatening, and fatal ILD/pneumonitis can occur in patients treated with GAVRETO. Pneumonitis occurred in 12% of patients who received GAVRETO, including 3.3% with Grade 3-4, and 0.2% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.
- Hypertension: Occurred in 35% of patients, including Grade 3 hypertension in 18% of patients. Overall, 8% had their dose interrupted and 4.8% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.
- **Hepatotoxicity:** Serious hepatic adverse reactions occurred in 1.5% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 49% of patients, including Grade 3 or 4 in 7% and increased alanine aminotransferase (ALT) occurred in 37% of patients, including Grade 3 or 4 in 4.8%. The median time to first onset for increased AST was 15 days (range: 5 days to 2.5 years) and increased ALT was 24 days (range: 7 days to 3.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.
- **Hemorrhagic Events:** Serious, including fatal, hemorrhagic events can occur with GAVRETO. Grade ≥3 events occurred in 4.1% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.
- Tumor Lysis Syndrome (TLS): Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

IMPORTANT SAFETY INFORMATION (Cont.)

- Risk of Impaired Wound Healing: Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.
- Embryo-Fetal Toxicity: Based on findings from animal studies and its mechanism of action, GAVRETO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the last dose.
- Common adverse reactions (≥25%) were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia, and cough. Common Grade 3/4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased leukocytes, decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased calcium (corrected), decreased platelets, increased alkaline phosphatase, increased potassium, decreased potassium, and increased bilirubin.
- Avoid coadministration of GAVRETO with strong or moderate CYP3A inhibitors, P-gp inhibitors, or combined P-gp and strong or moderate CYP3A inhibitors. If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with strong or moderate CYP3A inducers. If coadministration cannot be avoided, increase the GAVRETO dose.
- Lactation: Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the last dose.
- Pediatric Use: Monitor open growth plates in adolescent patients. Consider interrupting or discontinuing GAVRETO if abnormalities occur.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



Please see https://www.GAVRETO.com/ for full Prescribing Information.





Thank You

www.rigel.com

