Corporate Presentation

January 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 for the fourth quarter and fiscal year ended December 31, 2023; 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 TAVALISSE® (fostamatinib) as therapeutics for chronic ITP and other conditions; the regulatory approval and commercialization of fostamatinib or olutasidenib in the U.S. and international markets; and Rigel's ability to further develop its clinical stage and early-stage product candidates and Rigel's partnering 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 or olutasidenib; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding fostamatinib or olutasidenib; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that fostamatinib or olutasidenib may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop, 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 and subsequent filings. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. Rigel does not undertake any obligation to update forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise, and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein, except as required by law.

Growing Our Business: Hematology/Oncology Focus

Commercial Execution

TAVALISSE® in ITP

Tavalisse® (fostamatinib disodium hexahydrate) tablets

REZLIDHIA® in R/R AML

REZLIDHIA® (olutasidenib) 150 mg capsules

Development & Expansion

Development Programs[1]

- Evaluate REZLIDHIA in a broad range of IDH1-mutant cancers including AML, MDS and glioma
- R289 IRAK1/4 inhibitor Phase 1b trial in lower-risk MDS

In-license Opportunities

- New late-stage assets which leverage current capabilities and capacity

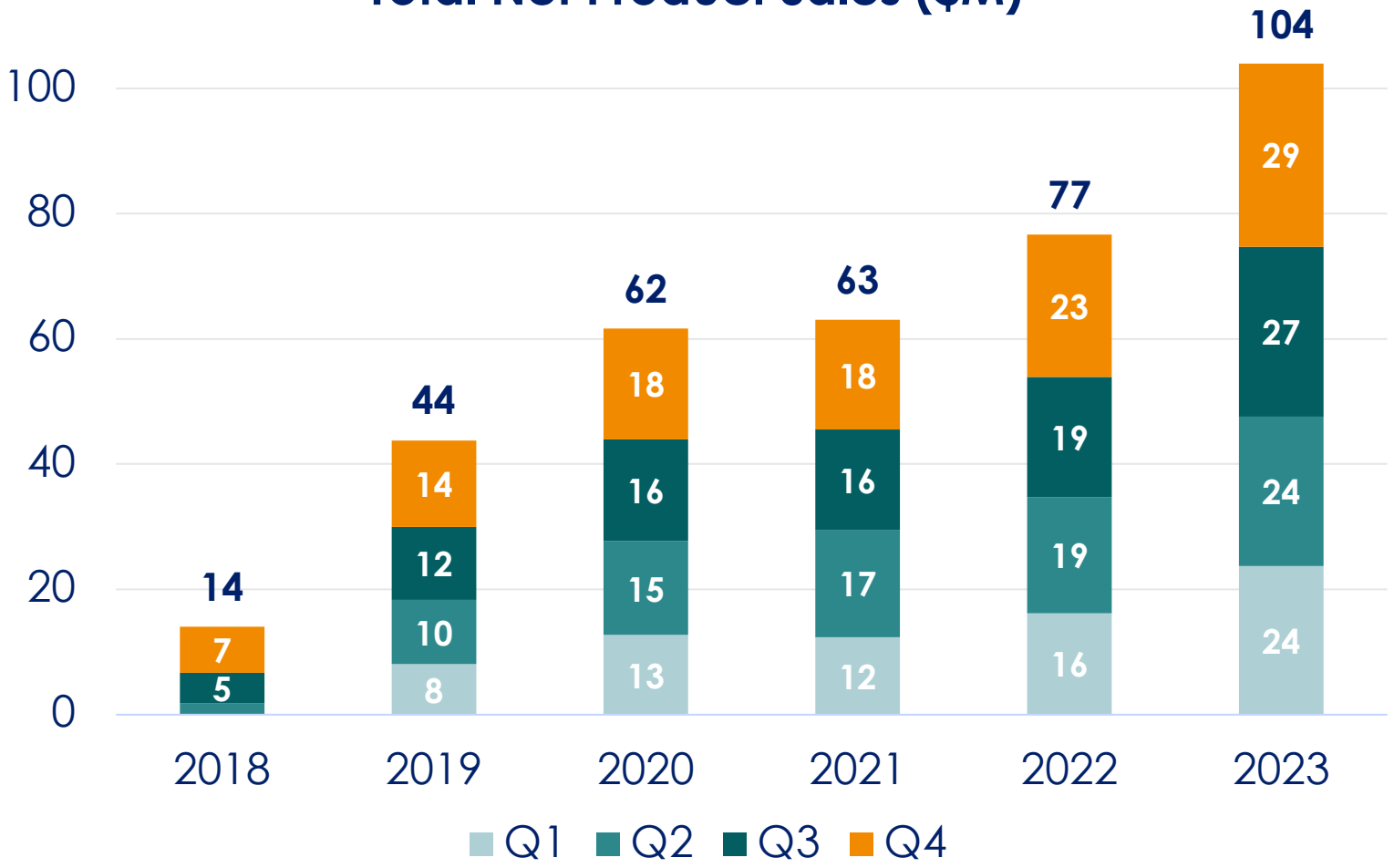
Partnered Programs

- RIPK1 inhibitor program in immune and CNS diseases with partner Eli Lilly

1. investigational compounds in these indications and not approved by the FDA. Please see Important Safety Information on slides 37-39. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

Growing Annual Sales of TAVALISSE and REZLIDHIA

Total Net Product Sales ($M)



2023 Highlights

- Generated $104M in full-year net product sales
  - 36% ($28M) growth vs. 2022
- TAVALISSE generated $93.7M
  - 24% ($18M) growth vs. 2022
- REZLIDHIA generated $10.6M
  - 45% growth in Q4 vs. Q3

Grow Sales of TAVALISSE in ITP

Tavalisse®

(fostamatinib disodium hexahydrate) tablets

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.

Please see Important Safety Information on slide 37. Please visit www.TAVALISSE.com for Full Prescribing Information.

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Creating Opportunities to Gain Market Share

Tavalisse® (fostamatinib disodium hexahydrate) tablets

81,300 US Adult cITP Patients[1]

37,000
Watchful Waiting

20,000
1st Line

11,400
2nd Line

6,900
3rd Line

3,500
4th Line

2,500
5L+

~75% of Post-Steroid Market

44,300 Patients Actively Treated[2]

- 24,300 patients are 2L or later

Patient Moving through Therapies Creates New Patient Opportunities

TAVALISSE is Now Preferred on Key Commercial National Formularies

- Significant National Commercial Coverage
- Reinforces TAVALISSE's proven efficacy and safety
- Strengthens Reimbursement Confidence
- Spreading awareness among customers through personal and non-personal channels

1. Symphony Health, PatientSource®, 10 years ending September 2019; **2.** Internal market research conducted in October 2020. Please see Important Safety Information on slide 37. Please visit www.TAVALISSE.com for full prescribing information.

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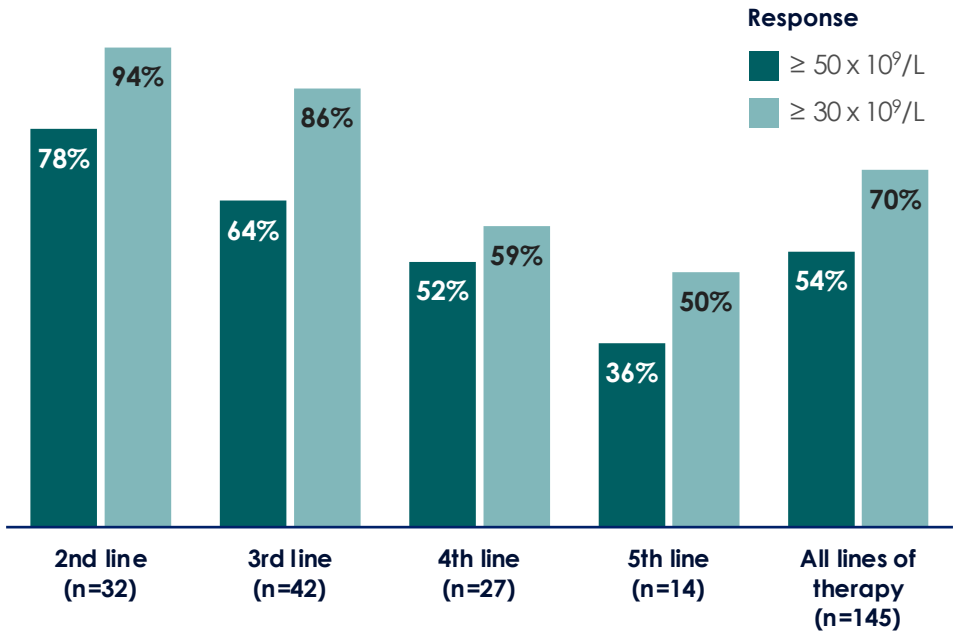
Promotion Efforts Highlight Data Supporting Use in Earlier Lines

