

Q3 2026 Financial Results Presentation

November 5, 2026

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 relating to, among other things, Rigel's financial performance and outlook for 2026, including anticipated total revenues, net product sales, contract revenues and profitability; projected long-term revenue growth, market opportunities and potential product sales; the commercialization of VEPPANU, TAVALISSE, REZLIDHIA and GAVRETO, expected commercial growth and execution of Rigel's commercial strategy; the potential for VEPPANU to become Rigel's largest product and for R289 to represent a $1 billion-plus opportunity in lower-risk myelodysplastic syndrome; the anticipated timing, progress and results of R289 clinical development, including completion of dose expansion enrollment and selection of a recommended Phase 2 dose by the end of 2026, subsequent opening of an exploratory cohort and discussions with the FDA regarding potential registrational studies, and evaluation in other potential indications; the timing and content of anticipated data presentations; the potential therapeutic benefits of Rigel's products and product candidates, alone or in combination with other therapies; ongoing and potential future development of vepdegestrant and olutasidenib; Rigel's ability to fund existing and future clinical development programs; anticipated benefits and efficiencies from integrating VEPPANU into Rigel's commercial and operating infrastructure; and potential partnering, licensing, collaboration, acquisition and other business development opportunities. Any statements contained in this presentation that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "anticipates," "believes," "expects," "intends," "may," "plans," "potential," "will" and similar expressions are intended to identify such forward-looking statements.

Forward-looking statements are neither historical facts nor assurances of future performance. They are based on Rigel's current beliefs, expectations and assumptions and involve significant risks and uncertainties that are difficult to predict and, in many cases, are beyond Rigel's control. Actual results and the timing of events could differ materially from those expressed or implied by these forward-looking statements as a result of various risks and uncertainties, including, without limitation, risks associated with the commercialization and marketing of VEPPANU, TAVALISSE, REZLIDHIA and GAVRETO, including physician adoption, patient demand, market acceptance, competition, reimbursement and pricing; risks that early launch activity, prescription trends, refills and patient access metrics may not be indicative of sustained demand or future commercial performance; uncertainties in estimates of market size, eligible patient populations, market penetration and long-term revenue growth; risks that R289 may not obtain regulatory approval or achieve the commercial opportunity anticipated; risks associated with the transfer and integration of development, manufacturing and commercialization responsibilities for VEPPANU and reliance on Arvinas, Pfizer and other third parties; variability in product sales and the timing and amount of collaboration revenues, expenses and other items affecting financial performance; risks that clinical studies may be delayed, may not be initiated or conducted as anticipated, or may not enroll or retain patients as anticipated; risks that preclinical findings and preliminary or limited clinical data may not be predictive of final results, results in other indications or patient populations, results in subsequent clinical trials or real-world outcomes; risks that additional data, analyses or experience may alter assessments of safety, tolerability, efficacy, dose selection or therapeutic potential; risks that Rigel's products or product candidates, alone or in combination with other therapies, may have unintended side effects or adverse reactions; risks that regulatory authorities may make adverse decisions regarding Rigel's products or development programs, including study designs, dose selection, approvals or continued marketing; risks associated with reliance on third parties for clinical development, manufacturing, supply and other services; the availability and allocation of financial, personnel and other resources; risks that potential business development transactions may not be identified, completed or yield anticipated benefits; unanticipated business needs or developments that may affect Rigel's funding needs or internal resource requirements; and other risks described in the "Risk Factors" section of Rigel's Quarterly Report on Form 10-Q for the quarter ended June 30, 2026 and subsequent filings with the Securities and Exchange Commission, including Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2026, which is expected to be filed later today.

Any forward-looking statement in this presentation speaks only as of the date on which it is made. Rigel undertakes no obligation to update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise, except as required by law.

Please visit www.VEPPANU.com for Full Prescribing Information. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING. Please visit www.GAVRETO.com for Full Prescribing Information, including Boxed WARNING.

Rigel Participants



Raul Rodriguez

President &
Chief Executive Officer



Ray Furey, J.D.

Executive Vice President,
General Counsel & Corporate Secretary



Dave Santos

Executive Vice President &
Chief Commercial Officer



Alison Hannah, M.D.

Executive Vice President &
Chief Medical Officer



Dean Schorno

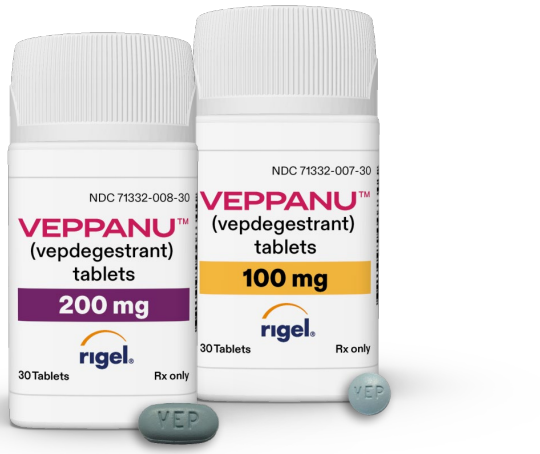
Executive Vice President &
Chief Financial Officer

Executing VEPPANU's U.S. Commercial Launch

$6.6M

Q3 2026 Net Product Sales

(6 weeks of commercial availability)



- Launch activities began in mid-June, driving awareness ahead of commercial availability
- VEPPANU incorporated into existing efficient distribution network
- Shipped VEPPANU to >100 patients and clinics in Q3; majority of early patients have already refilled
- Strong coverage across commercial payers and Medicare
- HCP engagement going well; focusing on high prescribers in ER+/HER2-, *ESR1*m mBC
- Executing marketing campaigns focused on education and VEPPANU's differentiated mechanism of action

HCP, healthcare provider; ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; mBC, metastatic breast cancer.
Please visit www.VEPPANU.com for Full Prescribing Information.

Rigel's Transformational Growth Strategy

Grow Commercial Business



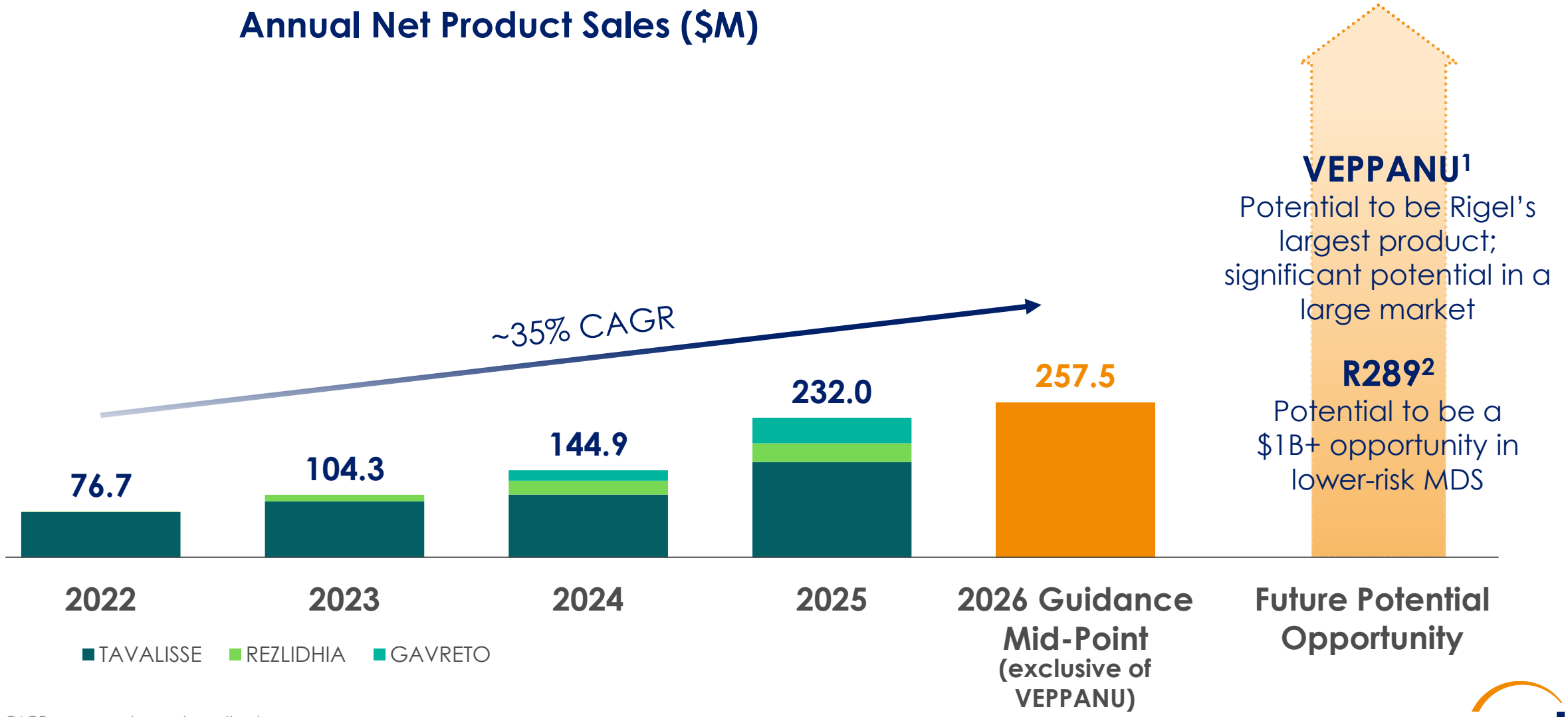
In-Licensing / Business Development

Maintain Financial Discipline

Advance Development Pipeline

Advancing Rigel's Long-Term Growth Potential

Annual Net Product Sales ($M)



