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): October 22, 2023

Arvinas, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-38672**	**47-2566120**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

5 Science Park **395 Winchester Ave.** **New Haven, Connecticut**	**06511**
(Address of principal executive offices)	**(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):

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

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. o

Item 7.01 Regulation FD Disclosure.

On October 22, 2023, Arvinas, Inc. (the "Company") issued a press release announcing the presentation of interim data from the Company's Phase 1/2 clinical trial for bavdegalutamide (ARV-110) in men with metastatic castration-resistant prostate cancer ("mCRPC") in a poster session at the European Society for Medical Oncology Congress being held in Madrid from October 20 – 24, 2023. The Company hosted a conference call to discuss these data and present new data from an updated analysis of its ongoing Phase 1/2 clinical trial with ARV-766 in men with mCRPC.

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 into this Item 7.01 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.

The Second Amended and Restated Bylaws also include certain technical, conforming and clarifying changes. The foregoing description of the Second and Amended Restated Bylaws is qualified in its entirety by reference to the full text of the Second Amended and Restated Bylaws, which is attached hereto as Exhibit 3.1 and incorporated herein by reference.

Item 8.01. Other Events.

On October 22, 2023, the Company announced interim data from the Company's Phase 1/2 clinical trial for bavdegalutamide (ARV-110) in men with mCRPC in a poster session at the European Society for Medical Oncology Congress being held in Madrid from October 20 – 24, 2023. Bavdegalutamide is an investigational, once-daily, orally bioavailable PROTAC® protein degrader designed to selectively target and degrade the androgen receptor ("AR"), and degrades wild type and all clinically relevant AR ligand binding domain ("LBD") mutations except AR L702H, a mutation associated with resistance to abiraterone and other AR-pathway novel hormonal agents ("NHA").

Data from the Phase 1/2 clinical trial with bavdegalutamide (data cut-off date Aug. 11, 2023) in a post-NHA (median prior therapies = 4) mCRPC population and at the recommend Phase 2 dose (420 mg, oral, once-daily), showed median radiographic progression free survival ("rPFS") of 11.1 months in a subgroup of patients harboring AR 878/875 mutations (AR 878/875; T878X=T878A or T878S) and without co-occurring AR L702H mutations (n=26) and median rPFS of 8.2 months in patients with tumors harboring any AR LBD mutation except L702H alone (n=45). The data also showed that 54% of patients with tumors harboring AR 878/875 mutations and without co-occurring AR L702H achieved reductions in prostate specific antigen ("PSA") levels of greater than or equal to than 50% or ("PSA50"), and 36% of patients with tumors harboring any AR LBD mutation except L702H alone achieved PSA50. The presence of AR L702H mutations greatly diminished the signals of efficacy of bavdegalutamide; in patients with any tumor harboring an AR L702H mutation, the PSA_{50} was 8%. Bavdegalutamide showed a manageable tolerability profile with no grade > 4 treatment-related adverse events ("TRAEs"). The most common TRAEs were grade 1 and 2 and included nausea (56%), fatigue (35%), vomiting (33%), decreased appetite (25%) and diarrhea (24%). The discontinuation rate due to TRAEs was 10%.

Also on October 22, 2023, the Company presented interim data from an updated analysis of its ongoing Phase 1/2 clinical trial with its second-generation PROTAC AR degrader, ARV 766 (data cut-off date Aug. 23, 2023), demonstrating broad signals of efficacy and excellent tolerability in mCRPC patients with tumors harboring any AR LBD mutations, including AR L702H. ARV-766 is an investigational orally bioavailable PROTAC® protein degrader designed to degrade all clinically relevant resistance-driving point mutations of the AR, including L702H, which improves upon the degradation profile of bavdegalutamide. The data showed a PSA50 of 41% in patients with tumors harboring any AR LBD mutation and a PSA_{50} of 50% in patients with any tumor harboring an AR L702H mutation. ARV-766 was well-tolerated, with no grade > 4 TRAEs. The most common TRAEs were grade 1 or 2 and included fatigue (29%), nausea (14%), vomiting (11%), and diarrhea (11%). The discontinuation rate due to TRAEs was 4%.

Based on signs of superior tolerability and efficacy in clinical settings to date, Arvinas believes that ARV-766 will be a superior PROTAC® AR degrader versus bavdegalutamide for both metastatic castration-sensitive prostate cancer "(mCSPC") and mCRPC. Arvinas will prioritize the initiation of a Phase 3 clinical trial with ARV-766 in mCRPC instead of the previously planned Phase 3 clinical trial for bavdegalutamide. The Company plans to initiate discussions with regulatory authorities to align on the Phase 3 program by 2Q 2024. Ongoing trial activities with bavdegalutamide

(ARV-110-101 and ARV-110-103) are not expected to be impacted and are expected to continue as planned. Arvinas also expects to advance ARV-766 to treat patients with mCSPC in the future.

Forward-Looking Statements.

This Current Report on Form 8-K, including the documents furnished as Exhibit 99.1 and 99.2 hereto, contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the potential advantages and therapeutic benefits of bavdegalutamide and ARV-766, Arvinas' plans to prioritize Phase 3 plans for ARV-766 over bavdegalutamide, the Company's expectations for ARV-766 to treat patients with mCRPC and mCSPC, the Company's expectations with respect to continuing ARV-110 activity, and plans for discussions with regulatory authorities. 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," "expect," "intend," "may," "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 and complete clinical development for bavdegalutamide and ARV-766, including whether the Company initiates and completes clinical trials for the Company's product candidates, and receives 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.