Tavalisse® (fostamatinib disodium hexahydrate) tablets

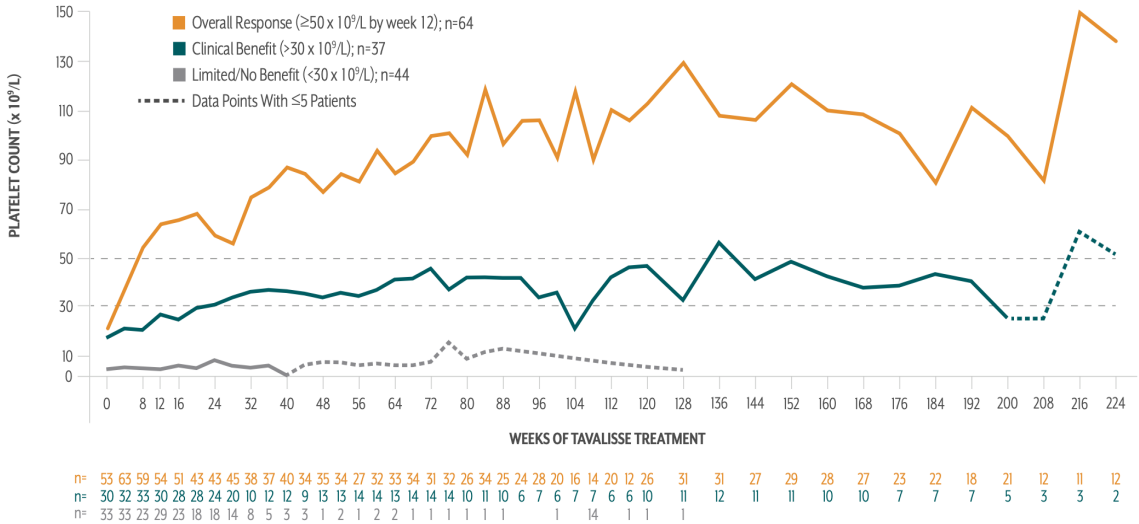
Post-hoc Data Analysis Demonstrated Use as 2nd-Line Therapy Resulted in Higher Response Rates[1,2]



Durable Efficacy was Observed in Responders to TAVALISSE in the FIT Studies

(combined results from FIT-1, FIT-2, and FIT-3)[3]

Median Platelet Counts Over Time



1. Fostamatinib is an effective 2nd-line therapy in patients with immune thrombocytopenia, British Journal of Haematology. **2.** Percentage of Patients Achieving Target Platelet Counts at Any Visit. **3.** Assessment of thrombotic risk during long-term treatment of immune thrombocytopenia with fostamatinib, Therapeutic Advances in Hematology, 4/30/21. Please see Important Safety Information on slide 37. Please visit www.TAVALISSE.com for Full Prescribing Information.

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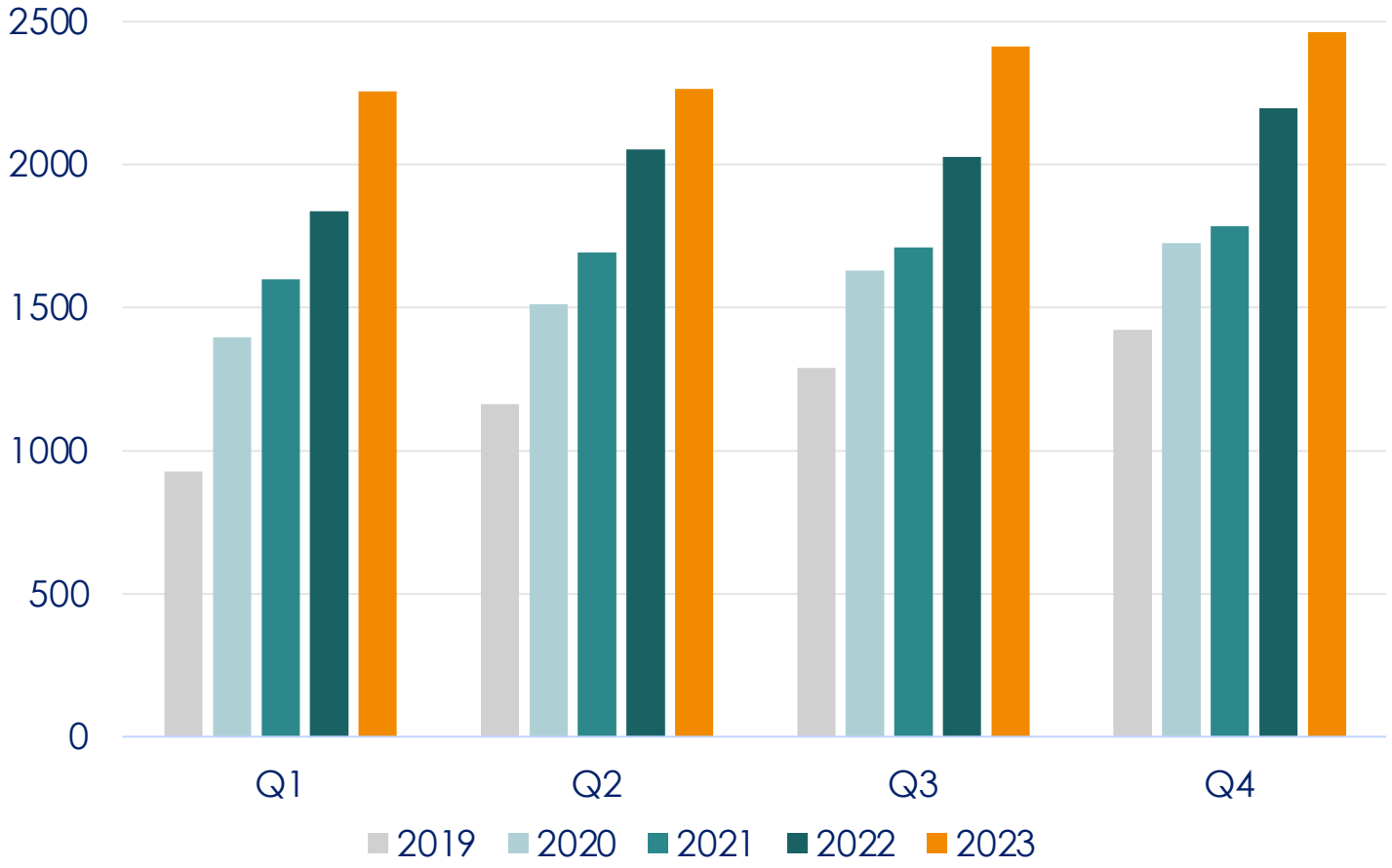
TAVALISSE Q4 2023 Performance

Tavalisse® (fostamatinib disodium hexahydrate) tablets

Bottles Shipped to Patients and Clinics



2,463 Bottles Shipped to Patients and Clinics in Q4 2023

12% Growth Versus Q4 2022

$25.7M Q4 2023 Net Product Sales

Sales grew $3.8M (17%) vs Q4 2022

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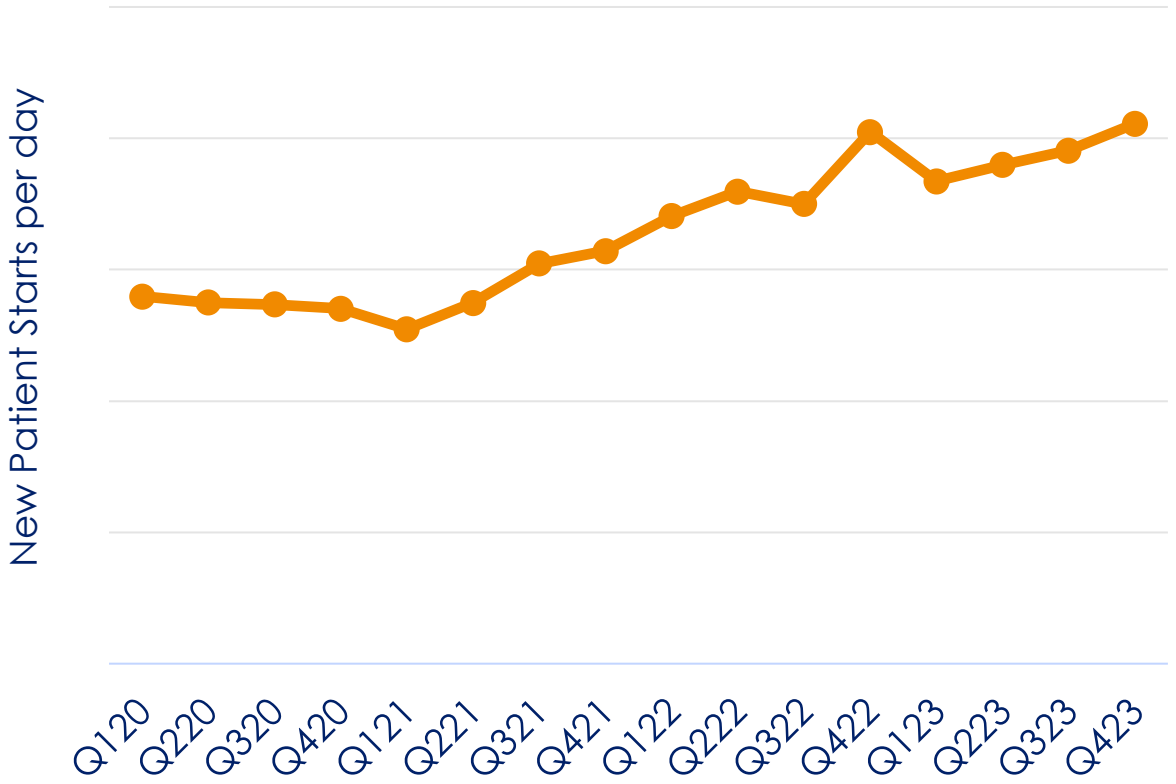
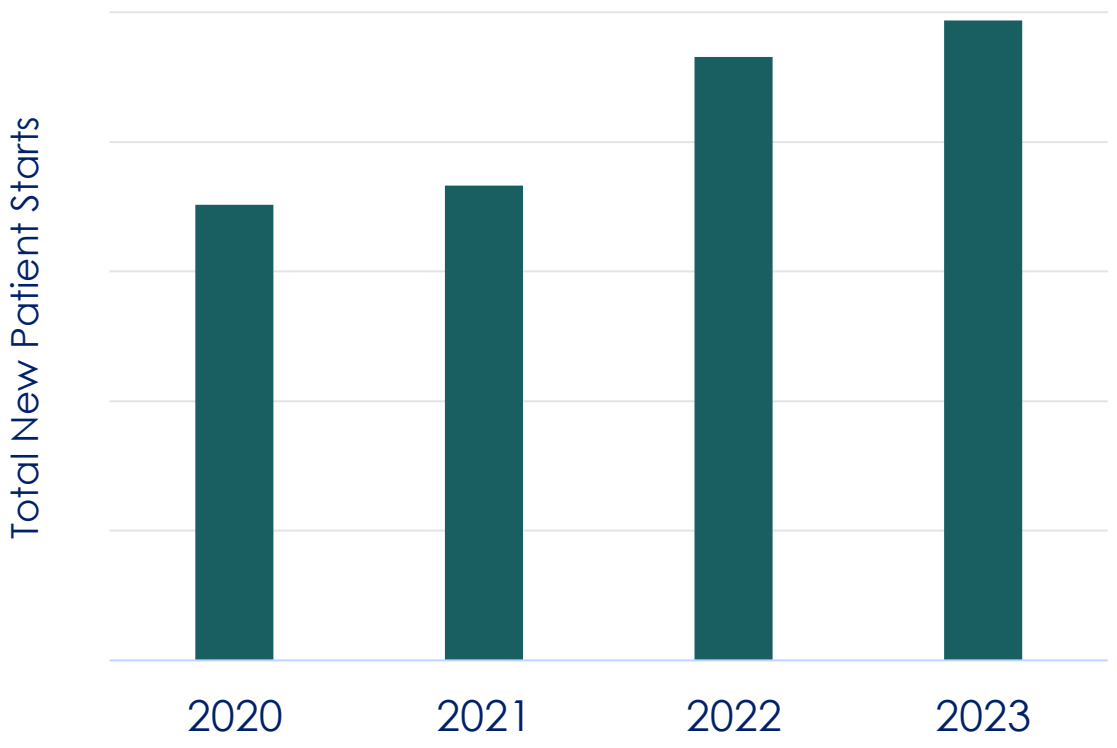
New Patient Starts Drove Growth in 2023

