ARVINAS

Pioneering Today
with a different kind of medicine

Transforming Tomorrow
for patients who need us

NASDAQ LISTED ARVN

February 2024

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 our expectation of brining the first PROTACT® protein degrader to market in partnership with Pfizer; the plans for and anticipated timings related to our planned clinical trials, including second-line Phase 3 clinical trials of vepdegestrant in combination with palbociclib and potentially other CDK4/6 inhibitors, a first-line Phase 3 clinical trial of vepdegestrant in combination with Pfizer's CDK4 inhibitor (PF-07220060), our Phase 3 clinical trial for ARV-766 as a monotherapy, and our Phase 1 dose escalation trial of ARV-393 (BCL6); our plans and timing related to commercial launch of vepdegestrant; the potential for vepdegestrant as an oral best-in-class targeted therapy and to become a backbone estrogen receptor therapy in the metastatic breast cancer space; the planned timing of data readouts for our ongoing clinical trials, including our Phase 3 VERITAC-2 monotherapy trial in the second-line setting; the potential therapeutic benefits and market opportunity of our product candidates, including vepdegestrant, ARV-766, ARV-393 and ARV-102; the opportunity for ARV-766 in both post- and pre-novel hormonal agent settings to potentially treat metastatic castrate-sensitive prostate cancer and metastatic castrate-resistant prostate cancer; the potential for androgen receptor (AR)-targeting PROTAC degraders to address the unmet need of patients with prostate cancer across multiple stages of disease and surpass the benefits of other AR inhibitors; the timing to receive progression free survival data for the ARV-766 dose expansion trial; whether our BCL6 PROTAC® degrader will be a first-in-class potential therapy for non-Hodgkin Lymphoma and additional opportunities for BCL6; the timing to initiate a Phase 1 trial for ARV-393; whether a KRAS-targeting PROTAC may provide an advance in treatment for multiple cancers; whether PROTAC-induced LRRK2 degradation could be a a potential treatment for idiopathic Parkinson's disease and Progressive Supranuclear Palsy; our plans and anticipated timing of clinical starts for KRAS, G12D and other programs; and our plans with respect to timing of key program catalysts,.

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 and Pfizer will be able to successfully conduct clinical development for vepdegestrant (ARV-471) and receive results from our clinical trials on our expected timelines, or at all; whether we will be able to successfully conduct and complete development for our other product candidates, including 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 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 quarterly and annual 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.

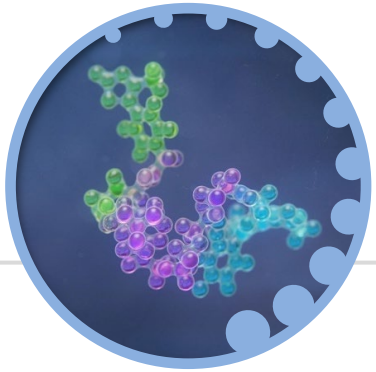
Arvinas: Advancing a new therapeutic modality to patients

PIONEER IN THE FIELD

- **Most advanced protein degradation platform**
- **Expecting to bring the first PROTAC® protein degrader to market** (in partnership with Pfizer)
- **First neuroscience PROTAC® degrader** advanced to the clinic in 2024