VEPPANU[1]
Potential to be Rigel's largest product; significant potential in a large market

R289[2]
Potential to be a $1B+ opportunity in lower-risk MDS

CAGR, compound annual growth rate.

1. VEPPANU became commercially available from Rigel on August 13, 2026. Rigel reported $6.6 million of VEPPANU net product sales for Q3 2026. **2.** Investigational compound not approved by the FDA.

Grow Commercial Business





VEPPANU™
vepdegestrant 200 mg 100 mg



Tavalisse®
(fostamatinib disodium hexahydrate) tablets



REZLIDHIA®
(olutasidenib) 150 mg capsules



GAVRETO®
pralsetinib 100 mg capsules

Please see Indications and Important Safety Information on slides 33-38. Please visit www.VEPPANU.com for Full Prescribing Information. Please visit www.TAVALISSE.com for Full Prescribing Information. Please visit www.REZLIDHIA.com for Full Prescribing Information, including Boxed WARNING. Please visit www.GAVRETO.com for Full Prescribing Information, including Boxed WARNING.

rigel.

Q3 2026 Commercial Performance

VEPPANU vepdegestrant 200 mg 100 mg

$6.6M
Q3 Net Product Sales

n/a[1]
Growth vs. Q3 2025

Tavalisse (fostamatinib disodium hexahydrate) tablets

$46.0M
Q3 Net Product Sales

3%
Growth vs. Q3 2025

REZLIDHIA (olutasidenib) 150 mg capsules

$9.9M
Q3 Net Product Sales

20%
Growth vs. Q3 2025

GAVRETO pralsetinib 100 mg capsules

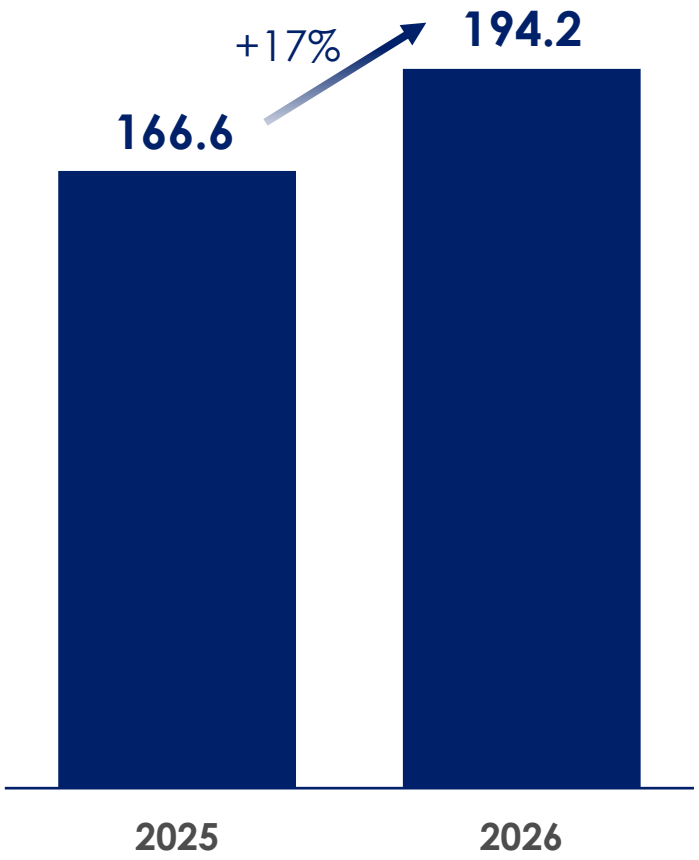
$9.8M
Q3 Net Product Sales

(11)%
Growth vs. Q3 2025

$72.3M Q3 2026 Net Product Sales

13% Growth vs. Q3 2025

YTD Net Product Sales ($M)

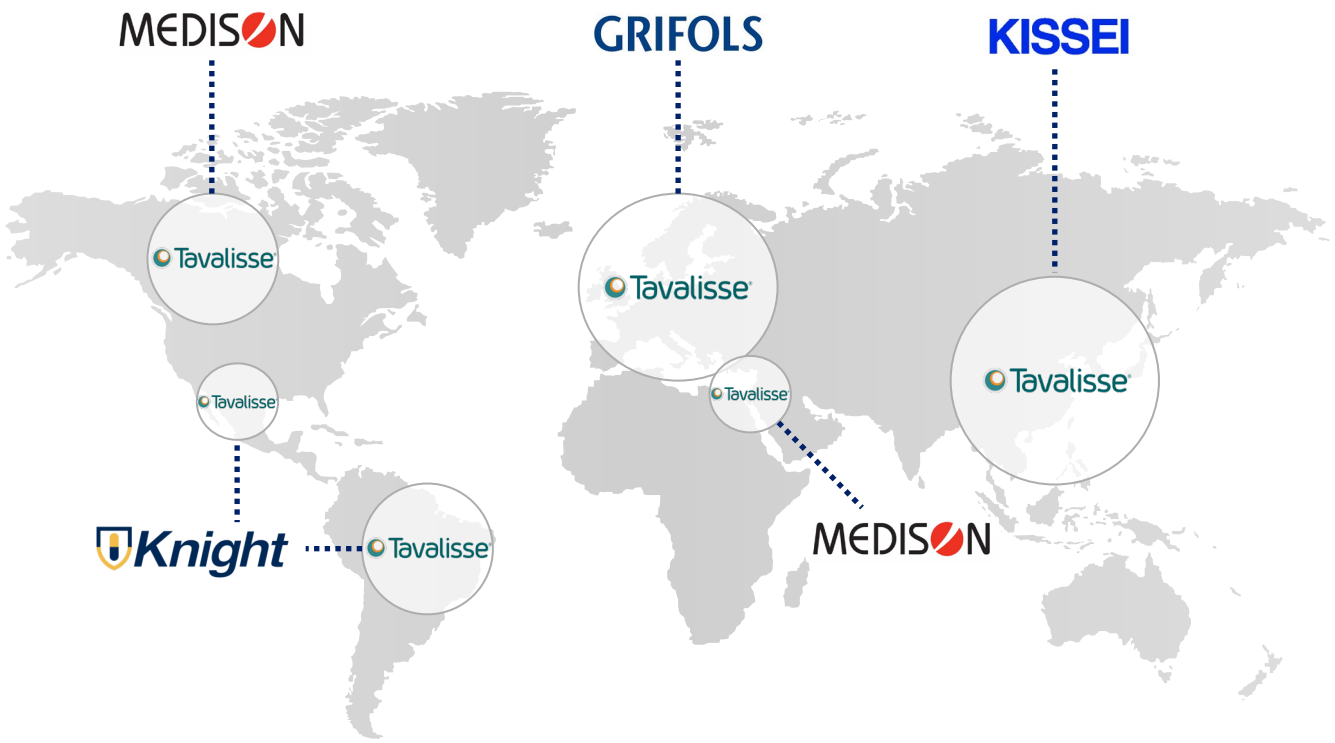


YTD, year-to-date.