Item 9.01 **Financial Statements and Exhibits.**

(d) Exhibits

Exhibit Number	Description of Exhibit
99.1	Press Release, dated October 22, 2023
99.2	Company Presentation, dated October 22, 2023
104	Cover Page Interactive Data File (formatted as Inline XBRL)

SIGNATURES

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

ARVINAS, INC.

Date: October 23, 2023

By: /s/ Sean Cassidy

Sean Cassidy
Chief Financial Officer

Potential of Arvinas' PROTAC® AR Degraders Reinforced by 11.1 months rPFS with Bavdegalutamide and Updated Positive Interim Data from Second Generation ARV-766 in mCRPC

– Data presented at the European Society for Medical Oncology from the Phase 1/2 trial with bavdegalutamide showed 11.1 months radiographic progression free survival in mCRPC patients with tumors harboring AR 878/875 mutations –

– Interim data from the Phase 1/2 trial of Arvinas' second PROTAC AR degrader, ARV-766, showed robust efficacy in a broader mCRPC patient population with a tolerability profile well-suited to both early- and late-line settings –

– Company to prioritize the initiation of a Phase 3 trial with ARV-766 in mCRPC –

– Arvinas will host conference call to discuss results on Sunday, October 22 at 3:00 p.m. CEST / 9:00 a.m. ET –

NEW HAVEN, Conn., October 22 -- Arvinas, Inc. (Nasdaq: ARVN), a clinical-stage biotechnology company creating a new class of drugs based on targeted protein degradation, today announced the presentation of interim data from the Company's Phase 1/2 clinical trial for bavdegalutamide (ARV-110), a novel PROTAC® protein degrader targeting the androgen receptor (AR), in a poster session at the European Society for Medical Oncology Congress being held in Madrid from October 20 – 24, 2023. The Company will host a conference call to discuss these data and present new data from an updated analysis of its ongoing Phase 1/2 clinical trial with its second-generation PROTAC AR degrader, ARV-766, showing clinical activity extending across patients harboring tumors with AR LBD mutations and a tolerability profile that is superior to bavdegalutamide.

Extended follow-up of data from the Phase 1/2 clinical trial with bavdegalutamide showed radiographic progression free survival (rPFS) of 11.1 months in a subgroup of patients with metastatic castration-resistant prostate cancer (mCRPC) and tumors harboring AR T878X/H878Y mutations (AR 878/875; T878X=T878A or T878S) in the absence of co-occurring AR L702H mutations. AR L702H is a common AR ligand-binding domain (LBD) mutation that is not potently degraded by bavdegalutamide. In patients with tumors harboring any AR LBD mutation except L702H alone, bavdegalutamide showed an rPFS of 8.2 months.

"We are incredibly pleased with the results from bavdegalutamide's Phase 1/2 trial as they demonstrate the promise of our AR PROTAC degraders to help patients with prostate cancer," said John Houston, Ph.D., chairperson, chief executive officer, and president of Arvinas. "While bavdegalutamide's efficacy is very exciting, its breadth of activity could be limited to a small patient population in a late-line setting. Our second generation PROTAC AR degrader, ARV-766, has demonstrated a broader efficacy profile and even better tolerability compared to bavdegalutamide in clinical settings. Arvinas is committed to bringing forward the best PROTAC AR degrader for patients with prostate cancer. We believe ARV-766 has the potential to be a first- and best- in-class treatment for patients with castrate-sensitive and

castrate-resistant prostate cancer, and we are prioritizing the initiation of a Phase 3 clinical trial in mCRPC with ARV-766."

Bavdegalutamide is a once-daily, oral, first-in-class PROTAC AR degrader that degrades wild type and all clinically relevant AR LBD mutations except AR L702H. ARV-766 was designed to improve upon the degradation profile of bavdegalutamide by also degrading AR L702H. The prevalence of all AR LBD mutations, especially AR L702H, has increased over time, and these mutations are present in approximately 25% of tumors after initial treatment with a novel hormonal agent (NHA) such as enzalutamide or abiraterone. This represents a potential addressable patient population for ARV-766 that is approximately three times that of bavdegalutamide in the post-NHA population due to its broader degradation profile.

New data from the ongoing Phase 1/2 clinical trial of ARV-766 continues to show robust efficacy in tumors with all LBD mutations (41% PSA_{50}) and in patients with tumors harboring AR L702H mutations (50% PSA_{50}). In addition to a tolerability profile that is superior to bavdegalutamide, early durability data for ARV-766 are encouraging and provide additional support for prioritizing ARV-766 over bavdegalutamide, with PFS data anticipated in 2024.

"I've been involved in trials with both bavdegalutamide and ARV-766. It's gratifying to see these innovative therapies developed in advanced prostate cancer where there remains a significant need for better treatments," said Daniel Petrylak, M.D., Professor of Medicine and Urology at Yale School of Medicine and investigator in the Phase 1/2 studies with bavdegalutamide and ARV-766. "In my experience, these novel therapies have the potential to be an important treatment choice for patients whose tumors harbor androgen receptor LBD mutations, which may be present in up to 25% of metastatic castration resistant prostate cancer. The increasing prevalence of the L702H mutation means that more patients could potentially benefit from the broader efficacy profile offered with ARV-766. The improvement in tolerability that ARV-766 has shown in clinical trials compared to bavdegalutamide is also a big advantage for patients with prostate cancer."