NEW MECHANISM

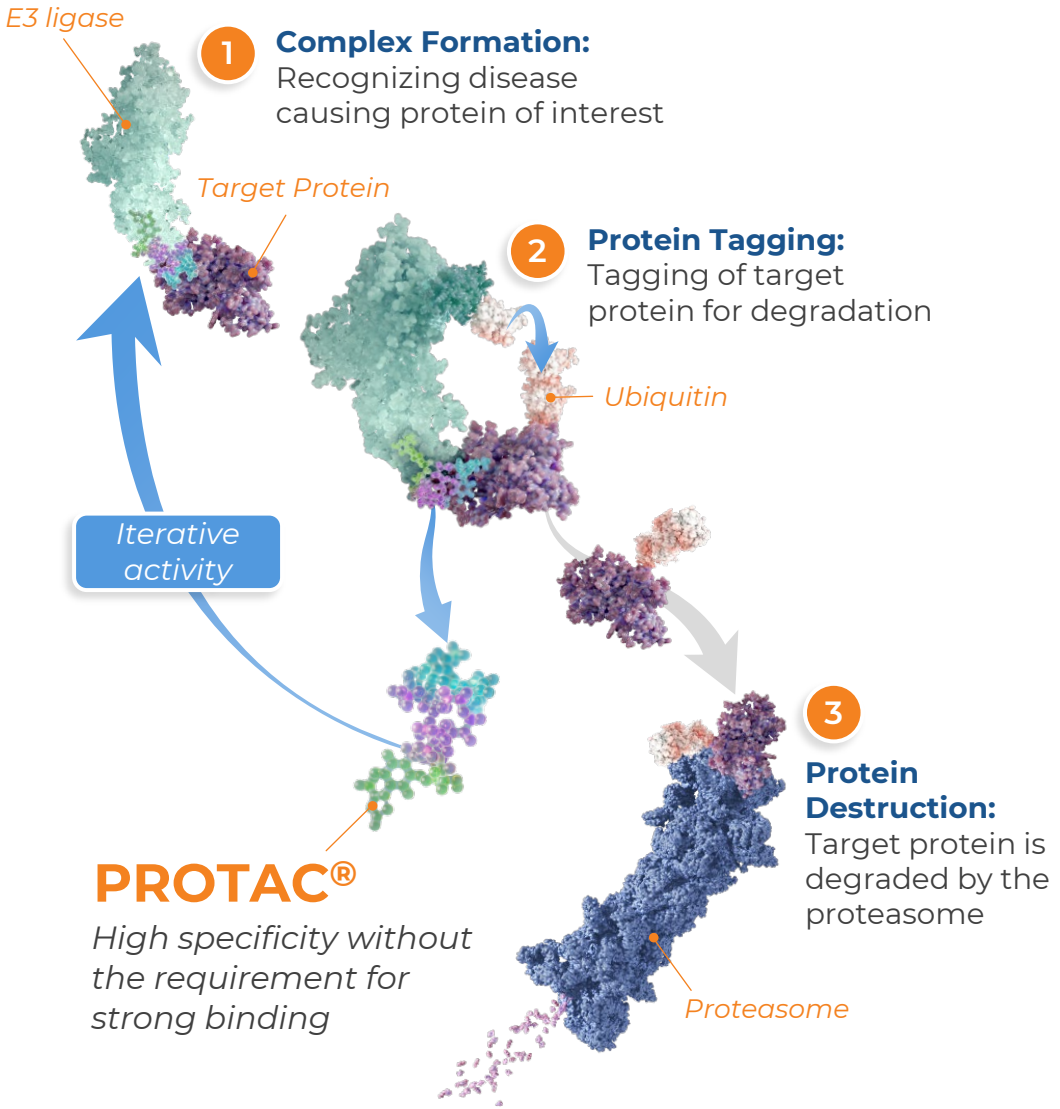
- PROTAC® protein degraders **eliminate** vs. inhibit disease-causing proteins
- Combines the **power of genetic knockdown** technology with the **benefits of small-molecule** therapeutics



DEEP PIPELINE

- **Clear efficacy signals** in patients with difficult-to-treat breast and prostate cancers
  - 2 ongoing Phase 3 trials
  - 10+ ongoing Phase 1 & 2 trials
- **Pipeline of programs** across oncology, neuroscience, hematology, and immuno-oncology

PROTAC® protein degraders combine the benefits of small molecules and gene-based knockdown technologies



Arvinas' proteolysis-targeting chimera (PROTAC®) degraders can:

- Eliminate (rather than inhibit) disease-causing proteins
- Disrupt scaffolding functions of target proteins
- Bind and degrade classically "undruggable" proteins
- Act iteratively (catalytically)
- Be delivered orally and achieve broad tissue distribution, including across the blood-brain-barrier

