Pfizer Logo

Arvinas and Pfizer Announce Updated Clinical Data from Phase 1b Trial of Vepdegestrant in Combination with Palbociclib (IBRANCE®)

Thursday, May 16, 2024 - 06:00am

– After six months of additional follow-up, clinical benefit rate (63%), overall response rate (41.9%), median progression-free survival (11.2 months), and safety profile of vepdegestrant in combination with palbociclib were consistent with data previously reported at SABCS in December 2023 –

– At the recommended Phase 3 dose of 200 mg vepdegestrant in combination with palbociclib, patients achieved a median progression-free survival of 13.9 months (95% CI: 8.1-NR) –

– Across all vepdegestrant dose groups, circulating tumor DNA analyses showed marked reduction in tumor fraction after one treatment cycle, regardless of ESR1 gene mutation status; at the 200 mg vepdegestrant dose, robust on-treatment decreases in mutant ESR1 circulating tumor DNA were sustained through multiple treatment cycles –

NEW HAVEN, Conn. and NEW YORK, May 16, 2024 – Arvinas, Inc. (Nasdaq: ARVN) and Pfizer Inc. (NYSE: PFE) today announced updated clinical data from a Phase 1b combination cohort evaluating vepdegestrant, an investigational oral PROteolysis TArgeting Chimera (PROTAC®) estrogen receptor (ER) degrader, in combination with palbociclib (IBRANCE®). After six months of additional follow-up, these data are consistent with data presented at the San Antonio Breast Cancer Symposium (SABCS) in December 2023, and show that vepdegestrant plus palbociclib continue to demonstrate encouraging clinical activity in heavily pre-treated patients with a median of four lines of prior therapy with locally advanced or metastatic ER positive (ER+)/human epidermal growth factor 2 (HER2) negative (ER+/HER2-) breast cancer. These updated data were presented at the 2024 European Society for Medical Oncology (ESMO) Breast Cancer Annual Congress.

“We're encouraged by the clinical activity and safety profile observed with vepdegestrant in combination with palbociclib in patients being treated for advanced ER+/HER2- breast cancer,” said Noah Berkowitz, M.D., Ph.D., Chief Medical Officer at Arvinas. “The median progression-free survival and duration of response data suggest a promising therapeutic benefit for these patients regardless of ESR1 mutation status.”

Vepdegestrant is an investigational PROTAC ER degrader designed to harness the body’s natural protein disposal system to specifically target and degrade the estrogen receptor. Vepdegestrant is being co-developed by Arvinas and Pfizer and is being evaluated as a monotherapy in the second-line setting in the ongoing Phase 3 VERITAC-2 trial and in the first-line setting in combination with palbociclib in the ongoing study lead-in cohort of the Phase 3 VERITAC-3 trial.

“Pfizer is focused on advancing the next generation of treatment breakthroughs for people with breast cancer,” said Roger Dansey, M.D., Chief Development Officer, Oncology, Pfizer. “With vepdegestrant, we hope to establish a new standard-of-care endocrine therapy backbone for patients with ER+/HER2- breast cancer, and the data shared at ESMO Breast Cancer continue to reinforce its potential.”

“This study evaluating vepdegestrant in combination with palbociclib among heavily pre-treated patients with advanced ER+/HER2- metastatic breast cancer is consistent with the clinical activity, safety, and tolerability outcomes reported at SABCS 2023,” said Erika Hamilton, M.D., Director Breast Cancer Research and Executive Chair, Breast Cancer Research Executive Committee, Sarah Cannon Research Institute in Nashville, Tennessee, and a lead investigator in the vepdegestrant clinical program and presenting author on the data presentation at ESMO Breast Cancer. “The data show promise that vepdegestrant could be a potential addition to current treatment options for this patient population, where there are significant unmet needs.”

Vepdegestrant + Palbociclib Phase 1b Study
The Phase 1b cohort of the ARV-471-mBC-101 study (NCT04072952) is designed to assess the safety, tolerability, and anti-tumor activity of vepdegestrant in combination with palbociclib among 46 patients with heavily pre-treated locally advanced or metastatic ER+/HER2- breast cancer. Patients in the study received a median of four prior therapies (median of three in the metastatic setting); 87% were previously treated with a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor; 80% were previously treated with fulvestrant; and 78% were previously treated with chemotherapy, including 48% in the metastatic setting.

Patients were treated once daily with oral doses of vepdegestrant at 180 mg (n=2), the recommended Phase 3 dose (RP3D) of 200 mg (n=21), 400 mg (n=3) or 500 mg (n=20), plus 125 mg of palbociclib given orally once daily for 21 days, followed by seven days off treatment in 28-day cycles. Initial data were presented at SABCS 2023 based on a data cutoff of June 6, 2023.

After six months of additional follow-up with a data cutoff of December 18, 2023, updated data from the study continue to demonstrate an encouraging clinical benefit rate, objective response rate and progression-free survival, and a consistent safety profile as previously reported at SABCS 2023.