Tavalisse® (fostamatinib disodium hexahydrate) tablets

Consistent Quarterly Progress since Q2 2021



12% Compounded Annual Growth Rate (CAGR)



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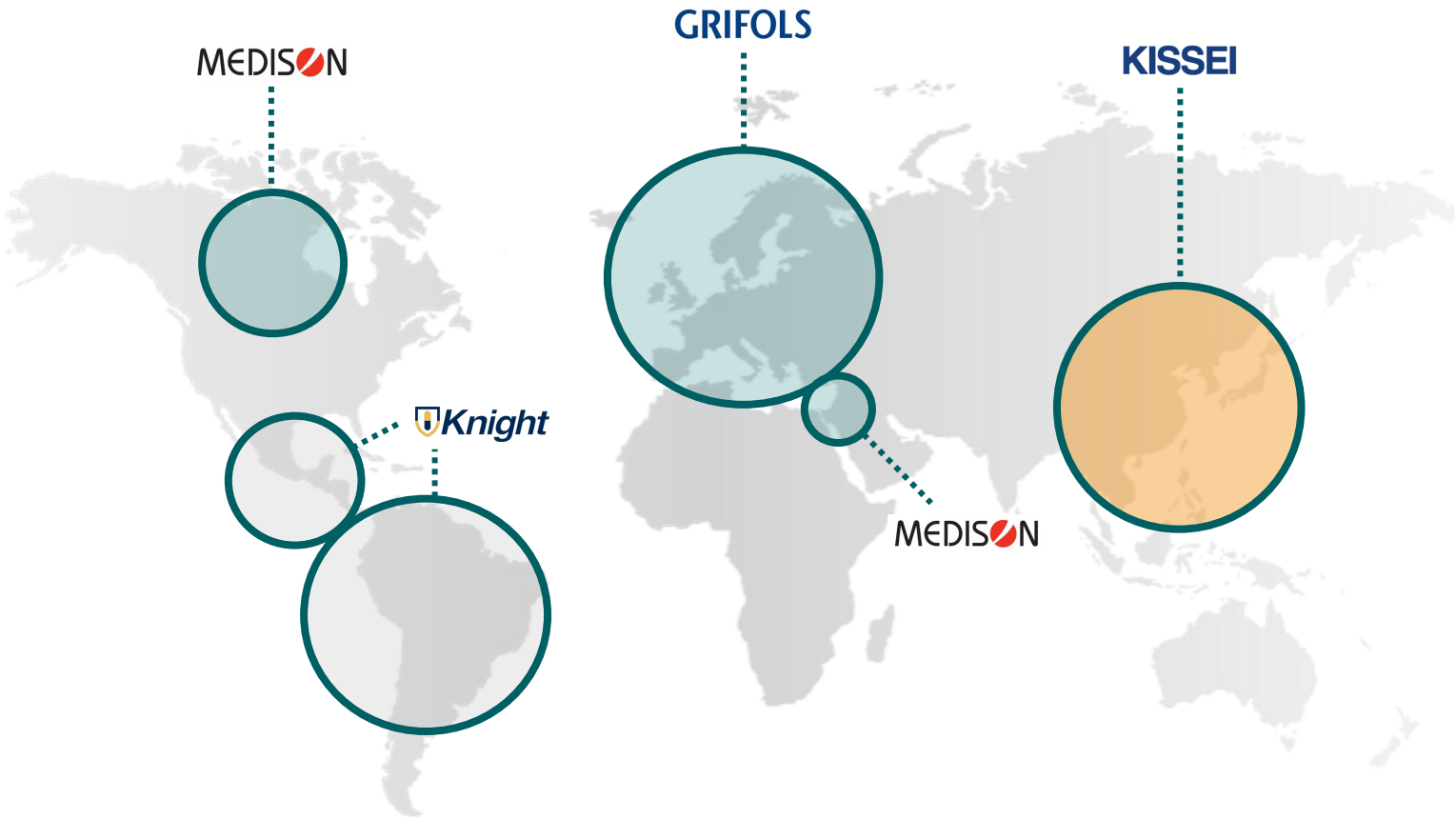
Expanding Access in Global Markets

Tavalisse® (fostamatinib disodium hexahydrate) tablets



Recent Progress

- In April 2023, Kissei launched TAVALISSE in Japan for the treatment of chronic ITP

- TAVALISSE is also commercially available in key European countries (TAVLESSE), Canada and Israel

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Expanding Our Commercial Heme/Onc Portfolio with REZLIDHIA

REZLIDHIA®

(olutasidenib) 150 mg capsules

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 38 & 39, including Boxed WARNING regarding differentiation syndrome

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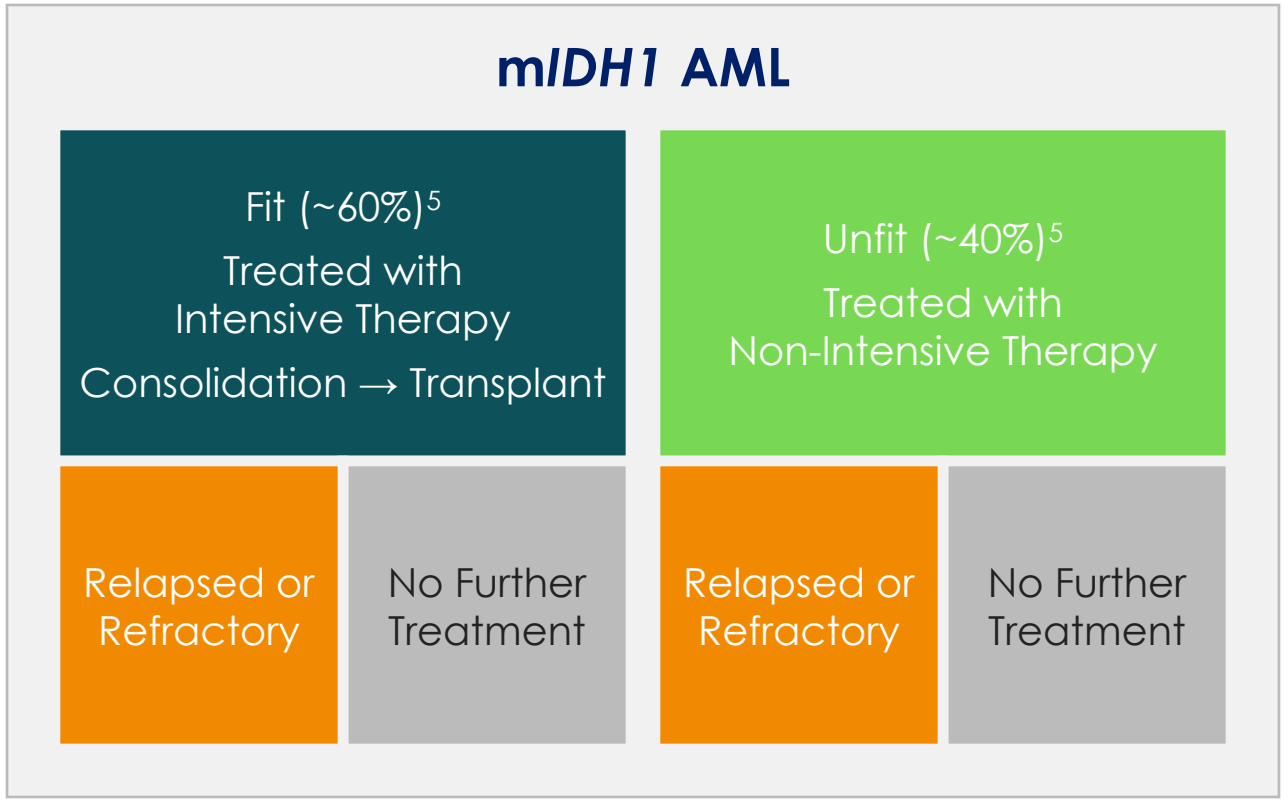
m*IDH1* Relapsed/Refractory AML Background

