November 24, 2026

Rigel to Present New Data for VEPPANU™ (vepdegestrant) in Patients with ER+/HER2-, ESR1-Mutated Advanced or Metastatic Breast Cancer at SABCS 2026

- *In a post hoc analysis of the Phase 1/2 VERITAC clinical study, vepdegestrant showed encouraging clinical activity in patients with ER+/HER2-, ESR1-mutated advanced breast cancer previously treated with SERD therapy*
- *Final Phase 1b results for vepdegestrant in combination with palbociclib showed an objective response rate of 42.9%, a CBR of 78.6% and a median PFS of 16.5 months among patients with ESR1-mutated disease*

SOUTH SAN FRANCISCO, Calif., Nov. 24, 2026 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL), a commercial stage biotechnology company focused on hematologic disorders and cancer, today announced data for VEPPANU™ (vepdegestrant) in patients with estrogen receptor-positive/human epidermal growth factor receptor 2-negative (ER+/HER2-), estrogen receptor 1 (*ESR1)*-mutated advanced or metastatic breast cancer (mBC) and data demonstrating the clinical impact of *ESR1* mutations in metastatic breast cancer will be presented in five upcoming poster presentations at the San Antonio Breast Cancer (SABC) Symposium 2026 taking place in San Antonio, Texas and virtually from December 8 to December 11, 2026.

Four poster presentations will present data for vepdegestrant in four key areas of interest, including patients previously treated with selective estrogen receptor degrader (SERD) therapy, patients treated with vepdegestrant in combination with palbociclib, QTc risk assessment and the association between baseline circulating tumor DNA (ctDNA) and progression-free survival (PFS).

"These presentations broaden the evidence base for VEPPANU, the first and only FDA-approved PROTAC, and deepen our understanding of *ESR1*-mutated advanced breast cancer," said Alison L. Hannah, M.D., Rigel's chief medical officer. "The findings demonstrate encouraging activity, both following prior SERD therapy and in combination with palbociclib, while additional analyses further characterize relevant biomarkers and QTc risk at the approved dose. Together with real-world findings showing an association between *ESR1* mutations and poorer clinical outcomes, these data underscore the need to improve treatment sequencing and continue evaluating rational combination strategies for patients

with ER-positive, HER2-negative advanced breast cancer."

Key highlights from the presentations at the SABC Symposium include:

- A post hoc analysis of 19 patients with ER+/HER2-,*ESR1*-mutated advanced breast cancer that had prior SERD exposure in the Phase 2 expansion cohort of the Phase 1/2 VERITAC clinical study showed that vepdegestrant at 200 mg/day achieved a clinical benefit rate (CBR) of 63.2% and a median PFS of 5.5 months. Notably, efficacy was maintained in the subgroup previously treated with fulvestrant (n=13), with a median PFS of 5.5 months and a CBR of 61.5%. These findings suggest activity following prior SERD exposure. The median PFS in both *ESR1*-mutated patients and in the subset previously exposed to a SERD was consistent with what was observed among patients treated in the VERITAC-2 registrational trial.
- Final Phase 1b results for vepdegestrant 200 mg/day in combination with 125 mg/day palbociclib in a heavily pre-treated patient population (median of 4 prior lines of therapy) showed an objective response rate (ORR) of 42.9%, a CBR of 78.6% and a median PFS of 16.5 months among patients with *ESR1*-mutated disease (n=14). Across the overall combination cohort (n=21), the ORR was 40%, the CBR was 66.7% and the median PFS was 13.9 months. The safety profile was consistent with the known profiles of both agents. The only grade 3/4 treatment-related adverse event (TRAE) occurring in ≥10% of patients was neutropenia (42.9%), and 1 patient experienced grade 3 febrile neutropenia. No grade 5 TRAEs occurred.
- Integrated VERITAC and VERITAC-2 analyses predicted a mean Fridericia-corrected QT interval (QTcF) increase of 11.1 msec at the observed median steady-state concentration following vepdegestrant 200 mg once daily. The upper bound of the 90% confidence interval (CI) was below 20 msec, indicating no large effect on QTc at the approved dose. VEPPANU can cause QTc prolongation, and labeled electrocardiogram (ECG) monitoring and dose-management precautions remain applicable.
- Exploratory VERITAC-2 ctDNA analyses identified *ESR1* mutation status as the key biologic subgroup associated with PFS benefit for vepdegestrant versus fulvestrant. Vepdegestrant benefit was generally consistent across major *ESR1* variants, *ESR1* variant allele frequency levels and most evaluated genomic subgroups, including *PIK3CA* and *GATA3*. Higher baseline ctDNA burden predicted poorer PFS across treatment arms.
- In a retrospective U.S. real-world study of 2,206 patients between 2014 and 2024, *ESR1* mutations were associated with shorter overall survival, real-world time to next treatment and real-world time to treatment discontinuation compared with *ESR1* wild-type disease. Co-occurring actionable mutations were associated with further reductions in time to next treatment and treatment discontinuation, highlighting the need for effective therapies in this setting.

