

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): December 10, 2021

Arvinas, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-38672
(Commission
File Number)

47-2566120
(IRS Employer
Identification No.)

**5 Science Park
395 Winchester Ave.
New Haven, Connecticut**
(Address of principal executive offices)

06511
(Zip Code)

Registrant's telephone number, including area code: (203) 535-1456

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.001 per share	ARVN	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On December 10, 2021, Arvinas, Inc. (the “Company”) issued a press release announcing clinical program updates for its PROTAC® protein degrader ARV-471, including updated data. The Company will present the updates on a conference call and webcast on December 10, 2021. Copies of the press release and presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K and are incorporated herein by reference.

The information in this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On December 10, 2021, the Company announced updated data, as of the data cut-off date of September 30, 2021, from the dose escalation portion of its Phase 1/2 clinical trial of ARV-471 in patients with locally advanced or metastatic ER+/HER2- breast cancer to be presented as a virtual spotlight poster session at the 2021 San Antonio Breast Cancer Symposium (SABCS).

The dose escalation portion of the Company’s Phase 1/2 clinical trial of ARV-471 is designed to assess safety, tolerability and pharmacokinetics (“PK”) of ARV-471 in patients with locally advanced or metastatic ER+/HER2- breast cancer, as well as measures of anti-tumor activity as secondary endpoints.

Enrollment

As of the data cut-off date, 60 adult patients with locally advanced or metastatic ER+/HER2- breast cancer were treated in the Phase 1 dose escalation portion of the study with total daily ARV-471 doses ranging from 30 mg to 700 mg. This patient group is heavily pretreated, with a median of four prior therapies. All patients were previously treated with cyclin-dependent kinase (“CDK”) 4/6 inhibitors; 80% of patients received prior fulvestrant; and 78% received prior chemotherapy.

Efficacy

Of 47 patients who were evaluable for clinical benefit (confirmed complete response, partial response, or stable disease ³ 24 weeks) the clinical benefit rate was 40%. As of the data cutoff date, 14 patients were continuing to receive study treatment, including two patients who had been on treatment for over 18 months. Three confirmed partial responses were observed among the 38 patients with baseline response evaluation criteria in solid tumors (RECIST) measurable disease and at least one on-treatment tumor assessment.

Safety

Patients were treated in the monotherapy escalation at total daily doses of 30 mg (n=3), 60 mg (n=3), 120 mg (n=7), 180/200 mg (n=11), 360 mg (n=15), 500 mg (n=17), and 700 mg was administered BID (300 mg in the morning / 400 mg in the evening) (n=4). A maximum tolerated dose was not reached and no dose limiting toxicities or Grade ³4 treatment-related adverse events (“TRAEs”) were observed. Of the 60 patients, 37% had Grade 1 TRAEs and 57% had Grade ² TRAEs, and the most common TRAEs were nausea (29%), fatigue (20%), and vomiting (10%). No Grade 1 or 2 TRAEs led to discontinuation or dose reduction of ARV-471. Four patients experienced six Grade 3 TRAEs that were potentially related to ARV-471, including: headache lasting 1-day, single occurrence of asymptomatic increased amylase and lipase, nausea and asymptomatic QTc prolongation, and post-biopsy venous embolism. The patient with the venous embolism was the only Grade 3 patient who discontinued ARV-471 due to a TRAE, and the patient with Grade 3 nausea was the only patient with a dose reduction due to a TRAE (reduced from 500 mg to 400 mg daily).

ER Degradation

In paired biopsies from 14 patients across all doses up to 500 mg daily, robust ER degradation of up to 89% was observed, regardless of ESR1 mutation status. Median and mean ER degradation across dose levels were 67% and 64%, respectively.

Pharmacokinetics

ARV-471 demonstrated a dose-related increase in plasma exposure, with doses from 30 mg to 500 mg daily, resulting in steady-state C_{max} and AUC₂₄ that exceeded the exposure associated with tumor regression in preclinical breast cancer models. Mean exposure on day 15 exceeded the nonclinical efficacious range at doses ³60 mg daily.