Data presented at the 2024 ESMO Breast Cancer Annual Congress:

Clinical Benefit Rate (CBR):

- CBR, defined as the rate of confirmed complete response, partial response, or stable disease ?24 weeks across all dose levels (n = 46) was 63% (95% CI: 47.5 - 76.8), with a CBR of 72% in patients with mutant ESR1 (n=29; 95% CI: 52.8 - 87.3) and a CBR of 53% in patients with wild-type ESR1 (n=15; 95% CI: 26.6 – 78.7).
- CBR in patients dosed at the RP3D of 200 mg (n=21) was 67% (95% CI: 43.0 - 85.4) with a CBR of 79% in patients with mutant ESR1 (n=14; 95% CI: 49.2 - 95.3) and a CBR of 43% in patients with wild-type ESR1 (n=7; 95% CI: 9.9 - 81.6)

Objective Response Rate (ORR) and Duration of Response (DOR):

- The ORR in evaluable patients with measurable disease at baseline (n=31) was 42% (95% CI: 24.5 - 60.9) with a median DOR in 13 responders of 14.6 months (95% CI: 9.5 – not reached). At the RP3D of 200 mg (n=15), the ORR was 53% (95% CI: 25.6 – 78.7).
    - ORR in patients with mutant ESR1 (n=17): 47% (95% CI: 23.0 - 72.2).
        - ORR at the RP3D of 200 mg (n=10): 60% (95% CI: 26.2 - 87.8).
    - ORR in patients with wild-type ESR1 (n=12): 42% (95% CI: 15.2 - 72.3).

- ORR at the RP3D of 200 mg (n=5): 40% (95% CI: 5.3 - 85.3).

Progression-free Survival (PFS):

- Median PFS (mPFS) based on 27 (59%) events across all dose levels was 11.2 months (95% CI: 8.2 – 16.5) with a mPFS of 13.7 months (95% CI: 8.2 - NR) in patients with ESR1 mutation (n=29) and mPFS of 11.1 months (95% CI: 2.8 - 19.3) in patients with wild-type ESR1 (n=15).
- mPFS in patients dosed at the RP3D of 200 mg (n=21) based on 12 events (57%) was 13.9 months (95% CI: 8.1 - NR) with a mPFS of 13.9 months (95% CI: 8.1 - NR) in patients with ESR1 mutation (n=14) and mPFS of 11.2 months (95% CI: 1.8 - NR) in patients with wild-type ESR1 (n=7).

Circulating Tumor DNA (ctDNA):

- Exploratory ctDNA analyses found marked reduction (median change, ?98.9%) in tumor fraction after one treatment cycle (all dose groups) regardless of ESR1 mutant status and robust on-treatment decreases in mutant ESR1 ctDNA levels sustained through cycle 7 (evaluated in patients in 200 mg dose cohort), as presented in the poster session.

Safety Profile:

- The safety profile of vepdegestrant plus palbociclib was consistent with what was previously reported with Grade 3/4 treatment-related adverse events (TRAEs) ?10% of neutropenia (91%) and decreased white blood cell count (15%); no grade 5 TRAEs or febrile neutropenia were reported.
- The majority of Grade 4 neutropenia events occurred in the first cycle of treatment and occurrences of Grade 3/4 neutropenia decreased following palbociclib dose reductions as described in the prescribing label.
- The safety profile of vepdegestrant in combination with palbociclib was otherwise consistent with the profile of palbociclib and what has been observed in other clinical trials for vepdegestrant. Three of 46 patients discontinued palbociclib due to neutropenia including one out of 21 patients treated with the RP3D of vepdegestrant (200 mg) plus palbociclib 125 mg.

About Vepdegestrant

Vepdegestrant is an investigational, orally bioavailable 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 and as part of combination therapy across multiple treatment settings for ER+/HER2- metastatic breast cancer.

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- locally advanced or metastatic breast cancer previously treated with endocrine-based therapy.

About IBRANCE® (palbociclib) 125 mg tablets and capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,[1] which are key regulators of the cell cycle that trigger cellular progression. [2,3] In the U.S., IBRANCE is a prescription medicine indicated for the treatment of adults with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as the first hormonal based therapy; or with fulvestrant in people with disease progression following hormonal therapy.

The full U.S. Prescribing Information for the IBRANCE tablets and the IBRANCE capsules can be found here and here.

IMPORTANT IBRANCE®(palbociclib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. One death due to neutropenic sepsis was observed in PALOMA-3. Inform patients to promptly report any fever.
Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 15 of first 2 cycles and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) and/or pneumonitis** can occur in patients treated with CDK4/6 inhibitors, including IBRANCE when taken in combination with endocrine therapy. Across clinical trials (PALOMA-1, PALOMA-2, PALOMA-3), 1.0% of IBRANCE-treated patients had ILD/pneumonitis of any grade, 0.1% had Grade 3 or 4, and no fatal cases were reported. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.
Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g., hypoxia, cough, dyspnea). In patients who have new or worsening respiratory symptoms and are suspected to have developed pneumonitis, interrupt IBRANCE immediately and evaluate the patient. Permanently discontinue IBRANCE in patients with severe ILD or pneumonitis.