REZLIDHIA® (olutasidenib) 150 mg capsules

- 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 2023[2]
- IDH1 mutations are found in 6-9%[3,4] of AML
- m*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 m*IDH1* 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), 2023.
3. Abbas S et al. Acquired mutations in the genes encoding IDH1 and IDH2 both are recurrent aberrations in acute myeloid leukemia: prevalence and prognostic value. *Blood* (2010) 116 (12): 2122-2126.
4. Chotirat S et al. Molecular alterations of isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) metabolic genes and additional genetic mutations in newly diagnosed acute myeloid leukemia patients. *J Hematol Oncol* 5, 5 (2012). **5.** Rigel HCP Quantitative Market Research, 2022 (Data on File).

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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: Summary

- 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

REZLIDHIA Potential

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

- CR/CRh of 35% (32% CR, 48% ORR)
- 25.9 months median duration of CR/CRh (28.1 months for CR)
- Estimated 18-month survival rate for CR/CRh of 78%

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

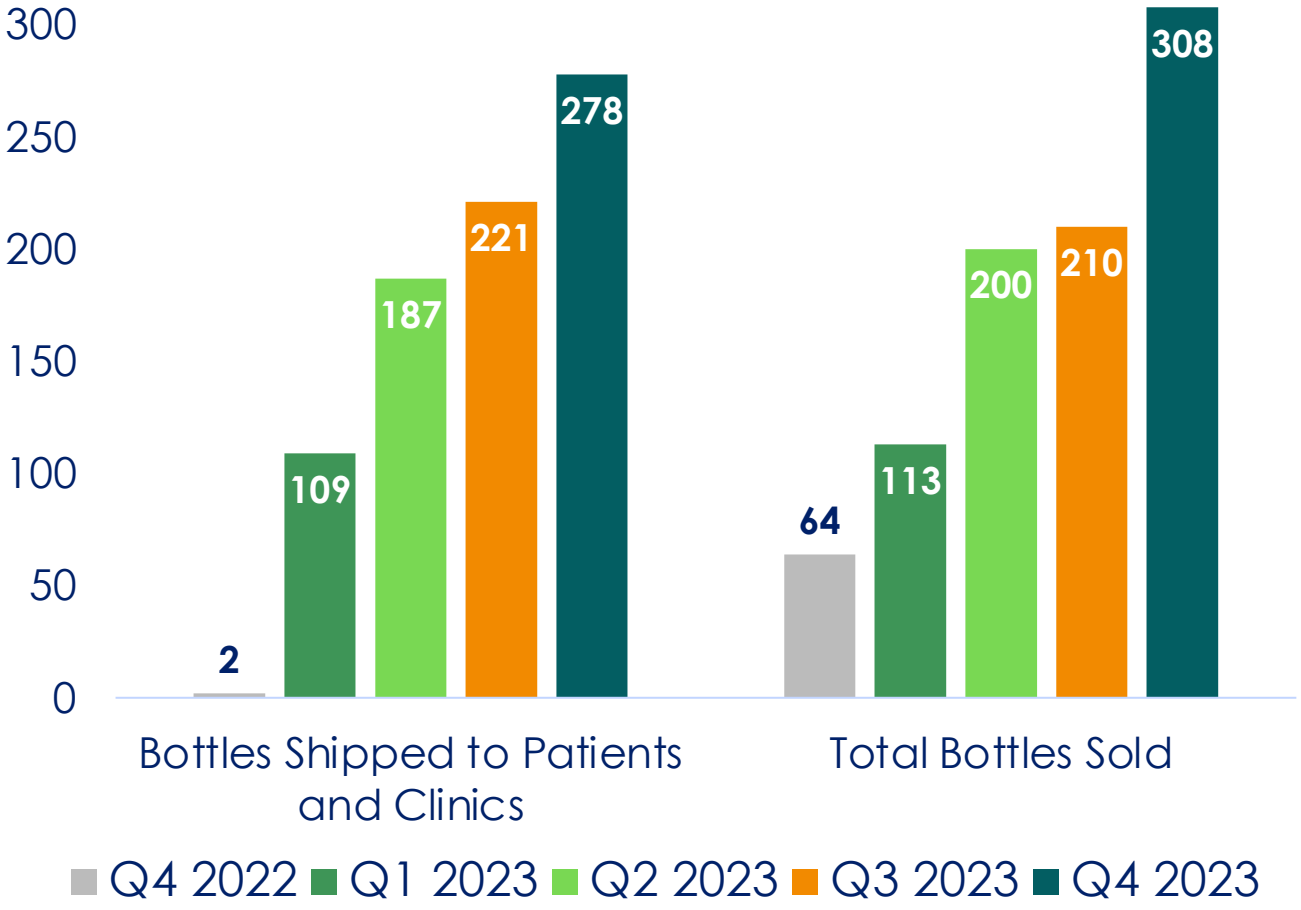
REZLIDHIA has the potential to address many patient and HCP needs

Please see Important Safety Information on slides 38 & 39. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

REZLIDHIA Q4 2023 Performance

REZLIDHIA® (olutasidenib) 150 mg capsules

Rezlidhia Launch-to-Date Sales



278 Bottles Shipped to Patients and Clinics in Q4 2023

▲ 26% vs. Q3 2023

$3.9M Q4 2023 Net Product Sales

▲ 45% vs. Q3 2023

$11.4M Launch Sales To-Date

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Driving Continued Growth

REZLIDHIA® (olutasidenib) 150 mg capsules

Promotional Activities

Institutional Team Fully Deployed:

- Leading REZLIDHIA promotional activities with top leukemia treaters and facilitating formulary placement at key AML accounts
- Continued progress with key institutions and leukemia treaters in Q4 2023, with numerous engagements at ASH

Other Key Activities:

- Speaker programs
- Leukemia and hematology conferences
- Increase REZLIDHIA awareness upon diagnosis
- Continue to maximize access for patients

Scientific Activities

Additional Phase 2 Publications

- Key m*IDH1* R/R patient populations (i.e. post Venetoclax)
- Other key populations from non-pivotal cohorts (i.e. MDS)

Supportive Data Generation

- Bolster available data in important, difficult-to-treat m*IDH1* R/R patient populations through Real World Evidence

Other Key Activities

- Providing relevant scientific information and education for HCPs
- Gathering insights from KOLs to better understand how to develop olutasidenib

Please see Important Safety Information on slides 38 & 39. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

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Development Programs Update

Hematology/Oncology Pipeline Expansion

Development Opportunities[1]

Olutasidenib

- Evaluate REZLIDHIA in a broad range of IDH1-mutant cancers including AML, MDS and glioma

IRAK1/4

- Evaluate in lower-risk MDS

Fostamatinib

- Evaluate heme/onc opportunities through investigator sponsored trials

Leverage Heme/Onc Capabilities

In-Licensing Criteria

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

1. Investigational compounds in these indications and not approved by the FDA

Strategic Alliance with MD Anderson to Advance REZLIDHIA (olutasidenib) in AML and Other Cancers[1]

- Rigel and The University of Texas MD Anderson Cancer Center will evaluate olutasidenib, in combination with other agents, to treat newly diagnosed and relapsed or refractory patients with:
  - AML
  - Higher-risk MDS and advanced MPN
- The collaboration will also support the evaluation of olutasidenib as:
  - Monotherapy in lower-risk MDS
  - Maintenance therapy in post-HSCT patients

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

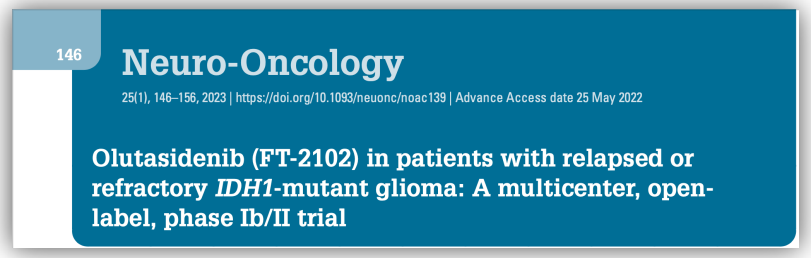
1. Investigational compound in these indications and not approved by the FDA. Please see Important Safety Information on slides 38 & 39. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

Potential Olutasidenib Opportunity in Glioma

High Unmet Need Remains in Glioma

- Gliomas are a heterogeneous group of primary brain tumors that are associated with diffuse brain infiltration and premature death.[1,2]
- Diffuse gliomas are the most common primary brain tumor in adults, affecting about 20,000 people in the US each year.[3]
- More than 70% of patients with grades II/III and approximately 5–7% of patients with grade IV harbor IDH1 mutations.[4,5]
- Standard of care for gliomas is best supportive care based on surgery, radiation, and chemo-therapies that are not very effective.
- There is a significant unmet need to improve survival.

