



Q2 2026 Financial Results Presentation

August 4, 2026



Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 ("PSLRA") relating to, among other things, expected commercial launches and commercial availability, commercial, financial and clinical results, projections of financial performance and outlook for 2026, expectations for growing our commercial business and successfully executing our commercial strategy, continued enrollment of our R289 study, presentation of study data, expectation of clinical outcomes, continued ability to develop and commercialize VEPPANU, TAVALISSE, GAVRETO, REZLIDHIA and R289 domestically and in certain international markets, the Company's ability to fund its existing and future clinical development programs, and expectations for our partnering, licensing, commercialization and collaboration efforts.

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", "outlook", "anticipates", "expects", "will", "promising" 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, anticipated financial performance and profitability for 2026; expected product sales and commercial growth; the anticipated timing, progress and results of clinical development activities for R289, including enrollment, dose selection and data readouts; the Company's ability to fund its existing and future clinical development programs; the anticipated commercial launch and commercialization of VEPPANU, including expectations regarding its market opportunity, physician adoption, commercial performance and potential contribution to Rigel's commercial portfolio; the Company's ability to successfully execute its commercial strategy; and its partnering, licensing, commercialization, collaboration and potential business development activities. 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 VEPPANU, TAVALISSE, GAVRETO and REZLIDHIA, including uncertainties relating to physician adoption, patient demand, market acceptance, reimbursement and pricing; risks that the FDA, European Medicines Agency, PMDA or other regulatory authorities may make adverse decisions regarding VEPPANU, TAVALISSE, GAVRETO, REZLIDHIA or R289; operational, regulatory or other risks that can affect the timing of enrollment and data availability for R289 clinical development; risks that clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that VEPPANU, TAVALISSE, GAVRETO, REZLIDHIA or R289 may have unintended side effects, adverse reactions or incidents of misuse; the availability of resources to develop or market Rigel's product candidates; market competition; product demand variability; pricing/reimbursement dynamics; unanticipated business needs and other developments, including potential partnering, licensing or other collaboration arrangements, which could impact Rigel's funding needs or other internal resource demands, as well as 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 June 30, 2026 and subsequent filings. Any forward-looking statement made by us in this presentation 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.

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.

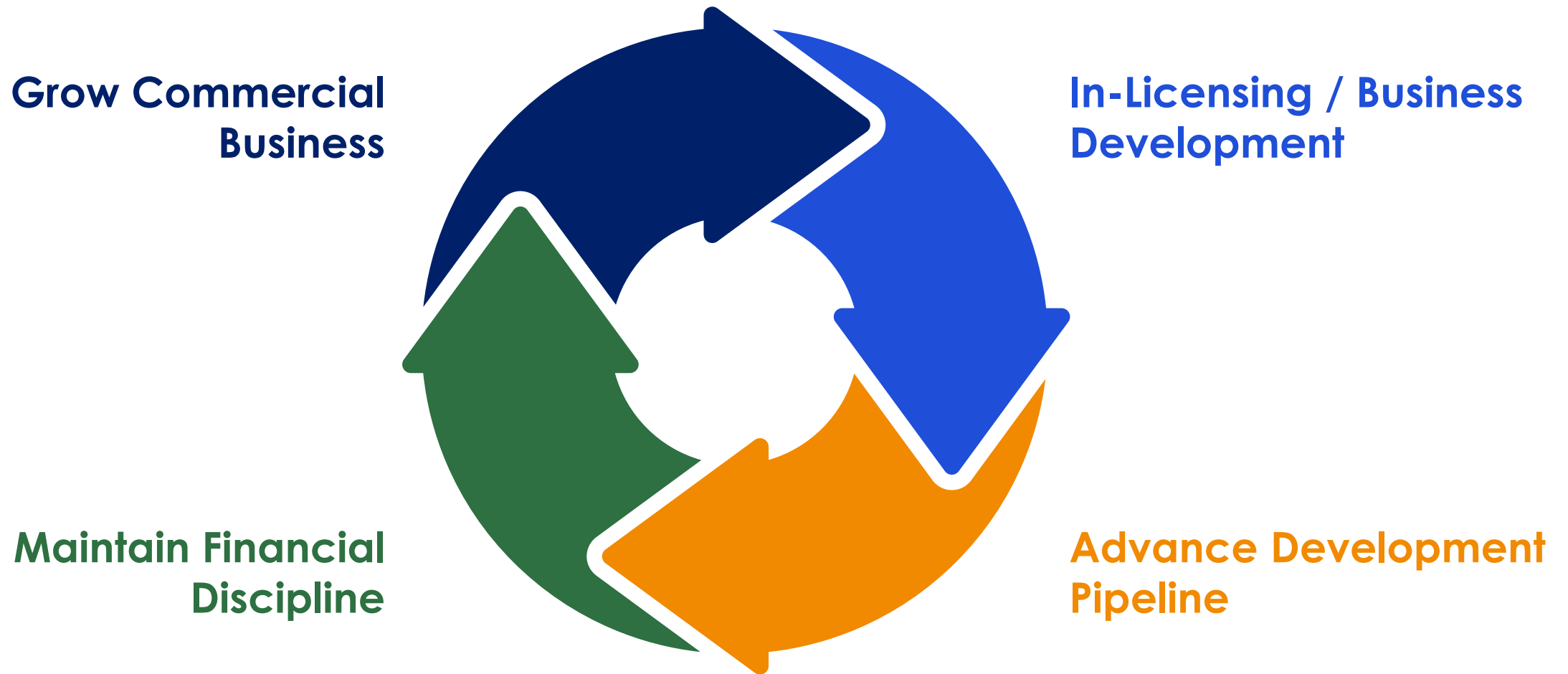
Executive Vice President &
Chief Medical Officer



Dean Schorno

Executive Vice President &
Chief Financial Officer

Rigel's Transformational Growth Strategy



In-License of VEPPANU™ (Vepdegestrant)

VEPPANU will be commercially available in mid-August

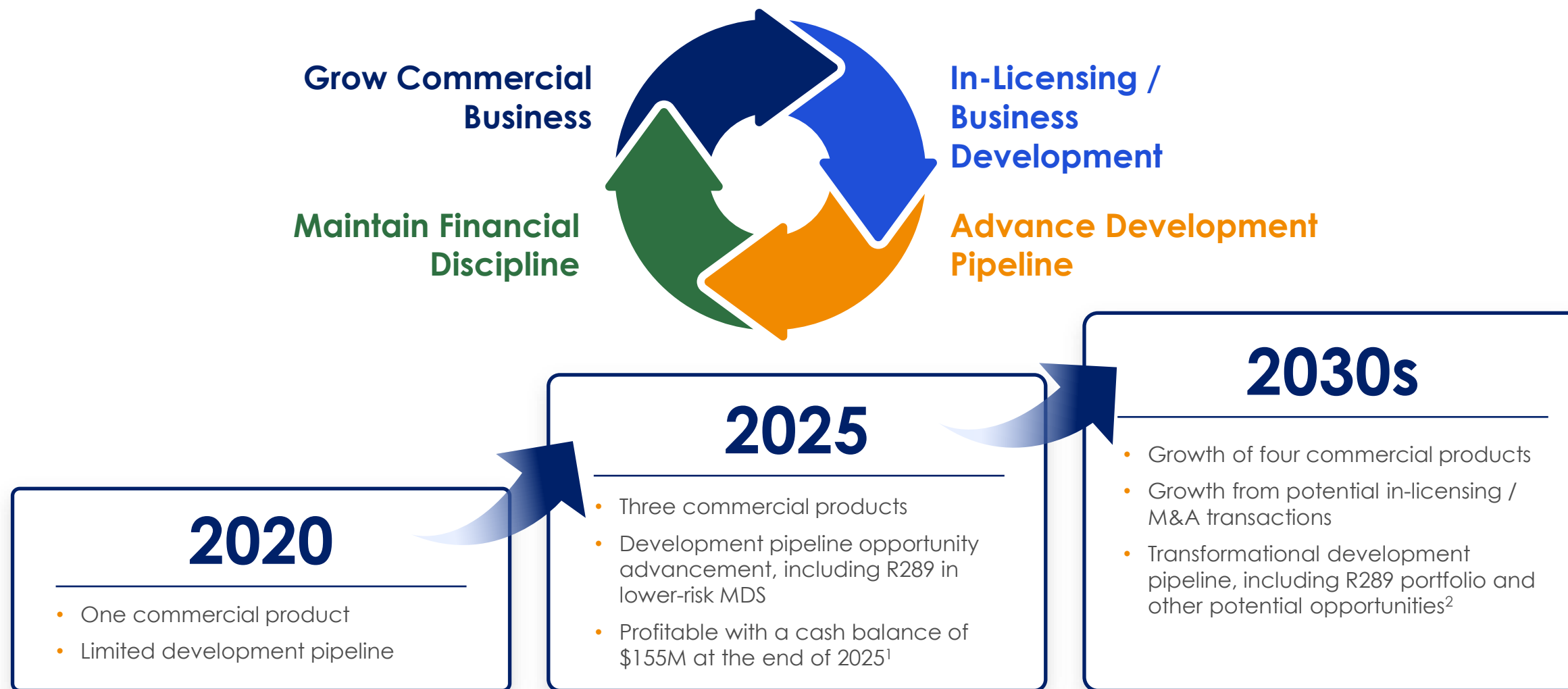


- Entered into **exclusive, global license agreement** with Arvinas and Pfizer to **develop, manufacture and commercialize VEPPANU™ (vepdegestrant)** for the treatment of 2L+ ER+/HER2-, *ESR1*m advanced or metastatic breast cancer, effective June 11, 2026
 - VEPPANU is **the first and only FDA-approved oral PROTAC**
- VEPPANU has a novel mechanism of action and differentiated data; has the **potential to become a market-leading treatment**
- Rigel has engaged with HCPs for early awareness and is ready to drive rapid adoption to execute a successful commercial launch

2L+, second line-plus; ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; FDA, U.S. Food and Drug Administration; PROTAC, PROteolysis TArgeting Chimera; HCP, healthcare provider.

