Arvinas Announces ARV-471 Achieves a Clinical Benefit Rate of 38% in Evaluable Patients and Continues to Show a Favorable Tolerability Profile in its Phase 2 Expansion Trial (VERITAC)

November 22, 2022

ARV-471 continues to show activity in heavily pre-treated patients with locally advanced or metastatic ER+/HER2- breast cancer

Median progression free survival of 3.7 months in all patients and 5.7 months in patients with ESR1 mutant tumors support the initiation of two Phase 3 registrational trials

NEW HAVEN, Conn., Nov. 22, 2022 (GLOBE NEWSWIRE) -- Arvinas, Inc. (Nasdaq: ARVN) today announced initial results from the Phase 2 cohort expansion portion (VERITAC) of a phase 1/2 study with ARV-471, a novel PROTAC® estrogen receptor (ER) protein degrader. ARV-471 is being co-developed with Pfizer Inc. (NYSE: PFE) for the treatment of patients with locally advanced or metastatic ER positive / human epidermal growth factor receptor 2 (HER2) negative (ER+/HER2-) breast cancer.

This disclosure was originally planned for December 8, 2022. However, on November 21, 2022, the 2022 San Antonio Breast Cancer Symposium (SABCS) incorrectly published the abstract, omitting a key safety data table, and inadvertently released the corresponding full data presentation on the SABCS website. These full data are scheduled to be presented on December 8, 2022 at 9:00 a.m. CT in an oral presentation titled “ARV-471, a PROTAC® estrogen receptor (ER) degrader in advanced ER-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer: phase 2 expansion (VERITAC) of a phase 1/2 study.”

As a result of the early release of the full data presentation, Arvinas will host a conference call and webcast today, November 22, 2022, at 4:30 p.m. ET to discuss these data. Those wishing to examine the data in more detail are welcome to access our 8K filed last evening located here.

In the VERITAC trial, ARV-471 shows a favorable tolerability profile and demonstrates a clinical benefit rate of 38% (total n=71) (CBR: rate of confirmed complete response, confirmed partial response, or stable disease ≥ 24 weeks), the primary endpoint in the trial. These results are consistent with the Phase 1 portion of this trial.

Patients in VERITAC had a median of four lines of prior therapies, in a population where 100% of patients were treated with prior cyclin-dependent kinase (CDK4/6) inhibitors, 79% with prior fulvestrant, and 73% with prior chemotherapy.

At the time of data cutoff (June 6, 2022), ARV-471 administered at 200 mg (n=35) and 500 mg (n=36) demonstrated:

- Antitumor activity in 100% CDK4/6 inhibitor-pretreated patients, as measured by a CBR of 38% (total n=71) in all patients and 51.2% in patients with mutant *ESR1* tumors (n=41).
- Preliminary median progression-free survival (mPFS) of 3.7 months, a key secondary endpoint, in all evaluable patients and 5.7 months in patients with mutant *ESR1* tumors (n=41).
- A favorable tolerability profile, with the majority of treatment-related adverse events (TRAEs) reported as Grade 1 or 2.

“I’m gratified to see the continued differentiated profile of ARV-471 and its potential to become an important new standard of care for patients with ER+/HER2- breast cancer,” said John Houston, Ph.D., President and Chief Executive Officer at Arvinas. “The positive VERITAC results, in a heavily pre-treated population in which 100% of the patients received at least one prior CDK4/6 inhibitor and many who had progressed on or after chemotherapy, and fulvestrant, reinforce our confidence in ARV-471 as we prepare to initiate two pivotal trials, with the goal of working to give patients and physicians a potential new option in the fight against breast cancer.”

“These data validate the early data which led us to enter into the collaboration with Arvinas and give us the confidence needed to initiate two Phase 3 registrational trials," said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology and Rare Disease, Pfizer Global Product Development.

ARV-471 Clinical Update

Study Design

VERITAC is the Phase 2 cohort expansion portion of a Phase 1/2 single-arm trial of ARV-471 alone and in combination with palbociclib in patients with ER+/HER2- locally advanced or metastatic breast cancer (mBC) (NCT04072952). In VERITAC, patients were treated with either 200 mg or 500 mg ARV-471 with a primary endpoint of CBR (CR, PR or SD ≥ 24 weeks). Secondary endpoints include ORR, DOR, PFS and OS as well as safety (AEs) and pharmacokinetics.

Enrollment

As of the data cut-off date of June 6, 2022, 71 patients with locally advanced or metastatic ER+/HER2- breast cancer in the VERITAC expansion cohort were treated once-daily with oral doses of ARV-471 at 200 mg (n=35) or 500 mg (n=36).