Olutasidenib Activity in Enhancing Gliomas[6]



- 26 patients with R/R glioma received olutasidenib 150 mg orally BID
- No DLTs were observed in the single-agent glioma cohort
- Disease control rate (OR+ SD) was 48%.
  - 2 PR and 8 SD for at least 4 months.
  - Grade 3–4 adverse events (≥10%) included alanine aminotransferase increased (12%) and aspartate aminotransferase increased (12%)
- Olutasidenib was well tolerated, demonstrated preliminary evidence of clinical activity, and prolonged disease control in patients with predominantly enhancing gliomas with IDH1 mutation

1. van den Bent et al., Diffuse infiltrating oligodendroglioma and astrocytoma. J. Clin. Oncol. 2017;35:2394–2401. doi: 10.1200/JCO.2017.72.6737. 2. Wen et al. Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions. NeuroOncology. 2020;22:1073–1113. doi: 10.1093/neuonc/noaa106. 3. Lapointe et al.,Primary brain tumours in adults. Lancet. 2018 Aug 4;392(10145):432-446. doi: 10.1016/S0140-6736(18)30990-5. 4. Yan et al., IDH1 and IDH2 mutations in gliomas. N Engl J Med. 2009 Feb 19;360(8):765-73. doi: 10.1056/NEJMoa0808710. 5. Myung et al., IDH1 mutation of gliomas with long-term survival analysis. Oncol Rep. 2012 Nov;28(5):1639-44. doi: 10.3892/or.2012.1994. 6. de la Fuente et al., Olutasidenib (FT-2102) in patients with relapsed or refractory IDH1-mutant glioma: A multicenter, open-label, phase Ib/II trial. Neuro Oncol. 2023 Jan 5;25(1):146-156. doi: 10.1093/neuonc/noac139.

Pediatric/AYA Glioma Treatment Landscape

- Glioma account for 29-35% of the CNS tumors in pediatric, adolescents and young adult patients, with approximately 1/3 being high grade gliomas (HGG) (800-1000 new cases/year)[1]
- Overall IDH1 mutations are found in 6% of pediatric HGG and up to 36% of HGGs in adolescents and young adult[2,3,4]

1

Newly diagnosed high grade glioma

Treatment includes maximal safe surgical resection, standard radiation therapy and adjuvant temozolomide

2

Recurrent or progressive disease

Diffuse or multiple → systemic therapy or surgery for symptomatic large lesions
Local → resection → brain MRI → clinical trials or systemic therapy

X

Palliative/best supportive care

HGGs are a leading cause of cancer-related death in children and adolescents. Despite intensive multimodal therapy, prognosis for pediatric, adolescent, and young adult patients diagnosed each year in the US with HGG remain dismal, with 5-year overall survival (OS) <10%[5,6]

1. Epidemiology, diagnosis, and optimal management of glioma in adolescents and young adults, Tejan P. Diwanji et al, Adolesc Health Med Ther 2017; 8:99-113 2. Mackay A, et al. Integrated Molecular Meta-Analysis of 1,000 Pediatric High-Grade and Diffuse Intrinsic Pontine Glioma. Cancer Cell. 2017; 32(4):520-537.e525. 3. Korshunov A, et al. Integrated analysis of pediatric glioblastoma reveals a subset of biologically favorable tumors with associated molecular prognostic markers. Acta Neuropathol. 2015; 129(5):669-678. 4. Hartmann C, et al. Type and frequency of IDH1 and IDH2 mutations are related to astrocytic and oligodendroglial differentiation and age: a study of 1,010 diffuse gliomas. Acta Neuropathol. 2009; 118(4):469-474.5. Fangusaro J. Pediatric high grade glioma: a review and update on tumor clinical characteristics and biology. Front Oncol. 2012; 2:105. 6. Jones C, et al. Pediatric high-grade glioma: biologically and clinically in need of new thinking. Neuro Oncol. 2017; 19(2):153-161.

Collaboration with CONNECT to Conduct a Phase 2 Trial of Olutasidenib in Glioma[1]

- Olutasidenib will be included in CONNECT's TarGeT-D, a molecularly guided Phase 2 umbrella clinical trial for HGG
- Rigel and CONNECT will evaluate olutasidenib in newly diagnosed pediatric and young adult patients (<39 years) with high-grade glioma (HGG) harboring an IDH1 mutation
- The Rigel-sponsored arm will study post-radiotherapy administration of olutasidenib in combination with temozolomide followed by olutasidenib monotherapy as maintenance treatment

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

1. Investigational compound in this indication and not approved by the FDA. 2. de la Fuente M, et al. Olutasidenib (FT-2102) in patients with relapsed or refractory IDH1-mutant glioma: A multicenter, open-label, phase Ib/II trial. Neuro Oncol. 2023 Jan 5;25(1):146-156. doi: 10.1093/neuonc/noac139.

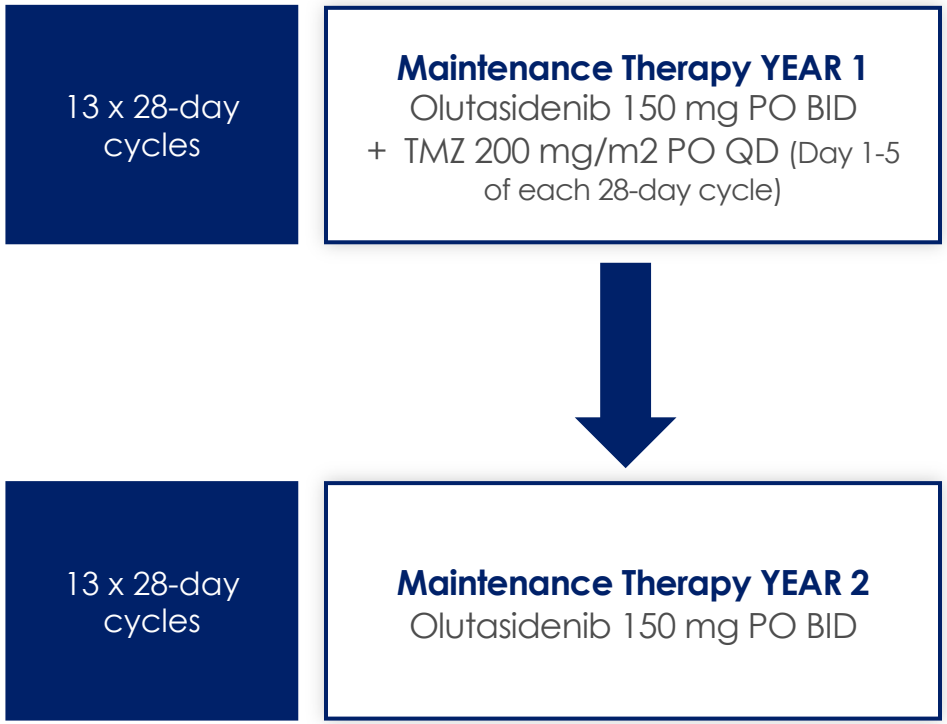
CONNECT Phase 2 Clinical Study Design

Olutasidenib in combination with temozolomide (TMZ) followed by olutasidenib monotherapy as maintenance treatment in newly diagnosed pediatric and young adult patients (<39 years) with IDH1 mutation positive HGG

Phase 2 Open-Label Study Design

(Post-radiotherapy)

N=~60



Primary objectives:

- Estimated progression-free survival vs historical controls
- Characterize plasma PK properties of olutasidenib in pediatric patients

Multiple secondary objectives include:

- Assess and characterize safety and toxicities of olutasidenib
- Evaluate the radiographic objective response rate and health-related quality of life outcomes
- Overall survival vs historical controls

Initiation:

- Estimated in the first half of 2024

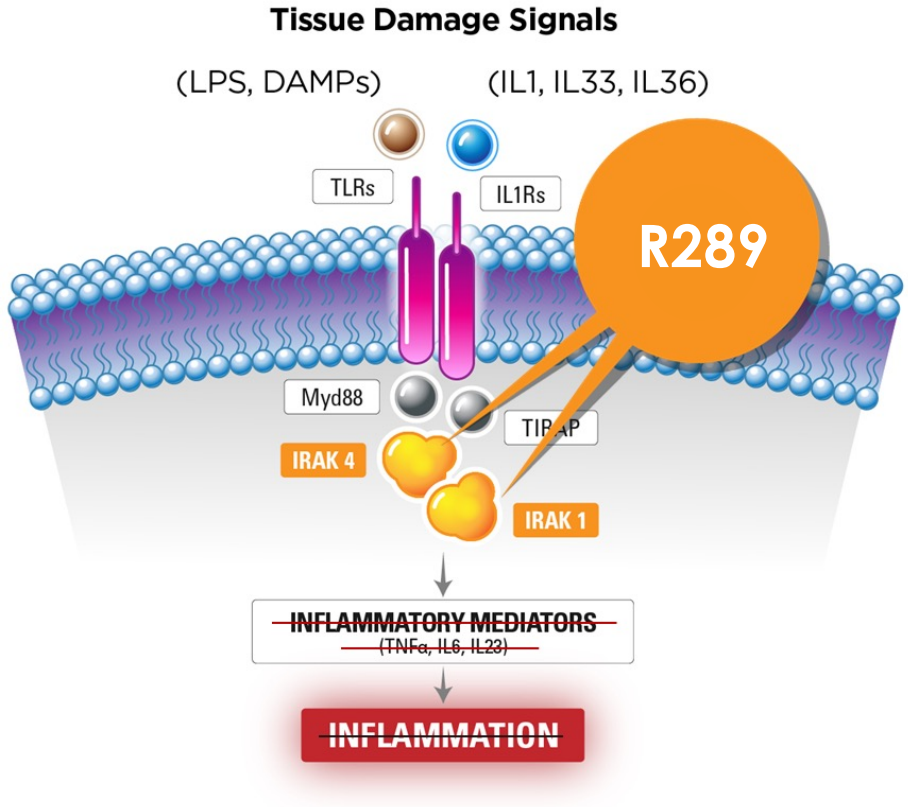
Targeting IRAK1 & IRAK4 Pathways in Heme/Onc