ARV-471 currently is being evaluated as a treatment for metastatic breast cancer in a Phase 1 dose escalation study, a Phase 1b combination study with IBRANCE® (palbociclib), and a Phase 2 monotherapy dose expansion study. In 2022, the Company expects to initiate Phase 3 studies across lines of therapy in metastatic breast cancer, as both a monotherapy and in combination; initiate two additional trials of ARV-471, including a Phase 1b combination trial with everolimus in 2L/3L metastatic breast cancer, potentially as part of a planned umbrella study to explore multiple combination agents, and a Phase 2 neoadjuvant trial in early breast cancer; and present data from the ongoing Phase 1b combination study with IBRANCE® (palbociclib) and from the ongoing Phase 2 monotherapy dose expansion study.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, dated December 10, 2021
99.2	Company Presentation, dated December 10, 2021
104	Cover Page Interactive Data File (formatted as Inline XBRL)

Forward-Looking Statements

This Current Report on Form 8-K, including the documents furnished as Exhibit 99.1 and Exhibit 99.2 hereto, contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the development and regulatory status of ARV-471 and other candidates in the Company's pipeline, and the timing of clinical trials and data from those trials and plans for registration for the Company's product candidates, the therapeutic potential of the Company's product candidates and the potential commercialization of any of the Company's product candidates. All statements, other than statements of historical facts, contained in this Current Report on Form 8-K, including statements regarding the Company's strategy, future operations, 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.

The Company may not actually achieve the plans, intentions or expectations disclosed in its 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 the Company makes as a result of various risks and uncertainties, including but not limited to: whether the Company and Pfizer will be able to successfully conduct and complete clinical development for ARV-471, initiate and complete other clinical trials for the Company's product candidates, and receive results from the Company's clinical trials on the Company's expected timelines, or at all, and other important factors discussed in the "Risk Factors" sections contained in the Company's quarterly and annual reports on file with the Securities and Exchange Commission. The forward-looking statements contained in this Current Report on Form 8-K reflect the Company's current views with respect to future events, and the Company 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 the Company's views as of any date subsequent to the date of this Current Report on Form 8-K.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: December 10, 2021

ARVINAS, INC.

By: /s/ Sean Cassidy
Sean Cassidy
Chief Financial Officer



Arvinas and Pfizer Announce PROTAC® Protein Degradar ARV-471 Continues to Demonstrate Encouraging Clinical Benefit Rate in Patients with Locally Advanced or Metastatic ER+/HER2- Breast Cancer

– ARV-471 continues to show a favorable tolerability profile and robust ER degradation in updated phase 1 dose escalation data presented at San Antonio Breast Cancer Symposium –

– ARV-471 is expected to enter two Phase 3 registrational clinical trials in 2022 –

NEW HAVEN, Conn., and NEW YORK, December 10, 2021 — Arvinas, Inc. (Nasdaq: ARVN) and Pfizer Inc. (NYSE: PFE) today announced an update on Phase 1 dose escalation data of ARV-471, a novel PROTAC® estrogen receptor (ER) degrader, which is being co-developed for the treatment of patients with locally advanced or metastatic ER-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer (ER+/HER2-). These data were presented as a virtual spotlight poster session at the 2021 San Antonio Breast Cancer Symposium (SABCS) and showed:

- ARV-471 demonstrated antitumor activity in CDK4/6 inhibitor-pretreated patients with a clinical benefit rate (CBR) of 40% in 47 evaluable patients. This heavily pretreated patient group had a median of four prior therapies.
- Three patients exhibited confirmed partial responses (PR) among the 38 patients with response evaluation criteria in solid tumors (RECIST) measurable lesions and at least one on-treatment tumor assessment.
- ARV-471 continues to demonstrate a favorable tolerability profile. Robust ER degradation was observed at all dose levels, reaching 89% reduction of ER.

Erika P. Hamilton, MD, Director of the Breast Cancer and Gynecologic Cancer Research Program and Principal Investigator, Sarah Cannon Research Institute, provided an overview of these data.

“These results continue to suggest that ARV-471 has the potential to become a first-in-category treatment, and a new standard of care, for ER+/HER2- breast cancer patients.” said John Houston, Ph.D., Chief Executive Officer at Arvinas. “The profile we see emerging for this drug candidate continues to validate our PROTAC® protein degrader platform, with ARV-471 showing clear signals of clinical benefit in a heavily pretreated patient population, including tumor shrinkage and good tolerability.”

These data support and further validate the evaluation of ARV-471 as a potential treatment for metastatic breast cancer that is ongoing in a Phase 1b combination study with IBRANCE® (palbociclib) and a Phase 2 monotherapy dose expansion study.

“We are excited by these results and believe ARV-471 is a promising ER-targeting investigational medicine,” said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “It is encouraging to see ARV-471 continuing to show durable efficacy and tolerability in heavily pre-treated patients with ER+ breast cancer who have limited treatment choices.”

ARV-471 Clinical Update

Enrollment

As of the data cut-off date of September 30, 2021, 60 adult patients with locally advanced or metastatic ER+/HER2- breast cancer were treated in the Phase 1 dose escalation portion of the study with total daily ARV-471 doses ranging from 30 mg to 700 mg. This patient group is heavily pretreated, with a median of four prior therapies. All patients were previously treated with cyclin-dependent kinase (CDK) 4/6 inhibitors; 80% of patients received prior fulvestrant; and 78% received prior chemotherapy.