Highlights from the Phase 1/2 trial with bavdegalutamide (data cut-off date Aug. 11, 2023):
In a post-NHA (median prior therapies = 4) mCRPC population, bavdegalutamide at the recommend Phase 2 dose (420 mg, oral, once daily) demonstrated:

- Median rPFS of 11.1 months in patients harboring AR 878/875 mutations and without co-occurring AR L702H mutations (n=26), and median rPFS of 8.2 months in patients with tumors harboring any AR LBD mutation except L702H alone (n=45)
- PSA_{50} rates of 54% in patients with tumors harboring AR 878/875 mutations and without co-occurring AR L702H, and 36% in patients with tumors harboring any AR LBD mutation except L702H alone
- The presence of AR L702H mutations greatly diminished the efficacy of bavdegalutamide
    - In patients with any tumor harboring an AR L702H mutation, the PSA_{50} was 8%
- Bavdegalutamide had a manageable tolerability profile with no grade $\geq$ 4 treatment-related adverse events (TRAEs). The most common TRAEs were grade 1 and 2 and included nausea (56%), fatigue (35%), vomiting (33%), decreased appetite (25%) and diarrhea (24%). The discontinuation rate due to TRAEs was 10%.

Interim data from the ongoing Phase 1/2 dose escalation and expansion trial of ARV-766 (data cut-off date Aug. 23, 2023)
Data from an updated analysis of the ongoing Phase 1/2 clinical trial demonstrate broad efficacy and excellent tolerability in mCRPC patients with tumors harboring AR LBD mutations, including AR L702H:

- PSA_{50} of 41% in patients with tumors harboring any AR LBD mutation, and a PSA_{50} of 50% in patients with any tumor harboring an AR L702H mutation
- ARV-766 was well-tolerated, with no grade $\geq$ 4 TRAEs. The most common TRAEs were grade 1 or 2 and included fatigue (29%), nausea (14%), vomiting (11%), and diarrhea (11%). The discontinuation rate due to TRAEs was 4%.

Based on ARV-766's superior tolerability profile and encouraging efficacy data to date, Arvinas believes ARV-766 will be a superior PROTAC AR degrader versus bavdegalutamide for both metastatic castration-sensitive prostate cancer (mCSPC) and mCRPC. Arvinas will prioritize the initiation of a Phase 3 clinical trial with ARV-766 in mCRPC instead of the previously planned Phase 3 clinical trial for bavdegalutamide. The Company will initiate discussions with regulatory authorities by 2Q 2024.

Bavdegalutamide Phase 1/2 Poster Presentation
Data from the Phase 1/2 trial is available during a poster session at the 2023 European Society for Medical Oncology (ESMO) Annual Congress in Madrid:

- Date: Sunday, October 22, 2023
- Presentation number: 1803P
- Time: 12:00 – 1:00 p.m. CEST / 6:00 – 7:00 a.m. EDT
- Speaker: Daniel Petrylak, M.D.

The Company will host a conference call and webcast call at 3:00 p.m. CEST / 9:00 a.m. EDT on October 22 to discuss these data as well as previously undisclosed data from the ongoing Phase 1/2 clinical trial with ARV-766. Participants are invited to listen by going to the Events and Presentation section under the Investor page on the Arvinas website at www.arvinas.com. A replay of the webcast will be archived on the Arvinas website following the presentation.

About bavdegalutamide (ARV-110) and ARV-766
Bavdegalutamide (ARV-110) and ARV-766 are investigational orally bioavailable PROTAC® protein degraders designed to selectively target and degrade the androgen receptor (AR). Bavdegalutamide and ARV-766 are being developed as potential treatments for men with prostate cancer. Preclinically, both investigational agents have demonstrated activity in models of wild type androgen receptor tumors in addition to tumors with AR mutations or amplification, both common potential mechanisms of resistance to currently available AR-targeted therapies.

About Arvinas
Arvinas is a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development, and commercialization of therapies that degrade disease-causing proteins. Arvinas uses its proprietary PROTAC® Discovery Engine platform to engineer proteolysis targeting chimeras, or PROTAC targeted protein degraders, that are designed to harness the body's own natural protein disposal system to

selectively and efficiently degrade and remove disease-causing proteins. In addition to its robust preclinical pipeline of PROTAC protein degraders against validated and "undruggable" targets, the company has three investigational clinical-stage programs: bavdegalutamide and ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer; and vepdegestrant (ARV-471) for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer. For more information, visit www.arvinas.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the potential advantages and therapeutic benefits of Arvinas' PROTAC® androgen receptor (AR) degraders, bavdegalutamide and ARV-766; the potential for bavdegalutamide and ARV-766 as treatment choices for patients whose tumors harbor AR ligand binding domain mutation; the potential breadth of activity of bavdegalutamide in a late-line setting; whether ARV-766 will be a first- and best-in class treatment for patients with early- and late-line prostate cancer; the addressable patient population for ARV-766, bavdegalutamide and ARV-766 as compared to bavdegalutamide; the timing of progression free survival data for ARV-766; whether ARV-766 will be a superior PROTAC® AR degrader versus bavdegalutamide for both metastatic castration-sensitive prostate cancer and metastatic castration-resistant prostate cancer; and the timing for Arvinas to initiate discussions with regulatory authorities. All statements, other than statements of historical facts, contained in this press release, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "expect," "intend," "may," "plan," "predict," "target," "potential," "will," "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 and complete development for ARV-766 and bavdegalutamide; whether we initiate and complete clinical trials for our product candidates and receive results from our clinical trials on our expected timelines or at all; our ability to obtain marketing approval for and commercialize our androgen receptor program product candidates on our current timelines or at all; our ability to maintain, expand and protect our intellectual property portfolio; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors, and other important factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2022 and subsequent other 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 release.