1. VEPPANU became commercially available from Rigel on August 13, 2026.

Expanding Commercial Availability in Global Markets

TAVALISSE is commercially available in key European countries (TAVLESSE), Japan, South Korea, Canada, Israel and Mexico



Q3 2026 Collaboration Revenues: $8.6M

- Grifols $3.8M
- Kissei $3.2M
- Others $1.6M

TAVALISSE Regulatory Approval

- Knight announced regulatory approval in Colombia in September

TAVALISSE Commercial Launch

- Knight announced launch in Brazil in October

REZLIDHIA Opportunity[1]

- Executing on ex-U.S. opportunities for development and commercialization
  - Expanded relationship with Kissei to include REZLIDHIA in Japan, South Korea, and Taiwan
    - Kissei submitted NDA in Japan in May
  - Entered relationship with Dr. Reddy's in Latin America and other territories[2]

NDA, New Drug Application.
1. Forma, now Novo Nordisk, is entitled to a certain portion of Rigel's sublicensing revenue from olutasidenib.
2. Dr. Reddy's territory includes Latin America, South Africa, certain countries in the Commonwealth of Independent States (CIS), India, certain countries in Southeast Asia and North Africa, Australia and New Zealand.

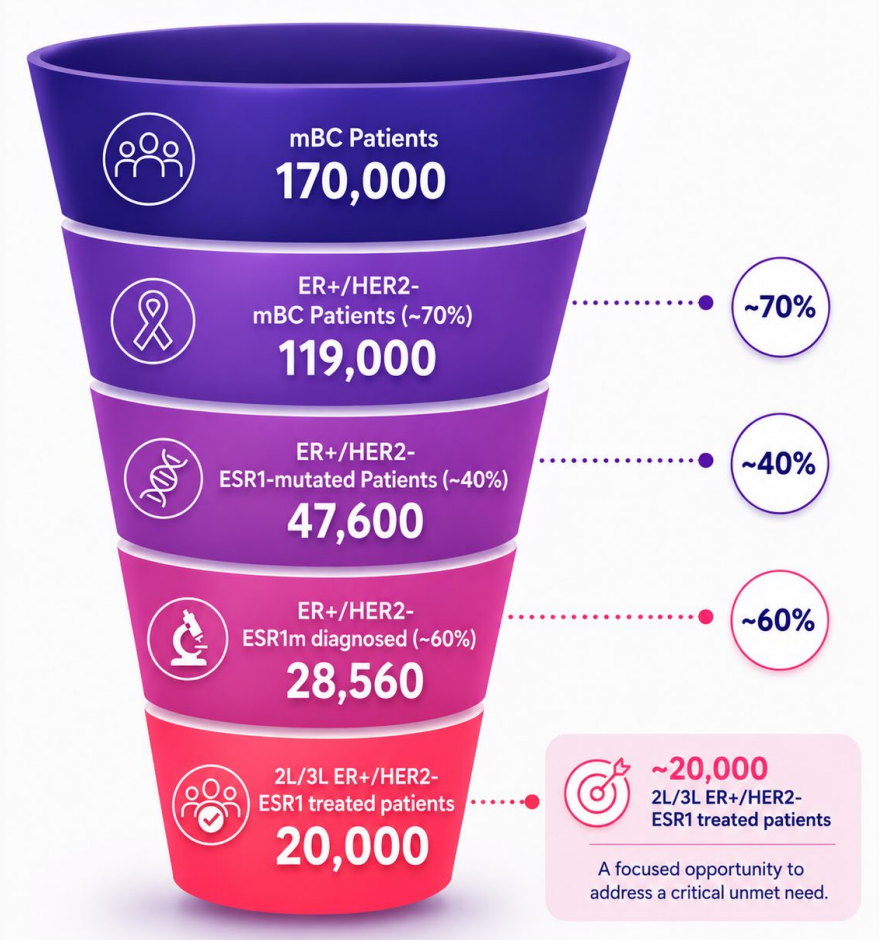


VEPPANU™

vepdegestrant 200 mg 100 mg

rigel

ER+/HER2-, *ESR1*m mBC Patient Opportunity



The largest segment of metastatic breast cancer

As patients become more exposed to endocrine and CDK4/6 inhibitor therapy, ESR1m resistance develops

ctDNA testing is increasing the proportion of patients diagnosed and treated in 2L

The majority of ER+/HER2- patients with ESR1m are in the 2L and later setting due to exposure to endocrine and CDK4/6 therapy

~20,000[1] patients with 2L/3L ER+/HER2-, *ESR1*m mBC represent potential $1B+ market in the U.S.

ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; mBC, metastatic breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; 2L, second line; 3L, third line; ctDNA, circulating tumor DNA.

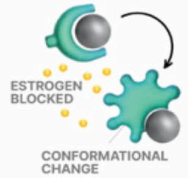
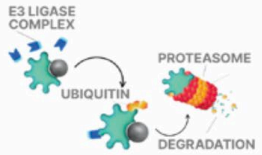
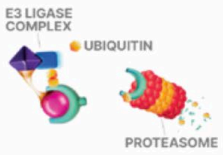
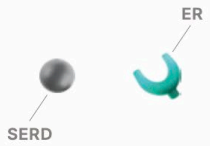
1. Internal market research.

PROTAC: A Different Mechanism to Eliminate Estrogen Receptors

ER degradation is an important therapeutic strategy for addressing endocrine resistance driven by *ESR1* mutations[1]

SERD AND PROTAC MECHANISMS

The clinical relevance of these mechanisms of action is unknown. No conclusions regarding clinical efficacy or safety should be drawn from these findings.

	Oral SERDs		PROTAC	
Binding mechanism		Binds to ER and causes a conformational change[14,15,19]		Binds to ER and an E3 ligase, initiating polyubiquitination[12, 15-17]
Mechanism of degradation		**INDIRECT** Degradation is a secondary effect of conformational change[2,14,15]		**DIRECT** Degradation occurs as the primary pharmacologic effect[2,14]
Repetitive function		SERDs rely on 1:1 binding for functionality[14]		PROTAC can degrade multiple ERs until metabolized[12,15,18]
Scale of ER degradation†	**8%-68%**	Oral SERDs degraded 8%-68% of ER in a preclinical study[20]	**79%-86%**	VEPPANU degraded 79%-86% of ER in a preclinical study[20]

PROTAC, PROteolysis TArgeting Chimera; ER, estrogen receptor; ESR1, estrogen receptor 1 gene; SERD, selective estrogen receptor degrader.

1. Bidard FC, et al. J Clin Oncol. 2022;40(28):3246–3256. doi:10.1200/JCO.22.00338 (phase 3 EMERALD trial).

Please visit www.VEPPANU.com for Full Prescribing Information, www.VEPPANUhcp.com to view full materials and slide 39 for citations in graphic.

EARLY LAUNCH SIGNALS

Encouraging Speed & Breadth of Uptake During Q3

VEPPANU™

Momentum built across prescribers and accounts

PATIENTS & CLINICS

Shipments began immediately at product availability

100+ patients and clinics received VEPPANU in the first 6 weeks

Most patients starting in Q3 have already received a second shipment

PRESCRIBERS

Academic and community oncologists prescribed VEPPANU

All 6 regions recorded a first prescriber on day 1, a second within week 1, and a third within 2 weeks

75% of territories had a Q3 prescriber

ACCOUNTS

Academic and community oncology accounts have ordered

All 6 regions had direct account orders in August

65% of territories placed account orders in Q3

Source: Rigel internal Q3 launch data.

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EARLY LAUNCH SIGNALS

Encouraging Early Patient Access Trends During Q3

VEPPANU™

High PA Approval Rates and Fast First Fill

PRIOR AUTHORIZATIONS

88%	Estimated overall PA approval rate
90%+	Estimated Medicare PA approval rate
80%+	Estimated Commercial PA approval rate

TIME TO FIRST FILL

4 DAYS	Overall median time to first fill
>80%	of prescriptions filled within 2 weeks
>1 IN 3	patients receive VEPPANU within 3 days