Efficacy

Of 47 patients who were evaluable for clinical benefit (confirmed complete response, PR, or stable disease ³ 24 weeks) the CBR was 40%. As of the data cutoff date, 14 patients were continuing to receive study treatment, including two patients who had been on treatment for over 18 months. Three confirmed PRs were observed among the 38 patients with baseline RECIST measurable disease and at least one on-treatment tumor assessment.

Safety

Patients were treated in the monotherapy escalation at total daily doses of 30 mg (n=3), 60 mg (n=3), 120 mg (n=7), 180/200 mg (n=11), 360 mg (n=15), 500 mg (n=17), and 700 mg (n= 4). All patients in the 700 mg cohort received ARV-471 twice-daily, a subset of patients who received 500 mg as a total daily dose received ARV-471 twice-daily, and other all doses were administered once-daily. A maximum tolerated dose was not reached and no dose limiting toxicities or Grade ^{3,4} treatment-related adverse events (TRAEs) were observed. Of the 60 patients, 37% had Grade 1 TRAEs and 57% had Grade \geq 2 TRAEs, and the most common TRAEs were nausea (29%), fatigue (20%), and vomiting (10%). No Grade 1 or 2 TRAEs led to discontinuation or dose reduction of ARV-471. Four patients experienced six Grade 3 TRAEs that were potentially related to ARV-471, including: headache lasting 1-day, single occurrence of asymptomatic increased amylase and lipase, nausea and asymptomatic QTc prolongation, and post-biopsy venous embolism. The patient with the venous embolism was the only Grade 3 patient who discontinued ARV-471 due to a TRAE, and the patient with Grade 3 nausea was the only patient with a dose reduction due to a TRAE (reduced from 500 mg to 400 mg daily).

ER Degradation

In paired biopsies from 14 patients across all doses up to 500 mg daily, robust ER degradation of up to 89% was observed, regardless of *ESR1* mutation status. Median and mean ER degradation across dose levels were 67% and 64%, respectively.

Pharmacokinetics

ARV-471 demonstrated a dose-related increase in plasma exposure, with doses from 30 mg to 500 mg daily, resulting in steady-state C_{max} and AUC_{24} that exceeded the exposure associated with tumor regression in preclinical breast cancer models. Mean exposure on day 15 exceeded the nonclinical efficacious range at doses ³60 mg daily.

Anticipated 2021/2022 Milestones

- ARV-471 currently is being evaluated as a treatment for metastatic breast cancer in a Phase 1 dose escalation study, a Phase 1b combination study with IBRANCE[®] (palbociclib), and a Phase 2 monotherapy dose expansion study.
- In 2022, we expect to:
 - Initiate Phase 3 studies across lines of therapy in metastatic breast cancer, as both monotherapy and in combination.
 - Initiate two additional trials of ARV-471, including a Phase 1b combination trial with everolimus in 2L/3L metastatic breast cancer, potentially as part of a planned umbrella study to explore multiple combination agents, and a Phase 2 neoadjuvant trial in early breast cancer.

- Present data from the ongoing Phase 1b combination study with IBRANCE® (palbociclib) and from the ongoing Phase 2 monotherapy dose expansion study.

Investor Conference Call Details

Arvinas will host a conference call and webcast at 8:30 AM ET on Friday, December 10, 2021, to discuss these data. Pfizer Oncology executives will also participate in this call. Participants are invited to listen by dialing (844) 467-7654 (domestic) or (602) 563-8497 (international) five minutes prior to the start of the call and providing the passcode 9122219.

Supporting materials for the conference call and webcast will be available on the Arvinas' website at www.arvinas.com under [Events + Presentations](#). 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 biopharmaceutical 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 clinical-stage programs: ARV-110 and ARV-766 for the treatment of men with metastatic castrate-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.

Arvinas Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the development and regulatory status of ARV-471 and other candidates in our pipeline, and the timing of clinical trials and data from those trials and plans for registration for our product candidates, the therapeutic potential of our product candidates, and the potential commercialization of any of our product candidates. All statements, other than statements of historical facts, contained in this press release, including statements regarding our strategy, future operations, 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.

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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 indicated for the treatment of adult patients with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or with fulvestrant in patients with disease progression following endocrine 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 Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

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 more than 170 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 Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

Pfizer Forward-Looking Statements

The information contained in this release is as of December 10, 2021. 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 ARV-471 and a global collaboration between Pfizer and Arvinas to develop and commercialize ARV-471, 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, 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; risks associated with interim 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 for ARV-471 for any potential indications in any jurisdictions; whether and when regulatory authorities may approve any potential applications that may be filed for ARV-471 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 ARV-471 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 ARV-471; 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, 2020 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.