Please visit www.VEPPANU.com for Full Prescribing Information.

Rigel's Transformation to Accelerated Growth



MDS, myelodysplastic syndrome.

1. Cash, cash equivalents & short-term investments. 2. Investigational compounds in these indications and not approved by the FDA.

Grow Commercial Business





Tavalisse[®]
(fostamatinib disodium
hexahydrate) tablets



GAVRETO[®]
pralsetinib | 100 mg
capsules



REZLIDHIA[®]
(olutasidenib) 150 mg
capsules

Q2 2026 Commercial Performance

Net Portfolio Sales grew \$8.1M (14%) vs. Q2 2025

Net Product Sales (\$M)

■ TAVALISSE ■ GAVRETO ■ REZLIDHIA



Tavalisse
(fostamatinib disodium hexahydrate) tablets

\$47.4M
Q2 2026 Net Product Sales

18%
Growth vs.
Q2 2025

GAVRETO
pralsetinib | 100mg capsules

\$10.7M
Q2 2026 Net Product Sales

(10)%
Growth vs.
Q2 2025

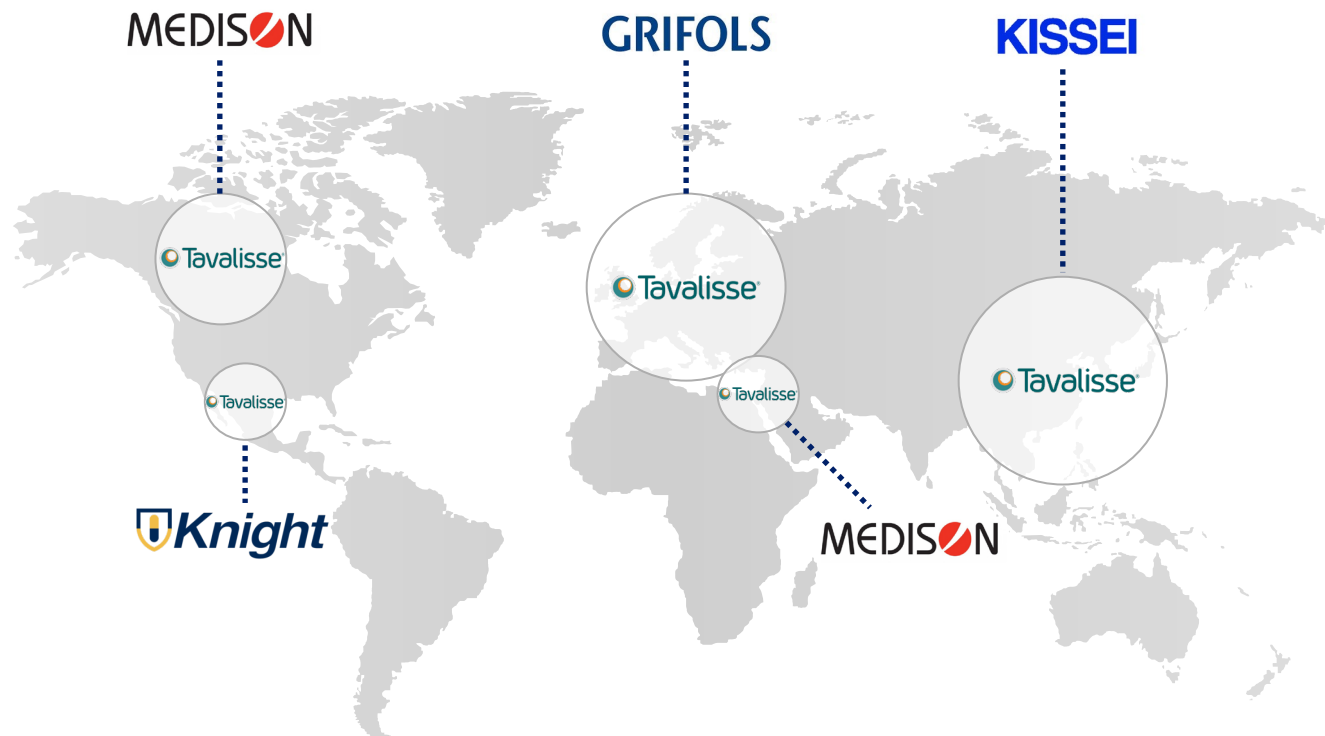
REZLIDHIA
(olutasidenib) 150mg capsules

\$8.9M
Q2 2026 Net Product Sales

27%
Growth vs.
Q2 2025

Expanding Commercial Availability in Global Markets

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



Q2 2026 Collaboration Revenues

- Kissei \$5.8M
- Grifols \$5.0M
- Medison \$0.3M
- Others \$0.6M

TAVALISSE Commercial Launch

- Knight announced launch of TAVALISSE in Mexico in May

TAVALISSE Regulatory Approval

- Knight announced regulatory approval in Brazil in May

REZLIDHIA Opportunity¹

- 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 territories²

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.



VEPPANUTM

vepdegestrant 200 mg
100 mg



APPROVED IN THE U.S.

VEPPANU is indicated for the treatment of adults with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-), 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.

Please see Important Safety Information on slide 44

VEPPANU™ has the Potential to Transform Rigel's Commercial Portfolio



The **first and only FDA-approved PROTAC**, a new class of targeted agents



A **novel and unique mechanism of action** with the **potential to be an important new therapy** for 2L and 3L ER+/HER2-, ESR1m metastatic breast cancer



Rigel's proven commercial and medical infrastructure and expertise are **enabling us to quickly and successfully launch**

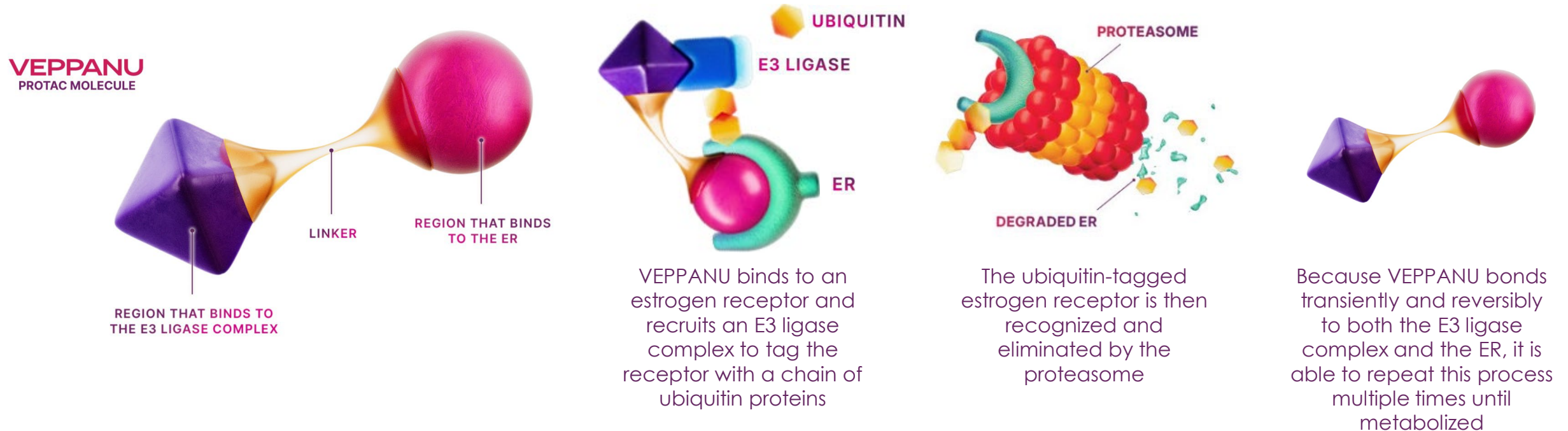


The **potential to drive portfolio growth** and become Rigel's **largest revenue producer**

