

**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 14, 2020

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 14, 2020, Arvinas, Inc. (the “Company”) issued a press release announcing clinical program updates for its PROTAC® protein degraders ARV-471 and ARV-110, including updated data. The Company will present the updates on a conference call and webcast on December 14, 2020. 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.*ARV-471 Clinical Update*

On December 14, 2020, the Company announced updated interim data from the dose escalation portion of its ongoing Phase 1/2 clinical trial of ARV-471 in patients with locally advanced or metastatic ER+/HER2- breast cancer. The dose escalation portion of the Company’s Phase 1/2 clinical trial of ARV-471 is designed to assess the safety, tolerability and pharmacokinetics (“PK”) of ARV-471 and also includes measures of anti-tumor activity as secondary endpoints.

As of the data cut-off date of November 11, 2020, 21 adult patients with locally advanced or metastatic ER+/HER2- breast cancer were dosed with ARV-471 (orally, once-daily) in the Phase 1 clinical trial. 100% of these patients were previously treated with a cyclin-dependent kinase (CDK) 4/6 inhibitor, 71% of patients also received prior fulvestrant, and 23% of patients were also pretreated with investigational selective estrogen receptor degraders (“SERDs”). Overall, patients had a median of five prior therapies.

One patient in the ARV-471 trial had a confirmed partial response, with a 51% reduction in target lesion size as assessed by Response Evaluation Criteria in Solid Tumors (RECIST), a standardized set of rules for response assessment based on tumor shrinkage. In addition to the confirmed partial response, two additional patients had unconfirmed partial responses and one additional patient demonstrated stable disease with greater than 50% target lesion shrinkage. For a clinical benefit rate (“CBR”) evaluation, 12 patients had sufficient follow-up to be included. Five of 12 patients (42%) achieved CBR. CBR is defined to include partial responses, complete responses and stable disease at 6 months. Three of these five patients had previously received fulvestrant, and another was treated with two investigational SERDs.

ARV-471 has also been well tolerated at all dose levels, as of the data cut-off date. The most common treatment-related Grade 1-2 adverse events were nausea (24%), arthralgia (19%), fatigue (19%), and decreased appetite (14%). None of these led to discontinuation or dose reduction of ARV-471. No patients reported treatment-related Grade 3 or 4 adverse events, and no dose-limiting toxicities have been reported. A maximum tolerated dose has not been reached and dose escalation continues.

The plasma exposures of ARV-471 have been dose proportional up to and including 360 mg orally once daily and have substantially exceeded the Company’s predicted thresholds of efficacy based on preclinical studies. The estimated half-life of ARV-471 is 28 hours, supporting a once-daily schedule of administration. Analysis of five paired tumor biopsies at doses up to 120 mg provide compelling proof of mechanism for ARV-471. At those doses, the Company has observed ER degradation up to 90% (average of 62%).

The Company believes that the interim data from its ongoing clinical trial compares favorably to previously reported Phase 1 clinical trial results of other SERDs with respect to tolerability, ER degradation and efficacy signals.

The Company expects to complete the dose escalation portion of the trial and initiate the dose expansion portion of the Phase 1/2 clinical trial of ARV-471 in the first half of 2021 and anticipates sharing interim data from the dose expansion portion in 2022.

The Company also expects to initiate a Phase 1b cohort expansion of ARV-471 in combination with Ibrance® (palbociclib) in December 2020. This trial will evaluate the safety and tolerability of ARV-471 in combination with palbociclib and seek to identify a recommended combination dose.

The Company expects to begin two additional studies of ARV-471 in the second half of 2021: a combination trial of ARV-471 and another targeted therapy in second line and/or third line metastatic breast cancer, and a window of opportunity study in adjuvant breast cancer.

The combined data from these studies will inform the Company's global development strategy and path forward toward the goal for ARV-471 to become the leading endocrine therapy in ER+/HER2- breast cancer.

ARV-110 Clinical Update

On December 14, 2020, the Company also announced updated interim data from the dose escalation portion of its ongoing Phase 1/2 clinical trial of ARV-110 in men with metastatic castrate resistant prostate cancer ("mCRPC"). The dose escalation portion of the Company's Phase 1/2 clinical trial of ARV-110 is designed to assess safety, tolerability and PK of ARV-110 in men with mCRPC who have progressed on standard of care therapies, as well as to identify a recommended Phase 2 dose.

The Company believes that ARV-110 continues to show promising activity in a very late-line population, with prostate specific antigen ("PSA") reductions equal to or greater than 50% (a "PSA50 response") observed at doses greater than 280 mg, the last cohort for which the Company had previously disclosed data.

ARV-110 exposures have risen dose proportionally, and at 420 mg oral daily dosing, exposures in nearly all patients have surpassed a threshold the Company associated with tumor responses with ARV-110 in enzalutamide-resistant preclinical models of prostate cancer.

In the dose escalation portion of the trial, 76% of patients had been treated with prior chemotherapy, and 82% previously received both abiraterone and enzalutamide. Patients had a median of five prior lines of therapy. Multiple lines of therapy in nonmetastatic and metastatic castrate resistant prostate cancer are associated with a decreased responsiveness to androgen receptor ("AR")-directed therapies and an increase in tumor heterogeneity, including in genetic mutations, which reduce the tumor's dependence on the AR signaling axis. Genetic profiling of trial patient tumors showed genetic variability, with 84% of patients in the trial having non-AR gene mutations. As such, these patients would not be expected to respond to AR-directed agents such as ARV-110. In addition, the Company found that rates of specific AR mutations have been found to be higher than the Company anticipated based on previously published studies of men with mCRPC.

The Company has identified a molecularly defined, late-line population with a particularly strong response to ARV-110. Two of five patients (40%) with T878 or H875 mutations in AR had a PSA50 response, including one patient with a tumor size reduction of 80%.

In addition, two of 15 patients (13%) with wild-type AR also had a PSA50 response, representing activity in a broader patient population. In the full group of patients with exposures above the minimum threshold the Company predicted to be efficacious by preclinical studies, four of 28 (14%) had PSA reductions greater than 50%. The Company believes that this PSA50 response rate is substantially higher than would be expected from approved AR-directed therapies in such late line patients. Specifically, PSA50 response rates from standard-of-care AR-directed therapies generally decrease to 8%—15% in mCRPC patients with fewer prior therapies.

The dual signals of ARV-110 activity in a molecularly defined population (T878/H875) and in wild-type patients support the Company's two-pronged strategy for ARV-110 development and suggest a robust opportunity to address unmet need in patients with mCRPC.

In October 2020, the Company initiated the ARDENT Phase 2 expansion portion of the trial comprising patient subgroups. T878/H875 patients will be enriched in a subgroup to ensure sufficient patient numbers in an effort to confirm the potential for accelerated regulatory approval for ARV-110 in this population. A separate subgroup will enrich for less-pretreated patients (i.e., no prior chemotherapy and with only one previous second-generation AR-directed therapy, such as enzalutamide or abiraterone), to ensure sufficient numbers of patients whose tumors are expected to be more AR-dependent, less genetically complex, and potentially more responsive to ARV-110.

The Company expects to provide complete data from the dose escalation portion of the Phase 1/2 trial in 2021 and provide interim data from the ARDENT Phase 2 expansion portion of the Phase 1/2 trial in the second half of 2021, with full data following in 2022. In 2021, the Company also expects to begin at least one Phase 1b combination trial with a standard-of-care prostate cancer therapy and provide data in 2022.

Other Anticipated Milestones

In addition, the Company expects to file an investigational new drug ("IND") application for ARV-766, an AR degrader with a different profile from ARV-110, and initiate a Phase 1 trial in the first half of 2021, and if ARV-766 progresses as planned, the Company expects to provide data from the Phase 1 trial and transition to Phase 2 in 2022. The Company anticipates filing IND applications for its B-cell lymphoma 6 protein (BCL6) and tau programs as well as a further undisclosed oncology program in 2022.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

| <u>Exhibit No.</u> | <u>Description</u> |
|--------------------|---|
| 99.1 | Press Release, dated December 14, 2020 |
| 99.2 | Company Presentation, dated December 14, 2020 |
| 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 Exhibits 99.1 and 99.2 hereto, contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the development and regulatory status of the Company's product candidates, such as statements with respect to the Company's lead product candidates, ARV-110, ARV-471 and ARV-766 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, and the Company's development programs that may lead to the Company's development of additional product candidates, the potential utility of the Company's technology and 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 will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-471, complete its clinical trials for its product candidates, and receive results from its clinical trials on the Company's expected timelines, or at all, whether the Company's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements, the Company's expected timeline 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 14, 2020

ARVINAS, INC.

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



Arvinas Releases Interim Clinical Data Further Demonstrating the Powerful Potential of PROTAC® Protein Degraders ARV-471 and ARV-110

- *ARV-471 demonstrates evidence of anti-tumor activity, and potential for best-in-class safety, and estrogen receptor (ER) degradation profile and robust efficacy signals in a heavily pretreated patient population –*
- *Initiation of a combination trial of ARV-471 and Ibrance® (palbociclib) expected this month; three additional trials of ARV-471 in patients with breast cancer expected to begin in 2021 –*
- *ARV-110 continues to demonstrate a favorable safety profile, tolerability, and anti-tumor activity in a heavily pretreated patient population as Phase 1 dose escalation continues in parallel with the ARDENT Phase 2 expansion –*
- *The ARDENT Phase 2 expansion trial for ARV-110 is designed to evaluate the potential for accelerated approval in a molecularly defined population and broader approval in earlier mCRPC –*

NEW HAVEN, Conn., December 14, 2020 – Arvinas, Inc. (Nasdaq: ARVN), a clinical-stage biopharmaceutical company creating a new class of drugs based on targeted protein degradation using its PROTAC® Discovery Engine, today announced clinical program updates for its PROTAC® protein degraders ARV-471 and ARV-110. For ARV-471, interim Phase 1 data show potential for best-in-class safety and tolerability, estrogen receptor (ER) degradation superior to that previously reported for the current standard of care agent (fulvestrant), and robust efficacy signals in heavily pretreated patients with locally advanced or metastatic ER positive / HER2 negative (ER+/HER2-) breast cancer. The efficacy signals include one Response Evaluation Criteria in Solid Tumors (RECIST) confirmed partial response (PR), two additional patients with unconfirmed PRs, and a clinical benefit rate (CBR) of 42%. For ARV-110, the ongoing dose escalation portion of the Phase 1/2 trial in men with metastatic castration-resistant prostate cancer (mCRPC) has provided additional evidence of anti-tumor activity and patient benefit, including a prostate specific antigen reduction of more than 50% (PSA50) rate of 40% in a molecularly defined patient population. Arvinas has initiated a Phase 2 dose expansion to explore a two-pronged development strategy, including the potential for accelerated approval in molecularly defined, late-line patients, and broader development in less-heavily pretreated mCRPC patients with fewer androgen receptor (AR)-independent mechanisms of tumor resistance.