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ARV-471: Phase 1 Dose
Escalation Clinical Trial
Results



San Antonio Breast Cancer Symposium
December 10, 2021

Safe harbor and forward-looking statements

This presentation 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 development and regulatory status of ARV-471 and other candidates in our pipeline, and the timing of clinical trials and data from those trials and plans for registration for our product candidates, the therapeutic potential of our product candidates and the potential commercialization of any of our product candidates. All statements, other than statements of historical facts, contained in this presentation, 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.

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The Arvinas name and logo are our trademarks. We also own the service mark and the registered U.S. trademark for PROTAC®. The trademarks, trade names and service marks appearing in this presentation are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks named in this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Agenda



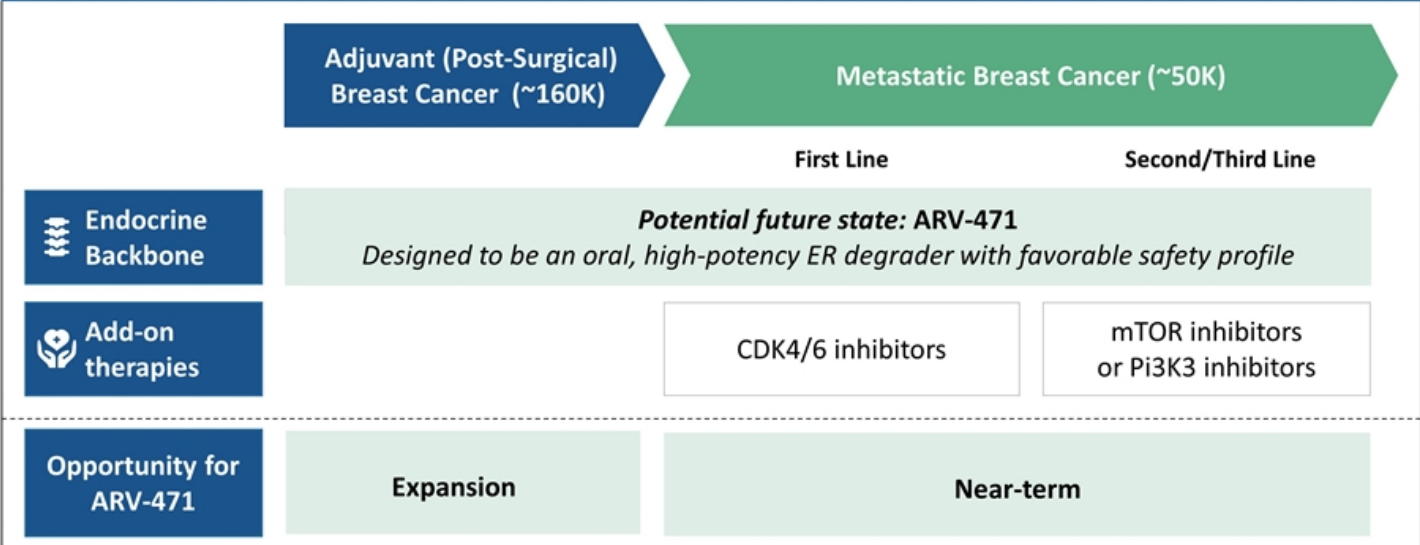
Topic	Participant	
Introduction	John G. Houston, Ph.D.	<i>President and Chief Executive Officer, Arvinas</i>
ARV-471 Clinical Data Update	Ron Peck, M.D.	<i>Chief Medical Officer, Arvinas</i>
	Chris Boshoff, M.D., Ph.D.	<i>Chief Development Officer, Pfizer Oncology</i>

 Q&A

ARV-471: Potential to be the endocrine backbone of choice for ER+/HER2- breast cancer treatment



Potential Future US ER+/HER2- Breast Cancer Treatment Paradigm with ARV-471



*US incident population per year from SEER database
 CDK: cyclin-dependent kinases, PI3K: phosphoinositide 3-kinase; mTOR: mammalian target of rapamycin

ARV-471: Potential best-in-class estrogen receptor-targeting therapy



December 2020: **21 patients**, clinical benefit rate of **42%** (5 of 12 evaluable patients)
December 2021: **60 patients**, clinical benefit rate of **40%** (19 of 47 evaluable patients)



Continued robust signals of efficacy in a patient population expected to have highly ER-independent disease, due to **100% pretreatment with CDK4/6 inhibitors**



Well-tolerated across all dose levels with **no dose limiting toxicities** up to 700mg

- Majority (89%) of AEs reported were grade 1/2



ER degradation **up to 89%** continues to exceed reported degradation in fulvestrant and clinical-stage SERDs[†]