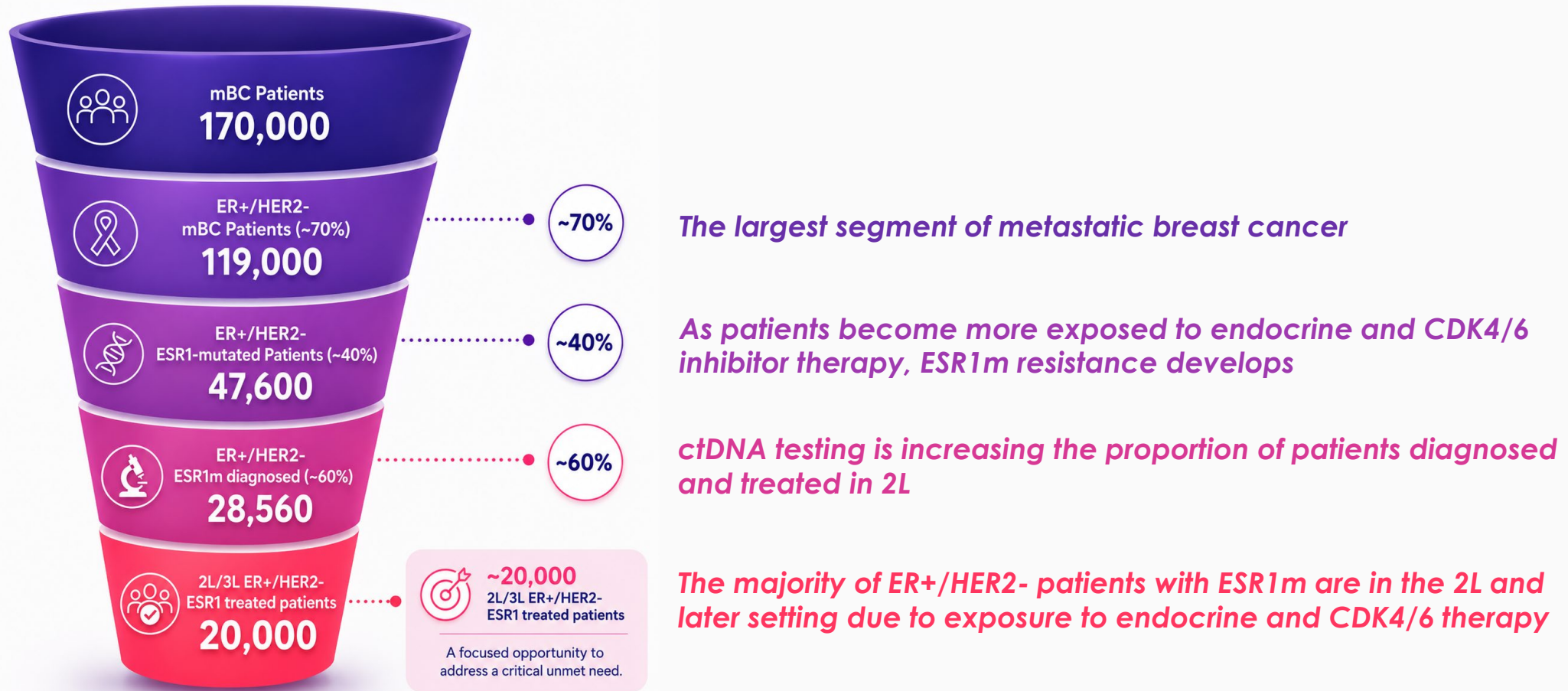
PROteolysis Targeting Chimera (PROTAC)

The FIRST in a novel class of drugs called heterobifunctional protein degraders

The novel bifunctional design of PROTAC represents a major innovation in ER degradation



ER+/HER2-, ESR1m mBC Patient Opportunity



~20,000¹ patients with 2L/3L ER+/HER2-, ESR1m mBC represent potential \$1B+ market in the U.S.

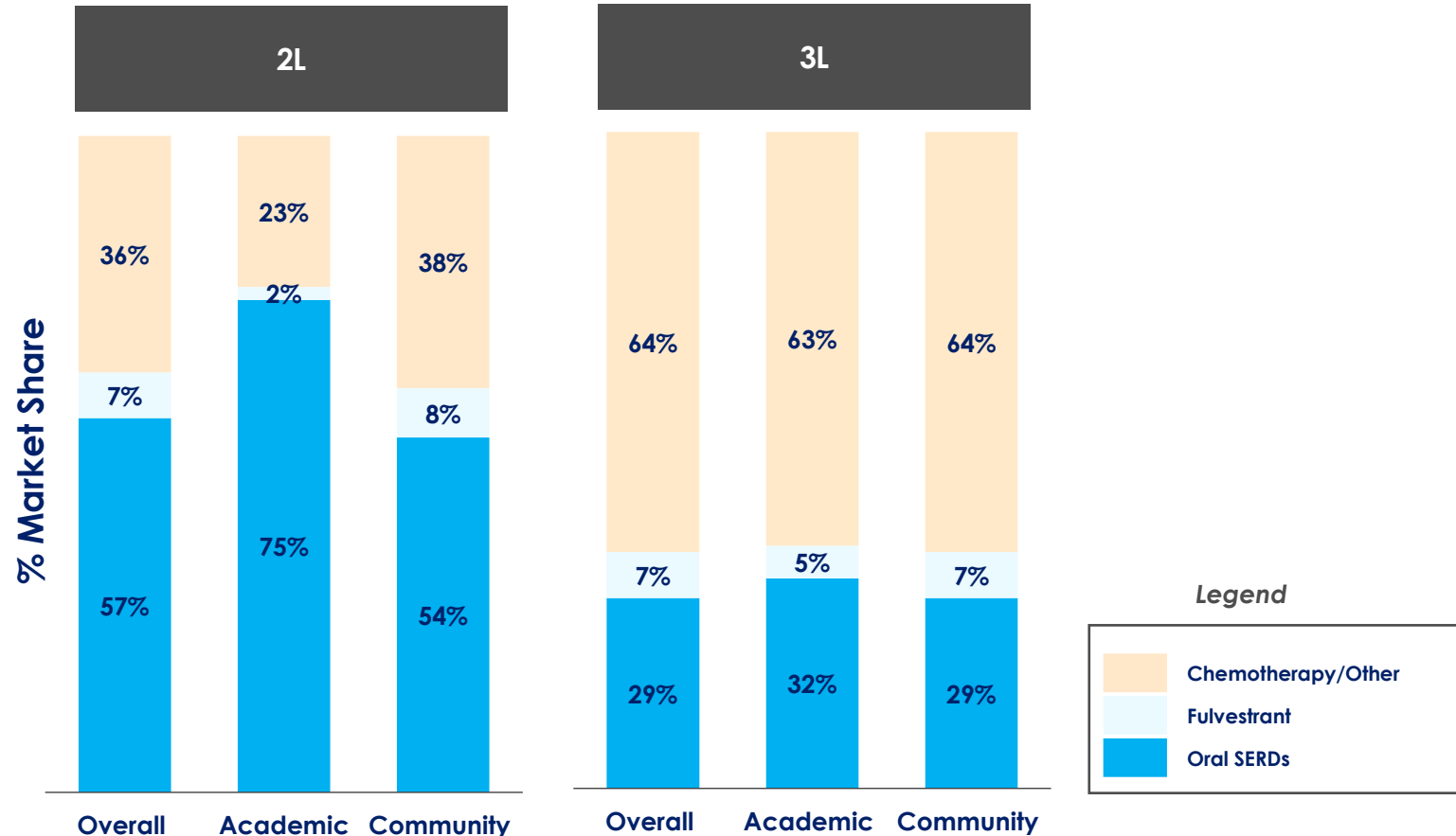
ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutation; mBC, metastatic breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; 2L, second line; 3L, third line; ctDNA, circulating tumor DNA.

1. Internal market research.



Will Enter a Dynamic Market Where Most Patients are Treated in the Community Setting

Current Therapies in 2L/3L ER+/HER2-, ESR1m mBC¹



Market Opportunity

- Oral SERDs have been rapidly adopted, and are used in the majority of patients in 2L and ~30% of patients in 3L
- Chemotherapy and other therapies still represent more than 25% of patients in 2L and 60% of patients in 3L
- Approximately 80% of patients are treated at community oncology practices, where nearly half of patients still do not receive oral SERDs in the 2L setting

2L, second line; 3L, third line; ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; MBC, metastatic breast cancer; SERD, Selective Estrogen Receptor Degradator.

