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Arvinas and Pfizer's Vepdegestrant Significantly Improves Progression-Free Survival for Patients with ESR1-Mutant, ER+/HER2- Advanced Breast Cancer

Saturday, May 31, 2025 - 08:00am

- *Pivotal Phase 3 VERITAC-2 clinical trial results presented at ASCO demonstrate 2.9-month improvement in median progression-free survival when compared to fulvestrant in second line-plus patients with an estrogen receptor 1 mutation*
- *Vepdegestrant was generally well tolerated, with few discontinuations and low rates of gastrointestinal-related adverse events*
- *Vepdegestrant is the first and only PROteolysis TArgeting Chimera (PROTAC) evaluated in a Phase 3 clinical trial and the first to show benefit in patients with breast cancer*
- *Data to be featured in a late-breaking oral presentation at ASCO and simultaneously published in the New England Journal of Medicine*
- *Arvinas will host a conference call to discuss these results on Monday, June 2, at 8:00 a.m. ET*

NEW HAVEN, Conn. and NEW YORK, May 31, 2025 – Arvinas, Inc. (Nasdaq: ARVN) and Pfizer Inc. (NYSE: PFE) today announced detailed results from the Phase 3 VERITAC-2 clinical trial (NCT05654623) evaluating vepdegestrant monotherapy versus fulvestrant in adults with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+/HER2-) advanced or metastatic breast cancer (MBC) whose disease progressed following prior treatment with cyclin-dependent kinase (CDK) 4/6 inhibitors and endocrine therapy. These data, which were highlighted in the American Society of Clinical Oncology (ASCO®) press briefing and selected for Best of ASCO, will be presented today in a late-breaking oral presentation (Abstract LBA1000) and have been simultaneously published in the New England Journal of Medicine.

In the trial, vepdegestrant demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) among patients with an estrogen receptor 1 (ESR1) mutation, reducing the risk of disease progression or death by 43% compared to fulvestrant [Hazard Ratio (HR)=0.57 (95% CI 0.42–0.77); 2-sided P<0.001]. The median PFS, as assessed by blinded independent central review (BICR), was 5.0 months with vepdegestrant versus 2.1 months with fulvestrant. Investigator-assessed PFS was consistent with the BICR-assessed PFS. In patients with ESR1 mutations, vepdegestrant demonstrated a consistent PFS benefit over fulvestrant across all pre-specified subgroups. The trial did not reach statistical significance in improvement in PFS in the intent-to-treat (ITT) population, with a median PFS of 3.7 months for vepdegestrant versus 3.6 for fulvestrant [HR=0.83 (95% CI 0.68–1.02); 2-sided P=0.07].

“Many patients with ER+/HER2- metastatic breast cancer who progress on endocrine therapy have tumors with ESR1 mutations, which drive resistance to standard treatments,” said Erika P. Hamilton, M.D., Director, Breast Cancer Research, Sarah Cannon Research Institute, and a principal investigator of the VERITAC-2 trial. “The VERITAC-2 results are promising and suggest that vepdegestrant could offer a much-needed treatment option

for these patients, with a low incidence of burdensome GI effects that can meaningfully affect daily life."

Vepdegestrant was generally well tolerated in the trial, with a safety profile consistent with what has been observed in previous studies, and mostly low-grade treatment-emergent adverse events (TEAEs). Rates and severity of gastrointestinal adverse events were low with vepdegestrant (nausea, 13.5%; vomiting, 6.4%; diarrhea, 6.4%). Grade 4 TEAEs were reported in 5 patients (1.6%) in the vepdegestrant arm versus 9 patients (2.9%) in the fulvestrant arm. The three most common TEAEs observed with vepdegestrant were fatigue (26.6%), increased alanine transaminase (ALT) (14.4%) and increased aspartate aminotransferase (AST) (14.4%). TEAEs leading to treatment discontinuation occurred in 2.9% of patients taking vepdegestrant versus 0.7% of patients taking fulvestrant.

"Based on these strong data from VERITAC-2, we believe that vepdegestrant has the potential to be a best-in-class monotherapy treatment for patients in the second-line ESR1-mutant setting," said John Houston, Ph.D., Chairperson, Chief Executive Officer and President at Arvinas. "We are excited to engage with regulatory authorities on next steps to potentially bring vepdegestrant to healthcare providers and their patients as swiftly as possible."