[†] When compared to published data with fulvestrant and the clinical-stage SERDs. ARV-471 has not been studied in clinical trials against fulvestrant and/or clinical stage SERDs. CDK4/6, cyclin-dependent kinases; SERD, selective estrogen receptor degrader

ARV-471: First-in-Human study “3+3” dose escalation study



Design

- “3 + 3” dose escalation with backfill
- ARV-471 orally administered with food
- Starting dose: 30 mg administered orally once daily
- Maximum administered daily dose: 700 mg

Endpoints

Primary:

- Maximum tolerated dose and recommended Phase 2 dose

Key Secondary:

- Safety
- Pharmacokinetics
- Pharmacodynamics: Quantify ER in paired biopsies (baseline and on-treatment)
- Efficacy: RECIST, Clinical Benefit Rate (CBR) defined as confirmed PRs and CRs + \geq 24-week SD

100% of patients in Phase 1 study were post- CDK4/6 inhibitor; high rate of potential ER-independent resistance mechanisms

Phase 1 Inclusion Criteria

- ER+/HER2- advanced breast cancer
- **Disease progression on CDK4/6 inhibitor**
- ≥ 2 prior endocrine therapies in any setting
- Up to 3 prior chemotherapy regimens in advanced breast cancer

Believed to be the only trial of an ER-targeting therapy requiring prior CDK4/6 treatment for all patients

- After CDK4/6 inhibitor treatment, **~66%** of breast cancers have ER-independent mechanisms of resistance[†]
- Previously disclosed data demonstrate poor outcomes following CDK4/6 inhibitor therapy, e.g., fulvestrant:
 - Median PFS = 1.9 months^{††}
 - CBR = 13.7%^{††}

[†] Wander 2020; ^{††} Lindeman ASCO 2021 results from VERONICA trial.
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor. PFS, progression-free survival; TTF, time to treatment failure; CBR, clinical benefit rate

ARV-471 Phase 1 patients received extensive prior therapy (N = 60)

Patient Characteristics	Parameter	N (%)	
Median age (years)		65.5 (38-80)	
ECOG performance status*	0	29	(48)
	1	30	(50)
Sites of metastases	Bone	33	(55)
	Liver	23	(38)
	Lung	13	(22)
	Other	13	(22)
Median prior lines of therapy total (range 1-9) †		4	(NA)
Median number of prior endocrine regimens		3	(NA)
Type of prior therapies in any setting			
	CDK 4/6 inhibitor	60	(100)
	Fulvestrant	48	(80)
	Chemotherapy	47	(78)
	Investigational SERD	6	(10)
	Aromatase inhibitors	52	(87)

*baseline value missing for 1 patient

†Median of 3 prior lines in the metastatic setting.

ECOG, Eastern Cooperative Oncology Group; CDK4/6, cyclin-dependent kinases; SERD, selective estrogen receptor degrader

ARV-471 was well tolerated at all dose levels; no dose limiting toxicities and MTD not reached

.....

TRAE in ≥ 10% of patients	30 mg (n=3)		60 mg (n=3)		120 mg (n=7)		180/200 mg (n=11)		360 mg (n=15)		500 mg (n=17)		700 mg (n=4)		Total (N=60)	
	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3	Gr 1/2	Gr 3
Any TRAE	0	0	3 (50%)	0	6 (86%)	0	6 (55%)	1 (9%)	10 (67%)	1 (7%)	7 (41%)	2 (12%)	2 (50%)	0	34 (57%)	4 (7%)
Nausea	0	0	2 (33%)	0	2 (29%)	0	4 (36%)	0	3 (20%)	0	4 (24%)	1 (6%)	1 (25%)	0	16 (27%)	1 (2%)
Fatigue	0	0	1 (17%)	0	0	0	1 (9%)	0	3 (20%)	0	5 (29%)	0	2 (50%)	0	12 (20%)	0
Vomiting	0	0	0	0	2 (29%)	0	1 (9%)	0	2 (13%)	0	1 (6%)	0	0	0	6 (10%)	0
AST increased	0	0	0	0	1 (14%)	0	2 (18%)	0	0	0	1 (6%)	0	2 (50%)	0	6 (10%)	0

- Discontinuation rate <2% (1 out of 60)
- Dose reductions <2% (1 out of 60)