1. Internal Market Research Apr 2026

VEPPANU™ has the Potential to Become a Market-leading Treatment in 2L+ ER+/HER2-, *ESR1*m Metastatic Breast Cancer (mBC)



Proven Efficacy

- Improved median Progression Free Survival (mPFS), Objective Response Rate (ORR) and Clinical Benefit Rate (CBR) vs. fulvestrant
 - Improved mPFS 2.4-fold, or 2.9 months (5.0 months vs. 2.1 months), ORR (19% vs. 4%) and CBR (42% vs. 20%) vs. fulvestrant



Demonstrated Tolerability

- Manageable safety profile with **low rates and severity of GI-related events**
- **Low rates of treatment discontinuation (3%) and dose reductions (2%)**



Real-World Applicability

- Patient characteristics of those enrolled in VERITAC-2 were **representative of real-world 2L+ setting, with 100% receiving prior CDK4/6i + ET**

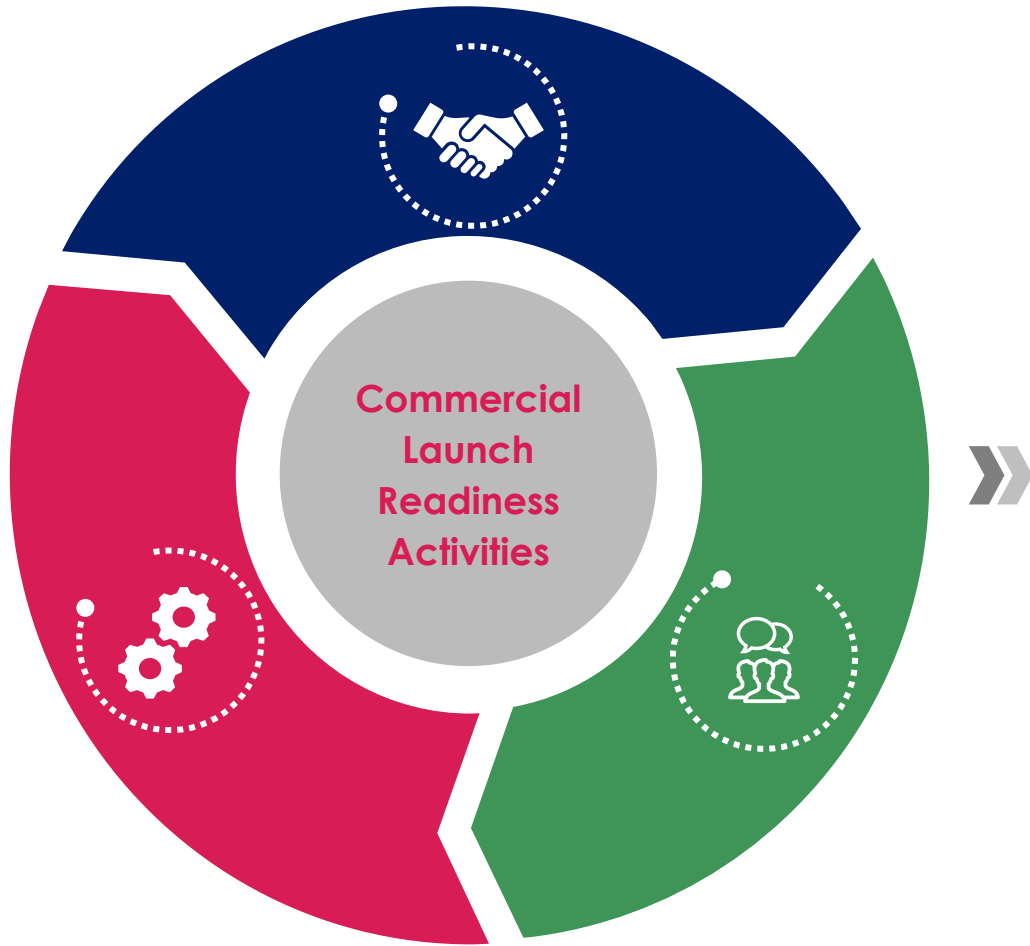
Breast Cancer NCCN Guidelines® include vepdegestrant as a Category 2A Targeted Therapy treatment option for HR-positive/HER2-negative *ESR1* mutation for recurrent unresectable or stage IV (M1) disease¹

2L+, second line-plus; ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; *ESR1*, estrogen receptor 1 gene; *ESR1*m, *ESR1* mutated; GI, gastrointestinal; 2L, second line; 3L, third line; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ET, endocrine therapy; NCCN, National Comprehensive Cancer Network® (NCCN®).

1. NCCN Clinical Practice Guidelines in Oncology® for Breast Cancer V.5.2026. Accessed July 30, 2026.

Commercialization Plans Now Being Implemented

Executing activities to ensure successful launch upon product availability



Collaboration Enabling Expedited Product Availability

Strong relationships with partners and execution against detailed transition plans have ensured we are ON TRACK to have VEPPANU in our specialty distribution channel and available to patients and clinics in mid-August

Coordinated Engagement with Key Customers

Meetings with Breast Cancer KOLs, Payers, GPOs and other key customers have been ongoing since ASCO to prepare for launch

Key accounts and top customer targets have been identified and refined through analytics and ongoing market research

Leveraged Capabilities to Immediately Operationalize

VEPPANU.COM live immediately upon June 16th deal close

Sales Force fully deployed on June 17th to spread VEPPANU awareness

Rigel ONECARE Patient Services hub, Copay Card services, and Specialty Pharmacy network now able to serve providers and patients, enabling patients access to VEPPANU upon availability



Commercial Launch Phases ON TRACK

Phase 1: Now Approved

Since Deal Close

- **Websites:** VEPPANU.com, rigelonecare.com, rigelmedinfo.com,
- **Initial Sales Force Materials:** USPI, Now Approved promotional materials

Phase 2: Now Available

Upon Product Availability

- **Additional Materials to Facilitate Patient Starts**
Publication Overview, Dosing and Admin Guide, Getting Started Patient Brochure, Distribution Guide

Phase 3: Branded Campaign

Post-Launch (Q4)

- **Expand Awareness and Adoption through an Omnichannel Approach**
Dedicated HCP and Patient websites
Additional Promotional Materials for HCPs and Patients

3

HCP Campaign

Drive patient identification, utilization

2

Patient Campaign

Drive request, activation and support positive outcomes

Personal

Non-Personal

VEPPANU
vepdegestrant

For 2L+ treatment of ESR7m, ER+/HER2- mBC

NOW APPROVED: the First-and-Only FDA-approved PROTAC

A PROTAC is a type of heterobifunctional protein degrader, a novel treatment class.

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.

[View Prescribing Information](#) [Read Full Release](#)

2L+ treated line, ER+/HER2- negative receptor-positive human epidermal growth factor receptor 2-negative, 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.

Contact Rigel Medical Information for Product Questions or Medical Inquiries
Call Rigel Medical Information Center at 1-800-983-1329 or email productinfo@rigel.com
You may also report adverse events associated with taking our prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Contact Rigel

VEPPANU
vepdegestrant

NOW APPROVED

Scan to visit VEPPANU.com and to view the full Prescribing Information

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VEPPANU is a registered trademark of Rigel Pharmaceuticals, Inc.
USPI Ref: VEPPANU-000001-0001

rigel

VEPPANU
vepdegestrant

VEPPANU, a PROTAC Estrogen Receptor Degradar, in Advanced Breast Cancer

Campos M, De Laurentis M, Jhaveri K, et al. The New England Journal of Medicine. Published online May 31, 2025. doi:10.1056/NEJMoa2505725

"In the context of studies in this patient population, our findings appear to support vepdegestrant as a new endocrine therapy with a differentiated mechanism of action and safety profile for patients who currently have limited treatment options in this disease setting."

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 QTc (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 >450 msec. Repeat ECG approximately 4 weeks after initiating treatment and as clinically indicated.
Avoid concomitant use of VEPPANU with strong CYP3A4 inhibitors or drugs known to prolong the QTc interval.

VEPPANU
vepdegestrant

DOSING AND ADMINISTRATION GUIDE
Information on dosing, administration, and management of potential adverse reactions with VEPPANU tablets

Getting started with VEPPANU
As you begin your journey with VEPPANU, this guide can help you get the most benefit from your medication—understanding how this medication works, how to take it as prescribed, and what to expect once treatment begins.

Please see full Prescribing Information including Patient Information at VEPPANU.com

DISTRIBUTION INFORMATION

VEPPANU
vepdegestrant

Description	15-Day RDC	30-Day RDC
VEPPANU 200 mg	71332-0008-30	71332-0008-30
VEPPANU 100 mg	71332-0007-30	71332-0007-30

Pharmacies can purchase VEPPANU from the following Specialty Distributors:

Distributor	Phone
Cardinal Health	877-453-3972
Cencora (ASD Healthcare)	800-745-6273
(Oncology Supply)	800-633-7555
Plasma and Biologics	877-625-2586
in Specialty Health	800-482-6700

Pharmacies are authorized to dispense VEPPANU directly to patients:

Pharmacy	Phone	Fax
by McKesson	800-850-4306	800-823-4506
ology Pharmacy	877-662-5633	877-662-5355
ry MedPlus Specialty	787-523-2900	787-777-1580
rtner of Onc360		

IECARE provides support to VEPPANU patients.

Contact RIGEL, ONECARE at 855-744-9562 (855-853-8562) for patient support services including:

- Benefits investigation, prior authorization, and appeals resources
- Copay assistance
- Temporary and long-term free drug supply
- Additional support and product education phone calls

Learn more and access the enrollment form at RIGELCARE.com.

"As part of our commitment to patient support, we have created RIGELCARE."

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VEPPANU is a registered trademark of Rigel Pharmaceuticals, Inc.
USPI Ref: VEPPANU-000001-0001

USPI, U.S. Prescribing Information; HCP, healthcare provider.