RIGEL ONECARE® SUPPORT

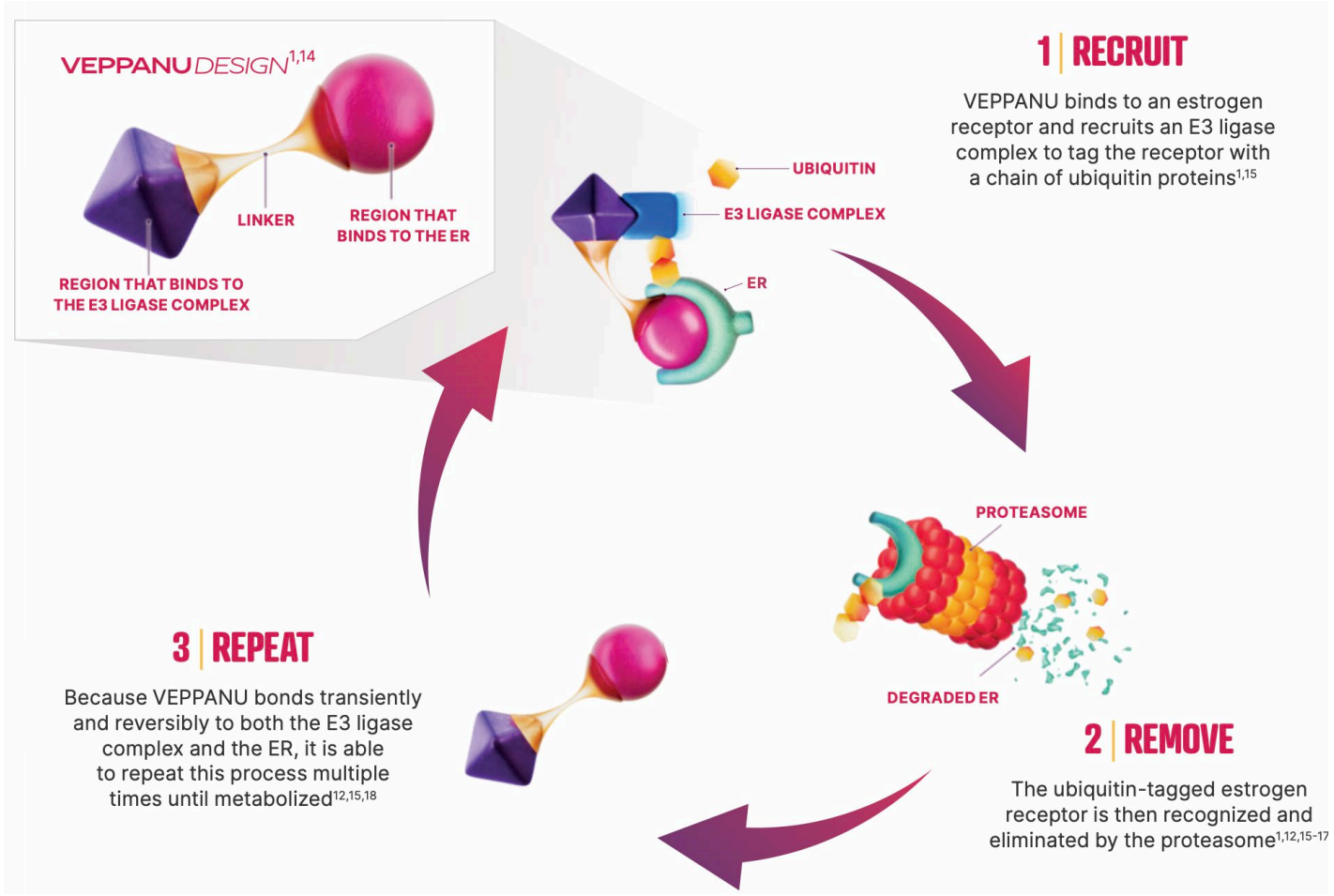
- Benefits verification and coverage support
- Prior authorization support
- Temporary drug supply for eligible patients
- Copay and financial assistance
- Adherence support during treatment

PA, prior authorization.

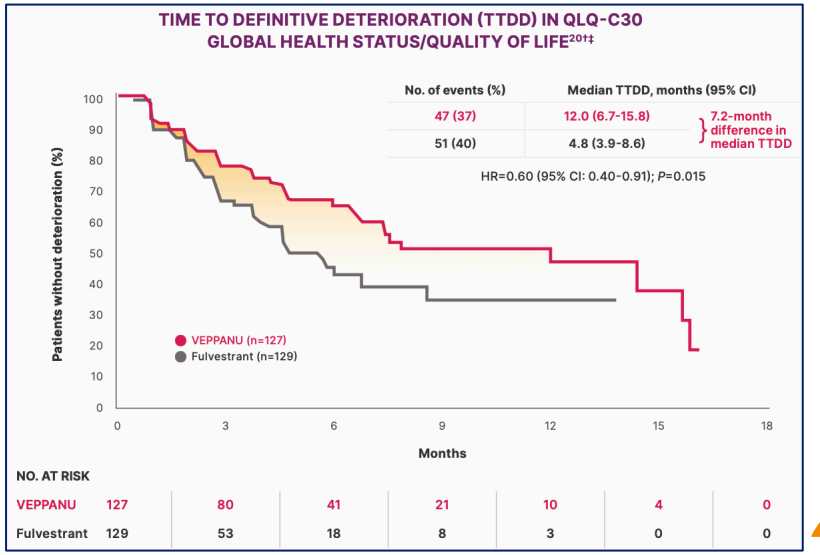
Source: Rigel internal Q3 launch data; Rigel OneCare program materials.

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VEPPANU is the FIRST and ONLY FDA-Approved PROTAC







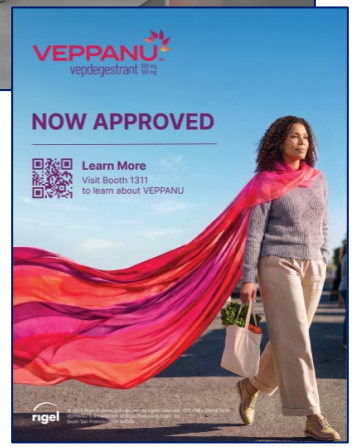
FDA, U.S. Food and Drug Administration; PROTAC, PROteolysis TArgeting Chimera; ER, estrogen receptor.

Continuing to Expand VEPPANU Awareness in Q4

Reaching Breast Cancer Audience at SABCS

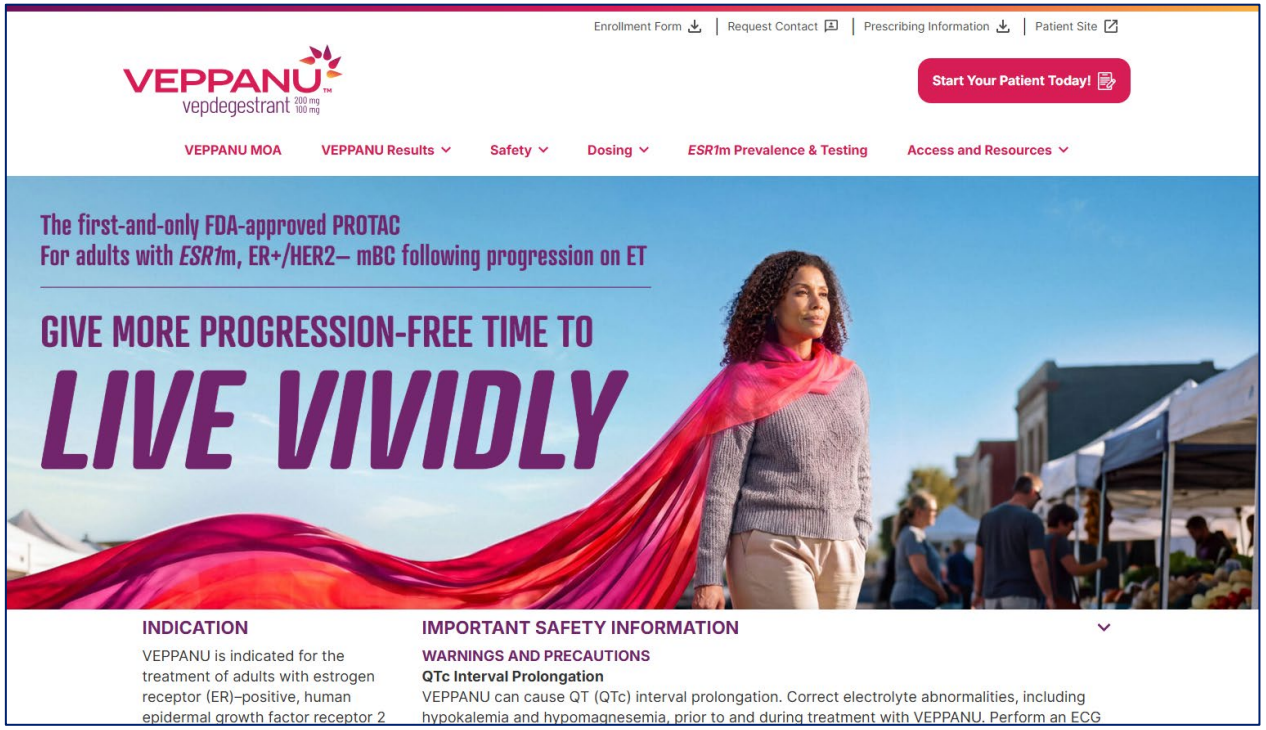






Rigel Booth #1311

New Healthcare Provider Campaign Just Launched



www.VEPPANUhcp.com IS NOW LIVE

Advance Development Pipeline



Hematology and Oncology Focus Areas[1]

R289
IRAK1/4 Inhibitor Development Program

- Evaluating in a Phase 1b study for patients with R/R lower-risk MDS
  - Granted Fast Track and Orphan Drug designations by the FDA[2]
- Other potential indications under consideration

Vepdegestrant
PROTAC Development Program

- Ongoing studies include combination therapy and other studies[3]
  - Pfizer and Arvinas remain responsible for current studies[4]
- Rigel will evaluate future development opportunities for vepdegestrant

Olutasidenib
m*IDH1* Inhibitor Strategic Collaborations

- Evaluating as monotherapy or combination therapy in m*IDH1* AML and other hematologic malignancies
- Evaluating as combination therapy in m*IDH1* high-grade glioma

IRAK1/4, interleukin receptor-associated kinases 1 and 4; R/R, relapsed/refractory; MDS, myelodysplastic syndrome; FDA, U.S. Food and Drug Administration; PROTAC, PROteolysis TArgeting Chimera; IDH1, isocitrate dehydrogenase-1; mIDH1, mutated IDH1; AML, acute myeloid leukemia.