Both ARV-471 and ARV-110 have been well tolerated, neither has reached a maximum tolerated dose, and the Phase 1 dose escalation trials for both programs continue. A Phase 1b combination trial of ARV-471 and Ibrance® (palbociclib) is expected to begin in December 2020, and a Phase 2 expansion cohort for ARV-471 is scheduled to begin in the first half of 2021.

“After initiating our clinical efforts just last year, we now have what we believe are clear signals of efficacy in both of our clinical-stage development programs,” said John Houston, Ph.D., Chief Executive Officer at Arvinas. “The clinical benefits we’ve seen in both patient populations, including tumor shrinkage and low incidence of adverse effects, are compelling and reinforce our belief that our PROTAC protein degraders could dramatically change the lives of patients who have few or no therapeutic options.”

“Based on data to date, we believe ARV-471 is the most promising ER-targeting therapy in the clinic, showing early signs of efficacy, a favorable tolerability profile, and better ER degradation than that previously reported for fulvestrant, the current standard of care,” said Ron Peck, Ph.D., Chief Medical Officer at Arvinas. “It is exciting to see that ARV-110 continues to be active and well tolerated in what we believe is the most heavily pretreated patient population that has ever been studied with an AR-directed therapy. Our recently initiated ARDENT Phase 2 cohort expansion is specifically designed to investigate the potential of a precision medicine approach in molecularly defined, late-line patients with few available treatment options, while also fully characterizing the safety and activity of ARV-110 in earlier line patients irrespective of molecular profile, setting ARV-110 on a potential two-pronged registrational path.”

ARV-471 Clinical Update

As of the data cut-off date of November 11, 2020, 21 adult patients with locally advanced or metastatic ER+/HER2- breast cancer completed at least one treatment cycle with ARV-471 (orally, once-daily) in the Phase 1 clinical trial. 100% of these patients were previously treated with a cyclin-dependent kinase (CDK) 4/6 inhibitor, 71% of patients received prior fulvestrant, and 23% of patients were pretreated with investigational selective estrogen receptor degraders (SERDs). Overall, patients had a median of five prior therapies.

In metastatic breast cancer, prior treatment with CDK4/6 inhibitors predicts high tumor ER-independence, rendering ER-targeting therapies ineffective. However, one patient in the ARV-471 trial had a confirmed PR with a 51% reduction in target lesion size as assessed by RECIST. Two additional patients had unconfirmed PRs and one additional patient demonstrated stable disease with >50% target lesion shrinkage. For evaluation of CBR, 12 patients had sufficient follow-up to be included. Five of 12 patients (42%) achieved CBR (CBR defined as PRs + complete responses + stable disease at 6 months). Three of these five patients had previously received fulvestrant, and another was treated with two investigational SERDs.

ARV-471 has been well tolerated at all dose levels, as of the data cut-off date. The most common treatment-related Grade 1-2 adverse events were nausea (24%), arthralgia (19%), fatigue (19%), and decreased appetite (14%). None of these led to discontinuation or dose reduction of ARV-471. No patients reported treatment-related Grade 3 or 4 adverse events, and no dose-limiting toxicities (DLTs) have been reported. A maximum tolerated dose (MTD) has not been reached and dose escalation continues.

The plasma exposures of ARV-471 have been dose proportional up to and including 360 mg orally once daily and have substantially exceeded Arvinas' predicted thresholds of efficacy based on preclinical studies. The estimated half-life of ARV-471 is 28 hours, supporting a once-daily schedule of administration. Analysis of five paired tumor biopsies at doses up to 120 mg provide compelling proof of mechanism for ARV-471, which has demonstrated ER degradation up to 90% (average of 62%) at those doses, while dose escalation continues.

The combined profile of ARV-471, including efficacy signals in a highly refractory population, excellent tolerability profile, and high levels of ER degradation, support a potential best-in-class ER-targeting therapy.

A Phase 2 dose expansion of ARV-471 is expected to begin in the first half of 2021. Arvinas also expects to initiate a Phase 1b cohort expansion of ARV-471 in combination with Ibrance® (palbociclib) in December 2020. This trial will evaluate the safety and tolerability of ARV-471 in combination with palbociclib and seek to identify a recommended combination dose. Arvinas expects to begin two additional studies of ARV-471 in the second half of 2021: a combination trial of ARV-471 and another targeted therapy in 2L/3L metastatic breast cancer, and a window of opportunity study in adjuvant breast cancer. The combined data from these studies will inform Arvinas' global development strategy and path forward toward the goal for ARV-471 to become the leading endocrine therapy in ER+/HER2- breast cancer.

ARV-110 Clinical Update

In the Phase 1 clinical trial in men with mCRPC, ARV-110 continues to show promising activity in a very late-line population, with PSA reductions >50% observed at doses greater than 280 mg, the last reported cohort.

In the dose escalation, ARV-110 exposures have risen dose proportionally, and at 420 mg oral daily dosing, exposures in nearly all patients have surpassed a threshold associated with tumor responses with ARV-110 in enzalutamide-resistant preclinical models of prostate cancer. Increases in exposure are associated with increased frequency of PSA reductions.

In the Phase 1 dose escalation trial, 76% of patients had been treated with prior chemotherapy, and 82% previously received both abiraterone and enzalutamide. Patients had a median of five prior lines of therapy. Multiple lines of therapy in nonmetastatic and metastatic castrate resistant prostate cancer are associated with a decreased responsiveness to AR-directed therapies and an increase in tumor heterogeneity, including in genetic mutations, which reduce the tumor's dependence on the AR signaling axis. Genetic profiling of trial patient tumors has led to significant learnings about the ARV-110 Phase 1 patient population, especially regarding genetic variability. 84% of patients in the trial have non-AR gene mutations, and as such, they would not be expected to respond. In addition, rates of specific AR mutations have been found to be higher than reported in publications that have characterized prevalence of AR mutations in men with mCRPC.

Despite the highly heterogeneous nature of the Phase 1 patient population, Arvinas has identified a molecularly defined, late-line population with a particularly strong response to ARV-110. Two of five patients (40%) with T878 or H875 mutations in AR had PSA reductions >50%, including one patient with a confirmed PR by RECIST and tumor size reduction of 80%.

In addition, two of 15 patients (13%) with wild-type AR also had PSA reductions >50%, representing activity in a broader patient population. In the full group of patients with exposures above the minimum threshold Arvinas predicted to be efficacious by preclinical studies, four of 28 (14%) had PSA reductions >50%. These PSA50 rates are higher than would be expected from approved AR-directed therapies in such late-line patients. Specifically, PSA50 response rates from standard-of-care AR-directed therapies generally decrease to 8-15% in mCRPC patients with fewer prior therapies than the patients in the ARV-110 trial.

The dual signals of ARV-110 activity in a molecularly defined population (T878/H875) and in wild-type patients supports Arvinas' two-pronged strategy for ARV-110 development and suggest a robust opportunity to address unmet need in patients with mCRPC.

A daily dose of 420 mg was selected as a Phase 2 expansion dose based on pharmacokinetics, safety profile, and the activity signals in both T878/H875 and wild-type patients. In the ARDENT Phase 2 expansion, T878/H875 patients will be enriched in a subgroup to ensure sufficient patient numbers to support the potential for accelerated approval in this population. A separate subgroup will enrich for less-pretreated patients (i.e., no prior chemotherapy and with only one previous second-generation AR-directed therapy, such as enzalutamide or abiraterone), to ensure sufficient numbers of patients whose tumors are expected to be more AR-dependent, less genetically complex, and more responsive to ARV-110.

The ARDENT Phase 2 expansion (N = ~100) began enrolling in October 2020, and Arvinas expects to provide interim data from the trial in the second half of 2021. In 2021, Arvinas also expects to begin at least one Phase 1b combination trial with a standard-of-care prostate cancer therapy and provide complete data from the Phase 1 dose escalation.

Anticipated 2020/2021 Milestones

ARV-471

- Initiation of a Phase 1b trial in combination with Ibrance® (palbociclib) (December 2020)
- Initiation of a Phase 2 dose expansion (1H21)
- Completion of the Phase 1 dose escalation (1H21)
- Safety data from the Phase 1b trial in combination with Ibrance® (palbociclib) (2H21)
- Initiation of a window of opportunity study in adjuvant breast cancer (2H21)
- Initiation of a combination trial of ARV-471 and another targeted therapy in 2L/3L metastatic breast cancer (2H21)

ARV-110

- Completion of the Phase 1 dose escalation (1H21)
- Interim data from the ARDENT Phase 2 dose expansion at 420 mg (2H21)
- Initiation of combination trial(s) with standards-of-care (2021)

Other clinical milestones

- First-in-human start for ARV-766, an AR degrader with a different profile from ARV-110 (1H21)

Arvinas Webcast Investor Meeting

Arvinas will host a conference call and webcast at 8:00 AM ET on Monday, December 14, 2020 to discuss these data. 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 9681734. A live webcast presentation will be available [here](#) or on the Company's 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-110

ARV-110 is an investigational orally bioavailable PROTAC® protein degrader designed to selectively target and degrade the androgen receptor (AR). ARV-110 is being developed as a potential treatment for men with metastatic castration-resistant prostate cancer.

ARV-110 has demonstrated activity in preclinical models of AR mutation or overexpression, both common mechanisms of resistance to currently available AR-targeted therapies.

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.

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 two clinical-stage programs: ARV-110 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.

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 our product candidates ARV-110, ARV-471, ARV-766, and other candidates in our pipeline, the conduct of and plans for our ongoing Phase 1/2 clinical trials for ARV-110 and ARV-471, our planned Phase 1b combination trial for ARV-471, our planned Phase 1b combination trials for ARV-110, the plans for presentation of data from our Phase 1/2 clinical trials for ARV-110 and ARV-471, the planned first-in-human start for ARV-766, and the potential advantages and therapeutic potential 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.

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: whether we will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-471 and Phase 1b combination trials for ARV-110 or ARV-471, complete our clinical trials for our other product candidates, and receive results from our clinical trials on our expected timelines, or at all, and other important factors discussed in the “Risk Factors” sections contained in our quarterly and annual reports on file with the 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 press release.

Contacts for Arvinas**Investors**

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Media

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Clinical Program Update:
ARV-471 & ARV-110



14 December 2020

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 our product candidates, such as statements with respect to our lead product candidates, ARV-110, ARV-471 and ARV-766 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, and our discovery programs that may lead to our development of additional product candidates, the potential utility of our technology and therapeutic potential of our product candidates, and 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.