Contacts
Investors:
Jeff Boyle

+1 (347) 247-5089
Jeff.Boyle@arvinas.com

Media:
Kirsten Owens
+1 (203) 584-0307
Kirsten.Owens@arvinas.com

Exhibit 99.2

ARVINAS

AR Franchise Update

Bavdegalutamide and ARV-766

October 22, 2023

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 potential advantages, therapeutic benefits and development of bavdegalutamide and ARV-766; the potential for ARV-766 to be first- and best-in class PROTAC® AR degrader in mCRPC; whether bavdegalutamide will be a better choice than bavdegalutamide for patients with both early- and late-line prostate cancer; the market opportunity for ARV-766 in prostate cancer (mCRPC + mCSPC), including when compared with bavdegalutamide; the timing of data progression free survival data for ARV-766. 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 and complete development for ARV-766 and bavdegalutamide; whether we initiate and complete clinical trials for our product candidates and receive results from our clinical trials on our expected timelines or at all; our ability to obtain marketing approval for and commercialize our androgen receptor program product candidates on our current timelines or at all; our ability to maintain, expand and protect our intellectual property portfolio; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors, 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 Annual Report on Form 10-K for the year ended December 31, 2022 and subsequent other reports on file with the U.S. 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. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of 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. This presentation is intended for the investor community only. It is not intended to promote the products referenced herein or otherwise influence healthcare prescribing decisions. Cross-trial comparisons are not based on head-to-head studies and no direct comparisons can be made.

In the clinic, bavdegalutamide and ARV-766 both show strong profiles in mCRPC; ARV-766 has shown broader efficacy and superior tolerability

- Bavdegalutamide has proven the concept for a PROTAC® AR degrader in prostate cancer
  - Updated Phase 2 data demonstrate **11.1 months rPFS** in patients with AR 878/875 mutations
  - Manageable tolerability suitable for patients with mCRPC
- However, bavdegalutamide's potential in late-line settings may be limited
  - In clinical settings, efficacy was reduced in patients with tumors harboring AR L702H mutations
- Our next generation pan-AR degrader, ARV-766, has shown to have an expanded efficacy profile and improved tolerability profile versus bavdegalutamide, suggesting that it could impact 3x more patients in mCRPC
  - **Early signals of efficacy: 41% PSA_{50}** in all patients with AR LBD mutations; **50% PSA_{50}** in patients with AR L702H
  - **Superior tolerability** versus bavdegalutamide
- We will prioritize a Phase 3 trial for ARV-766 in mCRPC
- ARV-766 could potentially benefit ~120,000 patients with prostate cancer (mCRPC + mCSPC)

ARVINAS

AR = androgen receptor; rPFS = radiographic progression-free survival; mCRPC = metastatic castrate-resistant prostate cancer; LBD = ligand binding domain; mCSPC = metastatic sensitive-resistant prostate cancer; PSA = prostate-specific antigen

Phase 1/2 trial with bavdegalutamide, an oral PROTAC® AR degrader

European Society for Medical Oncology (ESMO) 2023

ARVINAS

Bavdegalutamide has proven the concept of a PROTAC® AR degrader in mCRPC

Existing options leave unmet need in post-NHA mCRPC

- NHA retreatment is associated with limited benefit (e.g., rPFS ~ 4 months)[1-4]
- Emerging non-AR agents have better outcomes (e.g., rPFS 7-9 months post-taxane therapy), but are limited due to tolerability challenges, IV route of administration, or patient selection considerations[5]

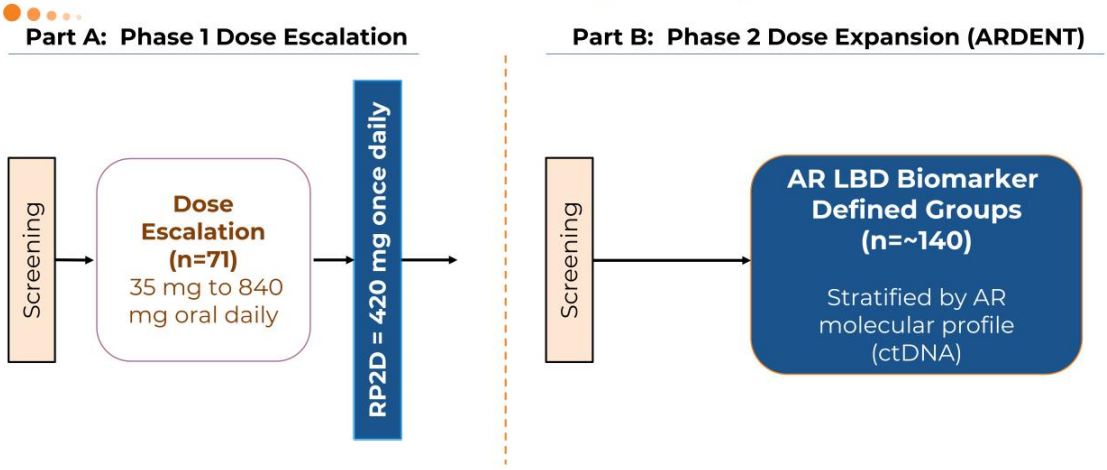
Bavdegalutamide is a PROTAC® AR degrader that degrades all AR LBD mutations except L702H

Bavdegalutamide demonstrates strong antitumor activity in post-NHA patients

- 11.1 months rPFS in patients with 878/875 AR LBD mutations, which are associated with worse survival in mCRPC[6]