R289/835[1] is a Dual Inhibitor of Both IRAK1 and IRAK4 Pathways

- Inhibition of IRAK1/4 kinases has therapeutic potential for multiple diseases
- In a preclinical study, dual Inhibition of IRAK1 & IRAK4 demonstrated greater suppression of inflammatory cytokines compared to an IRAK4-selective inhibitor[2]

Attractive Opportunities in Heme/Onc and Rare Immune Diseases Align with Development Strategy

- Activation of innate immune system through TLRs and IL-1Rs plays an important role in myelodysplastic syndrome (MDS) pathogenesis
- The downstream IRAK1/4 signaling network mediates NLRP3 inflammasome-driven pyroptosis, which drives bone marrow inflammation in lower-risk MDS[3]
- The first patients dosed in an open-label, Phase 1b clinical trial of study in lower-risk MDS[4]. The primary endpoint for this trial is safety with key secondary endpoints including preliminary efficacy

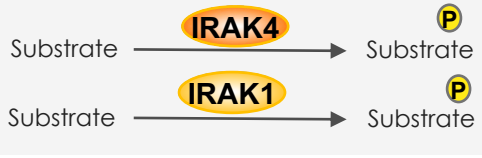


1. R289/R835 are investigational compounds not approved by the FDA. **2.** Rigel data on file. **3.** Sallman DA, Unraveling the Pathogenesis of MDS: The NLRP3 Inflammasome and Pyroptosis Drive the MDS Phenotype. *Front. Oncol.* 6:151. **4.** https://www.clinicaltrials.gov/ct2/show/NCT05308264

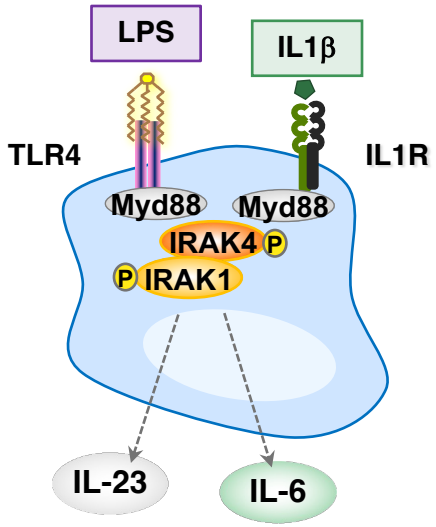
Targeting IRAK1 & IRAK4 Pathways in Inflammatory Disease

Dual Inhibition of IRAK1 and IRAK4 Provides Stronger Suppression of Inflammatory Cytokines Compared to IRAK4-selective Inhibitor[2]

Kinase Assays



Cell-Based Assays

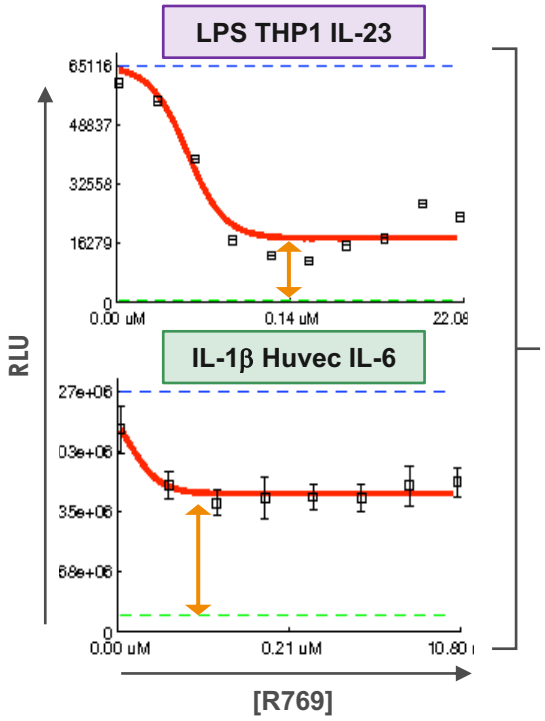


IRAK4-Selective Inhibitor

PF-06650833

IRAK4 IC_{50} = 0.2nM

IRAK1 IC_{50} = Inactive



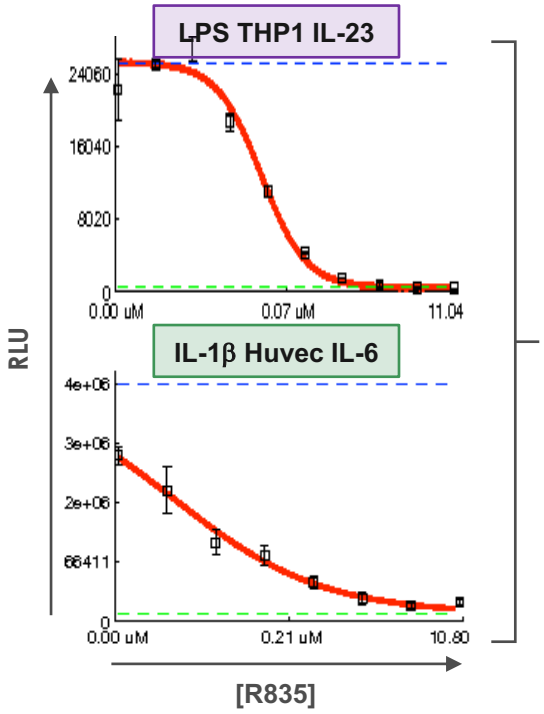
40-80%
Inhibition of Cytokine Release

IRAK1/ IRAK4 Dual Inhibitor

Rigel R835[1]

IRAK4 IC_{50} = 15nM

IRAK1 IC_{50} = 14nM

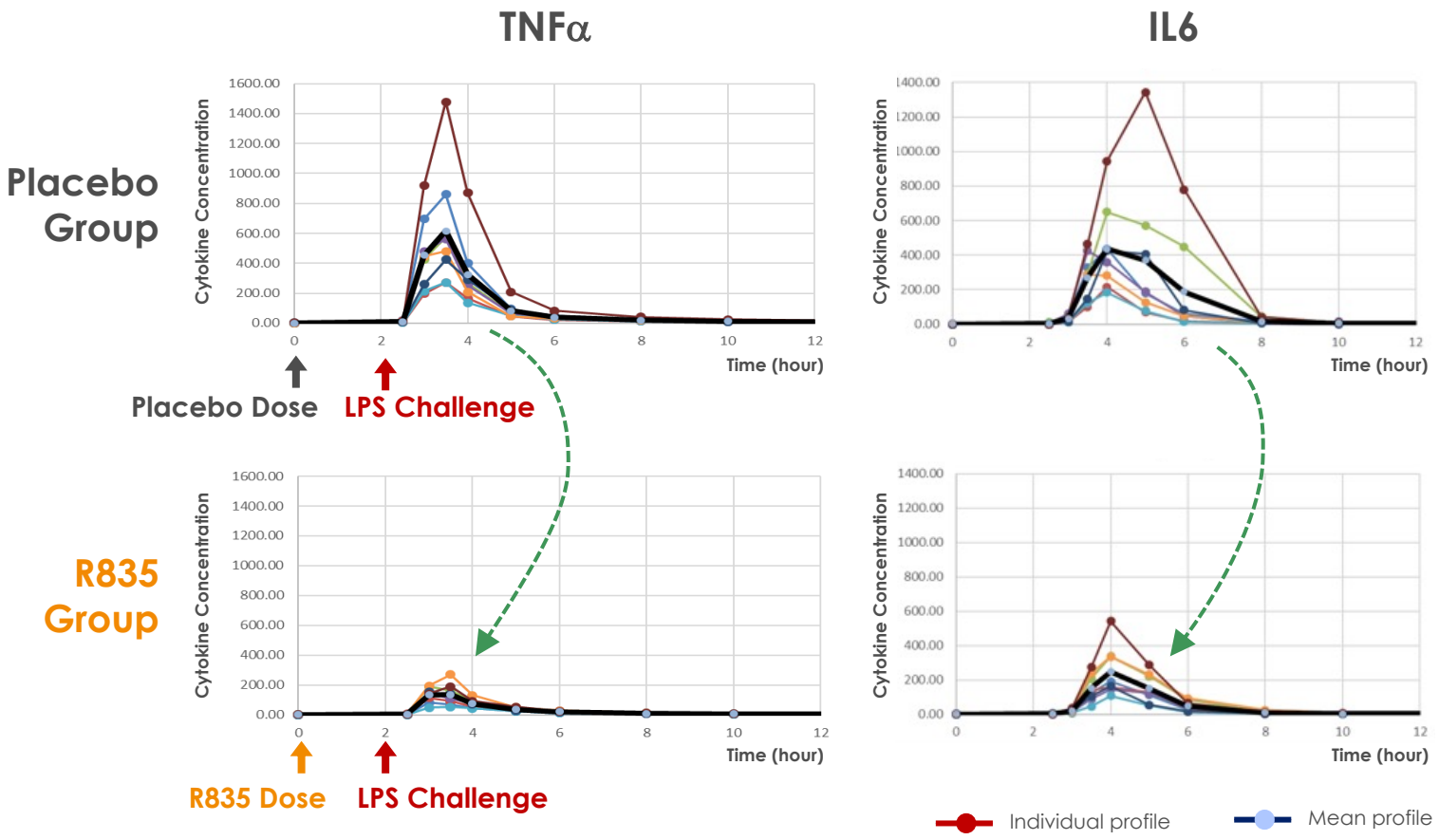


100%
Inhibition of Cytokine Release

1. R835 is an investigational compound not approved by the FDA. **2.** Rigel data on file.

R835[1] Proof-of-Mechanism and First-in-Human Studies[3]