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: whether we will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-471, complete other clinical trials for our product candidates, and receive results from our clinical trials on our expected timelines, or at all, whether our cash resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, discussed in the “Risk Factors” section of our quarterly and annual reports on file with the Securities and Exchange Commission. The forward-looking statements contained in this presentation reflect our current views as of the date of this presentation with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

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.



• • • • •
Introduction

Agenda

| Topic | Participant |
|-------------------------------------|---|
| Introduction | John G. Houston, Ph.D. <i>President and Chief Executive Officer</i> |
| ARV-471 Clinical Data Update | Ron Peck, M.D. <i>Chief Medical Officer</i> |
| ARV-110 Clinical Data Update | Ian Taylor, Ph.D. <i>Chief Scientific Officer</i> |
| Conclusion | John G. Houston, Ph.D. <i>President and Chief Executive Officer</i> |

 Q&A

ARV-471 and ARV-110: Opportunities to benefit patients in large areas of unmet need

ARV-471

Estrogen receptor-degrading
PROTAC®

Breast Cancer



Potential best profile of any ER-targeting therapy:

- Tolerability
- ER degradation
- Clinical benefit



Potential future endocrine therapy of choice in both adjuvant and metastatic settings



Phase 1 ongoing in a highly refractory patient population



>200k patients[†] per year with high unmet need

ARV-110

Androgen receptor-degrading
PROTAC®

Prostate Cancer



AR degradation and clear signals of efficacy observed in late-line mCRPC



Initiated Phase 2 ARDENT trial; two potential paths to registration: 3L molecularly defined, and broader 1L/2L



Extensive molecular profiling of tumors to understand drivers of resistance



>250k patients[†] per year with high unmet need

[†] US incidence data from SEER database
AR, androgen receptor; ER, estrogen receptor



ARV-471 Clinical Data Update

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



Potential endocrine therapy for ER+/HER2- breast cancer; >200k patients per year in the US alone[†]



Outstanding tolerability profile observed, with potential for adjuvant and metastatic breast cancer settings



Better ER degradation than fulvestrant and clinical-stage SERDs^{††}



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

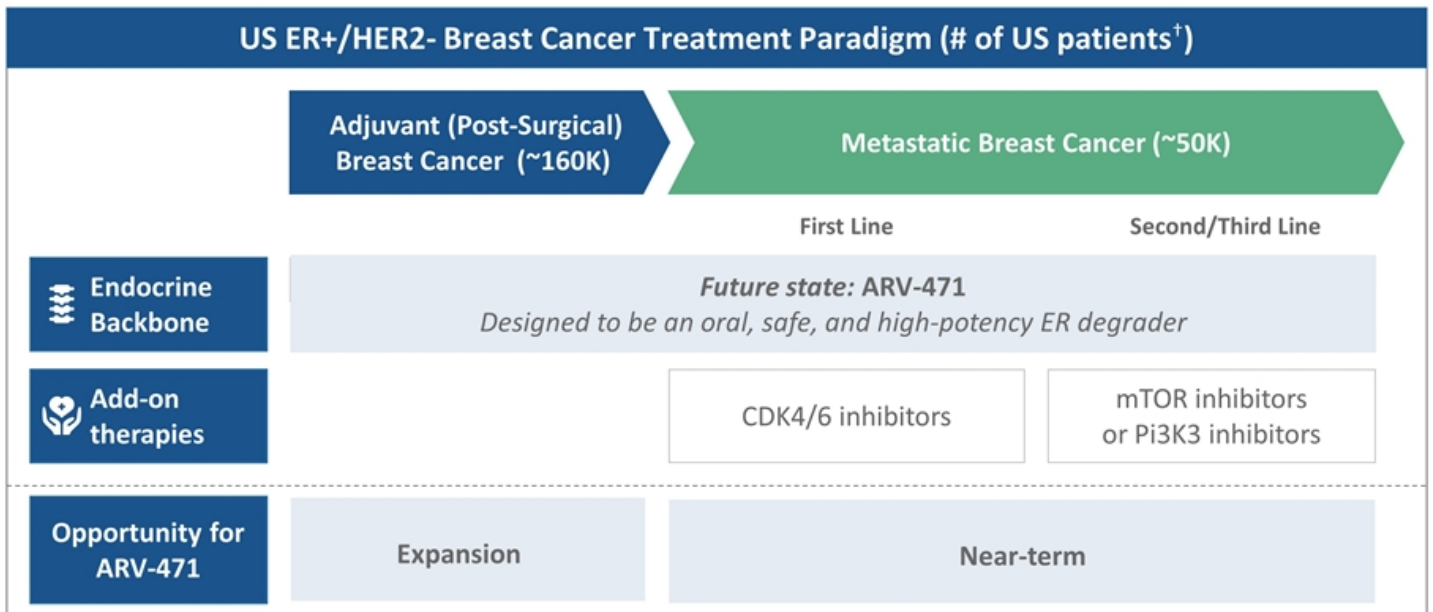
- One confirmed partial response, and two unconfirmed partial responses
- 42% clinical benefit rate



Phase 1 dose escalation continues

[†] US incidence data from SEER database. ^{††} As compared to previously reported data

We are developing ARV-471 to be the endocrine backbone of choice for ER+/HER2- breast cancer treatment



[†] US incidence from SEER Database
 CDK: cyclin-dependent kinases, PI3K: phosphoinositide 3-kinase; mTOR: mammalian target of rapamycin

ARV-471 First-in-Human study is a traditional “3+3” dose escalation study

Design

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

Endpoints

Primary:

- Maximum tolerated dose and recommended Phase 2 dose

Key Secondary:

- Safety and tolerability
- 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

All Phase 1 patients were post- CDK4/6 inhibitor treatment; high rate of ER-independent resistance

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

- After CDK4/6 inhibitor treatment, ~**66%** of breast cancers have ER-independent mechanisms of resistance[†]
- Outcomes are poor following CDK4/6 inhibitor therapy, e.g., for fulvestrant:
 - Median PFS = 1.8 months^{††}
 - CBR estimated $\leq 20\%$ ^{††}

[†] Wander 2020; ^{††} Juric SABCS 2018 Subset Analysis of SOLAR1.
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 = 21)

| Patient Characteristics | Parameter | N (%) | |
|---|-----------------------------|-------|-------|
| Median age (years) | | 64 | |
| ECOG performance status | 0 | 10 | (48) |
| | 1 | 11 | (52) |
| Prior visceral disease (liver, lung) | | 10 | (48) |
| Median prior lines of therapy total (range 1-9) | | 5 | (NA) |
| Median number of prior endocrine regimens | | 3 | (NA) |
| Type of prior therapies in advanced settings | | | |
| | <i>CDK 4/6 inhibitor</i> | 21 | (100) |
| | <i>Fulvestrant</i> | 15 | (71) |
| | <i>Chemotherapy</i> | 8 | (38) |
| | <i>Investigational SERD</i> | 5 | (24) |
| | <i>Other therapies</i> | 14 | (67) |

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

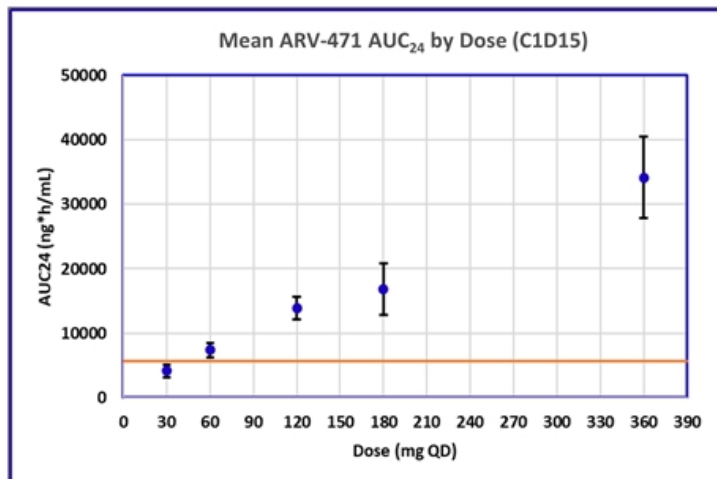
ARV-471 is well tolerated at all dose levels; no Grade 3 adverse events

| TRAE in ≥ 10% of Patients | 30 mg (N=3) | | 60 mg (N=3) | | 120 mg (N=7) | | 180 mg (N=5) | | 360 mg (N=3) | | Total (N=21) |
|---------------------------------|-------------|------|-------------|------|--------------|------|--------------|------|--------------|------|--------------|
| | Gr 1 | Gr 2 | Gr 1 | Gr 2 | Gr 1 | Gr 2 | Gr 1 | Gr 2 | Gr 1 | Gr 2 | N (%) |
| Any | - | - | 2 | - | 4 | - | 2 | 1 | 2 | - | 11 (52) |
| Nausea | - | - | 2 | - | 1 | - | - | 1 | 1 | - | 5 (24) |
| Arthralgia | - | - | 1 | - | 2 | - | 1 | - | - | - | 4 (19) |
| Fatigue | - | - | 1 | - | - | - | 1 | - | 2 | - | 4 (19) |
| Decreased appetite | - | - | - | - | 1 | - | - | - | 2 | - | 3 (14) |

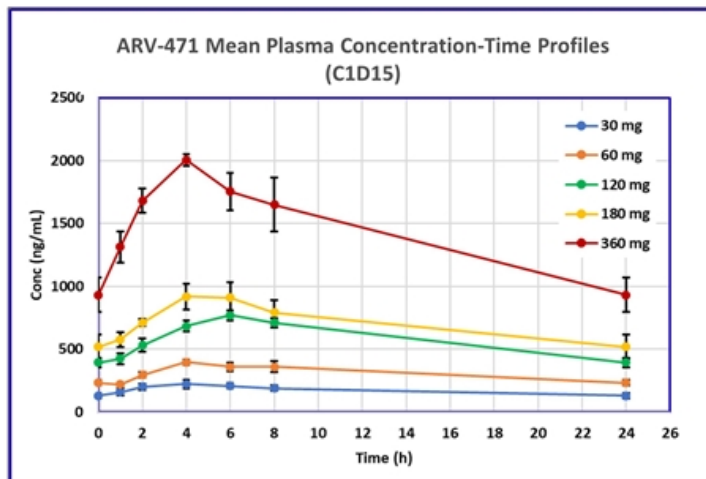
Adverse events were primarily Grade 1; No dose limiting toxicities

Data cut-off: November 11, 2020
TRAE, Treatment related adverse event

ARV-471's PK is dose proportional; exposures far exceed preclinical efficacy thresholds



The orange line represents the efficacious exposure for tumor regression in preclinical models †