Overall survival (OS), the key secondary endpoint in VERITAC-2, was immature at the time of the analysis, with less than a quarter of the required number of events having occurred. Additional secondary endpoints include clinical benefit rate (CBR) and objective response rate (ORR) and duration of response by BICR. In patients with an ESR1 mutation, CBR was 42.1% with vepdegestrant versus 20.2% with fulvestrant [odds ratio 2.88 (95% CI: 1.57–5.39); nominal P<0.001] and ORR was 18.6% with vepdegestrant versus 4.0% with fulvestrant [odds ratio 5.45 (95% CI: 1.69–22.73); nominal P=0.001]. The median duration of response was not reached.

"Patients whose tumors harbor ESR1 mutations can face a poor prognosis, often experiencing rapid disease progression on endocrine therapy," said Johanna Bendell, M.D., Chief Oncology Development Officer, Pfizer. "These results highlight the important role vepdegestrant may play in combating ESR1 mutation treatment resistance for these patients."

Approximately 2.3 million new breast cancer diagnoses were reported globally in 2022, and it is estimated there will be nearly 320,000 new diagnoses in the United States in 2025. ER+/HER2- breast cancer accounts for approximately 70% of all cases. Nearly 30% of women initially diagnosed with early-stage breast cancer will ultimately develop metastatic disease,[1] with resistance to current standard-of-care treatments often emerging during first-line therapy, leading to disease progression. ESR1 mutations are a common cause of acquired resistance and are found in approximately 40% of patients in the second-line setting.[2,3,4]

Vepdegestrant, an investigational oral PROTAC ER degrader for ER+/HER2- breast cancer being jointly developed by Arvinas and Pfizer, is designed to harness the body's natural protein disposal system to specifically target and degrade the ER. These detailed results follow the March 2025 announcement of the topline results from VERITAC-2. The companies plan to submit a New Drug Application (NDA) for vepdegestrant to the U.S. Food & Drug Administration (FDA) in the second half of 2025.

ASCO Presentation Details

"Vepdegestrant, a PROTAC Estrogen Receptor Degrader, vs Fulvestrant in ER-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Results of the Global, Randomized, Phase 3 VERITAC-2 Study" will be presented by Dr. Erika Hamilton, MD, Sarah Cannon Research Institute, in the Oral Abstract Session, Breast Cancer—Metastatic on Saturday, May 31, 1:15 – 4:15 p.m. CDT in Hall B1. Abstract LBA1000.

Investor Call and Webcast Details

Arvinas will host a conference call and webcast on June 2, 2025, at 8:00 a.m. ET to review these data. Participants are invited to listen by going to the Events and Presentation section under the Investors page on the Arvinas website at www.arvinas.com. A replay of the webcast will be available on the Arvinas website following the completion of the event and will be archived for up to 30 days.

About the VERITAC-2 Clinical Trial

The Phase 3 VERITAC-2 clinical trial (NCT05654623) is a global randomized trial evaluating the efficacy and safety of vepdegestrant (ARV-471) as a monotherapy compared to fulvestrant in patients with ER+/HER2- advanced or metastatic breast cancer. The trial enrolled 624 patients at sites in 26 countries who had previously received treatment with a CDK4/6 inhibitor plus endocrine therapy.

Patients were randomized 1:1 to receive either vepdegestrant once daily, orally on a 28-day continuous dosing schedule, or fulvestrant, administered intramuscularly on Days 1 and 15 of Cycle 1 and then on Day 1 of each 28-day cycle starting from Day 1 of Cycle 2. In the trial, 43% of patients (n=270) had ESR1 mutations detected. The primary endpoint was progression-free survival (PFS) in the ESR1-mutation and intent-to-treat populations as determined by blinded independent central review. Overall survival is the key secondary endpoint.

About Vepdegestrant

Vepdegestrant is an investigational, orally bioavailable PROteolysis TArgeting Chimera (PROTAC) protein degrader designed to specifically target and degrade the estrogen receptor (ER) for the treatment of patients with ER-positive (ER+)/human epidermal growth factor receptor 2 (HER2)-negative (ER+/HER2-) breast cancer. Vepdegestrant is being developed as a potential monotherapy for ER+/HER2- advanced or metastatic breast cancer with estrogen receptor 1 (ESR1) mutations in the second line-plus setting.

In July 2021, Arvinas announced a global collaboration with Pfizer for the co-development and co-commercialization of vepdegestrant; Arvinas and Pfizer will share worldwide development costs, commercialization expenses, and profits.

The U.S. Food and Drug Administration (FDA) has granted vepdegestrant Fast Track designation as a monotherapy in the treatment of adults with ER+/HER2- advanced or metastatic breast cancer previously treated with endocrine-based therapy.

