ARV-471: Phase 1 Dose Escalation Clinical Trial Results

ARVINAS

San Antonio Breast Cancer Symposium
December 10, 2021

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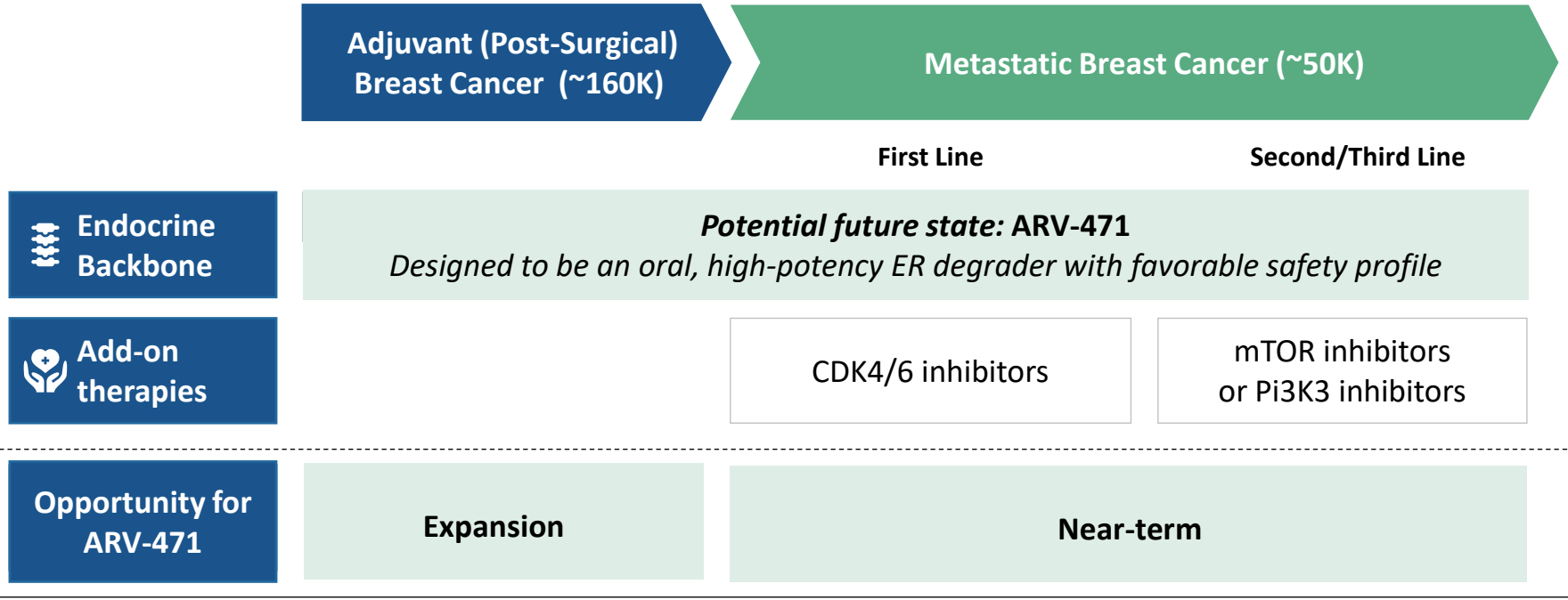
Agenda

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

? 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 + ≥ 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

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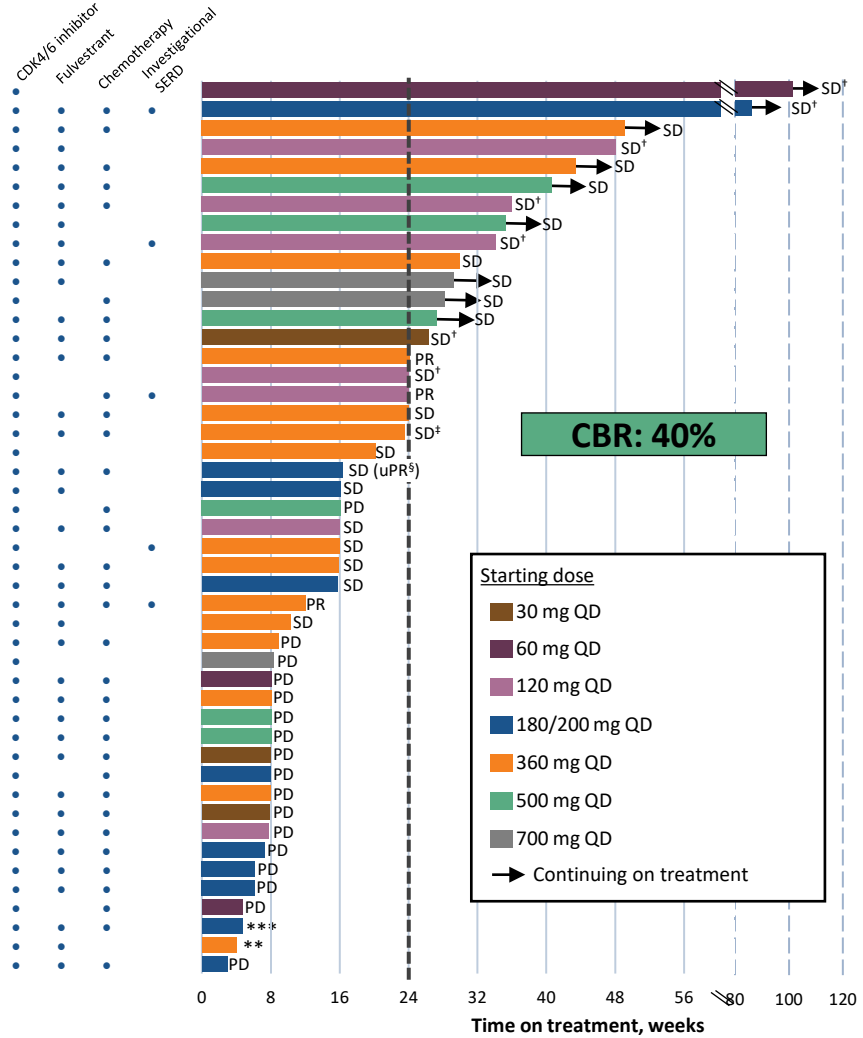
AVR-471: High CBR (40%) in heavily pretreated population