Advance Development Pipeline

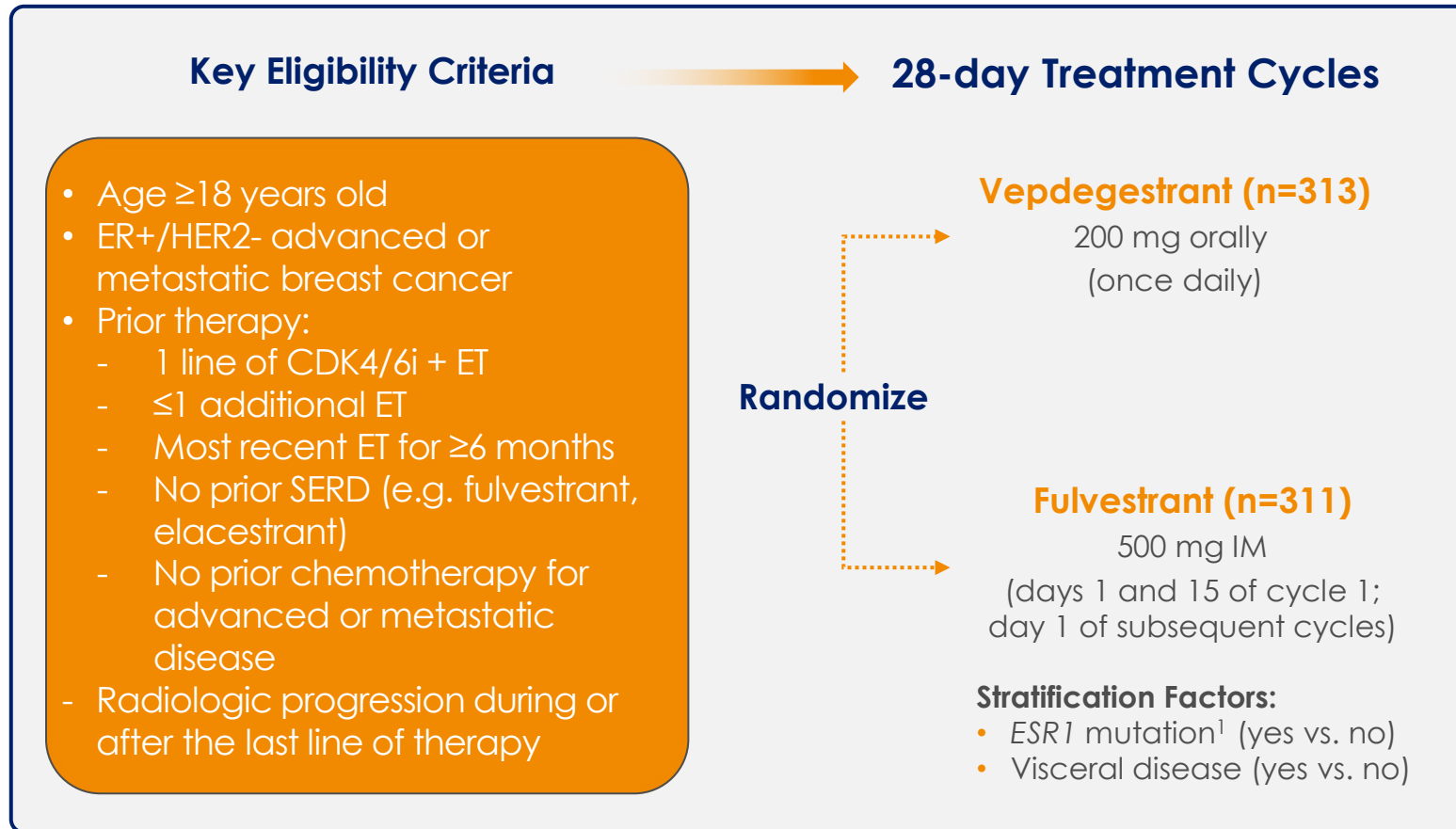




Vepdegestrant Clinical Overview

VERITAC-2 Phase 3 Clinical Trial Design

Randomized, open-label, multi-center trial evaluating efficacy and tolerability of vepdegestrant vs. fulvestrant in patients with ER+/HER2-, *ESR1*m advanced or metastatic breast cancer (NCT05654623)



Primary Endpoints

- Progression-free survival by BICR in:
 - *ESR1*m population
 - All patients

Secondary Endpoints

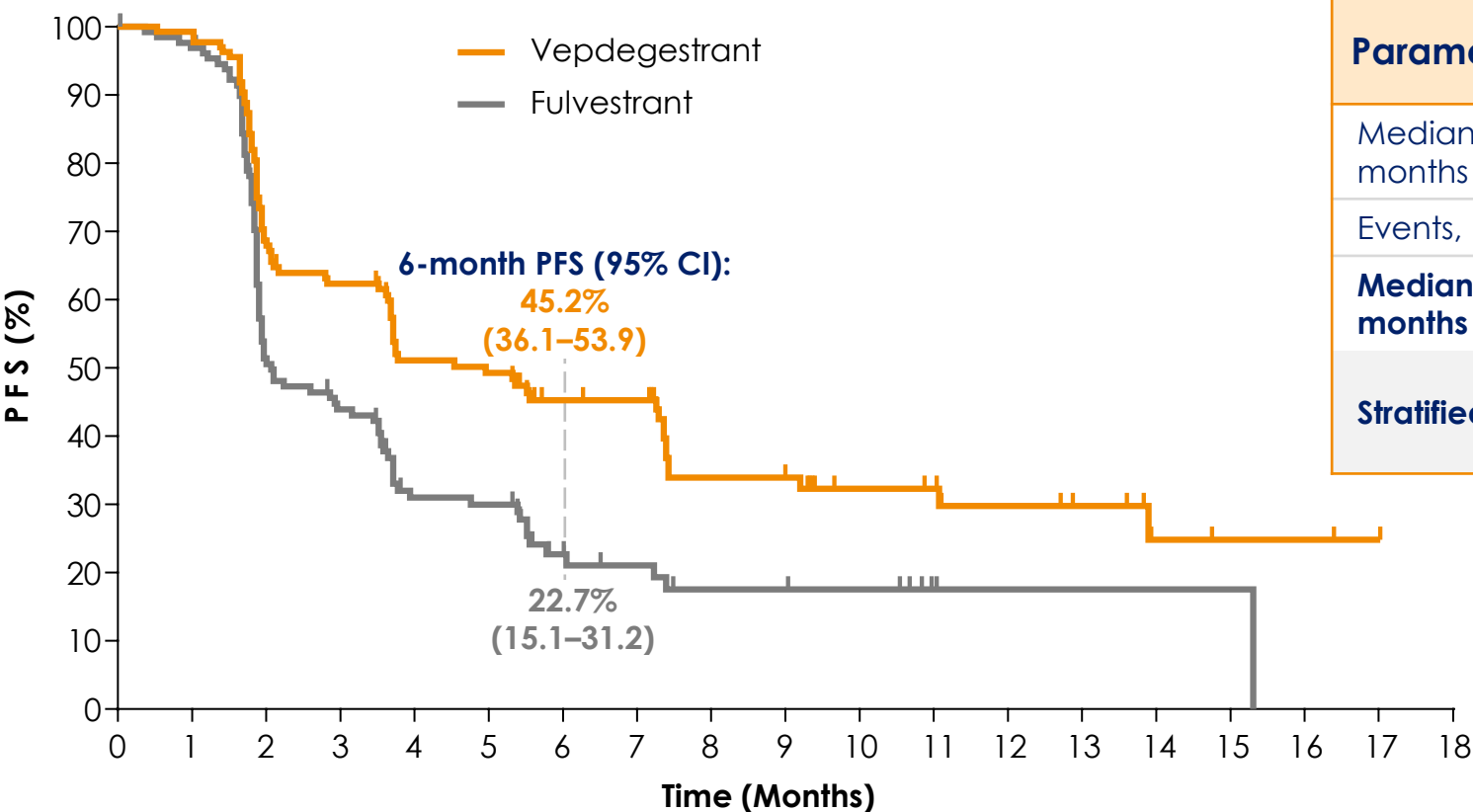
- Overall survival (key secondary)
- Clinical benefit rate and objective response rate by BICR
- Adverse events

Data cutoff date: Jan 31, 2025

ER+/HER2-, estrogen receptor-positive, human epidermal growth factor receptor 2-negative; *ESR1*, estrogen receptor 1 gene; *ESR1*m, *ESR1* mutated; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ET, endocrine therapy; SERD, selective estrogen receptor degrader; IM, intramuscularly; BICR, blinded independent central review.

1. *ESR1*m status was assessed in ctDNA by Foundation Medicine, except in China, where Origimed testing was used.