1. Investigational compounds in these indications and not approved by the FDA. **2.** R289 granted Fast Track designation for previously-treated transfusion dependent lower-risk MDS and Orphan Drug designation for MDS by the U.S. FDA. **3.** Studies include combination studies (abemaciclib, ribociclib, samuraciclib and atirmociclib), VERITAC-2, Japanese bridging study and hepatic impairment study. All studies are active, not enrolling, except for the hepatic study. VERITAC-2 study ongoing for time to event timepoints such as duration of response, progression-free survival and overall survival. **4.** Rigel will contribute up to $40 million over the next 4 years.

Vepdegestrant Development

Clinical Studies[1]

The following studies are active, not enrolling, except for the hepatic study:

- VERITAC-2[2]
- Combination studies
  - Abemaciclib
  - Ribociclib
  - Samuraciclib
  - Atirmociclib
- Japanese bridging study
- Hepatic impairment study

Development Plans

- Rigel will evaluate future development opportunities for vepdegestrant, including potential Rigel-led studies and new collaborations
- High-priority future clinical trials for vepdegestrant:
  - Combination studies
  - Studies in the post-SERD setting

SERD, selective estrogen receptor degrader.

1. Rigel will contribute up to $40 million over the next 4 years. **2.** VERITAC-2 study ongoing for time to event timepoints such as duration of response, progression-free survival and overall survival.

SABCS 2026 Key Data Presentations

Poster Presentations

Abstract #P4-14-19: Vepdegestrant in patients with ESR1-mutated, ER+/HER2− advanced breast cancer following prior selective estrogen receptor degrader (SERD) therapy: results from a Phase I/II study

- *Lead Author: Erika P. Hamilton, M.D., Sarah Cannon Research Center*

Abstract #P4-14-10: Vepdegestrant, a PROteolysis TArgeting Chimera (PROTAC) ER degrader, plus palbociclib in ER+/HER2− metastatic, recurrent, or locally advanced unresectable breast cancer: final safety and efficacy results from a phase 1b cohort

- *Lead Author: Erika P. Hamilton, M.D., Sarah Cannon Research Center*

Abstract #P4-15-15: Integrated QTc Risk Assessment of Vepdegestrant: Clinical and Concentration-QTc Analyses from VERITAC and VERITAC-2 Trials in ER+/HER2- Advanced or Metastatic Breast Cancer

- *Lead Author: Lana Tran, PharmD, Pfizer*

Abstract #P5-10-19: Baseline ctDNA biomarkers associated with PFS benefit from vepdegestrant, a PROteolysis TArgeting Chimera estrogen receptor (ER) degrader vs fulvestrant in ER+/HER2− advanced breast cancer: exploratory analysis from the phase III VERITAC-2 study

- *Lead Author: Seth A. Wander, M.D., Ph.D., Mass General Research Institute*

Abstract #P4-14-28: Clinical impact of estrogen receptor gene (ESR1) mutations in HR+/HER2− metastatic breast cancer previously treated with endocrine therapy (ET) and/or CDK4/6 inhibitors

- *Lead Author: Neal M. Iyengar, MD, Emory Winship Cancer Institute*

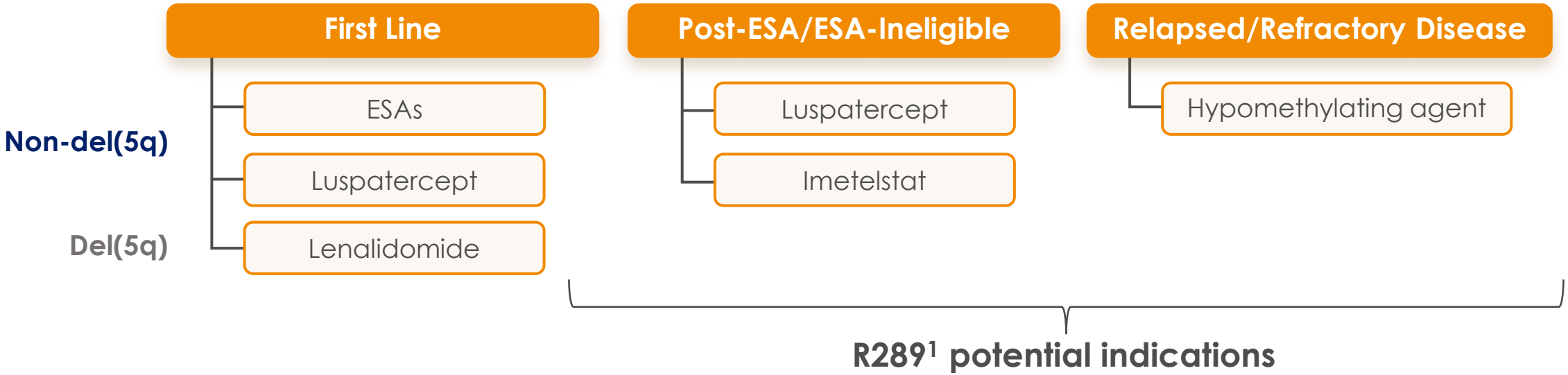
SABCS, San Antonio Breast Cancer Symposium.



R289
IRAK1/4 Inhibitor in Lower-Risk MDS

Lower-Risk MDS Treatment Landscape

- MDS is a clonal disorder of hematopoietic stem cells (HSCs) leading to dysplasia and ineffective hematopoiesis
  - Consequences: Cytopenias (anemia), infections, iron overload and organ dysfunction, progression to AML
- Primary goal of therapy: Reduce/limit transfusion-dependency
- Modest efficacy thus far with available therapies; there is room for improvement



New therapies needed for previously-treated TD LR-MDS patients that are R/R or ineligible for ESAs

MDS, myelodysplastic syndrome; AML, acute myeloid leukemia; ESAs, erythropoiesis-stimulating agents; TD, transfusion dependent; LR-MDS, lower-risk myelodysplastic syndrome; R/R, relapsed or refractory.