A History of Pioneering
To transform the treatments of tomorrow

ARVINAS

2001 Arvinas' founder Craig Crews publishes first paper describing PROTAC® degraders

2013 **Arvinas founded** to turn protein degraders into patient therapies

2016 Arvinas creates first oral PROTAC® protein degraders for clinical trial evaluation

2018 Arvinas creates first PROTAC® degraders to **cross blood-brain barrier**

2019 **First** PROTAC® degrader **clinical trials** initiated

2020 **Proof of concept** is achieved for AR and ER PROTAC® degraders

2020 **First Phase 2** trial initiated with AR PROTAC® degrader

2021 **First Phase 2** trial initiated with vepdegestrant

2021 Partnered with Pfizer to co-develop and co-commercialize vepdegestrant

2022 First PROTAC® degrader **Phase 3** trial initiated (vepdegestrant)

2023 IND cleared for BCL6 PROTAC® (ARV-393)

2023 CTA authorized for LRRK2 PROTAC® (ARV-102 - 1st neuroscience candidate)

2024 **First** Phase 1 trial with PROTAC® in development for **neurodegenerative diseases**

The agents mentioned above are currently under investigation; their safety and effectiveness have not yet been established
IND, investigation new drug application; CTA, clinical trial authorization

Our broad pipeline includes the first pivotal trials for PROTAC® degraders

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Program	Therapeutic Area / Indication	Preclinical	Phase 1/1b	Phase 2	Phase 3
Vepdegestrant (ARV-471) Global co-development/ co-commercialization partners with Pfizer	**Oncology:** ER+/HER2- Breast Cancer	★ **VERITAC-2:** vepdegestrant monotherapy 2L+ pivotal trial			
		★ ***Vepdegestrant plus palbociclib and potentially other CDK4/6 inhibitors in 2L[a]***			
		★ **VERITAC-3:** vepdegestrant + palbociclib as 1L combination therapy *(study lead-in)*			
		★ ***Vepdegestrant plus CDK4 inhibitor (PF-07220060) in 1L[a]***			
		VERITAC: vepdegestrant monotherapy dose expansion (2L+)			
		TACTIVE-K: vepdegestrant in combination with CDK4i (PF-7220060)			
		TACTIVE-N: vepdegestrant in neoadjuvant setting (to inform potential adjuvant plan)			
		TACTIVE-U: vepdegestrant in combination with ribociclib, abemaciclib and other targeted therapies			
		TACTIVE-E: vepdegestrant + everolimus			
ARV-766	**Oncology:** Prostate Cancer	★ ***ARV-766 monotherapy (mCRPC)***			
		ARV-766 monotherapy dose expansion (2L+)			
		ARV-766 Phase 1/2 combination with abiraterone (pre-NHA setting)			
ARV-393 (BCL6)	**Hematology**	**Phase 1 dose escalation**			
ARV-102 (LRRK2)	**Neuroscience**	**Phase 1 dose escalation**			
Preclinical programs	**Oncology and Neuroscience**	**20+ programs, including KRAS-G12D/V, AR-V7, Myc, HPK1, Tau, α-Synuclein, and mHTT**			

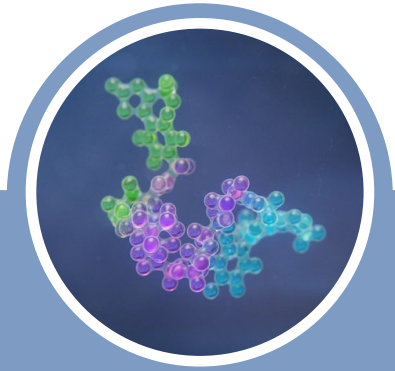
[a] Pending Health authority feedback on potential pivotal trial
NHA, novel hormonal agent
These agents are currently under investigation; their safety and effectiveness for these investigational uses have not yet been established.

★ *Pivotal Trial* ***Planned***

Arvinas' strategy positions us for the next stage of growth

Focused on Near-term Patient Impact

- Planning for multiple launches with vepdegestrant
- Strengthened by a best-in-class pipeline and research engine



Data-driven Approach to Resource Allocation

- Choose and invest in highest value drivers
- Use BD to enhance the value of our pipeline
- Invest for commercial success

Strong Capitalization

- Backed by a cash runway into 2027
- Capital to support us through the first years of our planned commercial launch