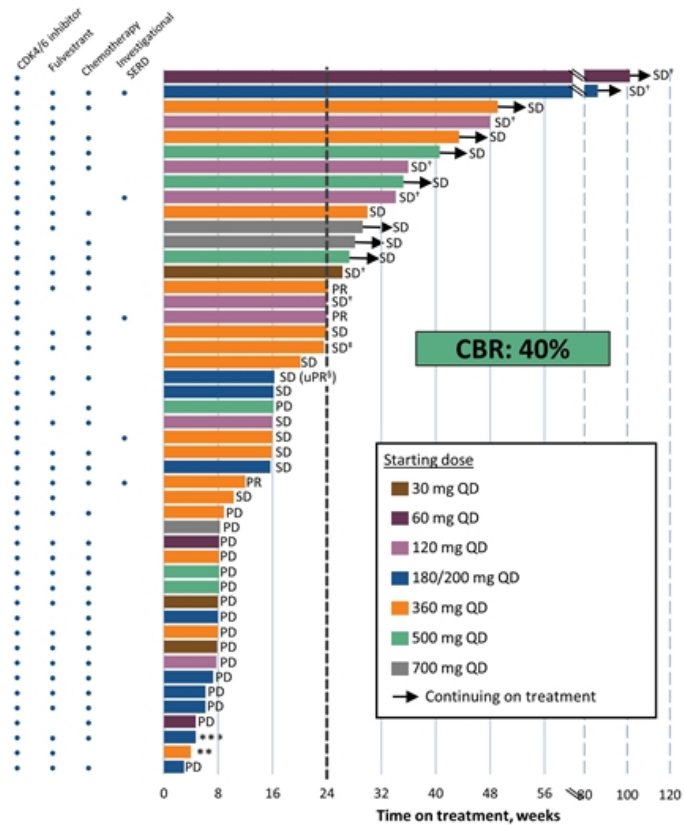
Four patients experienced Gr 3 events potentially related to ARV-471 (headache lasting 1-day, single occurrence of asymptomatic increased amylase and lipase, nausea and asymptomatic QTc prolongation, and venous embolism after a minor procedure*)

*Advanced breast cancer is highly associated with venous embolisms. Event was included as potentially treatment related, so treatment with ARV-471 was stopped.
Data cut-off: 09/30/21; TRAE, Treatment related adverse event

AVR-471: High CBR (40%) in heavily pretreated population

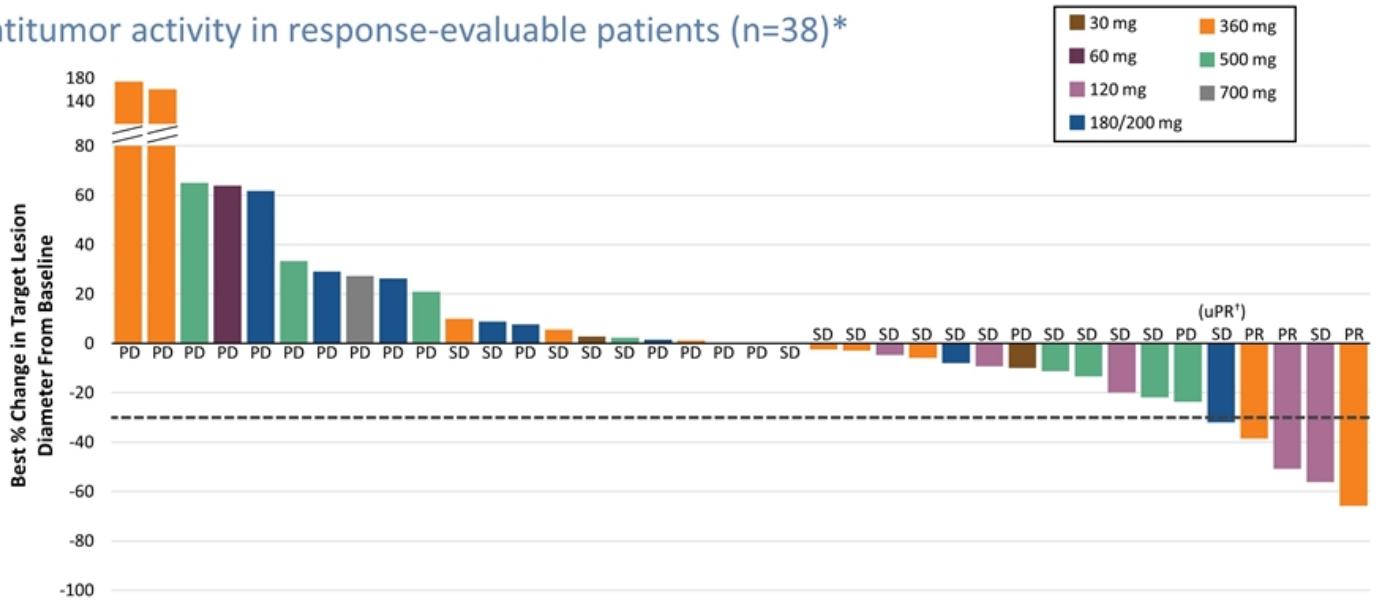
- **40% clinical benefit rate (CBR)** in 47 evaluable patients*
 - CBR = rate of confirmed CR or PR or SD ≥24 weeks
- **3 patients had confirmed PRs**
- **14 patients were ongoing at the time of data cutoff, including 2 who have been on treatment for >18 months**