1. Investigational compound not approved by the FDA.

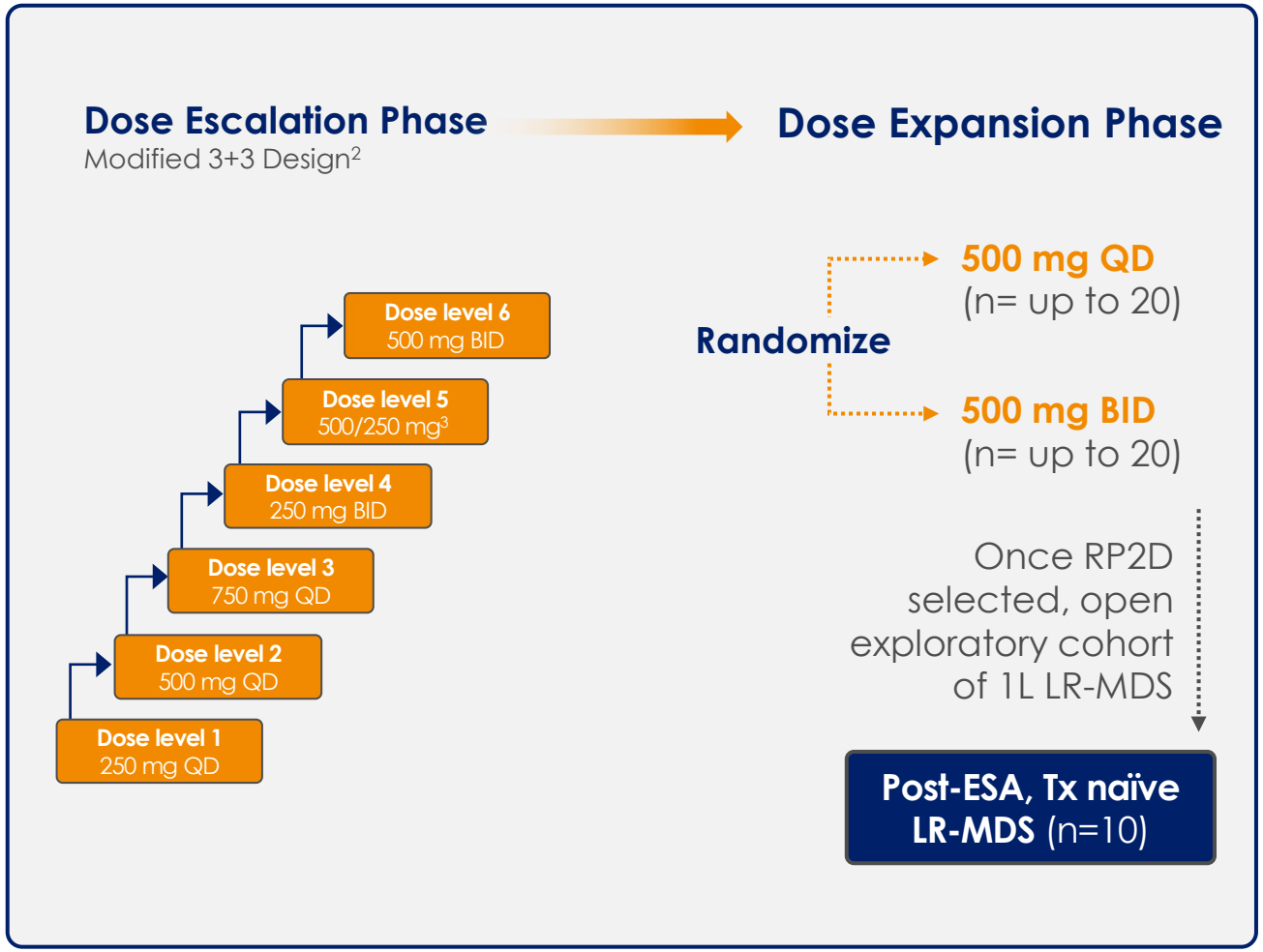
R289[1] Program Value Proposition for Lower-Risk MDS

Unmet Medical Need	• **~12,200 lower-risk MDS patients who have been previously treated**[2] • **Therapies for previously-treated transfusion dependent lower-risk MDS patients are lacking**
Novel Mechanism of Action	• **Dysregulated inflammatory signaling** is associated with MDS • **Co-targeting IRAK1/4 may suppress inflammation and LSPC function** and **restore hematopoiesis** • **Blocks TLR and IL-1R signaling** *in vitro*; **active in preclinical models of inflammation**[3]
Clinical Proof of Concept	• **Markedly suppressed LPS-induced cytokine release** was observed in a randomized controlled trial in healthy volunteers[4]
Regulatory Designations	• **Fast Track designation** for previously-treated transfusion dependent LR-MDS (Nov 2024) • **Orphan Drug designation** for treatment of myelodysplastic syndromes (Jan 2025)
Encouraging Clinical Profile	• **Promising preliminary safety and efficacy in a Phase 1b study** in elderly, heavily pre-treated patients with R/R LR-MDS (n=33) (presented at ASH 2025)[5]

MDS, myelodysplastic syndrome; LR-MDS, lower-risk myelodysplastic syndrome; ESAs, erythropoiesis-stimulating agents; LSPC, liver stem/progenitor cells; TLR, toll-like receptor; IL-1R, interleukin 1 receptor; LPS, lipopolysaccharide; R/R, relapsed or refractory. **1.** Investigational compound not approved by the FDA. **2.** Rigel data analysis on file. Patient population represents previously-treated patients. **3.** Sallman DA, et al. Front Oncol. 2016;6. **4.** Yan L et al. Ann Rheum Dis 2020;79 (suppl 1). **5.** Garcia-Manero et al. Blood (2025) 146 (Supplement 1): 489.

R289[1]: Phase 1b Study in Relapsed/Refractory Lower-Risk MDS

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



Key Eligibility Criteria

- R/R LR-MDS or inadequate response to prior therapies. Del(5q): R/R to lenalidomide
- Symptomatic anemia (Hb ≤9.0 g/dL) or TD (≥2u RBCs/16wks) in dose escalation; TD in dose expansion

Assessments

- Hematologic responses [TI and HI-E] per IWG 2018 criteria[4] and other responses per IWG 2006 criteria[5], from 8 weeks

Primary Endpoints

- Incidence of adverse events and dose-limiting toxicities

Secondary Endpoints

- Transfusion independence, hematologic improvement, response rates
- PK / PD
- Patient-reported outcomes (FACIT-Fatigue scale)

Updated data to be presented at ASH 2026

MDS, myelodysplastic syndrome; LR-MDS, lower-risk MDS; PK, pharmacokinetics; QD, daily; BID, twice daily; RP2D, recommended Phase 2 dose; Tx, treatment; Hb, hemoglobin; TD, transfusion dependent; TI, transfusion independence; HI-E, hematologic improvement - erythroid; PD, pharmacodynamics; FACIT-Fatigue scale, The Functional Assessment of Chronic Illness Therapy – Fatigue Scale.

1. Investigational compound not approved by the FDA. **2.** Jaki T et al. *Cancer Chemother Pharmacol.* 2013; 71. **3.** Split dose: 500 mg q AM, 250 mg q PM. **4.** Platzbecker U et al. Blood 2019;133(10). **5.** Cheson BD et al. Blood 2006;108.

ASH 2026: R289[1] Phase 1b Clinical Study Data Update

R289 continues to be generally well tolerated in an elderly, heavily pre-treated patient population with a high baseline transfusion burden

Abstract[2]

- 64 patients enrolled; 33 in dose escalation and 31 in dose expansion (randomized to 500 mg QD or BID)
  - Median # of prior therapies: 3 (1-8)
    - Prior therapies included luspatercept 84%, ESA 83%, azacitidine 38%, an investigational agent 29%, decitabine 24% and imetelstat 21%
- Most frequent TEAEs (≥20%, n=64) were diarrhea (31%) and cough (22%), all Grade 1/2
- No TEAEs leading to discontinuation occurred in dose expansion
- No dose limiting toxicities occurred in dose expansion
- The randomized comparison of 2 doses in dose expansion showed a similar, highly tolerable safety profile

Oral Presentation

- Updated data, including preliminary efficacy from dose expansion, will be presented during an oral session at ASH
  - Session: 637. Myelodysplastic Syndromes: Clinical and Epidemiological: Novel Therapeutic Strategies and Prognostic
  - Publication #251: Dose Escalating / Dose Expansion Study of R289, a Dual IRAK 1/4 Inhibitor, in Patients with Relapsed/Refractory (R/R) Lower Risk Myelodysplastic Syndrome (LR-MDS)
  - Presenter: Guillermo Garcia-Manero, MD Chair Ad Interim, Department of Leukemia, UT MDACC, Houston TX
  - Date: Saturday, December 12
  - Time: 3:00pm – 3:15pm CT

Source: ASH 2026 Publication #251: Dose Escalating / Dose Expansion Study of R289, a Dual IRAK 1/4 Inhibitor, in Patients with Relapsed/Refractory (R/R) Lower Risk Myelodysplastic Syndrome (LR-MDS).

ASH, American Society of Hematology Annual Meeting and Exposition; QD, once daily; BID, twice daily; TEAE, treatment emergent adverse events; UT MDACC, University of Texas MD Anderson Cancer Center.

1. Investigational compound not approved by the FDA. **2.** Abstract data as of July 16, 2026. Please see abstract for additional data.

R289 Development Next Steps

Lower-Risk MDS

- Complete enrollment of the dose expansion phase and selection of the recommended Phase 2 dose for future clinical studies (2H 2026)
  - Share updated top-line data from dose expansion phase by end of 2026
  - Open exploratory cohort of post-ESA, treatment naïve patients following selection of recommended Phase 2 dose
- Upon completion of Phase 1b study, follow-up with FDA about a potential registrational study

Other Potential Indications

- Evaluate R289 in other potential indications

MDS, myelodysplastic syndrome; ESA, erythropoiesis-stimulating agent; FDA, U.S. Food and Drug Administration.