NHA = novel hormonal agent; rPFS = radiographic progression-free survival; AR = androgen receptor; LBD = ligand binding domain; mCRPC = metastatic castrate-resistant prostate cancer; 1. de Bono et al. N Engl J Med. 2020 and prescribing information; 2. Fizazi et al. N Engl J Med. 2023. 3. de Wit et al. N Engl J Med. 2019; 4. Sartor et al. N Engl J Med. 2021 5. CARD, PROFOUND, VISION studies. 6. Stewart et al Abstract 1407P ESMO 2022

Bavdegalutamide's ARDENT Phase 2 trial has explored efficacy in patients with tumors that retain AR dependency



AR = androgen receptor; LBD = ligand-binding domain; RP2D = recommended phase 2 dose; ctDNA = circulating tumor DNA

Patients enrolled in the Phase 1/2 trial were NHA-experienced and included heavily pretreated patients (median prior therapies = 4)

Table 1: Baseline characteristics

Parameter	Total at 420 mg QD (n=153)	*AR* LBD patients[1] (n=45)
Age, median (range), y	73 (48–91)	72 (51–83)
ECOG PS, n (%)[2]		
0	81 (53)	25 (56)
1	71 (46)	20 (44)
Visceral disease	49 (32)	14 (31)
Prior lines of treatment, median (range)	4 (1–11)	4 (2–8)
Prior treatment, n (%)		
NHA	153 (100)	45 (100)
1 NHA	83 (54)	21 (47)
≥2 NHA	70 (46)	24 (53)
Abiraterone	105 (69)	36 (80)
Enzalutamide or other AR blocker	111 (73)	29 (64)
Taxane chemotherapy	51 (33)	16 (36)

AR = androgen receptor; ECOG PS = Eastern Cooperative Oncology Group performance status; LBD = ligand-binding domain; NHA = novel hormonal agent; QD = once daily
1. AR LBD patients: any AR ligand-binding domain (LBD) missense mutation except AR L702H alone
2. 1 patient who received bavdegalutamide 420 mf QD had ECOG status of 2

Bavdegalutamide's tolerability has been shown to be manageable in patients with mCRPC

- The most common treatment-related adverse events (TRAEs) with bavdegalutamide 420 mg QD were nausea, vomiting, and fatigue
- No grade ≥4 TRAEs
- 17 (11%) patients had a dose reduction due to an adverse event (AE) and 19 (12%) discontinued treatment due to any AE

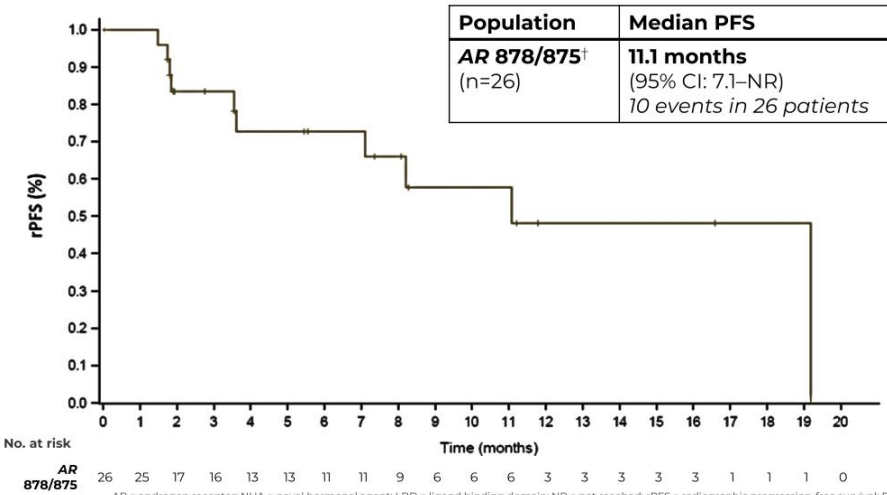
TRAEs reported in ≥10% of patients treated with bavdegalutamide 420 mg QD in the Phase 1/2 trial (n=153)

	Total n (%)	Grade 1	Grade 2	Grade 3
Any TRAE	135 (88)	45 (29)	66 (43)	24 (16)
Nausea	85 (56)	59 (39)	24 (16)	2 (1)
Fatigue	53 (35)	36 (24)	16 (10)	1 (1)
Vomiting	50 (33)	38 (25)	11 (7)	1 (1)
Decreased appetite	39 (25)	21 (14)	18 (12)	0
Diarrhea	37 (24)	27 (18)	7 (5)	3 (2)
Alopecia	28 (18)	24 (16)	4 (3)	NA
Anemia	23 (15)	10 (7)	6 (4)	7 (5)
Weight decreased	19 (12)	10 (7)	9 (6)	0
AST increased	18 (12)	13 (8)	4 (3)	1 (1)

AST = aspartate aminotransferase; NA = not applicable; QD = once daily; TRAE = treatment-related adverse event; AE = adverse event

In clinical settings, bavdegalutamide has demonstrated a robust rPFS of 11.1 months in an NHA-experienced mCRPC patient population

Population	Median PFS	PSA_{50}
***AR* 878/875**† (n=26)	**11.1 months** (95% CI: 7.1–NR) *10 events in 26 patients*	**14/26 (54%)**



No. at risk

AR 878/875	26	25	17	16	13	13	11	11	9	6	6	6	3	3	3	3	3	1	1	1	0

AR = androgen receptor; NHA = novel hormonal agent; LBD = ligand binding domain; NR = not reached; rPFS = radiographic progression-free survival; PFS = progression-free survival; PSA=prostate-specific antigen; mCRPC = metastatic castrate-resistant prostate cancer