Cytokine Response After LPS Challenge



Proof-of-Mechanism

In LPS[2] Challenge study in healthy volunteers, R835 profoundly inhibited inflammatory cytokine production[2]

- Inhibited TNFα, IL-6, and IL-8

First-in-Human

First-In-Human study enrolled 82 adults to characterize the safety, PK, PD of R835

- R835 was well tolerated
- Linear PK profile and dose proportional exposure

1. R835 is an investigational compound not approved by the FDA. **2.** Lipopolysaccharide (LPS, a TLR4 agonist). **3.** EULAR 2020 Poster Presentation -Abstract THU0219 - First-inhuman Study of Safety, Pharmacokinetics and Pharmacodynamics of IRAK1/4 Inhibitor R835 in Healthy Subjects.

Lower-Risk MDS Treatment Landscape

- MDS is a clonal disorder of hematopoietic stem cells (HSCs) leading to dysplasia and ineffective hematopoiesis in the bone marrow
- Risk of autoimmune abnormalities, cytopenias, progression to AML and death

1

First-Line Therapy: Transfusions and ESAs

treatment includes frequent blood transfusions and Erythropoiesis-Stimulating Agents (ESAs) for anemia

2

Second-Line Therapy: Lenalidomide, Luspatercept, Hypomethylating Agents (HMAs),

and immunosuppressive therapy provide limited hematologic response in selected subsets of patients, durable responses are not common, and these agents can result in significant adverse effects

X

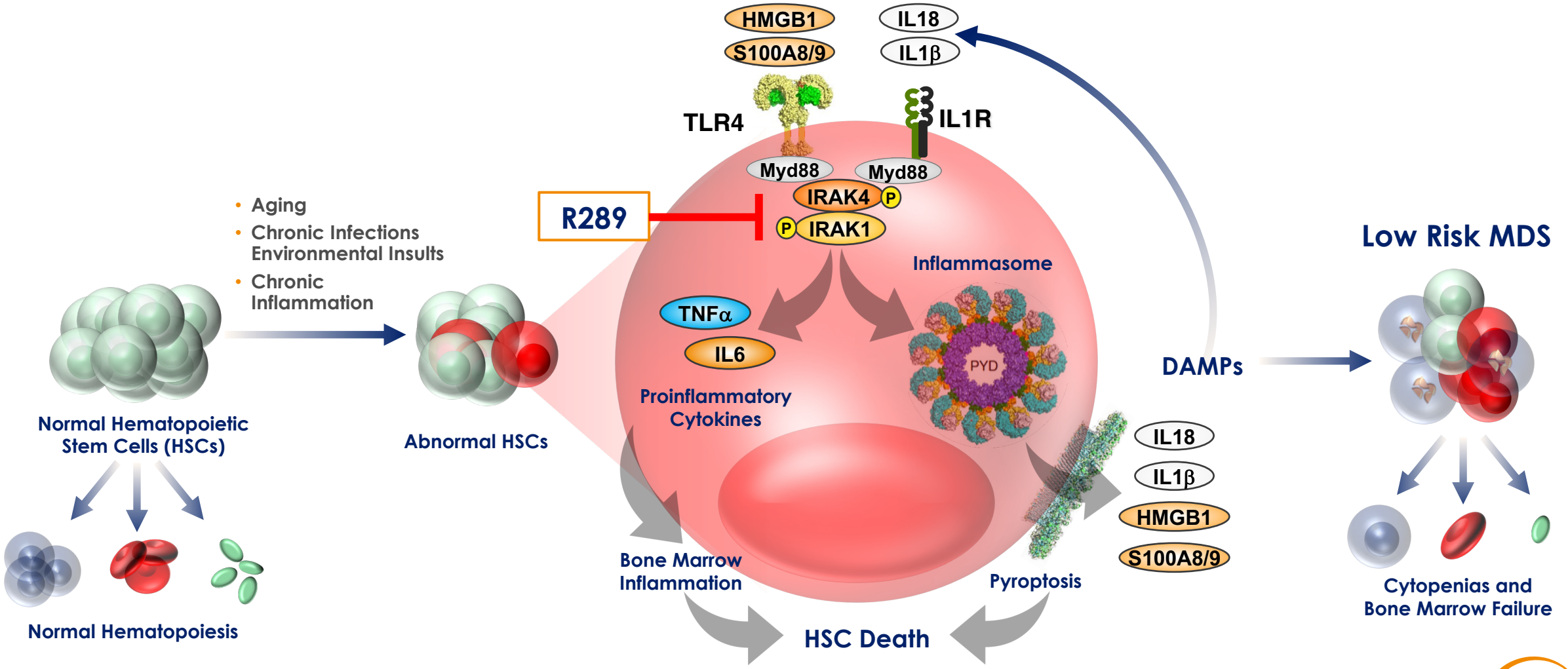
Loss of Response

is associated with significant morbidity and cytopenias[1]

There are currently no standard therapies for lower-risk MDS patients who are refractory/resistant to current second-line therapies

1. Volpe VO, Garcia-Manero G, Komrokji RS. SOHO State of the Art Updates and Next Questions: Treatment of Lower Risk Myelodysplastic Syndromes. Clin Lymphoma Myeloma Leuk. 2023 Mar;23(3):168-177. doi: 10.1016/j.clml.2023.01.001.

Bone Marrow Failure in Low Risk MDS is Driven by Chronic Inflammation and Pyroptosis of Normal Hematopoietic Stem Cells[1-3]

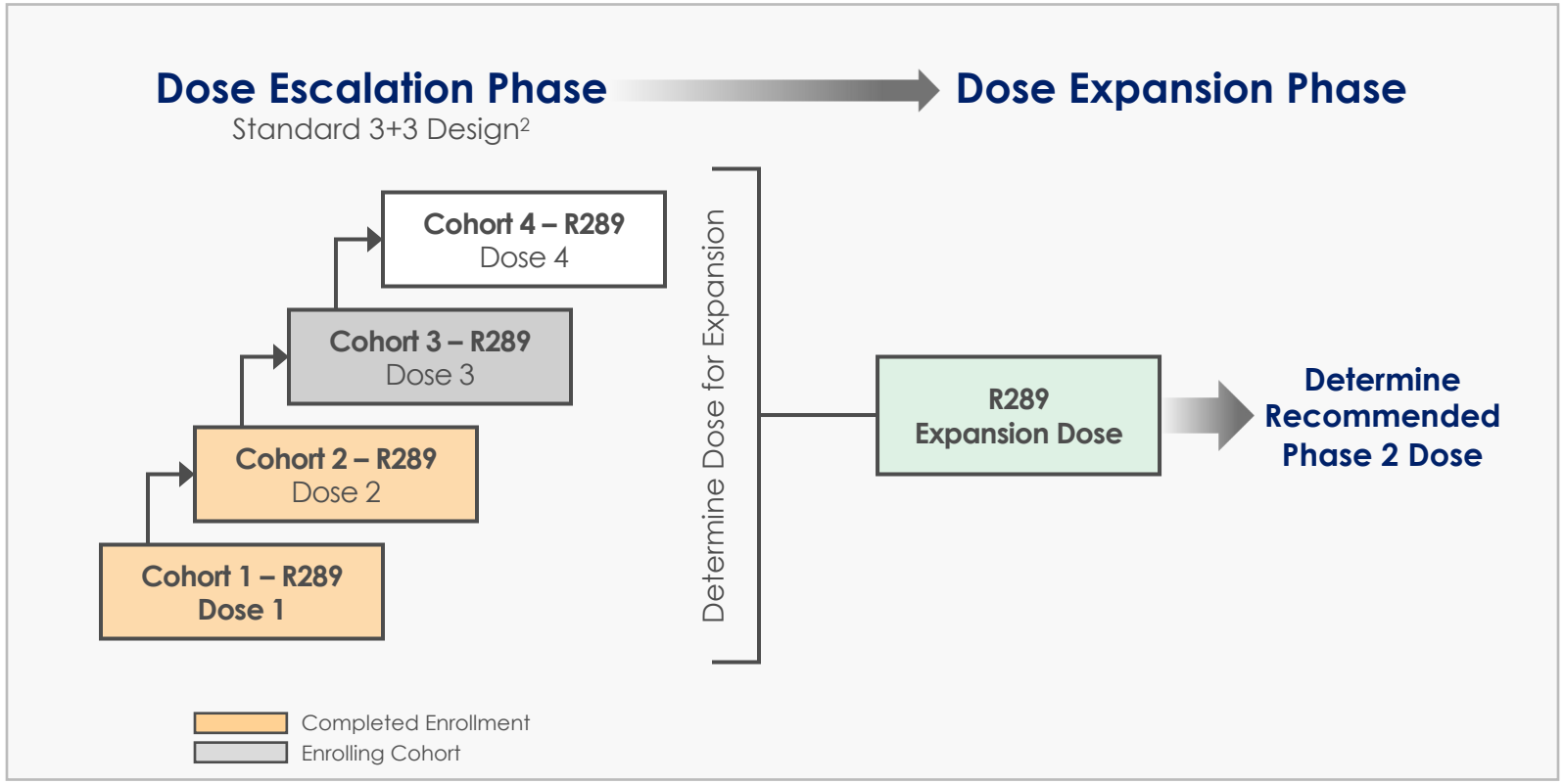


1. Sallman, DA, Front Oncol. 2016;6:151. **2.** Monlish DA, Front Immunol. 2016;7:390; **3.** Barreyro L, Blood. 2018;132(15):1553-60.