*Excludes patients unable to complete cycle 1 due to reasons other than PD, toxicity, or death
 **Patient discontinued treatment due to venous embolism before first on-study scan
 ***Patient discontinued treatment due to clinical progression before first on-study scan
 †Patient had dose escalation from starting dose
 †Week 24 imaging assessment performed at 23.4 weeks (within the window allowed per protocol)
 ‡Patient had disease progression on subsequent scan and discontinued treatment
 CBR=clinical benefit rate; CDK=cyclin-dependent kinase; PD=progressive disease; PR=confirmed partial response; SD=stable disease; SERD=selective estrogen receptor degrader; uPR=unconfirmed partial response



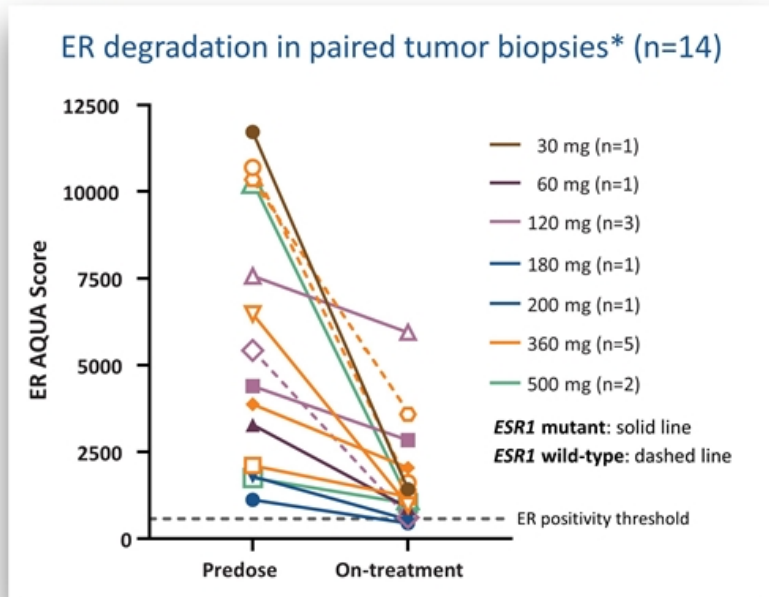
ARV-471 demonstrates promising anti-tumor activity in late-line patients

Antitumor activity in response-evaluable patients (n=38)*



*Patients with measurable disease at baseline who had a baseline and ≥1 on-treatment scan
 †Patient had disease progression on subsequent scan and discontinued treatment
 PD=progressive disease; PR=confirmed partial response; SD=stable disease; uPR=unconfirmed partial response

ARV-471 degraded ER up to 89% through the 500 mg dose level



Degradation up to **89%**;
median **67%**; mean of **64%**



Degradation **exceeds** reported
data for **fulvestrant**
(previously reported: 40-
50%)**



Degradation of **wild type ER**
and **ESR1 mutant proteins**

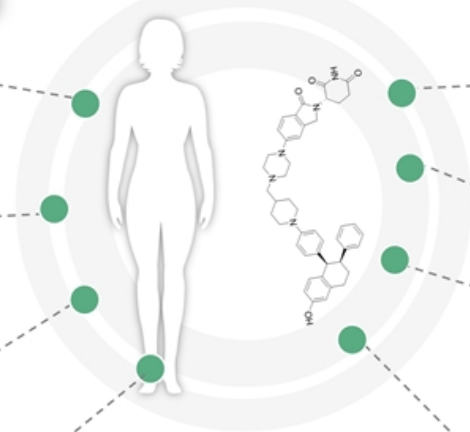
* Data available as of September 3, 2021; median time on treatment at biopsy: 31 days (range: 16–77). ER immunoreactivity analyzed by QIF using the AQUA method, and ER positivity threshold derived by examining AQUA scores and visually inspecting all samples in the dataset to determine a cut-point for ER positivity
 ** Fulvestrant degradation reported as 40-50% in Robertson et al., Breast Cancer Research (2013) and Kuter et al., Breast Cancer Res Treat (2012).
 AQUA=automated quantitative analysis; ER=estrogen receptor; QIF=quantitative immunofluorescence

Summary: ARV-471 has shown robust signals of efficacy in a challenging patient population

Data as presented 12/10/2021

ARV-471

Designed to be an oral, high-potency ER degrader with favorable safety profile



Heavily pretreated patient population

- 4** Median lines of prior therapies
- 100%** Of patients treated with CDK4/6 inhibitors
- 80%** Of patients with prior fulvestrant treatment