ASH 2026 Key Data Presentations

Oral Presentation

Publication #251: Dose Escalating / Dose Expansion Study of R289, a Dual IRAK 1/4 Inhibitor, in Patients with Relapsed/Refractory (R/R) Lower Risk Myelodysplastic Syndrome (LR-MDS)

- *Lead Author: Guillermo Garcia-Manero, M.D., UT MD Anderson Cancer Center*

Poster Presentations

Publication #1250: Platelet Responses with Combination Therapy of Fostamatinib and Thrombopoietin Receptor Agonists in Immune Thrombocytopenia: An Updated Real-World Analysis

- *Lead Author: David J. Kuter, M.D., Dphil, Massachusetts General Hospital*

Publication #1252: Real-world safety, effectiveness, and predictors of responses to fostamatinib in patients with ITP: interim analysis of a nationwide post-marketing surveillance in Japan

- *Lead Author: Masataka Kuwana, M.D., Nippon Medical School, Japan*

Publication #4619: Hemoglobin Responses With Fostamatinib in a Long-Term Extension Trial in Warm Autoimmune Hemolytic Anemia

- *Lead Author: David J. Kuter, M.D., DPhil, Massachusetts General Hospital*

ASH, American Society of Hematology Annual Meeting.

Maintain Financial Discipline



Q3 2026 Highlights

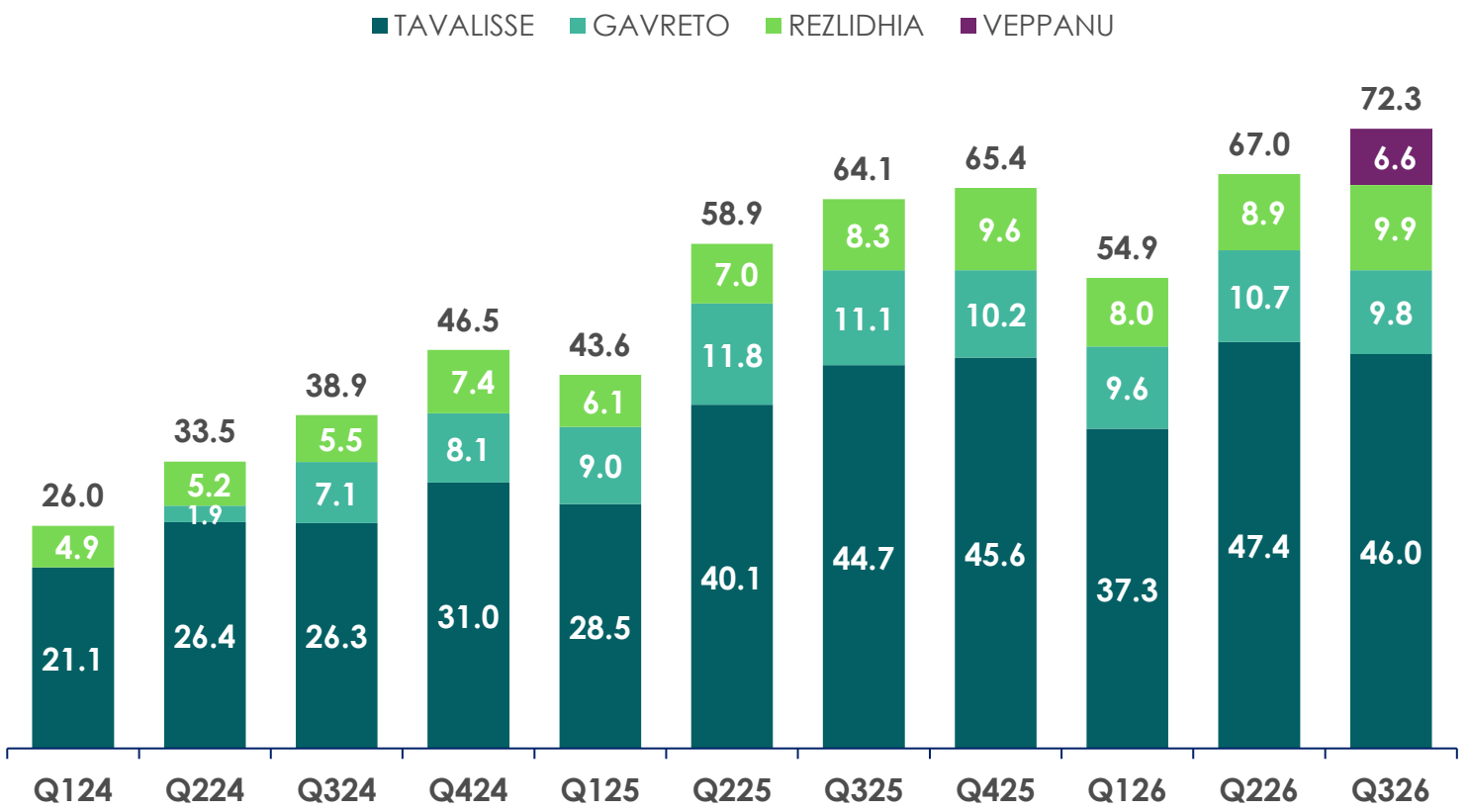
Q3 2026 Net Product Sales: $72.3M

- TAVALISSE $46.0M
- GAVRETO $9.8M
- REZLIDHIA $9.9M
- VEPPANU $6.6M

Q2 2026 Contract Revenues: $8.6M

- Grifols $3.8M
- Kissei $3.2M
- Others $1.6M

Net Product Sales ($M)



Q3 2026 Financial Overview

(in thousands)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2026	2025	2026	2025
Revenues				
Net Product Sales	$ 72,289	$ 64,067	$ 194,227	$ 166,565
Contract revenues from collaborations and other	8,601	5,395	24,184	57,915
Total revenues	80,890	69,462	218,411	224,480
Costs and expenses:				
Cost of product sales	10,783	4,753	23,914	13,666
Research and development	18,272	7,353	43,909	22,610
Selling, general and administrative	34,730	28,936	98,023	85,908
Total costs and expenses	63,785	41,042	165,846	122,184
Income from operations	17,105	28,420	52,565	102,296
Interest income	561	1,094	2,555	2,438
Interest expense and other	(257)	(1,894)	(2,469)	(5,621)
Income before income tax	17,409	27,620	52,651	99,113
Provision for (benefit from) income tax	4,224	(280)	13,522	154
Net income	$ 13,185	$ 27,900	$ 39,129	$ 98,959

	As of	
	September 30, 2026	December 31, 2025
Cash, Cash Equivalents and Short-term Investments	$ 99,305	$ 154,955

2026 Financial Outlook

- Total revenues of ~$290M to $295M (previously $285M to $295M)
  - Net product sales of ~$255M to $260M (previously ~$255M to $265M)
  - Contract revenues of ~$35M (previously ~$30M)
- Revenue guidance excludes VEPPANU
- Anticipate will report positive net income for the full year 2026, while funding existing and new clinical development programs

1. Cash, cash equivalents and short-term investments.

Note: Year-to-date 2025 contract revenues from collaborations and total revenues included $40M in non-cash contract revenues related to Rigel's agreement with Eli Lilly.

2026 Progress and Key Q4 2026 Priorities

Grow Commercial Business

- **VEPPANU™ (vepdegestrant) commercially available as of mid-August**
- **Drive rapid awareness and adoption of VEPPANU**

In-Licensing / Business Development

- **In-license of VEPPANU, the first and only FDA-approved PROTAC,** for patients with 2L+ ER+/HER2-, *ESR1*m advanced or metastatic breast cancer



Maintain Financial Discipline

- **Leverage existing commercial and operating infrastructure during integration of VEPPANU to drive financial synergies**
- **2026 Outlook: Total revenues: ~$290M to $295M[1]**
  - Net product sales of ~$255M to $260M
    Contract revenues of ~$35M

Advance Development Pipeline

- **R289 Phase 1b study in lower-risk MDS:**
  - Complete dose expansion and select RP2D for future clinical studies (2H 2026)
  - Share updated top-line data by end of 2026
  - Upon completion of the Phase 1b study, follow-up with FDA about a potential registrational study
- **Evaluate R289 in other potential indications**

FDA, U.S. Food and Drug Administration; PROTAC, PROteolysis TArgeting Chimera; 2L+, second line-plus; ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; MDS, myelodysplastic syndrome; RP2D, recommended Phase 2 dose.

1. Revenue guidance excludes VEPPANU.

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 https://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.