R289[1] Development: Open-label Phase 1b Study of Patients with Lower-Risk MDS

Patients with Lower-Risk MDS

Relapsed/Refractory or Inadequate Response to Prior Therapy with Known Clinical Benefit*



Primary Endpoint:

- Safety

Secondary Endpoints:

- Preliminary Efficacy
  - Transfusion Independence
  - Remission
  - Overall Response
  - Hematologic Improvement
- PK
- Biomarkers

*Thrombopoietin (TPO), erythropoietin (EPA), luspatercept, and HMAs (i.e., azacytidine or decitabine). Patients with del (5q) must have failed prior lenalidomide therapy. **1.** Investigational compound not approved by the FDA. **2.** Jaki T, Clive S, Weir CJ. Principles of dose finding studies in cancer: a comparison of trial designs. *Cancer Chemother Pharmacol.* 2013; 71(5): 1107-1114. doi:10.1007/s00280-012-2059-8.

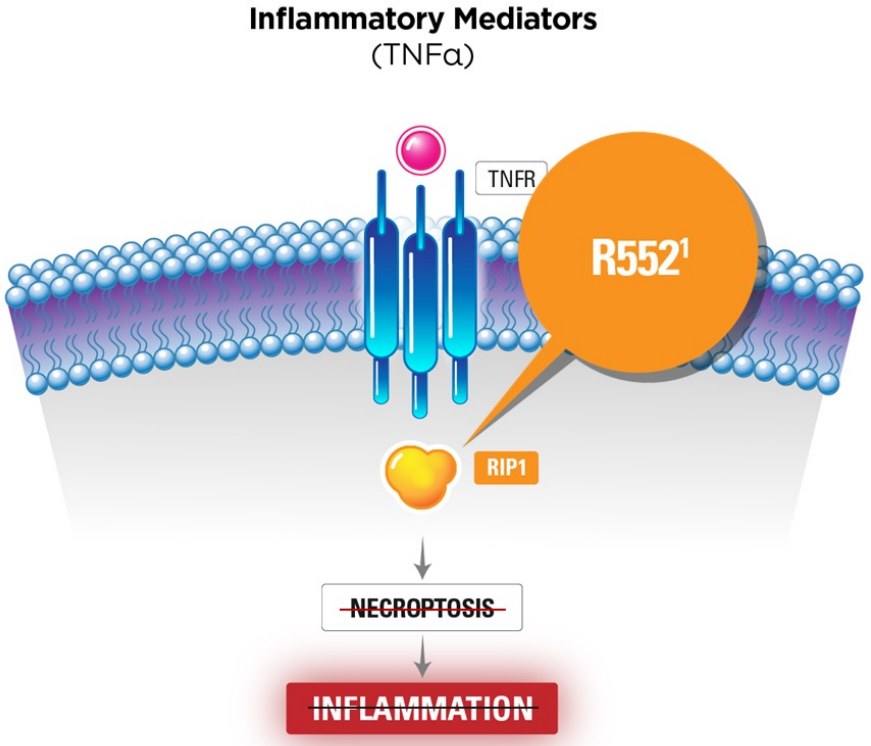
RIPK1 Inhibitor Programs in Immune and CNS Diseases with Partner Lilly

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 LY3871801 (previously R552) 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.

1. Investigational compound not approved by the FDA. https://www.clinicaltrials.gov/study/NCT05848258

Financials

Q4 2023 Financial Highlights[1]

Total Revenue: $35.7M

- **Net Product Sales: $29.5M**
- TAVALISSE: $25.7M
- REZLIDHIA: $3.9M
- **Contract revenues from collaborations: $6.0M**
- Grifols $3.7M
- Kissei $2.2M
- Medison $0.1M
- **Government contract revenue: $0.1M**

Total Bottles Shipped:

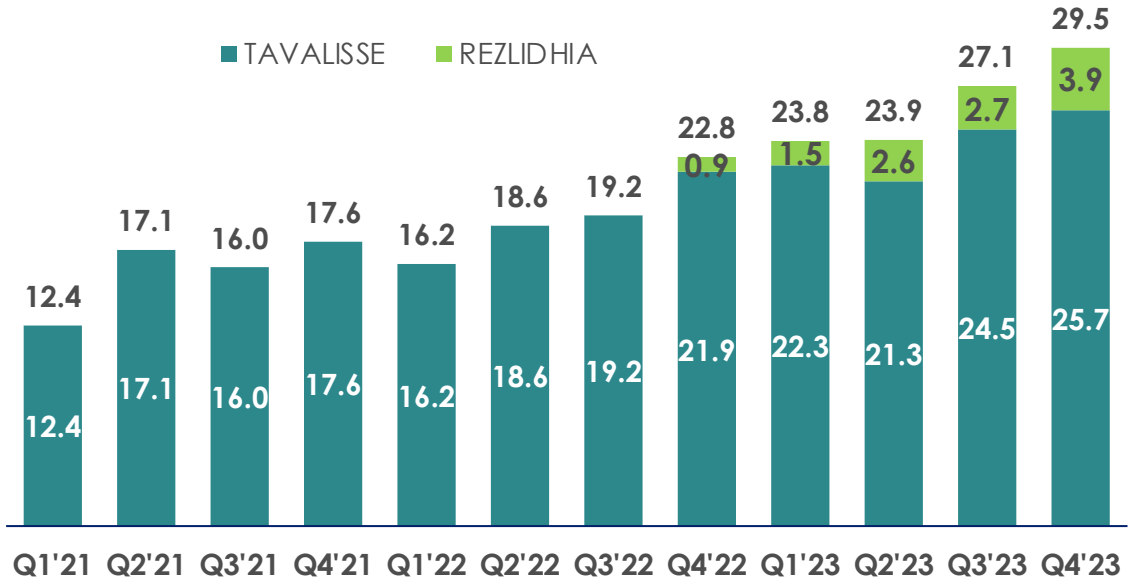
- TAVALISSE: 2,671
- REZLIDHIA: 308

Bottles Shipped to Patients and Clinics[2]:

- TAVALISSE: 2,463
- REZLIDHIA: 278

Cash, cash equivalents & short-term investment as of December 31, 2023 was **$56.9M** as of December 31, 2023 compared to $58.2M as of December 31, 2022

Net Product Sales ($M)



		Q1'21	Q2'21	Q3'21	Q4'21	Q1'22	Q2'22	Q3'22	Q4'22	Q1'23	Q2'23	Q3'23	Q4'23
Bottles Shipped to Patients & Clinics[1]	Tavalisse	1599	1693	1710	1785	1836	2054	2026	2196	2256	2265	2412	2463
	Rezlidhia								2	109	187	221	278
Change in Bottles in Distribution Channels	Tavalisse	-235	212	-53	29	-12	-1	46	221	25	-74	139	208
	Rezlidhia								62	4	13	-11	30
Total Bottles Shipped	Tavalisse	1364	1905	1657	1814	1824	2053	2072	2417	2281	2191	2551	2671
	Rezlidhia								64	113	200	210	308

1. This information is preliminary, has not been audited and is subject to change upon completion of the audit of the company's financial statements as of and for the year ended December 31, 2023

2. 1,374 total TAVALISSE bottles, net of returns, and 98 total REZLIDHIA bottles, net of returns, remained in distribution channels as of December 31, 2023.

2024 Value Drivers

Expanding Product Sales for TAVALISSE and REZLIDHIA

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

Continued Financial Discipline

Development Programs[1]

- Advance olutasidenib in AML, MDS, glioma and other cancers
- Evaluate additional clinical development opportunities and alliances for olutasidenib
- Evaluate heme/onc opportunities for fostamatinib
- Enroll and generate preliminary data for R289 Phase 1b study in lower-risk MDS

In-License Opportunities

- Actively pursue new late-stage assets which leverage current capabilities & capacity

Partnered Programs

- Phase 2a study of R552[1] in rheumatoid arthritis initiated by partner Eli Lilly

1. Investigational compounds in these indications and not approved by the FDA. Please see Important Safety Information on slides 37-39. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING.

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 http://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., 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 (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, 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

Thank You

www.rigel.com