Vepdegestrant Met the Primary Endpoint with a ~3-Month mPFS Improvement in Patients with Tumors Harboring *ESR1* Mutations



Parameter	Vepdeg (n = 136)	Fulv (n = 134)
Median follow up, months	7.4	6.0
Events, n (%)	79 (58)	95 (71)
Median PFS by BICR, months (95% CI)	5.0 (3.7-7.4)	2.1 (1.9-3.5)
Stratified HR (95% CI)	0.57 (0.42-0.77) 2-sided P <.001	

No. at risk

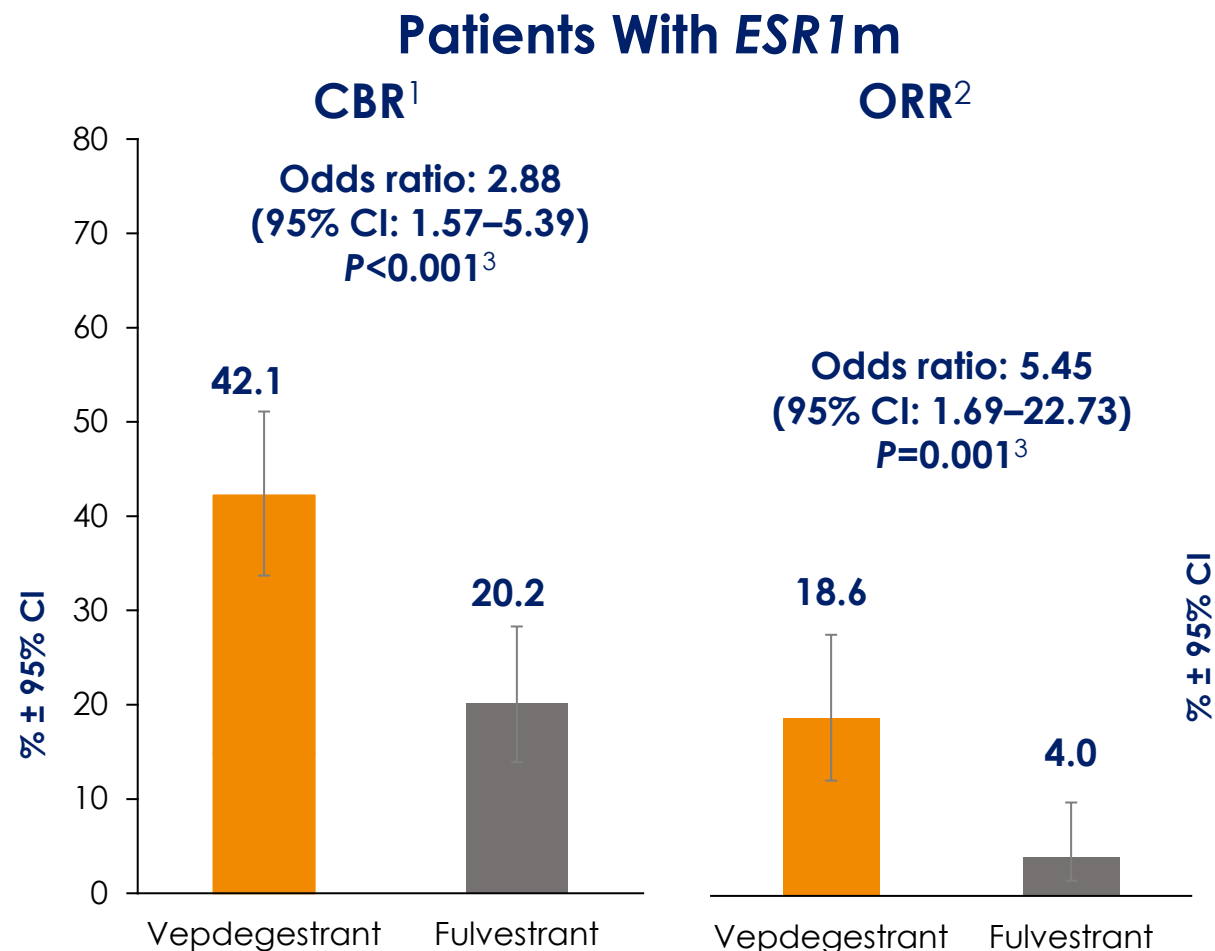
Vepdegestrant	136	134	87	78	55	53	38	37	22	22	15	14	10	8	4	3	3	2	0
Fulvestrant	134	125	62	52	30	29	15	12	8	8	7	2	1	1	1	1	0	0	0

Source: Hamilton. ASCO 2025. Abstr LBA1000.

Note: Vepdegestrant did not meet the primary endpoint in the intention-to-treat (ITT) population.

mPFS, median progression-free survival; ESR1, estrogen receptor 1 gene; ESR1m, ESR1 mutated; PFS, progression-free survival; CI, confidence interval; Vepdeg, vepdegestrant; Fulv, fulvestrant; BICR, blinded independent central review; HR, hazard ratio.

Vepdegestrant Showed Statistically Significant Improvements in CBR and ORR in the *ESR1*m Population



Source: Hamilton. ASCO 2025. Abstr LBA1000.

CBR, clinical benefit rate; ORR, objective response rate; *ESR1*, estrogen receptor 1 gene; *ESR1*m, *ESR1* mutated; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease.

1. CBR was defined as the rate of confirmed CR or PR at any time, or SD, non-CR, or non-progressive disease for ≥24 weeks and was estimated in CBR-evaluable patients (those enrolled for ≥24 weeks prior to data cutoff or those with confirmed CR or PR). 2. ORR was defined as the rate of confirmed CR or PR and was estimated in patients with measurable disease at baseline. 3. Nominal P-value.

Vepdegestrant Was Generally Well Tolerated, with Low Rates of Discontinuation and Dose Reductions

Adverse Events, %	Vepdegestrant (n = 312)	Fulvestrant (n = 307)
TEAEs		
Any	87	81
Grade ≥3	23	18
Serious	10	9
Leading to tx discontinuation	3	1
Leading to dose reduction	2	NA
TRAEs		
Any	57	40
Grade ≥3	8	3

QT Prolongation

- TEAEs: 10% in vepdegestrant and 1% in fulvestrant
- A QT interval substudy (n = 88) confirmed a mild increase (11.1 ms) from baseline in QTcF, with upper 90% CI (13.7 ms) <20 ms,^f **indicating no large QT-prolonging effect**

TEAEs in >10% of Patients in Either Group, %	Vepdegestrant (n = 312)		Fulvestrant (n = 307)	
	Any	Gr 3/4	Any	Gr 3/4
Fatigue^a	27	1	16	1
ALT increased^b	14	1	10	1
AST increased	14	1	10	3
Nausea	13	0	9	1
Anemia^{b,c}	12	2	8	3
Neutropenia^d	12	2 ^e	5	1 ^e
Back pain	11	1	7	<1
Arthralgia	11	1	11	0
Decreased appetite	11	<1	5	0

Source: Hamilton. ASCO 2025. Abstr LBA1000.

TEAEs, treatment-emergent adverse events; tx, treatment; QTcF, Fridericia-corrected QT interval; Gr, grade; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

a. Includes fatigue and asthenia. b. No between-group differences were observed for ALT/AST increases or anemia based on laboratory values. c. Includes anemia, hemoglobin decreased, and iron deficiency anemia. d. Includes neutropenia and neutrophil count decreased. No events led to dose reductions or treatment discontinuation in either treatment group. There were no events of febrile neutropenia in the vepdegestrant group and 1 event of grade 2 febrile neutropenia in the fulvestrant group. e. One patient with grade 4 event. f. Based on a concentration-QTc population modeling analysis.

Vepdegestrant Development

Current Clinical Studies

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

- VERITAC-2¹
- Combination studies
 - Abemaciclib
 - Ribociclib
 - Samuraciclib
 - Atfirmociclib
- Japanese bridging study
- Hepatic impairment study

Development Plans

- Pfizer and Arvinas remain responsible for current clinical studies²
- Combination studies are expected to provide additional safety and efficacy data
- Rigel will evaluate future development opportunities for vepdegestrant

Hematology and Oncology Focus Areas¹

R289 IRAK1/4 Inhibitor

- Evaluating in a Phase 1b study for patients with R/R lower-risk MDS
 - Granted Fast Track and Orphan Drug designations by the FDA²
- Other potential indications under consideration

- Strategic collaborations:
 - **MD Anderson:** Monotherapy or combination therapy in *mIDH1* AML and other hematologic malignancies
 - **CONNECT:** Combination therapy in *mIDH1* high-grade glioma
 - **MyeloMATCH:** Combination therapy in *mIDH1* AML and MDS

Olutasidenib *mIDH1* Inhibitor

IRAK1/4, interleukin receptor-associated kinases 1 and 4; R/R, relapsed/refractory; MDS, myelodysplastic syndrome; FDA, U.S. Food and Drug Administration; 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.