About Arvinas

Arvinas (Nasdaq: ARVN) is a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases. Through its PROTAC protein degrader platform, Arvinas is pioneering the development of protein degradation therapies designed to harness the body’s natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. Arvinas is currently progressing multiple investigational drugs through clinical development programs, including vepdegestrant, targeting the estrogen receptor for patients with locally advanced or metastatic ER+/HER2- breast cancer; ARV-393, targeting BCL6 for relapsed/refractory non-Hodgkin Lymphoma; and ARV-102, targeting LRRK2 for neurodegenerative disorders. Arvinas is headquartered in New Haven, Connecticut. For more information about Arvinas, visit www.arvinas.com and connect on LinkedIn and X.

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and bispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on X at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Arvinas Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding: vepdegestrant's development as a potential monotherapy for patients with estrogen receptor positive ("ER+"), human epidermal growth factor receptor 2 negative ("HER2-"), metastatic breast cancer with estrogen receptor 1 ("ESR1") mutations in the second-line plus setting; vepdegestrant's potential as a treatment option for patients with a low incidence of burdensome gastrointestinal effects; vepdegestrant's potential to be a best-in-class monotherapy treatment for patients with ER+/HER2- metastatic breast cancer in the second-line ESR1-mutant setting; and Arvinas' and Pfizer's plans to engage with regulatory authorities on next steps to potentially bring vepdegestrant to healthcare providers and patients, and the companies' plans to submit a New Drug Application to the U.S. Food and Drug Administration, and the timing thereof. All statements, other than statements of historical fact, contained in this press release, including statements regarding Arvinas' strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "target," "goal," "potential," "will," "would," "could," "should," "look forward," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Arvinas may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on such forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements Arvinas makes as a result of various risks and uncertainties, including but not limited to: whether Arvinas and Pfizer will successfully perform their respective obligations under the collaboration between Arvinas and Pfizer; whether Arvinas and Pfizer will be able to successfully conduct and complete clinical development for vepdegestrant as a monotherapy; whether Arvinas will be able to successfully conduct and complete development for its other product candidates, including ARV-393 and ARV-102; whether Arvinas and

Pfizer, as appropriate, will be able to obtain marketing approval for and commercialize vepdegestrant and other product candidates on current timelines or at all; Arvinas' ability to protect its intellectual property portfolio; Arvinas' reliance on third parties; whether Arvinas will be able to raise capital when needed; whether Arvinas' cash and cash equivalents will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors discussed in the "Risk Factors" section of Arvinas' Annual Report on Form 10-K for the year ended December 31, 2024 and subsequent other reports on file with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Arvinas' current views with respect to future events, and Arvinas assumes no obligation to update any forward-looking statements, except as required by applicable law. These forward-looking statements should not be relied upon as representing Arvinas' views as of any date subsequent to the date of this release.

Pfizer Disclosure Notice:

The information contained in this release is as of May 31, 2025. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology and vepdegestrant, including its potential benefits, detailed results from the Phase 3 VERITAC-2 clinical trial evaluating vepdegestrant monotherapy versus fulvestrant in adults with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+/HER2-) advanced or metastatic breast cancer whose disease progressed following prior treatment with cyclin-dependent kinase (CDK) 4/6 inhibitors and endocrine therapy and plans to submit a New Drug Application for vepdegestrant to the FDA in the second half of 2025 that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; whether the VERITAC-2 trial will meet the secondary endpoint for overall survival; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for any potential indication for vepdegestrant; whether and when any such applications that may be filed for vepdegestrant may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy, and, if approved, whether vepdegestrant will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of vepdegestrant; whether the collaboration between Pfizer and Arvinas will be successful; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on our business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov

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[2] Bidard F-C, et al. Elacestrant (oral selective estrogen receptor degrader) Versus Standard Endocrine Therapy

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[3] Kalinsky, K. Abemaciclib Plus Fulvestrant in Advanced Breast Cancer After Progression on CDK4/6 Inhibition: Results From the Phase III postMONARCH Trial. Journal of Clinical Oncology. 2024 Dec. https://doi.org/10.1200/JCO-24-0208.
[4] Tolaney, S. et al. AMEERA-3: Randomized Phase II Study of Amcenestrant (Oral Selective Estrogen Receptor Degrader) Versus Standard Endocrine Monotherapy in Estrogen Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Advanced Breast Cancer. Journal of Clinical Oncology. https://ascopubs.org/doi/full/10.1200/JCO.22.02746.

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