Based on the mechanism of action, IBRANCE can cause **fetal harm**. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may **impair fertility in males** and has the potential to cause genotoxicity. Advise male patients to consider sperm preservation before taking IBRANCE. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women **not to breastfeed** during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

The **most common adverse reactions (?10%)** of any grade reported in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (80% vs 6%), infections (60% vs 42%), leukopenia (39% vs 2%), fatigue (37% vs 28%), nausea (35% vs 26%), alopecia (33% vs 16%), stomatitis (30% vs 14%), diarrhea (26% vs 19%), anemia (24% vs 9%), rash (18% vs 12%), asthenia (17% vs 12%), thrombocytopenia (16% vs 1%), vomiting (16% vs 17%), decreased appetite (15% vs 9%), dry skin (12% vs 6%), pyrexia (12% vs 9%), and dysgeusia (10% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (66% vs 2%), leukopenia (25% vs 0%), infections (7% vs 3%), and anemia (5% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were decreased WBC (97% vs 25%), decreased neutrophils (95% vs 20%), anemia (78% vs 42%), decreased platelets (63% vs 14%), increased aspartate aminotransferase (52% vs 34%), and increased alanine aminotransferase (43% vs 30%).

The **most common adverse reactions (?10%)** of any grade reported in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (83% vs 4%), leukopenia (53% vs 5%), infections (47% vs 31%), fatigue (41% vs 29%), nausea (34% vs 28%), anemia (30% vs 13%), stomatitis (28% vs 13%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (66% vs 1%) and leukopenia (31% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Avoid concurrent use of **strong CYP3A inhibitors**. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided. Avoid concomitant use of strong CYP3A inducers. The dose of **sensitive CYP3A substrates** with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

For patients with **severe hepatic impairment** (Child-Pugh class C), the recommended dose of IBRANCE is 75 mg. The pharmacokinetics of IBRANCE **have not been studied** in patients **requiring hemodialysis.**

About Arvinas

Arvinas is a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development, and commercialization of therapies that degrade disease-causing proteins. Arvinas uses its proprietary PROTAC® Discovery Engine platform to engineer proteolysis targeting chimeras, or PROTAC® targeted protein degraders, that are designed to harness the body’s own natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. In addition to its robust preclinical pipeline of PROTAC protein degraders against validated and “undruggable” targets, the company has four investigational clinical-stage programs: vepdegestrant for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer; ARV-766 and bavdegalutamide for the treatment of men with metastatic castration-resistant prostate cancer; and ARV-102 for the treatment of patients with neurodegenerative disorders. For more information, visit www.arvinas.com.

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 ; the potential, pending regulatory approval, for vepdegestrant to address an area of high unmet need; Arvinas' and Pfizer's plans with respect to, the timing and results of ongoing and planned clinical trials of vepdegestrant, as a monotherapy and in combination studies; and statements regarding potential therapeutic benefits of vepdegestrant. All statements, other than statements of historical facts, 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," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "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: Arvinas' and Pfizer Inc.'s ("Pfizer") performance of the respective obligations with respect to Arvinas' collaboration with Pfizer; whether Arvinas and Pfizer will be able to successfully conduct and complete clinical development for vepdegestrant; whether Arvinas and Pfizer, as appropriate, will be able to obtain marketing approval for and commercialize vepdegestrant on current timelines or at all; Arvinas' ability to protect its intellectual property portfolio; whether Arvinas' cash and cash equivalent resources 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, 2023 , its Quarterly Report on Form 10-Q for the quarter ended March 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 16, 2024. 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 vepdegestrant, IBRANCE® (palbociclib), a global collaboration between Pfizer and Arvinas to develop and commercialize vepdegestrant and Pfizer Oncology, including their potential benefits, that involves 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, uncertainties regarding the commercial success of IBRANCE; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for 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; 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 the clinical studies; whether and when any applications may be filed in any jurisdictions for vepdegestrant for any potential indications or any other potential indications for IBRANCE; whether and when regulatory authorities may approve any potential applications that may be filed for vepdegestrant and/or IBRANCE in any jurisdictions, 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 such product 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 and IBRANCE; whether the collaboration between Pfizer and Arvinas will be successful; uncertainties regarding the impact of COVID-19 on Pfizer's 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, 2023 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 and www.pfizer.com.

Arvinas Contacts

Investor Contact:
Jeff Boyle
347-247-5089
Jeff.Boyle@arvinas.com

Media Contact:
Kathleen Murphy
+1 (760) 622-3771
Kathleen.Murphy@arvinas.com

Pfizer Contacts

Investor Contact:
+1 (212) 733-4848
IR@pfizer.com

Media Contact:
+1 (212) 733-1226

PfizerMediaRelations@pfizer.com

[1] IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: September 2023.
[2] Weinberg, RA. pRb and Control of the Cell Cycle Clock. In: Weinberg RA, ed. The Biology of Cancer. 2nd ed. New York, NY: Garland Science; 2014:275-329.
[3] Sotillo E, Grana X. Escape from Cellular Quiescence. In: Enders GH, ed. Cell Cycle Deregulation in Cancer. New York, NY: Humana Press; 2010:3-22.