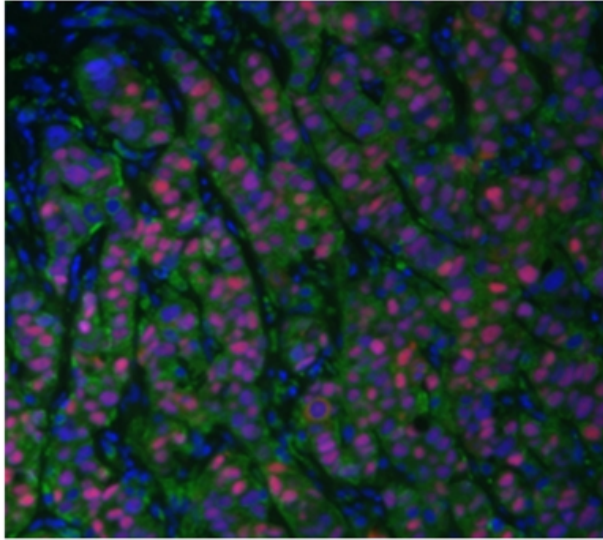


Effective half-life ($T_{1/2}$) \approx 28 hours

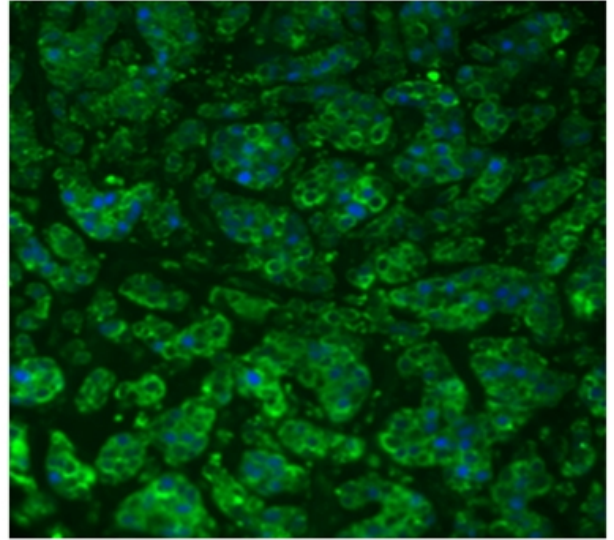
† AUC₂₄=5717 ng·h/mL for preclinical effective exposure in preclinical model (mice@30mpk). AUC, area under the curve; SE, standard error

ER degradation observed in patient tumor biopsies

Red: Estrogen receptor
Blue: Nuclei
Green: Tumor (cytokeratin)



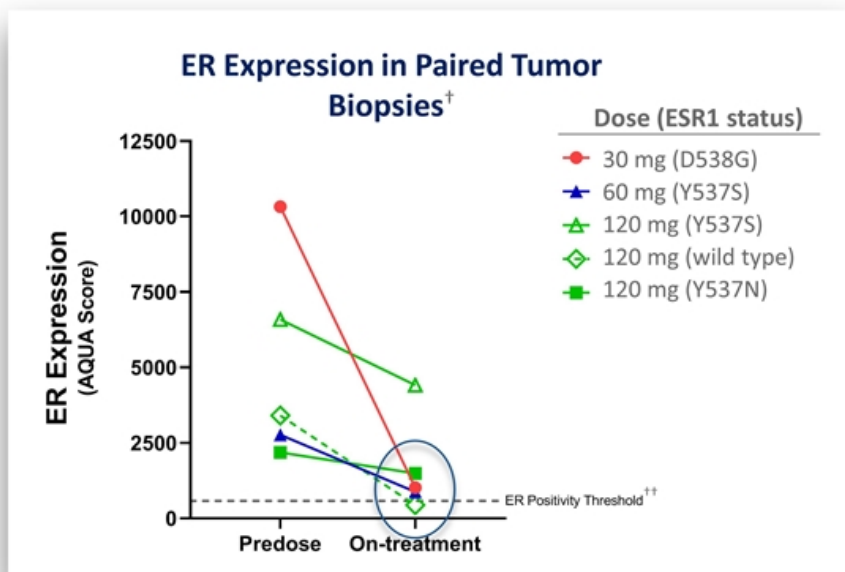
Baseline



After treatment with 60 mg ARV-471

Method: ER immunoreactivity analyzed by quantitative immunofluorescence (QIF) using the automated quantitative analysis (AQUA) method

ARV-471 degraded ER up to 90% through the 120 mg dose level



Degradation up to **90%**;
average of **62%**



Degradation **superior to fulvestrant** (previously reported: 40-50%)^{†††}



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

[†] ER immunoreactivity analyzed by quantitative immunofluorescence (QIF) using the automated quantitative analysis (AQUA) method. ^{††} 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).
ESR1, Estrogen Receptor 1

Confirmed RECIST Partial Response (cPR) in a patient with extensive prior therapy and an ESR1 mutation at 120 mg

Extensive prior therapy

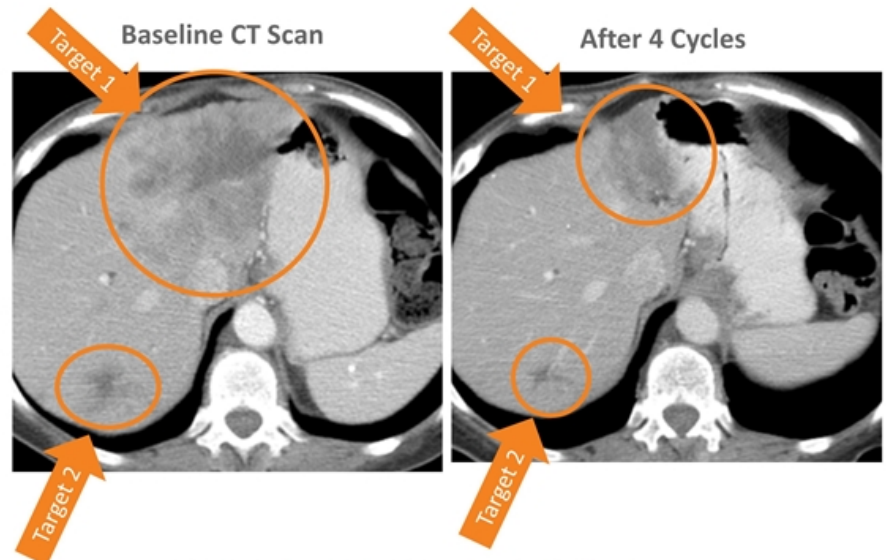
- CDK4/6 inhibitor: Palbociclib
- Endocrine therapies: 6 Agents
 - Aromatase inhibitors x 3
 - Tamoxifen
 - Investigational SERDs X 2[†]
- Other targeted agents: Everolimus
- Chemotherapy: 2 Regimens
 - 1 neoadjuvant + 1 metastatic

ESR1 mutations

- D538G

[†] Includes one selective ER α covalent antagonist.

CDK: cyclin-dependent kinases; SERD, selective estrogen receptor degrader



**51% reduction in target lesions
(RECIST partial response)**

Regression in chest wall lesions in a patient with extensive prior therapy and multiple ESR1 mutations at 180 mg

Extensive Prior therapy

- CDK4/6 inhibitor:
 - Palbociclib, Abemaciclib
- Endocrine therapies: 3 Agents
 - Aromatase inhibitors x 2
 - Fulvestrant
- Other targeted agents: Everolimus
- Chemotherapy: 4 Regimens
 - 1 neoadjuvant + 3 metastatic

ESR1 mutations

- D538G, E380Q, V422del, L536P

Baseline
(Associated Bleeding)

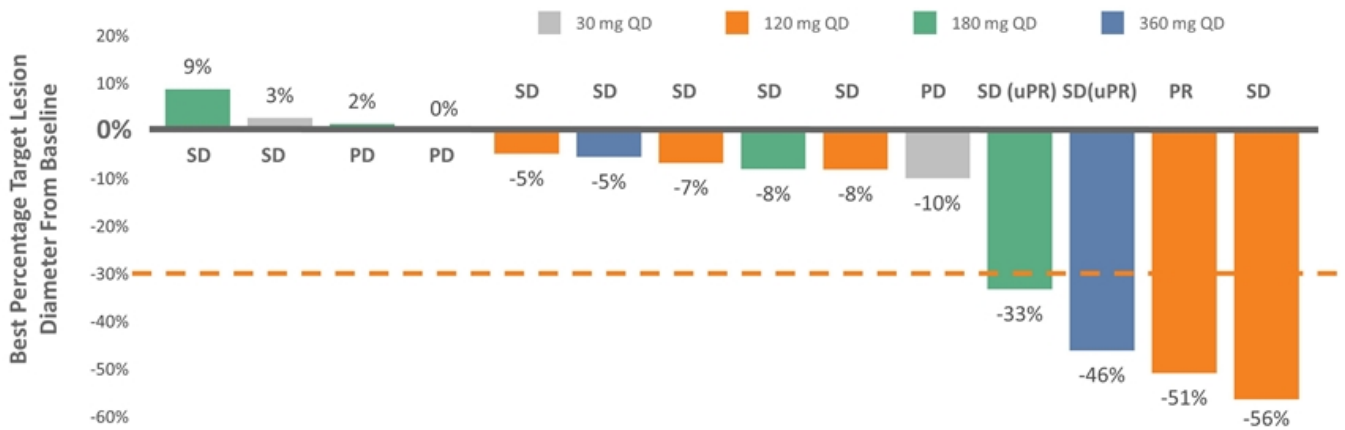


After 4 Cycles
(No Bleeding)