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

WARNING: SERIOUS INFECTIONS, INCLUDING OPPORTUNISTIC INFECTIONS

GAVRETO may increase the risk for serious infections, including bacterial, fungal, viral and opportunistic infections, which can lead to hospitalization or death. Withhold, reduce the dose or permanently discontinue GAVRETO based on severity.

WARNINGS AND PRECAUTIONS

- **Serious Infections, including Opportunistic Infections:** GAVRETO may increase the risk for serious infections, including fatal and opportunistic infections. In the AcceleRET-Lung trial, infections occurred in 72% of patients who received GAVRETO, including 18% with Grade 3 and 3.7% with Grade 4 and 7% with fatal outcomes. Among the patients who received chemotherapy/immunotherapy, infections occurred in 52%, including 10% with Grade 3. Infections in the GAVRETO arm included pneumonia, urinary tract infection, opportunistic infections (such as pneumocystis jirovecii pneumonia, and fungal infections) and others. Monitor patients for signs and symptoms of infection and treat appropriately. Withhold, reduce the dose, or permanently discontinue GAVRETO based on severity.
- **Interstitial Lung Disease (ILD)/Pneumonitis:** Severe, life-threatening, and fatal interstitial lung disease (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 which may be indicative of ILD (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.
- **Hypertension:** 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 AST occurred in 49% of patients, including Grade 3 or 4 in 7% and increased 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 for 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.

IMPORTANT SAFETY INFORMATION (Cont.)

- **Hemorrhagic Events:** Serious, including fatal, hemorrhagic events can occur with GAVRETO. Grade ≥ 3 hemorrhagic 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:** Cases of tumor lysis syndrome (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.
- **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. Oral administration of pralsetinib to pregnant rats during the period of organogenesis resulted in malformations and embryolethality at maternal exposures below the human exposure at the clinical dose of 400 mg once daily. 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.

ADVERSE REACTIONS

- **The most common adverse reactions (≥ 25%)** were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia and cough. **The most 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.

DRUG INTERACTIONS

- **Strong or moderate CYP3A inhibitors and/or P-gp inhibitors:** Concomitant use with a strong or moderate CYP3A inhibitor and/or a P-gp inhibitor increases pralsetinib exposure, which may increase the risk of adverse reactions related to GAVRETO. Avoid coadministration of GAVRETO with a strong or moderate CYP3A and/or P-gp inhibitor. If coadministration with any of the above inhibitors cannot be avoided, reduce the GAVRETO dose.
- **Strong or moderate CYP3A inducers:** Concomitant use with a strong CYP3A inducer decreases pralsetinib exposure, which may decrease efficacy of GAVRETO. Avoid concomitant use of GAVRETO with strong or moderate CYP3A inducers. If coadministration of GAVRETO with strong or moderate CYP3A inducers cannot be avoided, increase the GAVRETO dose.

USE IN SPECIFIC POPULATIONS

- **Lactation:** Advise not to breastfeed during treatment with GAVRETO and for 1 week after the last dose.
- **Pediatric Use:** The safety and effectiveness of GAVRETO have not been established in pediatric patients with RET fusion-positive NSCLC or in pediatric patients younger than 12 years old with RET fusion positive thyroid cancer.

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, including Boxed WARNING.

About VEPPANU™ (vepdegestrant)

INDICATION
VEPPANU is indicated for the treatment of adults with estrogen receptor (ER)–positive, human epidermal growth factor receptor 2 (HER2)–negative, estrogen receptor–1 (*ESR1*)–mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
QTc Interval Prolongation
VEPPANU can cause QT (QTc) interval prolongation. Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to and during treatment with VEPPANU. Perform an ECG prior to initiation of treatment with VEPPANU and do not initiate VEPPANU in patients with QTc >470 msec. Repeat ECG approximately 4 weeks after initiating treatment and as clinically indicated. Avoid concomitant use of VEPPANU with strong CYP3A inhibitors or drugs known to prolong the QTc interval.

Embryo-Fetal Toxicity
Based on findings from animal studies and its mechanism of action, VEPPANU can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VEPPANU and for 2 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with VEPPANU and for 2 weeks after the last dose.

ADVERSE REACTIONS
Serious adverse reactions occurred in 9% of patients who received VEPPANU. The serious adverse reactions included any fracture (1.3%), fall, hypercalcemia, hepatic injury, pneumonia, musculoskeletal pain (0.6% each), and QTc prolonged (0.3%). Fatal adverse reactions occurred in 1.0% of patients who received VEPPANU, including dyspnea, cerebral ischemia, and unknown cause (one patient each).

Permanent discontinuation of VEPPANU due to an adverse reaction occurred in 2.9% of patients, dosage interruptions of VEPPANU due to an adverse reaction occurred in 14% of patients, and dosage reductions of VEPPANU due to an adverse reaction occurred in 1.9% of patients.

The most common (≥10%) adverse reactions, including laboratory abnormalities, were decreased white blood cells, increased AST, musculoskeletal pain, fatigue, decreased hemoglobin, decreased neutrophils, increased ALT, increased alkaline phosphatase, nausea, decreased blood potassium, increased bilirubin, decreased appetite, electrocardiogram QT prolonged, decreased platelets, and constipation.

Clinically relevant adverse reactions in <10% of patients who received VEPPANU included headache, hot flush, diarrhea, vomiting, bradycardia, and urinary tract infection.

DRUG INTERACTIONS
- **Strong CYP3A Inhibitors:** Avoid concomitant use of VEPPANU with strong CYP3A inhibitors. If concomitant use cannot be avoided, reduce VEPPANU dosage.
- **Strong CYP3A Inducers:** Avoid concomitant use with strong CYP3A inducers in patients receiving VEPPANU. If concomitant use cannot be avoided, increase VEPPANU dosage.
- **Certain P-gp Substrates:** Avoid concomitant use with certain P-gp substrates where minimal increases in concentration may lead to serious adverse reactions.
- **Certain UGT1A9 Substrates:** Refer to the Prescribing Information for UGT1A9 substrates where minimal increases in the concentration may lead to serious adverse reactions.

Avoid concomitant use of VEPPANU with other drugs with a known potential to prolong the QTc interval.

LACTATION
Advise lactating women not to breastfeed during treatment with VEPPANU and for 2 weeks after the last dose.

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

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

PROTAC vs. Oral SERD Mechanism Image Citations

† In a preclinical trial with 2 wild-type ER+ breast cancer lines after 4 hours of treatment, the maximal degradation rates ranged between 8% and 68% for the oral SERDs approved at the time of the study (elacestrant and imlunestrant); the maximal degradation rates ranged between 79% and 86% for VEPPANU. In ESR1m ER+ breast cancer lines, maximal degradation rates ranged from 9% to 62% for elacestrant and from 79% to 85% for VEPPANU.

2. Campone M, De Laurentiis M, Jhaveri K, et al. Vepdegestrant, a PROTAC estrogen receptor degrader, in advanced breast cancer. *N Engl J Med*. 2025;393(6):556-568. doi: 10.1056/NEJMoa2505725

12. Békés M, Langley DR, Crews CM. PROTAC targeted protein degraders: the past is prologue. *Nat Rev Drug Discov*. 2022;21(3):181-200. doi:10.1038/s41573-021-00371-6

14. Hamilton EP, Jeselsohn RM, Vahdat LT, et al. PROteolysis TArgeting Chimera (PROTAC) estrogen receptor degraders for treatment of estrogen receptor–positive advanced breast cancer. *Target Oncol*. 2025;20(3):431-444. doi:10.1007/s11523-025-01137-5

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16. Burke MR, Smith AR, Zheng G. Overcoming cancer drug resistance utilizing PROTAC technology. *Front Cell Dev Biol*. 2022;10:872729. doi:10.3389/fcell.2022.872729

17. Liu Z, Hu M, Yang Y, et al. An overview of PROTACs: a promising drug discovery paradigm. *Mol Biomed*. 2022;3(7):46. doi:10.1186/s43556-022-00112-0

18. Chirnomas D, Hornberger KR, Crews CM. Protein degraders enter the clinic – a new approach to cancer therapy. *Nat Rev Clin Oncol*. 2023;20(4):265-278. doi:10.1038/s41571-023-00736-3

19. Wang Y, Tang SC. The race to develop oral SERDs and other novel estrogen receptor inhibitors: recent clinical trial results and impact on treatment options. *Cancer Metastasis Rev*. 2022;41:975-990. doi:10.1007/s10555-022-10066-y

20. Data on file, Rigel Pharmaceuticals, Inc. September 2026

PROTAC, PROteolysis TArgeting Chimera; SERD, selective estrogen receptor degrader.



Thank You

www.rigel.com