† 878/875 without co-occurring L702H

ARVINAS

Bavdegalutamide's efficacy profile is differentiated from those of non-AR agents

Cross-trial benchmarks are not based on head-to-head studies

Drug	Trial Name *Prior taxane status*	Route of Administration	Addressable Patient Segment	Clinical Activity		Safety Profile	
				Median rPFS (months)	% PSA_{50}	Grade ≥3 TEAE (%)	Discontinuation rate from TEAEs (%)
Bavdegalutamide Phase 1/2 clinical data (all post-NHA)							
Bavdegalutamide	ARDENT *Pre- or post-taxane*	Oral	AR 878/875[5]	11.1	54%	31	12
			AR LBD w/o L702H alone	8.2	36%		
Clinical data from currently approved non-AR targeted therapies used post-NHA							
Cabazitaxel (Jevtana®)	CARD[1] *Post-taxane*	IV	Post docetaxel	8.0	36%	56.3	19.8
Lu-177 RLT (Pluvicto®) + SoC	VISION[2] *Post-taxane*	IV	PSMA+ by PET-CT scan	8.7	46%	52.7	11.9
Olaparib (Lynparza®)	PROFOUND[3] *Pre- or post-taxane*	Oral	BRCA 1/2, ATM	7.5	43%	51	18
Rucaparib (Rubraca®)	TRITON-3[4] *Pre-taxane*	Oral	BRCA 1/2 , ATM	10.2	55%	60	15

Post-NHA, AR therapies historically achieve 3.5-4.5 months PFS[6]

NHA = novel hormonal agents; SoC = Standard of Care; IV = intravenous; PET-CT = Positron Emission Tomography and Computed Tomography; TEAE = treatment emergent adverse event; AR LBD = androgen receptor ligand binding domain; rPFS = radiographic progression-free survival; AR = androgen receptor; ATM = ataxia telangiectasia mutated; PSMA = prostate-specific membrane antigen
BRCA = BReast CAncer gene

1. de Wit R, NEJM 2019. 2. Sartor, O, NEJM 2021; 3. de Bono, J, NEJM 2020. 4. Fizazi, K, NEJM 2023. 5. 878/875 without co-occurring L702H. 6. Control arms of the CARD, VISION, and PROFOUND trials

The presence of AR L702H mutations diminishes the efficacy of bavdegalutamide

Mutation status	PSA_{50} rate
AR 878/875 alone (n=26)	**54%**
AR 878/875 with co-occurring L702H (n=11)	**9%**
Any tumor with AR L702H (n=24)	**8%**

Bavdegalutamide's diminished efficacy in patients harboring tumors with AR L702H may limit its ability to benefit a broad mCRPC patient population

ARVINAS

AR = androgen receptor; PSA=prostate-specific antigen; mCRPC = metastatic castrate-resistant prostate cancer

Bavdegalutamide has proven the concept for a PROTAC® AR degrader in AR LBD mCRPC

- In clinical settings, bavdegalutamide achieved a robust efficacy in post-NHA patients with most AR LBD mutations, with particularly strong responses in patients with tumors harboring AR 878/875 mutations alone
- Bavdegalutamide's suboptimal ability to degrade L702H will limit its addressable population (6-9% of mCRPC patients)

When compared with bavdegalutamide, our second-generation PROTAC AR degrader, **ARV-766**, has been shown in clinical settings to have **better tolerability** and a **broader efficacy profile** that could potentially reach **3x more patients in mCRPC**

AR = androgen receptor; mCRPC = metastatic castrate-resistant prostate cancer; NHA = novel hormonal agent; LBD = ligand binding domain

ARV-766 Clinical Update

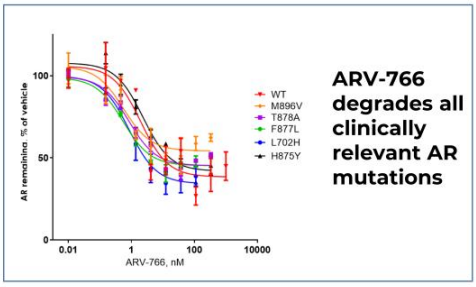
ARVINAS

ARV-766 is a pan-AR PROTAC® degrader designed to degrade wild-type AR and all clinically relevant AR mutations, including L702H

- The prevalence of AR LBD mutations is increasing, especially L702H
  - L702H is estimated at ~11% of mCRPC in 2023[3]
- In total, the prevalence of AR LBD mutations in mCRPC is 20-25%[4,5,6]

Estimates of AR LBD mutation prevalence

AR LBD mutation	2016[1]	2020[2]	2023[3]
L702H	**~2%**	**~9%**	**~11%**
T878X[7]	~6%	~6%	~8%
H875Y	~4%	~4%	~5%



ARV-766 degrades all clinically relevant AR mutations

AR = androgen receptor; mCRPC = metastatic castrate-resistant prostate cancer; LBD = ligand binding domain

1. Coutinho et al 2016 DOI: 10.1530/ERC-16-0422. 2. Ledet et al 2020 DOI: 10.1634/theoncologist.2019-0115. 3. Antonarakis et al, Abstract 395182, ASCO/GU 2023.
4. Beltran H. Eur Urol. 2013;63(5):920-926. 5. Wyatt AW. JAMA Oncol.2016;2(12):1598-1606. 6. Bernard-Tessier et al, Abstract 39698, ASCO/GU 2023. 7. T878X = T878A or T878S

ARV-766 has the potential to be first- and best-in-class PROTAC® AR degrader in mCRPC