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

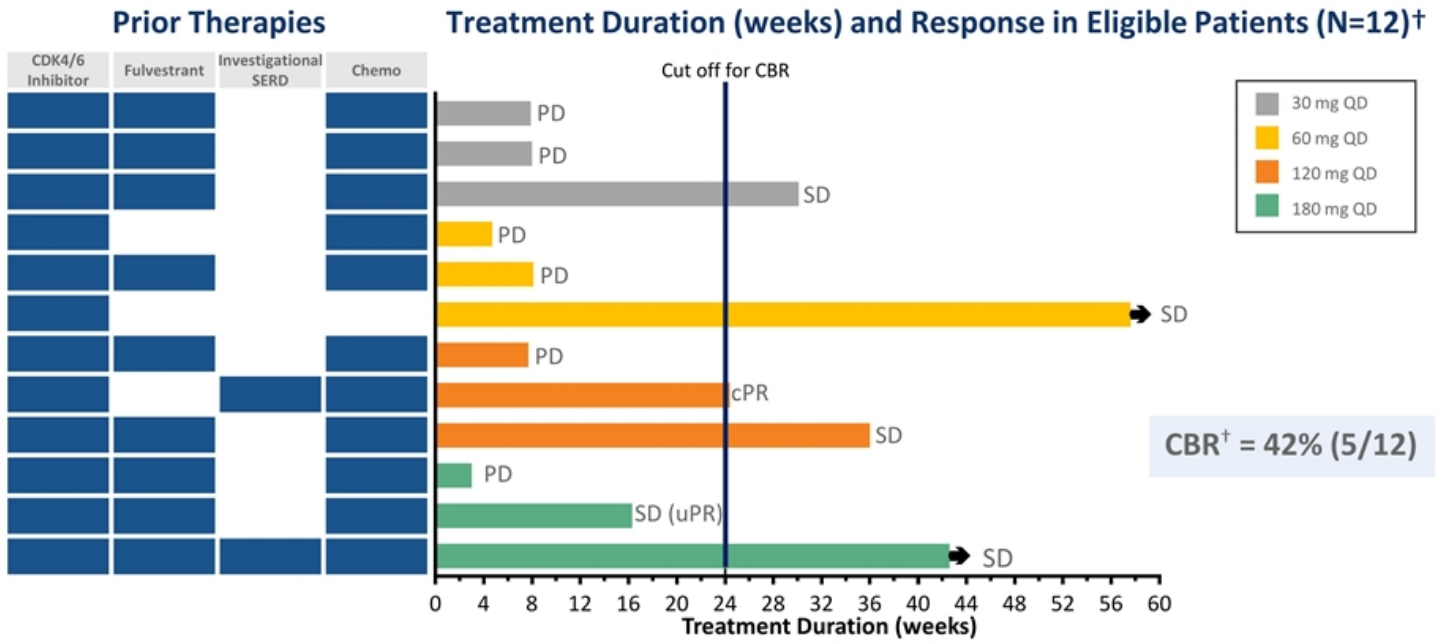
Antitumor Activity in Eligible Patients (N=14)[†]



| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|----------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|
| CDK4/6 inhibitor | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| Fulvestrant | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| Investigational SERD | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| Chemotherapy | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |

[†] 7 patients out of 21 are excluded from graph due to no measurable disease at baseline (n=4), discontinuation of treatment without post-treatment target lesion measurements (n=2), and discontinuation after 2 doses due to non-compliance (n=1).

ARV-471 achieves a high clinical benefit rate (42%) in this heavily pretreated population through the 180 mg dose level



† Excludes 8 patients enrolled < 24 weeks prior to the data cut-off of November 28, 2020 and 1 patient who received 2 doses of ARV-471 and discontinued due to non-compliance, †† CBR defined as SD persisting ≥ 24 weeks, or a best response of confirmed CR or PR.

Comparison of ARV-471 profile with Phase 1 data for preclinical SERDs

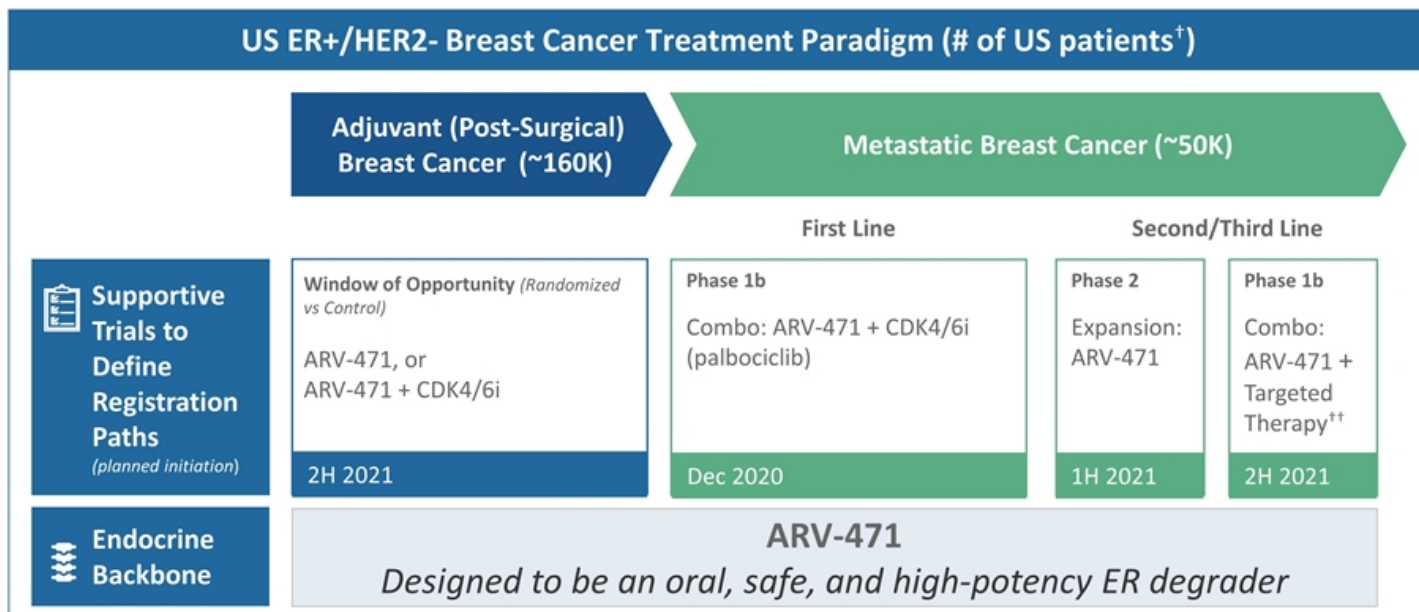
Phase 1 Data Comparison

| Drug Candidate | CDK4/6i Pretreated Patients (0 – 100%) | Clinical Benefit Rate | Mean ER Degradation in Patient Tumors | Select TRAEs (> 5% of Patients) | | | | |
|----------------------|--|-----------------------|---------------------------------------|---------------------------------|--------|----------|-------------|--------------------|
| | | | | Gastrointestinal (GI) AEs | | | Other AEs | |
| | | | | Diarrhea | Nausea | Vomiting | Bradycardia | Visual disturbance |
| ARV-471 | 100% | 42% | 62% <i>Interim</i> | | ● | ● | | |
| H3B-6545 | 87% | 34% | Not reported | ● | ● | ● | ● | |
| ZN-C5 | 87% | 40% | Not reported | ● | ● | ● | | |
| Rintodestrant | 70% | 30% | 28% | ● | ● | ● | | |
| SAR43989 | 63% | 34% | Not reported | ● | ● | ● | | |
| AZD9833 [†] | 62% | 35% | <50% ^{††} | | ● | ● | ● | ● |
| GDC9545 | 59% | 41% | <50% ^{††} | ● | ● | | ● | |

ARV-471 has the potential to be a best-in-class ER-directed therapy

Source: H3B-6545 SABCS 2020 Poster, ZN-C5 SABCS 2020 Poster, Rintodestrant SABCS 2020, SAR439859 SABCS 2020 Poster, AZD9833 SABCS 2020 and ASCO 2020 Posters, GDC-9545 SABCS 2019 Poster. This comparison utilizes data from different Phase 1 trials and presents a non-head-to-head summary comparison.
[†] Reported AEs are from ASCO 2020 Poster; ^{††} Visual estimation based on ER degradation data provided by each company.

We 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 alpelisib

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 fulvestrant and SERDs[†]
- Strong efficacy signal in a predominantly ER-independent population
- Well tolerated



Clear Development Path

- Potential for 2L/3L approval as monotherapy or in combination
- Planned combinations with CDK4/6 inhibitors 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

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



ARV-110 Clinical Data Update

ARV-110: 40% PSA50 in a molecularly defined subgroup, and additional opportunity in early-line mCRPC



Potential best-in-class therapy for prostate cancer, representing >250k patients per year in the US alone†



Well tolerated, escalating through the current dose of 700 mg



Continued patient benefit: 40% PSA50 in T878/H875 patients, and additional activity in wild-type tumors



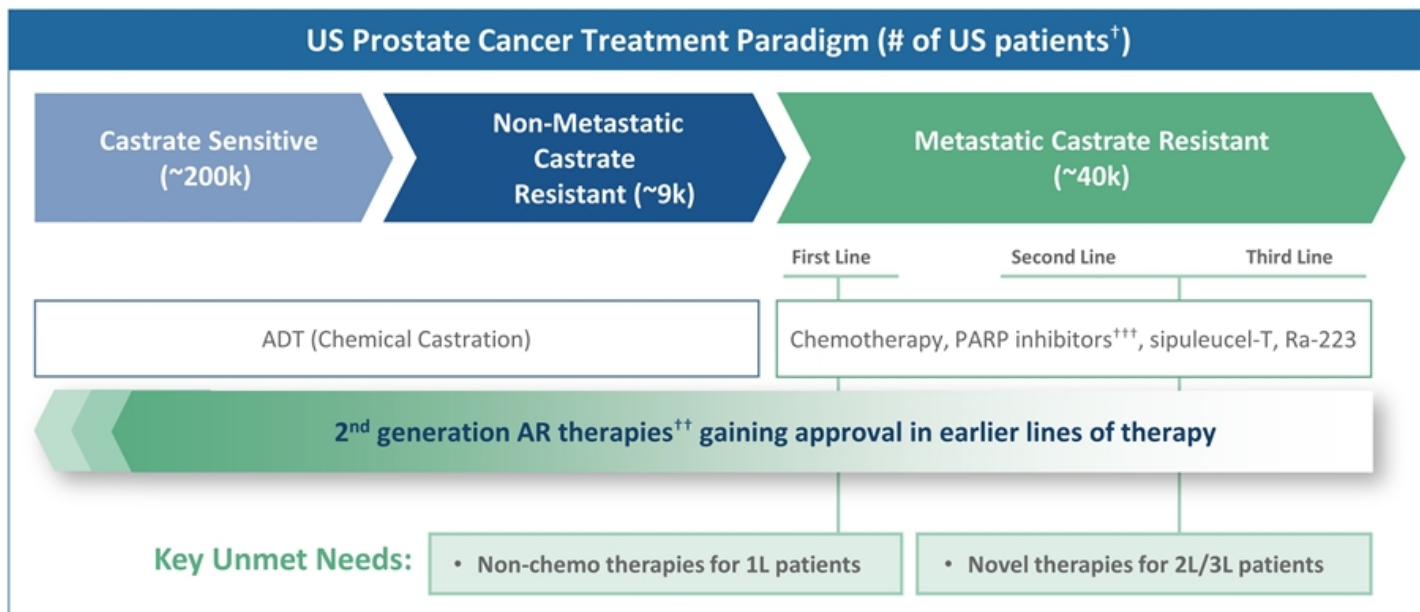
Building substantial learnings about our late-line patient population into our development strategy



The ongoing Phase 2 ARDENT trial is designed to confirm the potential for accelerated approval in a molecularly defined population, while also exploring the potential for approval in early-line mCRPC