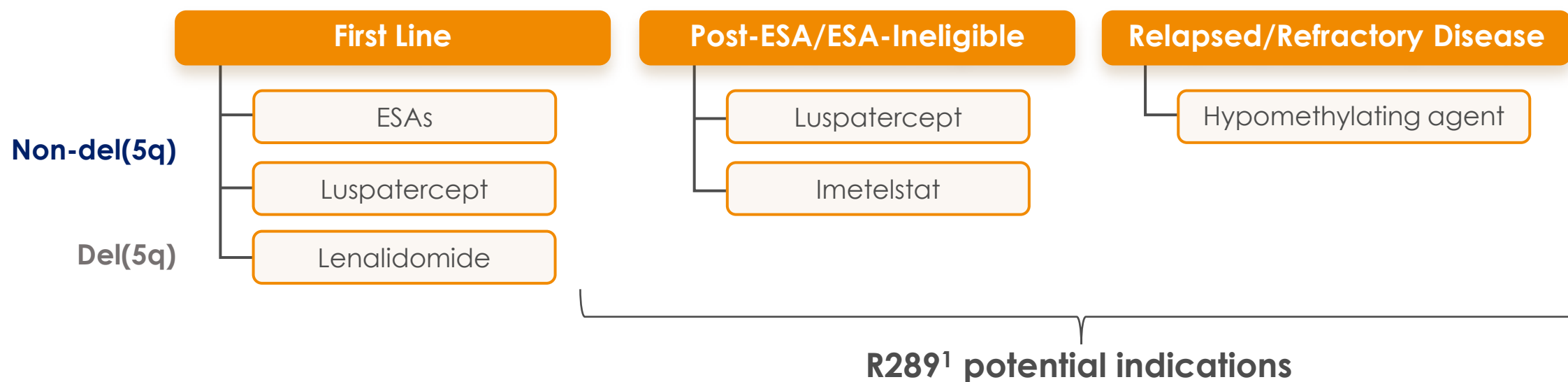


R289

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.

R289¹ Program Value Proposition for Lower-Risk MDS

Unmet Medical Need

- ~12,200 lower-risk MDS patients that have been previously treated²
- 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 volunteers⁴

Regulatory Designations

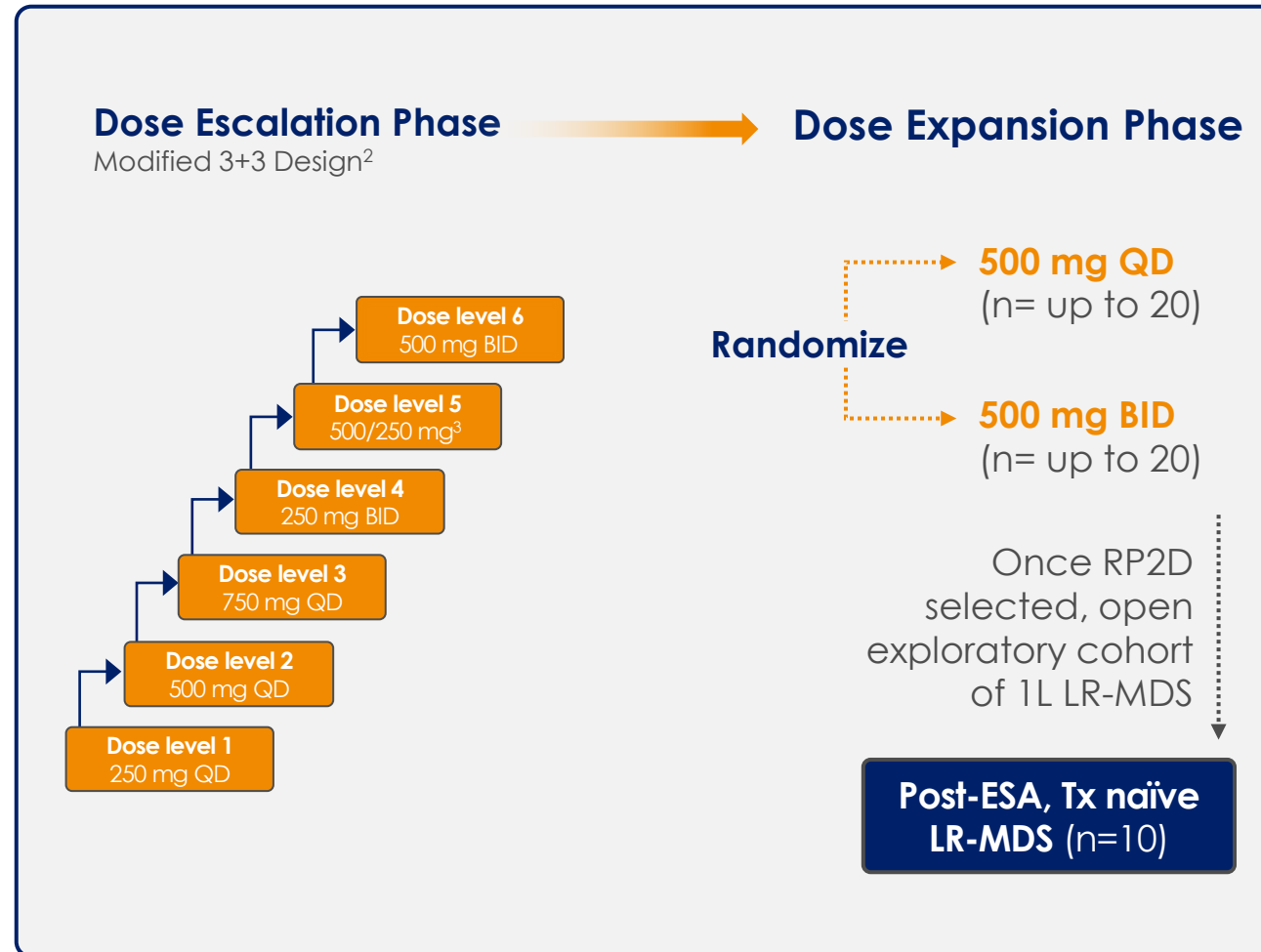
- **Fast Track designation** for previously-treated transfusion dependent LR-MDS (Nov 2024)
- **Orphan Drug designation** for treatment of myelodysplastic syndromes (Jan 2025)

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

R289¹: 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 (≥ 2 u RBCs/16wks) in dose escalation; TD in dose expansion

Assessments

- Hematologic responses [TI and HI-E] per IWG 2018 criteria⁴ and other responses per IWG 2006 criteria⁵, 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 presented at ASH 2025

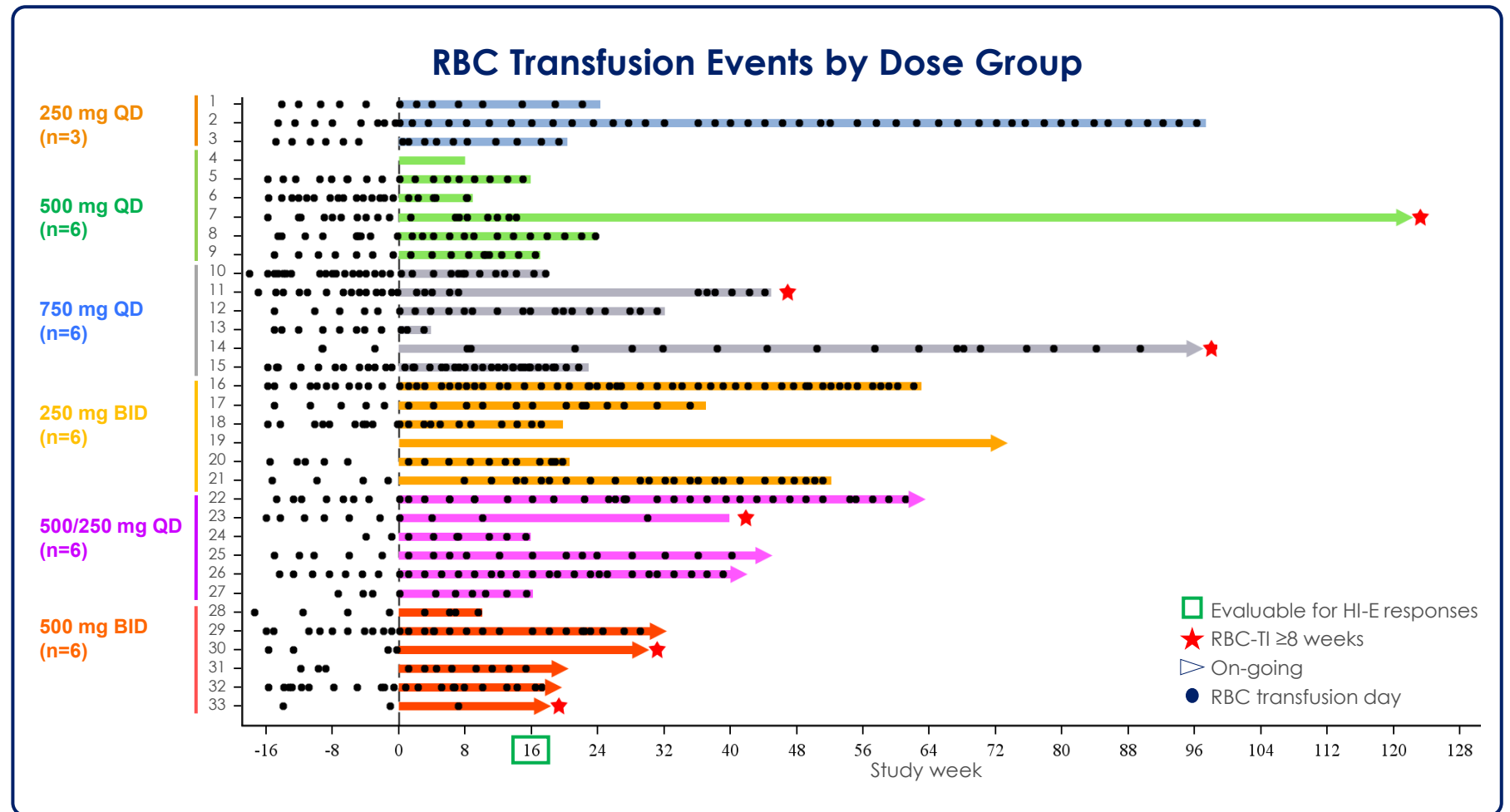
MDS, myelodysplastic syndrome; LR-MDS, lower-risk MDS; PK, pharmacokinetics; QD, daily; BID, twice daily; RP2D, recommended Phase 2 dose; Tx, treatment; Hb, hemoglobin; TD, transfusion dependent; TI, transfusion independence; HI-E, hematologic improvement - erythroid; PD, pharmacodynamics; FACIT-Fatigue 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.