June 2023† disclosure (N=47)

- Strong activity (**42% PSA_{50}**) in post-NHA patients across **all LBD** (including L702H) mutations
- **Low rates of Grade 2 and 3 TRAEs**; 1 discontinuation, 2 dose reductions

Data available today (N=84)‡

- Activity remains robust (**41% PSA_{50}**) across **all LBD**, **including in patients with L702H (50% PSA_{50})**
- **Highly differentiated tolerability** appears superior versus bavdegalutamide

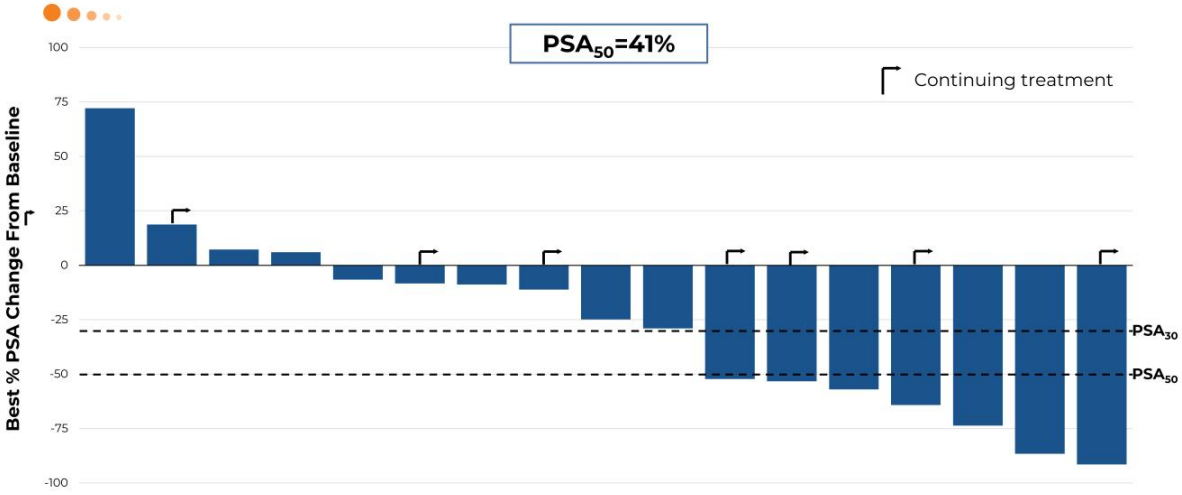
AR = androgen receptor; PSA_{50} = best PSA declines ≥50%; LBD = ligand binding domain; TRAE = treatment-related adverse event; mCRPC = metastatic castrate-resistant prostate cancer;
† Data as of April 15, 2023 (ARV-766 Phase 1/2 dose escalation and expansion trial)
‡ Data as of August 23, 2023 (ARV-766 Phase 1/2 dose escalation and expansion trial)

ARV-766's excellent tolerability profile surpasses that of bavdegalutamide in the clinical setting

TRAE ≥10% n (%)[1]	Bavdeg (n=153[2]) Any Grade	ARV-766 (n=84†) Any Grade	Bavdeg (n=153[2]) Grade 3+	ARV-766 (n=84†) Grade 3+
Any TRAE	135 (88)	55 (66)	24 (16)	7 (8)
Fatigue	53 (35)	24 (29)	1 (1)	2 (2)
Nausea	**85 (56)**	**12 (14)**	2 (1)	0 (0)
Diarrhea	**37 (24)**	**9 (11)**	3 (2)	1 (1)
Vomiting	**50 (33)**	**9 (11)**	1 (1)	0 (0)
Decreased appetite	39 (25)	9 (11)	0 (0)	0 (0)
Alopecia	28 (18)	8 (10)	0 (0)	0 (0)
Anemia	23 (15)	3 (4)	7 (5)	0 (0)
Weight decrease	19 (12)	1 (1)	0	0 (0)
AST increase	18 (12)	6 (7)	1 (1)	1 (1)
Any TRAE leading to discontinuation	16 (10)	3 (4)		

TRAE = treatment related adverse events; AST = aspartate aminotransferase
† As of August 23, 2023
1 .Table includes TRAEs (Treatment Related Adverse Events) greater than 10% for either bavdegalutamide or ARV-766. 2. Includes all patients treated at the RP3D of 400mg QD in Ph 1/2 trial

ARV-766: 41% of patients with AR LBD mutations achieve PSA_{50} (n=17†)



AR = androgen receptor; LBD = ligand-binding domain; PSA = prostate-specific antigen; QD = once daily; PSA_{30} = best PSA declines ≥30%; PSA_{50} = best PSA declines ≥50%
†Includes biomarker-evaluable patients with ≥4 weeks of PSA follow-up. Data from the ARV-766 Phase 1/2 dose escalation and expansion trial; data cut-off, August 23, 2023