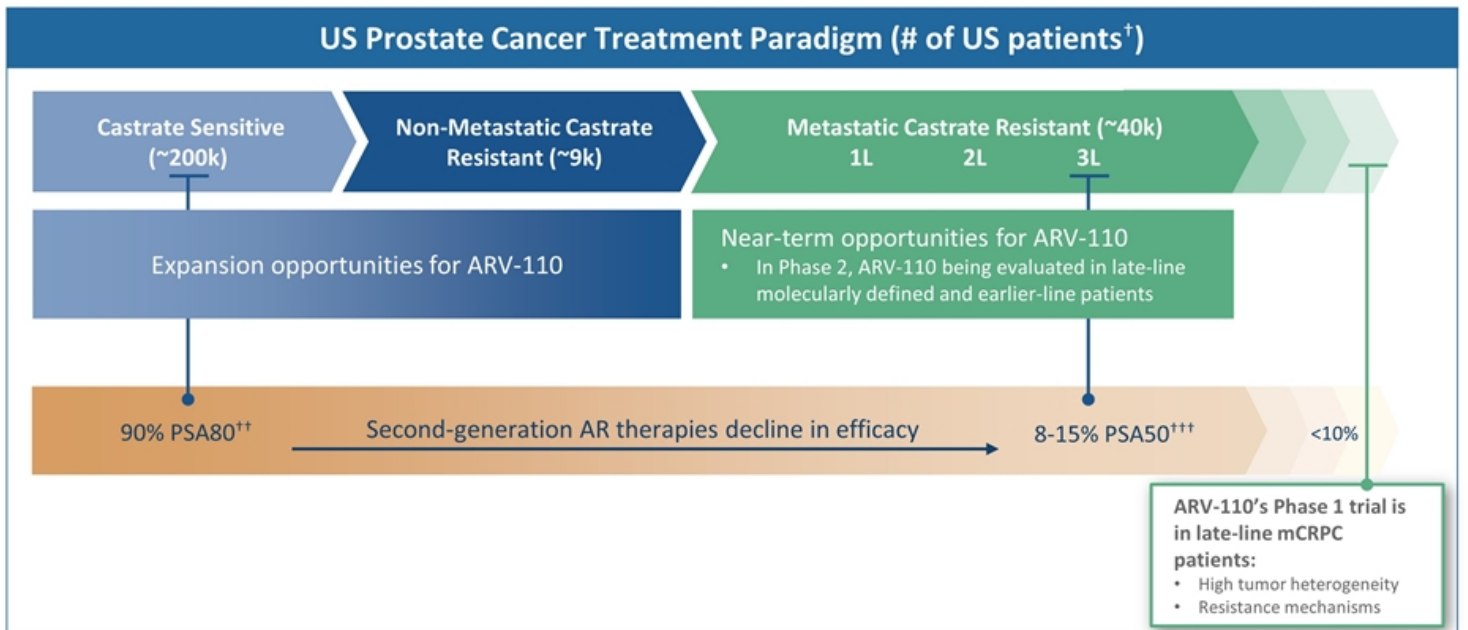
† US incidence data from SEER database

Migration of second-generation AR therapies to earlier settings has created substantial unmet need for new treatments in mCRPC



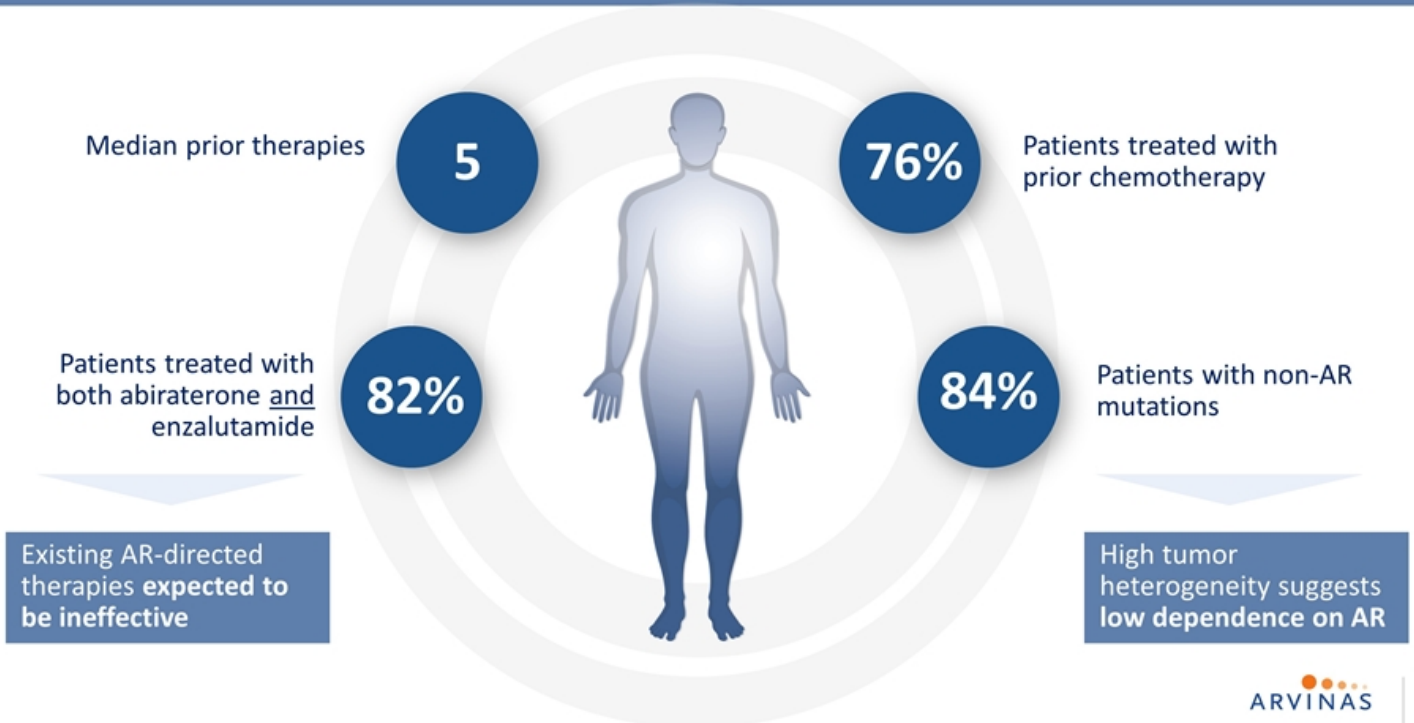
[†] SEER database, ^{††} Includes enzalutamide, abiraterone, darolutamide, apalutamide, ^{†††} Approved for BRCA mutant/DNA Deficient Repair (DDR) patients progressed on 2nd gen AR-directed therapies.
ADT, androgen deprivation therapy; mCRPC, metastatic castrate resistant prostate cancer

Our strategy is to develop ARV-110 across treatment settings of prostate cancer



[†] SEER database; ^{††} Tombal, Lancet Oncology 2014; ^{†††} de Wit R, N Engl J Med. 2019; Hussain, ESMO 2019.

ARV-110 is showing early clinical benefit in highly refractory patients

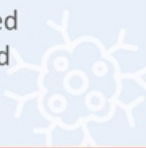


ARDENT Phase 2 has initiated with a once daily, oral dose of 420 mg

Design informed by Phase 1 learnings

Promising antitumor activity

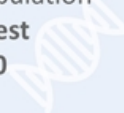
in heavily pre-treated patients with limited treatment options



PSA reduction is associated with plasma exposure



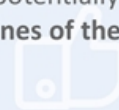
AR molecular profiling identifies a **molecularly defined**, late line population that may **have greatest response to ARV-110**



Activity in wild-type AR patients supports broader use

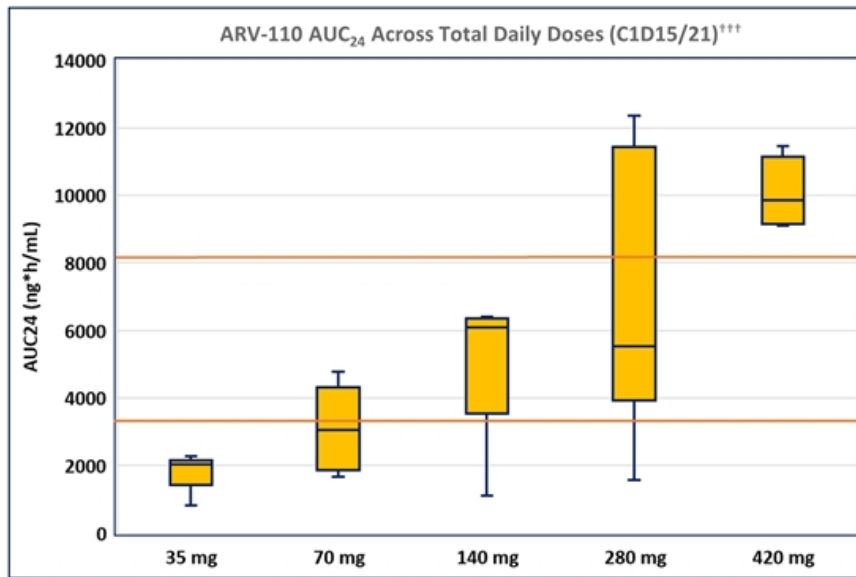


ARV-110 is well tolerated[†], allowing continued dose escalation up to current dose of 700 mg daily, and potentially supporting use in earlier lines of therapy



[†] Safety cut-off date: October 2, 2020

At 420 mg, exposures exceed the predicted efficacious threshold observed in a preclinical enzalutamide-resistant model