SABC Symposium 2026 abstracts may be accessed online via https://sabcs.org/events/.

Abstract Title	Lead Author	Presentation Type / Abstract #	Session Date / Time (CT)
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	Erika P. Hamilton, MD	Poster Presentation P4-14-19	Thursday, December 10, 2026, 5:00 PM - 6:30 PM
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	Erika P. Hamilton, MD	Poster Presentation P4-14-10	Thursday, December 10, 2026, 5:00 PM - 6:30 PM
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	Lana Tran, PharmD	Poster Presentation P4-15-15	Thursday, December 10, 2026, 5:00 PM - 6:30 PM
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	Seth A. Wander, MD, PhD	Poster Presentation P5-10-19	Friday, December 11, 2026, 12:30 PM - 2:00 PM
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	Neal M. Iyengar, MD	Poster Presentation P4-14-28	Thursday, December 10, 2026, 5:00 PM - 6:30 PM

About ER+/HER2-, *ESR1*-mutated Metastatic Breast Cancer

Breast cancer is the most common cancer in women in the United States, except for skin cancers.[1] The estrogen receptor-positive/human epidermal growth factor receptor 2-negative (ER+/HER2-) patient population represents the majority (70%) of breast cancer, where treatment with endocrine therapies (aromatase inhibitors) is the standard of care. While endocrine therapy remains a cornerstone of metastatic ER+/HER2- breast cancer treatment, up to 50% of patients treated with endocrine therapy and a CDK4/6 inhibitor acquire estrogen receptor 1 gene (*ESR1*) mutations, resulting in endocrine resistance and poor prognosis. Treatment options in second-line and later ER+/HER2-, *ESR1*-mutated advanced or metastatic breast cancer setting include chemotherapy, selective estrogen receptor degraders (SERDs), and as of May 2026, vepdegestrant, the first and only FDA-approved oral PROteolysis TArgeting Chimera (PROTAC).

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.

Click here **for Important Safety Information and Full Prescribing Information.**

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

VEPPANU is a trademark of Rigel Pharmaceuticals, Inc.

About Rigel
Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) is a biotechnology company dedicated to discovering, developing and providing novel therapies that significantly improve the lives of patients with hematologic disorders and cancer. Founded in 1996, Rigel is based in South San Francisco, California. For more information on Rigel, the Company's marketed products and pipeline of potential products, visit www.rigel.com.

1. The American Cancer Society. Key Statistics for Breast Cancer. Revised June 24, 2026. Accessed November 1, 2026: https://www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 relating to, among other things, the anticipated timing, content and availability of presentations at the 2026 San Antonio Breast Cancer Symposium; the potential therapeutic benefits and clinical utility of VEPPANU (vepdegestrant), including following prior selective estrogen receptor degrader therapy and in combination with palbociclib; the potential implications of biomarker analyses for treatment outcomes and patient selection; the potential implications of QTc analyses for the cardiac safety profile of vepdegestrant; and the potential role of these findings in informing treatment sequencing and further evaluation of combination strategies. Any statements contained in this press release 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 that data analyses or presentations may be delayed or may not proceed as anticipated; limitations of early-stage studies, post hoc, exploratory and subgroup analyses, and analyses involving small or selected patient populations; limitations of retrospective real-world studies, including

potential selection bias, confounding factors and incomplete data; risks that comparisons across studies or patient populations may not support conclusions regarding comparative efficacy or treatment sequencing; risks that clinical trial results may not be predictive of real-world outcomes or results in broader patient populations or subsequent clinical trials; risks that biomarker associations may not establish predictive utility or support treatment selection; limitations of exposure-response modeling and QTc analyses, which may not fully characterize cardiac risk in individual patients or broader clinical use; risks that additional data, analyses or experience may alter assessments of the safety, tolerability, efficacy, durability or therapeutic potential of vepdegestrant, alone or in combination with palbociclib; risks that vepdegestrant or combination therapy may have unintended side effects or adverse reactions; risks that clinical results or decisions by regulatory authorities may not support further development or approval for investigational uses; and other risks described in the "Risk Factors" section of Rigel's Quarterly Report on Form 10-Q for the quarter ended September 30, 2026 and subsequent filings with the Securities and Exchange Commission. Any forward-looking statement in this press release 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.

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