- 100% of patients were previously treated with CDK 4/6 inhibitors
- 79% of patients were previously treated with fulvestrant

- 73% of patients were previously treated with chemotherapy
    - 45% received chemotherapy in the metastatic setting

Efficacy Data

Clinical benefit rate (the primary endpoint, defined as a confirmed complete response, partial response, or stable disease ≥ 24 weeks) in all patients (n=71) and in patients with tumors harboring *ESR1* mutations (n=41):

- All patients (200 mg and 500 mg, n=71): 38%
    - Patients with tumors harboring *ESR1* mutations (n=41): 51.2%
    - Patients with *ESR1* wild-type tumors (n=25): 20%
- All patients at 200 mg (n=35): 37.1%
    - Patients with tumors harboring *ESR1* mutations (n=19): 47%
- All patients at 500 mg (n=36): 39%
    - Patients with tumors harboring *ESR1* mutations (n=22): 55%

Progression free survival

- All patients receiving 200 mg or 500 mg qd ARV-471 (n=71): median 3.7 months
    - Patients with mutant *ESR1* tumors (n=41): median 5.7 months
- Patients receiving 200 mg qd ARV-471 (n=35): median 3.5 months
    - Patients with mutant *ESR1* tumors (n=19): median 5.5 months
- At the time of the data cutoff, data for 500 mg cohort were immature and therefore not included in a separate analysis

Safety Data

ARV-471 was well tolerated across both dose levels. TRAEs were primarily Grade 1 and 2, with 5 patients experiencing Grade 3/4 TRAEs:

- 200 mg cohort:
    - Grade 1 (n=13): 37%
    - Grade 2 (n=13): 37%
    - Grade 3 or 4 (n=2): 6%
        - Grade 3/4 TRAEs in the 200 mg cohort were Grade 3 QT prolonged (n=1) and Grade 3 thrombocytopenia and Grade 4 hyperbilirubinemia (n=1).

- 500 mg cohort:
    - Grade 1 (n=11): 31%
    - Grade 2 (n=9): 25%
    - Grade 3 or 4 (n=3): 8%
        - Grade 3/4 TRAEs in the 500 mg cohort were Grade 3 fatigue (n=1), Grade 3 decreased appetite (n=1), and Grade 3 neutropenia (n=1).

There was 1 discontinuation due to a treatment-emergent adverse event (TEAE) and no dose reductions in the 200 mg cohort. There were 2 discontinuations and 3 dose reductions in the 500 mg cohort.

Anticipated 2022/2023 Milestones

- Initiate a Phase 3 trial (First Subject First Visit) with ARV-471 as a second-line treatment in patients with ER+/HER2- metastatic breast cancer (4Q 2022).
- Initiate a Phase 3 trial (First Subject First Visit) with ARV-471 in combination with palbociclib as a first-line treatment in patients with ER+/HER2- metastatic breast cancer (1Q 2023).
- Initiate the first two cohorts (First Subject First Visit) and initiate additional arms with other targeted therapies in the ongoing Phase 1b combination trial (TACTIVE-U) (2023).
- Present data from the Phase 1b combination trial with palbociclib (Part C of the Phase 1/2 trial) at a medical conference (1H 2023).

Investor Call & Webcast Details

A conference call and webcast will be held at 4:30 p.m. ET on Tuesday, November 22, 2022, with executives from Arvinas and Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology and Rare Disease, Pfizer Global Product Development. Participants are invited to listen by going to the Events and Presentation section under the Investor page on the Arvinas website at www.arvinas.com. A replay of the webcast will be archived on the Arvinas website following the presentation.

About ARV-471

ARV-471 is an investigational, orally-bioavailable PROTAC® protein degrader designed to specifically target and degrade the estrogen receptor (ER) for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer.

In preclinical studies, ARV-471 demonstrated near-complete ER degradation in tumor cells, induced robust tumor shrinkage when dosed as a single agent in multiple ER-driven xenograft models, and showed superior anti-tumor activity when compared to a standard of care agent, fulvestrant, both as a single agent and in combination with a CDK4/6 inhibitor. In July 2021, Arvinas announced a global collaboration with Pfizer for the co-development and co-commercialization of ARV-471; Arvinas and Pfizer will equally share worldwide development costs, commercialization expenses, and profits.

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 three investigational clinical-stage programs: bavdegalutamide (ARV-110) and ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer; and ARV-471 for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer. For more information, visit www.arvinas.com.

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 for ARV-471 to become a new standard of care for patients with ER+/HER-2 breast cancer; the timing of our and Pfizer Inc.'s ("Pfizer") plans to initiate two Phase 3 trials with ARV-471, one in combination with palbociclib, and additional arms with other targeted therapies in the ongoing Phase 1b combination trial (TACTIVE-U); and the timing of our and Pfizer's plans to present data from the Phase 1b combination trial with palbociclib. All statements, other than statements of historical facts, contained in this press release, including statements regarding our 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.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various risks and uncertainties, including but not limited to: our and Pfizer performance of our respective obligations with respect to our collaboration with Pfizer; whether we and Pfizer will be able to successfully conduct and complete clinical development for ARV-471; whether we obtain marketing approval for and commercialize ARV-471 on our current timelines or at all; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2021 and subsequent other reports on file with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect our current views with respect to future events, and we assume 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 our views as of any date subsequent to the date of this release.

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