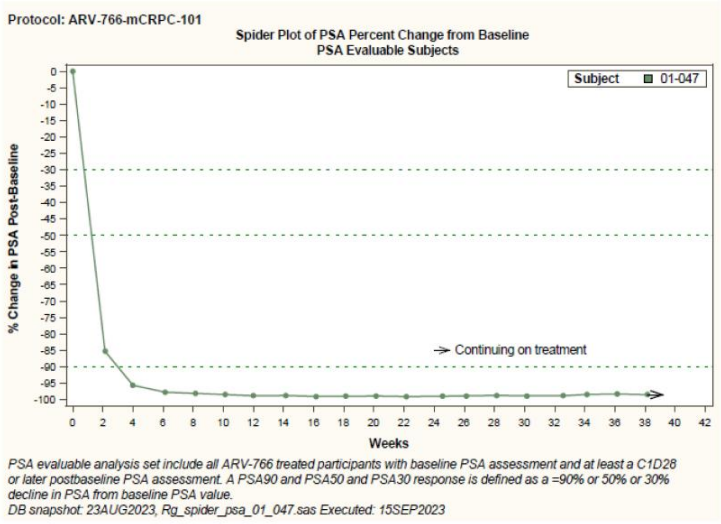
ARV-766 is demonstrating improved signals of efficacy in patients with tumors harboring AR L702H mutations compared to bavdegalutamide in the clinical setting

PSA_{50} rates (%)	Bavdegalutamide†	ARV-766‡
Patients with tumors with L702H	**8% (2 of 24)**	**50% (4 of 8)**

- 41% PSA_{50} (7 of 17) in patients with any AR LBD mutation
- Early durability data for ARV-766 are encouraging and provide additional support for prioritizing ARV-766 over bavdegalutamide
  - PFS data anticipated in 2024

AR = androgen receptor; LBD = ligand-binding domain; PSA = prostate-specific antigen; PFS = progression-free survival; PSA50 = best PSA declines ≥50%
† Includes patients treated at the RP2D ‡ Data as of August 23, 2023

Deep PSA decline in patient with mCRPC with wild-type AR supports development in pre-NHA settings, including mCSPC

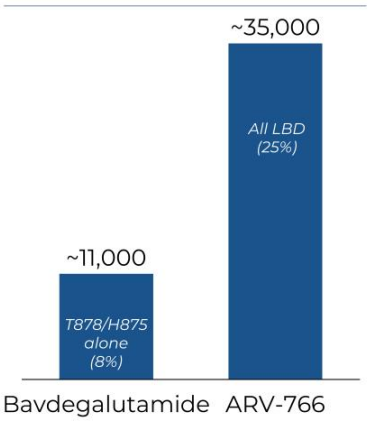


PSA evaluable analysis set include all ARV-766 treated participants with baseline PSA assessment and at least a C1D28 or later postbaseline PSA assessment. A PSA90 and PSA50 and PSA30 response is defined as a =90% or 50% or 30% decline in PSA from baseline PSA value.
DB snapshot: 23AUG2023, Rg_spider_psa_01_047.sas Executed: 15SEP2023

AR = androgen receptor; PSA = prostate-specific antigen; mCSPC = metastatic castrate-sensitive prostate cancer; mCRPC = metastatic castrate-resistant prostate cancer; NHA = novel hormonal agent

ARV-766 has the potential to reach 3X more patients in mCRPC than bavdegalutamide, with additional opportunity in mCSPC

Potential addressable patient populations in mCRPC†



ARV-766:

- **Strong signals of efficacy and excellent tolerability** in a population representing ~**25% of mCRPC**
- *Plus* an additional ~**87,000†** potentially addressable patients in mCSPC

mCSPC = metastatic castrate-sensitive prostate cancer; mCRPC = metastatic castrate-resistant prostate cancer;
† Kantar 2023 Epidemiology Database; includes US, EU4, UK, and Japan

Based on current clinical data, Arvinas believes ARV-766 will be a better choice than bavdegalutamide for patients with both early- and late-line prostate cancer

Potential for PROTAC® AR degrader to improve outcomes in patients with prostate cancer	Bavdegalutamide	ARV-766
Degrades wild type and amplified AR	✓	✓
Targets all AR LBD mutations	No L702H	✓
Tolerability suitable for mCRPC	✓	✓
Tolerability suitable for mCSPC		✓
Phase 3 ease of enrollment		✓
PSA_{50} in patients with tumors harboring L702H mutation	**7% (2 of 24)**	**50% (4 of 8)**
Addressable mCRPC patient population†	**~11,000 (6-9%)**	**~35,000 (~25%)**

† Kantar 20AR = androgen receptor; LBD = ligand-binding domain; mCSPC = metastatic castrate-sensitive prostate cancer; mCRPC = metastatic castrate-resistant prostate cancer;
PSA_{50} = best PSA declines ≥50%
23 Epidemiology Database; includes US, EU4, UK, and Japan

Path Forward for PROTAC® AR Degraders in mCSPC and mCRPC

ARVINAS

Arvinas will prioritize ARV-766 in mCSPC and mCRPC

- Arvinas is committed to advancing the best treatment for patients in both early- (mCSPC) and late-line (mCRPC) disease

- Based on our current clinical data, we believe that ARV-766 will be superior to bavdegalutamide in each setting, and can enroll and target a larger patient population

- Arvinas will prioritize the initiation of an ARV-766 Ph 3 trial in mCRPC instead of the planned Phase 3 for bavdegalutamide
  - Initiate discussions with regulatory authorities by 2Q 2024 to align on Phase 3 program

mCSPC = metastatic castrate-sensitive prostate cancer; mCRPC = metastatic castrate-resistant prostate cancer; PSA_{50} = best PSA declines ≥50%

Q&A

- John Houston, Ph.D, President and Chief Executive Officer, Arvinas
- Ron Peck, M.D., Chief Medical Officer, Arvinas
- Daniel P. Petrylak, M.D., Professor of Medicine (Medical Oncology) and of Urology; Chief, Genitourinary Oncology; at Yale School of Medicine
  - Investigator: bavdegalutamide Phase 1 dose escalation and Phase 2 ARDENT dose expansion
  - Investigator: ARV-766 Phase 1/2 trial