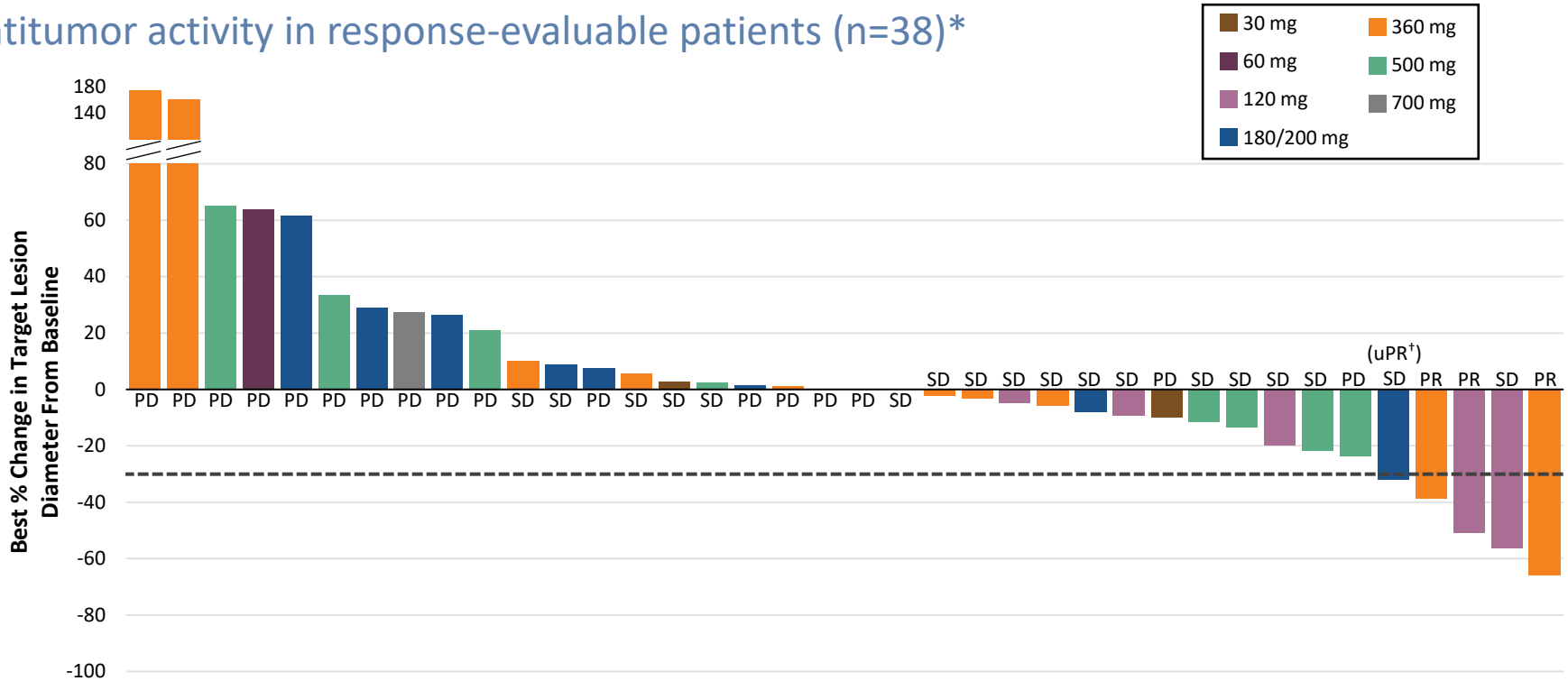
- **40% clinical benefit rate** (CBR) in 47 evaluable patients*
  - CBR = rate of confirmed CR or PR or SD ≥24 weeks
- **3** patients had **confirmed PRs**
- 14 patients were ongoing at the time of data cutoff, including ***2 who have been on treatment for >18 months***