66% Patients expected to have ER-independent disease[†]

Early clinical benefit Phase 1

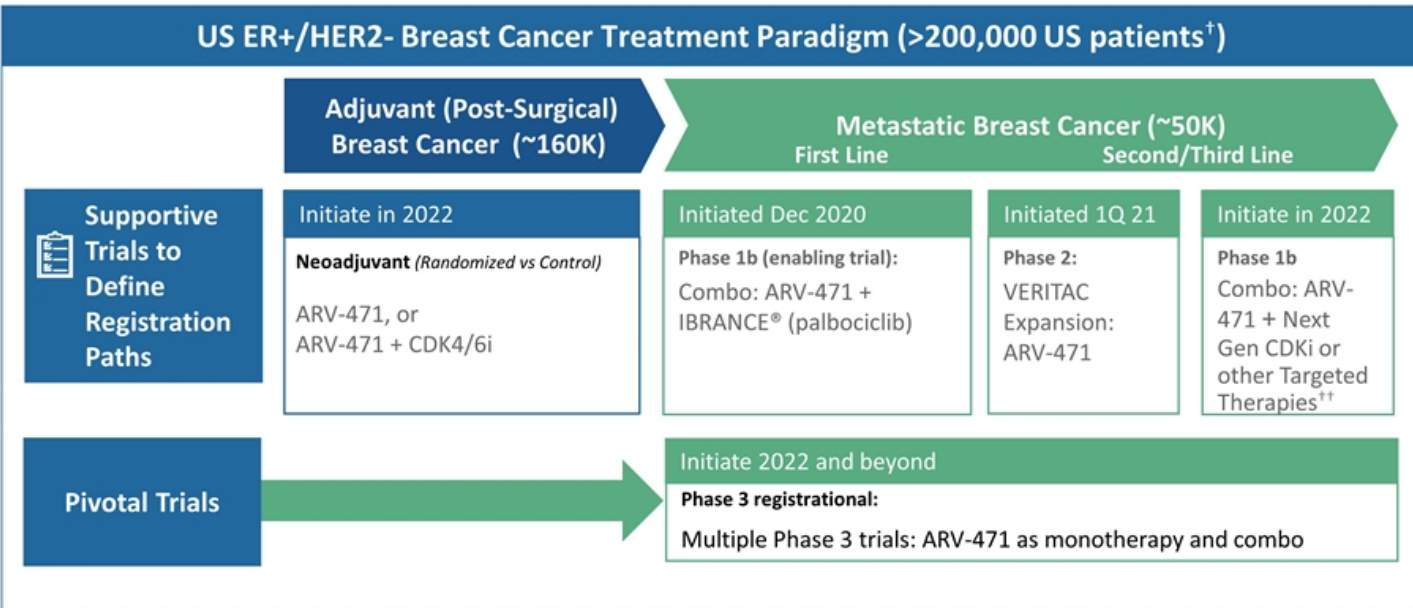
- 40%** Clinical benefit rate (CBR)^{††}; 14 patients ongoing at cutoff
- 3** Confirmed partial responses (PR); tumor shrinkage in other patients
- 89%** Maximum ER degradation (mean, 64%) in first 3 dose levels

89% Of TRAEs were grade 1/2 in severity with no DLTs

...with potential to become endocrine backbone of choice for ER+/HER2- breast cancer treatment

[†] Wander 2020; ^{††}CBR defined as SD persisting ≥ 24 weeks, or a best response of confirmed CR or PR.

Arvinas and Pfizer aim to characterize the activity of ARV-471 across ER+/HER2- breast cancer treatment lines



[†] SEER database; includes US patient population only, ^{††} E.g., everolimus or as part of umbrella study with multiple combination agents
 CDK, cyclin-dependent kinases PI3Ki; phosphoinositide 3-kinase inhibitor; mTORi: mammalian target of rapamycin inhibitors

ARV-471: Evidence for best-in-class potential in a large area of unmet need



STRONG EVIDENCE FOR BEST-IN-CLASS PROFILE

- Superior degradation to published fulvestrant and SERD data[†]
- Strong efficacy signal in a predominantly ER-independent population
- Well tolerated



CLEAR DEVELOPMENT PATH

- Potential for 1L/2L/3L approval as monotherapy or in combination
- Planned combinations with CDK inhibitors and other targeted therapies in adjuvant or early metastatic cancers



LARGE UNMET NEED AND OPPORTUNITY

- In the US alone, ER+/HER2- breast cancer represents an addressable patient population of >200K[†] per year and a market opportunity of >\$15B



[†] US incidence from SEER Database. ^{††} Fulvestrant degradation reported in Robertson et al., Breast Cancer Research (2013) and Kuter et al., Breast Cancer Res Treat (2012)

Thank You