Phase 1b Study Dose Escalation Phase Data Summary

Elderly, heavily pre-treated patient population with a high baseline transfusion burden

- R289 was generally well tolerated with a low incidence of Grade 3/4 cytopenias and infections
- 6/18 (33%) evaluable TD patients receiving ≥ 500 mg QD achieved RBC-TI >8 weeks; 4 >16 weeks; 3 >24 weeks
- Median duration of treatment: 5.5 months (range: 0.9 - 27.7 months)
- Median time to onset of RBC-TI: 1.9 months
- Median duration of RBC-TI: 22.9 weeks (9 - 104.3)



Note: Patients listed in order of enrollment.

TD, transfusion dependent; QD, once daily; RBC, red blood cell; RBC-TI, red blood cell transfusion independence; BID, twice daily; HI-E, hematologic improvement-erythroid.

Source: Garcia-Manero et al. Blood (2025) 146 (Supplement 1): 489.

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

Maintain Financial Discipline



Q2 2026 Highlights

Tavalisse
(fostamatinib disodium
hexahydrate) tablets

GAVRETO
pralsetinib 100mg
capsules

REZLIDHIA
(olutasidenib) 150mg
capsules

Q2 2026 Net Product Sales: \$67.0M

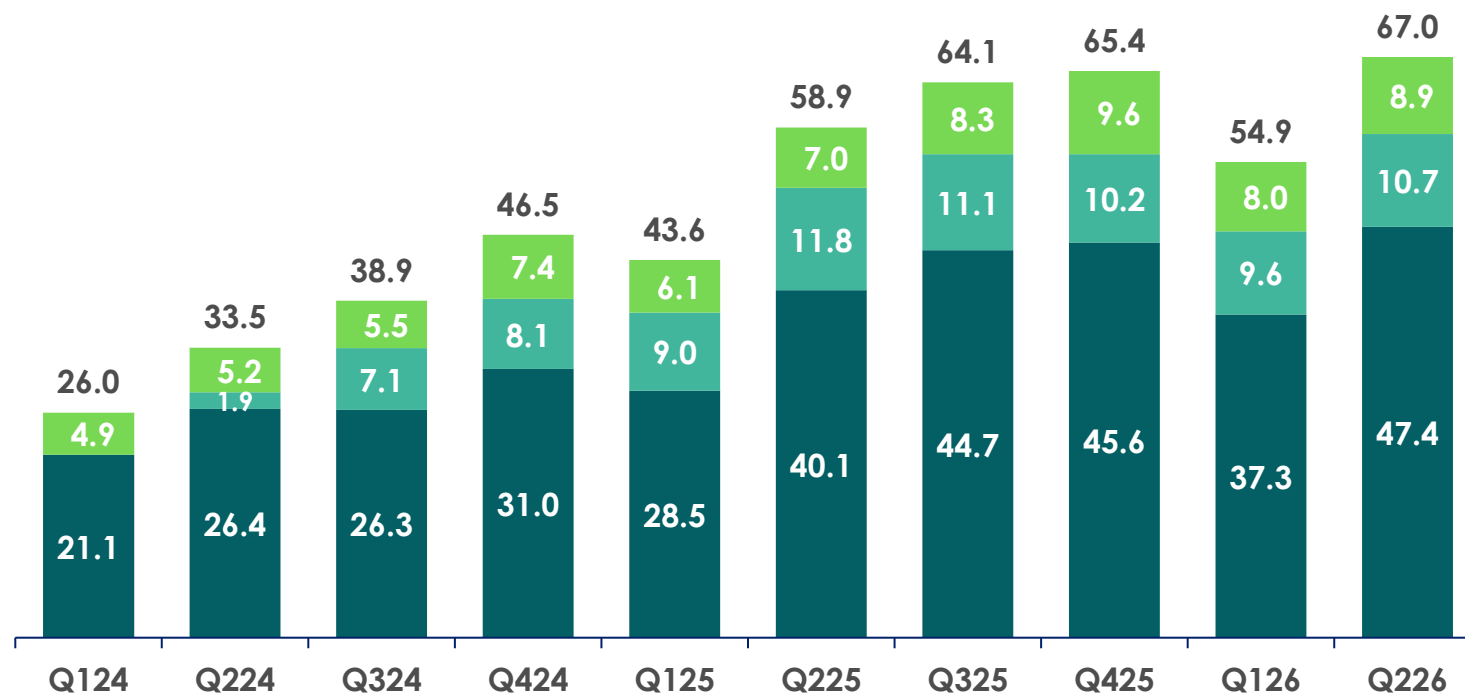
- TAVALISSE \$47.4M
- GAVRETO \$10.7M
- REZLIDHIA \$8.9M

Q2 2026 Contract Revenues: \$11.7M

- Kissei \$5.8M
- Grifols \$5.0M
- Medison \$0.3M
- Others \$0.6

Net Product Sales (\$M)

■ TAVALISSE ■ GAVRETO ■ REZLIDHIA



Q2 2026 Financial Overview

(in thousands)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2026	2025	2026	2025
Revenues				
Net Product Sales	\$ 67,015	\$ 58,948	\$ 121,938	\$ 102,498
Contract revenues from collaborations and other	11,688	42,737	15,583	52,520
Total revenues	78,703	101,685	137,521	155,018
Costs and expenses:				
Cost of product sales	8,525	4,504	13,131	8,913
Research and development	13,961	6,821	25,637	15,257
Selling, general and administrative	32,642	29,257	63,293	56,972
Total costs and expenses	55,128	40,582	102,061	81,142
Income from operations	23,575	61,103	35,460	73,876
Interest income	789	753	1,994	1,344
Interest expense and other	(779)	(1,874)	(2,212)	(3,727)
Income before income tax	23,585	59,982	35,242	71,493
Provision for income tax	6,295	369	9,298	434
Net income	\$ 17,290	\$ 59,613	\$ 25,944	\$ 71,059

	As of	
	June 30, 2026	December 31, 2025
Cash, Cash Equivalents and Short-term Investments	\$ 95,329	\$ 154,955

2026 Financial Outlook

- Total revenues of ~\$285M to \$295M
 - Net product sales of ~\$255M to \$265M
 - Contract revenues of ~\$30M (previously ~\$20M to \$25M)
- Revenue guidance excludes VEPPANU
- Anticipate will report positive net income for the full year 2026, while funding existing and new clinical development programs

Exclusive Global License Agreement to Develop, Manufacture and Commercialize VEPPANU™ (vepdegestrant)

Key Transaction Terms

Arvinas and Pfizer will receive:

- **\$70M** upfront fee (paid in Q2 2026)
- **\$15M** upon the successful completion of certain transition activities
- Additional potential milestone payments: **\$320M**
 - Regulatory Milestones: **\$60M**
 - Commercial Milestones: **\$260M**
- Tiered Royalties: Mid-teens to mid-twenties
- Pfizer and Arvinas remain responsible for current clinical trials
 - Rigel will contribute up to \$40 million over the next 4 years

2026 Progress and Key 2H 2026 Priorities

Grow Commercial Business

- Immediately initiated VEPPANU™ (vepdegestrant) launch activities upon close of transaction; to become commercially available in mid-August
- Drive rapid awareness and adoption of VEPPANU

In-Licensing / Business Development

- In-license of VEPPANU™ (vepdegestrant), an oral PROTAC with the potential to be an important new treatment option for patients with 2L+ ER+/HER2-, ESR1m 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: ~\$285M to \$295M¹**
 - Net product sales of ~\$255M to \$265M
 - Contract revenues of ~\$30M (previously \$20M to \$25M)

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**



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; FDA, U.S. Food and Drug Administration.

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 ($\geq$ 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 ($\geq 5\%$ 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 ($\geq 20\%$) 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 embryoletality 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 ($\geq 25\%$)** were musculoskeletal pain, constipation, hypertension, diarrhea, fatigue, edema, pyrexia and cough. **The most common Grade 3-4 laboratory abnormalities ($\geq 2\%$)** 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™ (vepdgestrant)

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.



Thank You

www.rigel.com