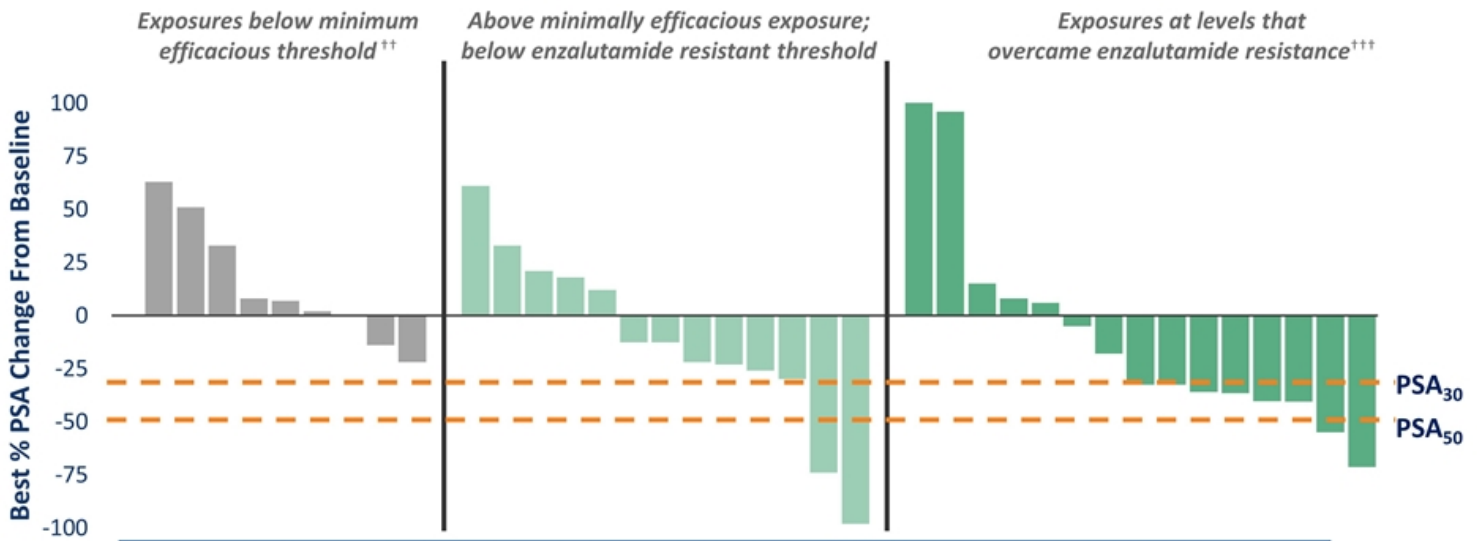
Predicted efficacious threshold based on an enzalutamide-resistant prostate cancer model^{††}

Predicted **minimum** efficacious threshold based on a standard prostate cancer model[†]

† The minimum preclinical efficacious threshold represents the AUC associated with tumor growth inhibition in standard VCAP models, †† This efficacious threshold represents the AUC associated with tumor growth inhibition in a preclinical enzalutamide-resistant VCaP model, ††† Includes both qd and bid dosing for the 420 mg total daily dose

Increased ARV-110 clinical activity at higher exposures

Best PSA Change By Preclinical Efficacious Threshold (N=37)[†]



Exposure-activity relationship informs and supports Phase 2 dose selection

[†] Data as of 30-Nov-2020, ^{††} Exposures in this range did not show anti-tumor activity, ^{†††} Preclinical exposures in this range were sufficient to overcome enzalutamide resistance in preclinical models.

We have identified ARV-110-sensitive populations despite significant tumor heterogeneity in our patient population

Genomic alterations are known to increase over time and with multiple treatments in mCRPC

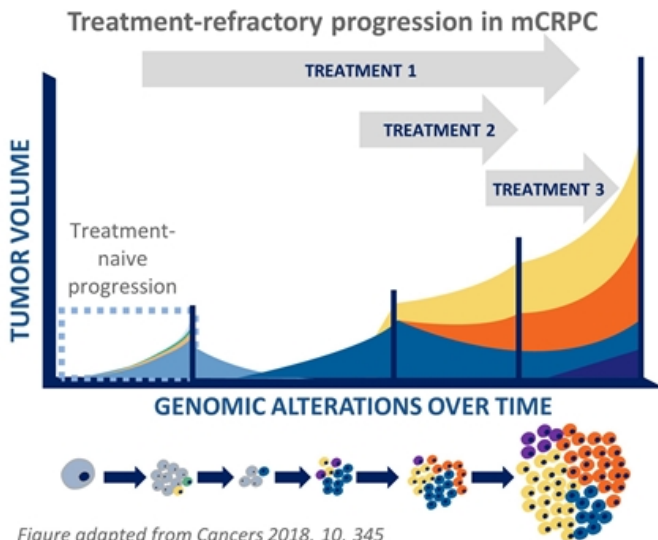


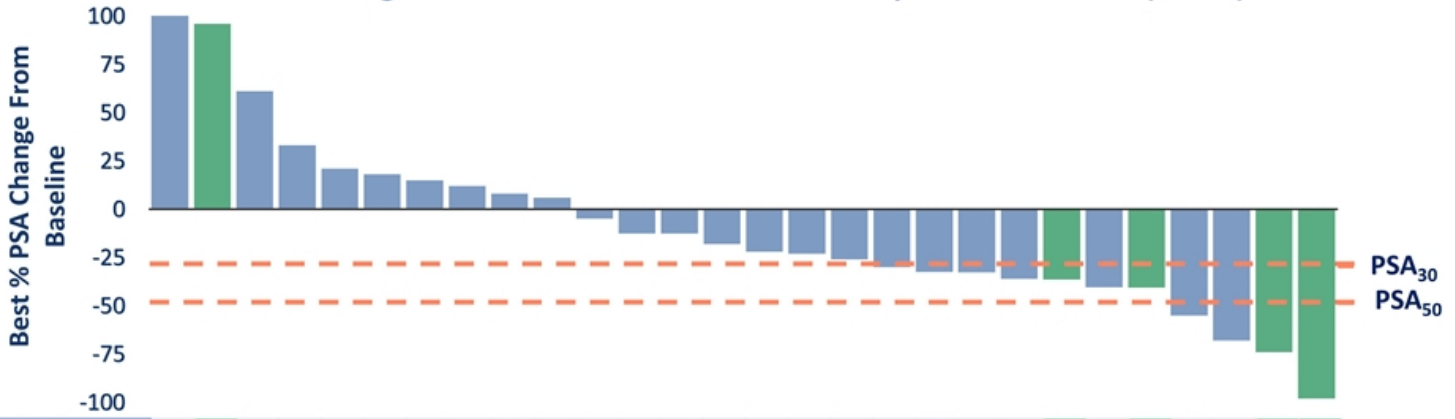
Figure adapted from *Cancers* 2018, 10, 345

† Genetic profiling for most Phase 1 patients was done using the FoundationOne®Liquid test (70-gene panel), additional Phase 1 and Phase 2 patients: FoundationOne®Liquid CDx (324-gene panel).

- Genetic context, an important determinant of response, is the basis for our Phase 2 patient selection strategy
- The tumors of patients in our Phase 1 dose escalation are highly heterogeneous
 - 84% have non-AR mutations
 - Potential for high AR-independence
 - <10% PSA response expected
- In our studies, we are testing for mutations using 70- and now 324 gene-panels[†]

In our late stage, genetically heterogeneous population, we have identified potential molecularly defined subgroups of patients sensitive to ARV-110

Best PSA Change In All Patients Above Minimum Exposure Threshold (N= 28) ^{†††}



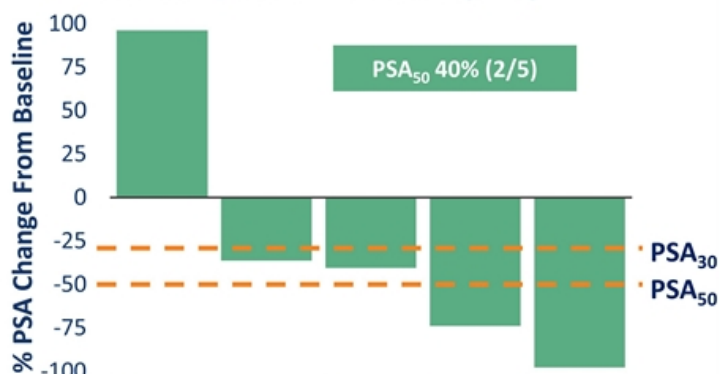
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------------------------|-----|---------------------|-----|----|----|-----|----------------|----|-----|-------|----------------|----|----|----|----|----------------|----|----|----------------|----|----|---------------------|----|----------------------------|----|----|--------------|--------------|--|
| AR Status | Amp | T878A, H875Y, L702H | Amp | WT | WT | Amp | Amp | WT | Amp | W742C | L702H | WT | WT | WT | WT | WT | WT | WT | Amp | WT | WT | T878A, T878S, L702H | WT | T878A, F877L, V716M, L702H | WT | WT | T878A, H875Y | T878A, H875Y | |
| AR-V7 ^{††} | | | + | + | + | | | | | | | | | | | | | | + | | | + | + | | | | | | |
| Other Genes Altered (n) | 1 | 2 | 1 | 2 | 2 | 0 | 2 [†] | 1 | 2 | 4 | 3 [†] | 0 | 2 | 0 | 1 | 1 [†] | 0 | 2 | 1 [†] | 1 | 3 | 5 [†] | 0 | 6 [†] | 2 | 0 | 3 | 1 | |

20/28 (71%) of patients have either T878/H875 or wild-type AR

Each column represents one patient. [†] Includes genes with multiple alterations, ^{††} Epic Sciences, Genetic profiling: FoundationOne[®]Liquid (70-gene panel), ^{†††} Data as of 30-Nov-2020.

Four of five (80%) patients with T878/H875 mutations had PSA reductions, representing a potential accelerated approval population

Best PSA Change In Patients with AR T878/H875 mutations (N=5)^{††}



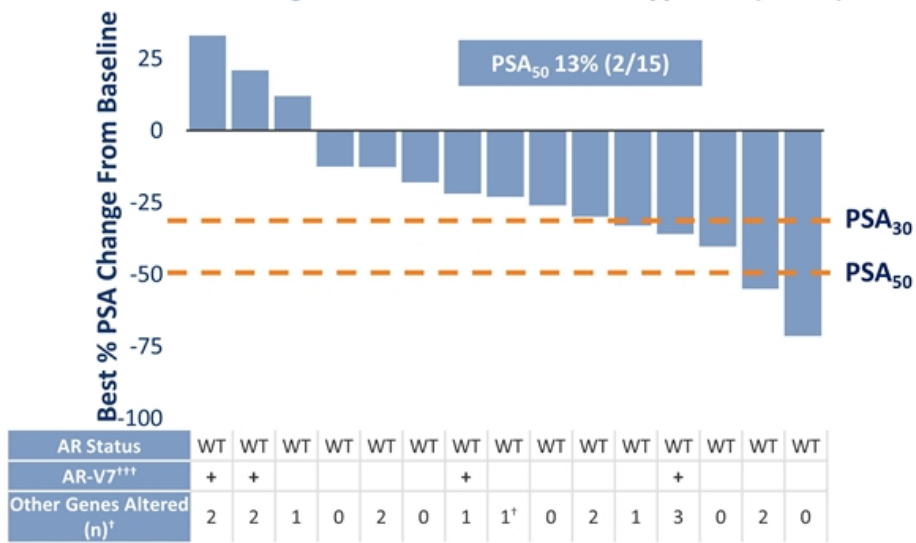
| AR Status | T878A, H875Y, L702H | T878A, T878S, L702H | T878A, F877L, L702H, V716M | T878A, H875Y | T878A, H875Y |
|-----------------------------|---------------------|---------------------|----------------------------|--------------|--------------|
| AR-V7 ^{†††} | | + | | | |
| Other Genes Altered (n) | 2 | 5 [†] | 6 [†] | 3 | 1 |
| Treatment Duration (months) | 1.4→ | 1.8 | 6.2→ | 7.7 | 10.1 |

- Multiple AR mutations could be a "signature" for continued AR dependence
- PSA levels declined even in the presence of significant tumor heterogeneity, AR-V7, and L702H
- T878/H875 patients are a molecularly defined population for enrichment in our ongoing Phase 2 dose expansion, and represent a potential path to accelerated approval

Each column represents one patient. † Includes genes with multiple alterations, †† Includes all patients dosed above the minimum efficacious threshold and with T878/H875 AR (may include other forms of AR), ††† Epic Sciences, Genetic profiling: FoundationOne®Liquid (70-gene panel), →Patient remained on treatment as of November 30 2020

ARV-110 is also active in refractory mCRPC patients with tumors expressing wild-type AR

Best PSA Change In Patients with Wild-Type AR (N=15)^{††}



Wild-type AR-containing tumors represent a broader population sensitive to ARV-110

Each column represents one patient. † Includes genes with multiple alterations, †† Includes all patients dosed above the minimum efficacious threshold and with wild type AR, ††† Epic Sciences, Genetic profiling: FoundationOne®Liquid (70-gene panel).