*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

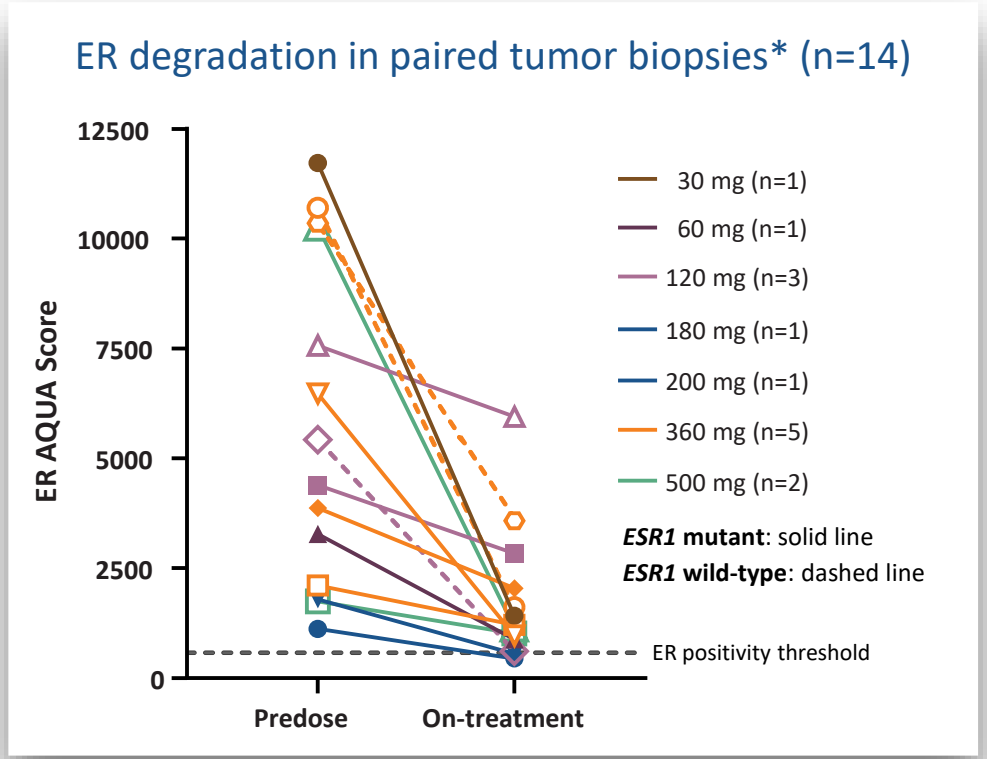
ARV-471 demonstrates promising anti-tumor activity in late-line patients

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

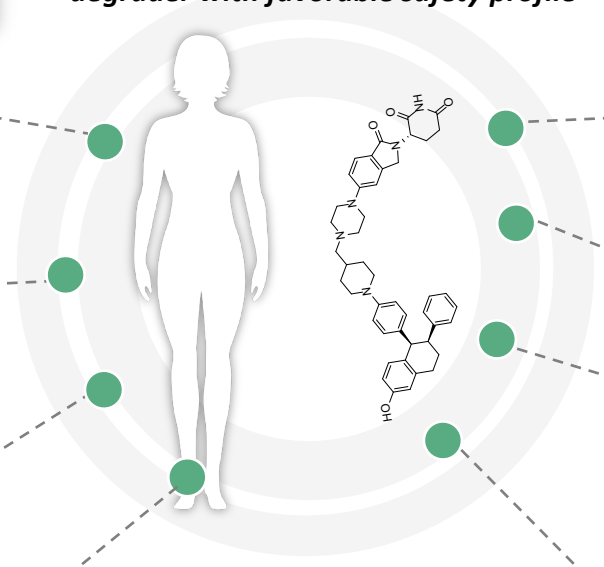
Data as presented 12/10/2021

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



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

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

66%	**Patients expected to have ER-independent disease[†]**
89%	**Of TRAEs were grade 1/2 in severity with no DLTs**

[†] 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

US ER+/HER2- Breast Cancer Treatment Paradigm (>200,000 US patients†)

	Adjuvant (Post-Surgical) Breast Cancer (~160K)	Metastatic Breast Cancer (~50K) First Line	Metastatic Breast Cancer (~50K) Second/Third Line		
Supportive Trials to Define Registration Paths	Initiate in 2022 **Neoadjuvant** *(Randomized vs Control)* ARV-471, or ARV-471 + CDK4/6i	Initiated Dec 2020 **Phase 1b (enabling trial):** Combo: ARV-471 + IBRANCE® (palbociclib)	Initiated 1Q 21 **Phase 2:** VERITAC Expansion: ARV-471	Initiate in 2022 **Phase 1b** Combo: ARV-471 + Next Gen CDKi or other Targeted Therapies††	
Pivotal Trials	Initiate 2022 and beyond **Phase 3 registrational:** Multiple Phase 3 trials: ARV-471 as monotherapy and combo				

† 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

Pfizer ARVINAS

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