Strong profile for ARDENT Phase 2 expansion trial at 420 mg, oral, once daily

| Parameter | Phase 1 Results |
|--|---------------------------------------|
| Safety Data [†] | ✓ (Well tolerated; no TRAEs Gr >2) |
| Dose Response and Exposure Threshold ^{††} | ✓ |
| Efficacy Data ^{††} | ✓ |
| Strong signal in molecularly defined patient populations | ✓ |
| High potential for patient benefit in earlier-line, more AR-dependent patients | ✓ |

Opportunity to select a second dose in 2021

[†] Safety cut-off date: October 2, 2020

^{††} For patients with molecular profiling, PK and PSA data as of 30-Nov-2020.

ARDENT will evaluate efficacy in both late-line, molecularly defined patients, and in a broader, early-line mCRPC population

Features of the ARDENT Phase 2 Design

- Enriches T878/H875 for exploration as a potential population for accelerated approval, and retains optionality for others
- Enrolls earlier, more AR-dependent populations
- Provides a subgroup for all screened patients

| Patient Subgroup [†] | Tumor Characteristics |
|--------------------------------|--|
| T878/H875 | T878 and/or H875 AR mutated |
| Less-pretreated patients | Chemo-naïve, and progressed on abiraterone OR enzalutamide (<i>not both</i>) |
| Other AR degradable by ARV-110 | AR wild type, amplified, and resistance-driving point mutations |
| AR not degradable by ARV-110 | Tumors with L702H and AR-V7 |
| Total N = ~100 | |

[†] Tumors are heterogeneous, so patients may fall into multiple subgroups for post-hoc analysis.

Potential registrational paths

1

**Late-line (3L),
molecularly defined
mCRPC**

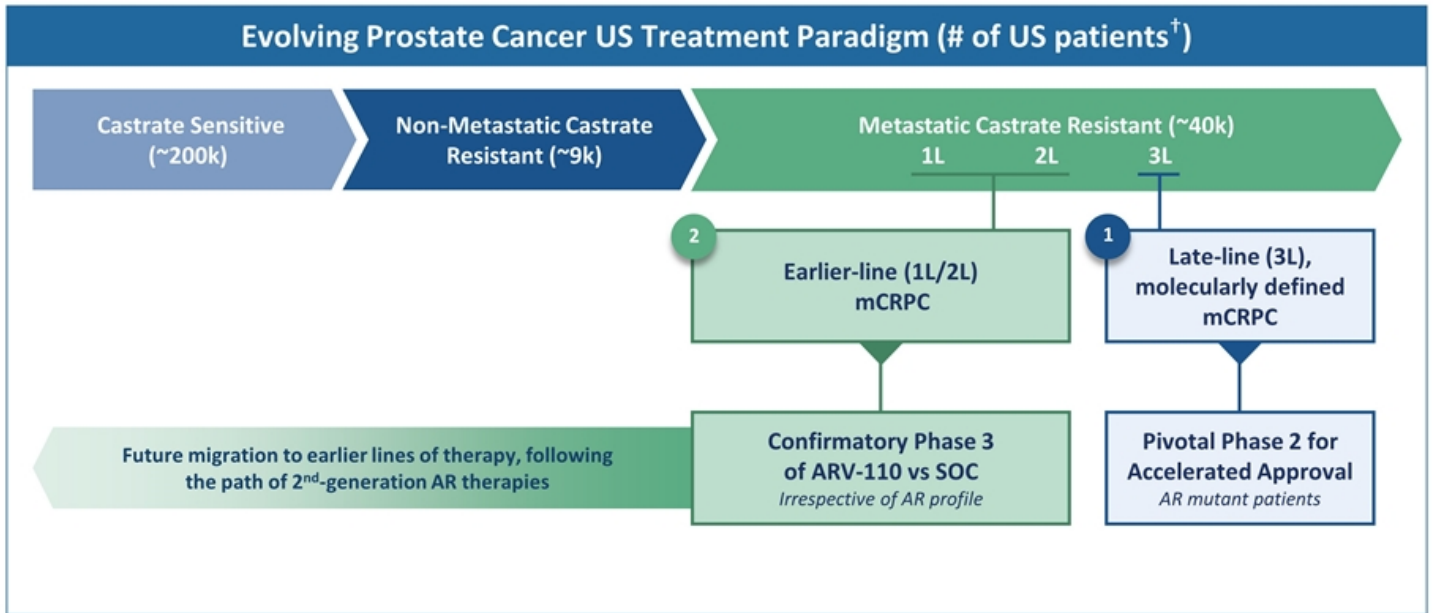
Potential for accelerated approval

2

**Earlier-line (1L/2L)
mCRPC**

Via confirmatory study

ARV-110's planned registrational path aligns with unmet need in mCRPC, and offers potential label expansion into earlier settings



[†] SEER database
SOC, standard of care; mCRPC, metastatic castrate resistant prostate cancer

ARV-110: Potential to address unmet need across multiple stage of prostate cancer



Potential for Best-in-Class Profile

- Driving **tumor responses and PSA reductions** in a molecularly defined, late-line mCRPC population
- **Late-line activity** suggests **strong potential in CSPC**
- **Well tolerated**



Clear Development Path

- **Two potential registrational paths**
 - **Accelerated approval** in molecularly defined mCRPC
 - **Broader 1L/2L mCRPC**



Large Unmet Need and Opportunity

- High unmet need across all stages of prostate cancer
- Including CSPC, addressable patient population of >250K[†] per year in the US alone translates into a >\$8B market opportunity

[†] US incidence from SEER Database
CSPC, castrate sensitive prostate cancer

Conclusion



Arvinas' current pipeline encompasses a range of validated and undruggable targets in oncology, I-O, and neuroscience

| | ARVN Program | Indication | Exploratory | Research | IND Enabling | Phase 1 | Phase 2 | Phase 3 | |
|----------------------------|-----------------|-------------------------|---|----------|--------------|---------|----------|---------|--|
| Oncology / Immuno-oncology | ARV-110 | mCRPC | [Progress bar from Exploratory to Phase 2] | | | | | | |
| | ARV-766 | Other AR indications | [Progress bar from Exploratory to Research] | | | | IND 2021 | | |
| | AR-V7 | mCRPC | [Progress bar from Exploratory to Research] | | | | | | |
| | ARV-471 | ER+/HER2- Breast Cancer | [Progress bar from Exploratory to Phase 1] | | | | | | |
| | BCL6 | B-cell Malignancies | [Progress bar from Exploratory to Research] | | | | IND 2022 | | |
| | KRAS | NSCLC, CRC, Pancreatic | [Progress bar from Exploratory to Research] | | | | IND 2023 | | |
| | Undisclosed | Solid Malignancies | [Progress bar from Exploratory to Research] | | | | IND 2022 | | |
| | Myc | Solid Malignancies | [Progress bar from Exploratory to Research] | | | | | | |
| Neuroscience | HPK1 | Solid Malignancies | [Progress bar from Exploratory to Research] | | | | | | |
| | Tau | FTLD-TAU, PSP, AD | [Progress bar from Exploratory to Research] | | | | IND 2022 | | |
| | Alpha Synuclein | MSA, Parkinson's | [Progress bar from Exploratory to Research] | | | | | | |
| | mHTT | Huntington's | [Progress bar from Exploratory to Research] | | | | | | |
| | Undisclosed | Neurodegeneration | [Progress bar from Exploratory to Research] | | | | | | |

Note: Pipeline is non-exhaustive and IND dates are anticipated.

mCRPC, metastatic castration-resistant prostate cancer; ER+/HER2-, estrogen receptor+/human epidermal growth factor receptor 2-; NSCLC, non-small-cell lung carcinoma; CRC, colorectal cancer; FTLD-tau, frontotemporal lobar degeneration-tau; PSP, progressive supranuclear palsy; MSA, multiple systems atrophy

ARV-110 and ARV-471 set up Arvinas for a remarkable 2021

Anticipated Milestones

| | 2020 Q4 | 2021 | 2022 |
|-------------------------|--|--|--|
| ARV-110 (AR PROTAC®) | | <ul style="list-style-type: none"> Complete Phase 1 data ARDENT Phase 2 interim data Initiation of combination study(s) | <ul style="list-style-type: none"> Full ARDENT Phase 2 data Combination study data |
| ARV-471 (ER PROTAC®) | <ul style="list-style-type: none"> Initiation of combination study with CDK4/6i | <ul style="list-style-type: none"> Complete Phase 1 data Initiation of Phase 2 CDK4/6i combination study data | <ul style="list-style-type: none"> Interim Phase 2 data |
| ARV-766 (AR PROTAC®) | | <ul style="list-style-type: none"> Initiate Phase 1 | <ul style="list-style-type: none"> Phase 1 data Initiate Phase 2 |
| INDs | | <ul style="list-style-type: none"> ARV-766 | <ul style="list-style-type: none"> BCL6 Tau Undisclosed (oncology) |

We are well on our way to our 2024 vision



Integrated biotech poised for launch

- Goal to have first PROTAC® degraders proven to benefit patients in registrational studies
- Sustainably nominating ≥ 1 clinical candidate per year
- PROTAC Discovery Engine delivering candidates with tissue- and disease-specific degradation
- Completing build-out of the resources and capabilities to bring PROTAC therapeutics to market

2019-2020

Proved the Concept of Our PROTAC Discovery Engine

2013-2018

Built Arvinas' Foundation as a Pioneer in Protein Degradation



Thank You