CLINICAL PROGRAMS

Vepdegestrant

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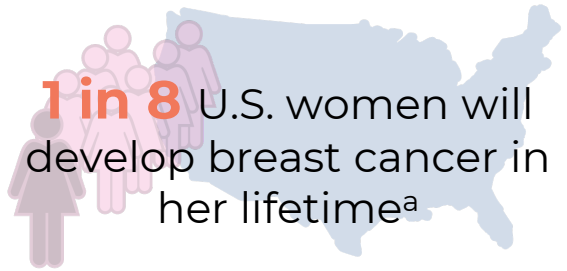
Pfizer

Vepdegestrant (ARV-471): First-in-class estrogen receptor (ER)-degrading PROTAC® in advanced breast cancer



1 in 8 U.S. women will develop breast cancer in her lifetime[a]

~80% of all newly diagnosed cases of breast cancer are ER-positive (ER+)[b]

Vepdegestrant is currently being evaluated in **two Phase 3 trials** in metastatic breast cancer

Vepdegestrant has the potential to become an oral, best-in-class targeted therapy

Vepdegestrant degrades **wild-type and ESR1-mutant** estrogen receptors (ER) to directly inhibit signaling pathways

More than **600 patients and healthy volunteers** have been treated with vepdegestrant across 12 clinical trials

Consistent and compelling data in **heavily pre-treated patients**

Vepdegestrant could be a backbone ER therapy in the ~$17B ER+/HER2- metastatic breast cancer space[c]

Vepdegestrant is an investigational compound. Its safety and efficacy has not been established

[a] ACS: https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html; accessed 01/06/24; [b] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4549764/, accessed 01/06/2024

[c] Clarivate/Decision Resources Group – Breast Cancer Disease Landscape & Forecast (Nov 2023). 2032 Projection.

ER, estrogen receptor; HER2, human epidermal growth factor 2; ESR1, estrogen receptor 1 gene

Our Phase 3 VERITAC-2 monotherapy trial in the 2L+ setting is on track for topline data in 2H24

Two ongoing monotherapy trials:

- VERITAC-2: Phase 3 trial
- VERITAC: Phase 2 trial (enrollment complete, N=71)
  - At RP3D (200mg), vepdegestrant showed favorable safety profile, with <6% Grade 3+ TRAEs, no dose reductions, and low rate of discontinuations

VERITAC Phase 2 subset analysis:

- In the 8 patients in VERITAC who would meet the eligibility criteria for the Phase 3 VERITAC-2 trial (*no prior fulvestrant, no prior chemotherapy for locally advanced/metastatic disease*)[a]:
  - **CBR: 62.5% (5 of 8 patients)**
  - **mPFS: 19 months (4 of 8 events)**
  - **ORR: 29% (7 evaluable patients, 2 confirmed responses)**

Study design for Phase 3 VERITAC-2
(Enrolling, NCT05654623)

Treatment (N = 560)

Randomize 1:1

Vepdegestrant
200 mg orally once daily

Fulvestrant
500 mg intramuscularly
Days 1 and 15 of cycle 1 and Day 1 of subsequent cycles

Select Patient Eligibility Criteria	Primary Endpoints
• Prior CDK4/6 inhibitor treatment • No prior fulvestrant • No prior chemotherapy for locally advanced / metastatic disease	Progression Free Survival (PFS) by Blinded Independent Central Review in: ○ ESR1 mutant population ○ All Comers (Intention To Treat) population

[a] Data cutoff, June 6, 2023;.Post-hoc analysis
RP3D, recommended phase 3 dose; TRAE, treatment related adverse events; CBR, clinical benefit rate; mPFS, media progression-free survival; ORR, objective response rate; ESR1, estrogen receptor 1; CDK, cyclin-dependent kinase

Our 1L Phase 3 VERITAC-3 trial in combination with palbociclib is currently enrolling its study lead-in

VERITAC-3 Phase 3 trial design (NCT05909397)

Study lead-in (SLI) N=50 | Randomized w/comparator arm (N~1130)

Randomize 1:1

Open-label SLI to assess:

- rate of Grade 4 neutropenia
- dose reductions
- dose discontinuations

Cohort A: Vepdegestrant 200 mg + palbociclib 100 mg (N=25)
Palbociclib 100 mg daily 3/1 schedule + vepdegestrant 200 mg daily in 28-day cycle

Cohort B: Vepdegestrant 200 mg + palbociclib 75 mg (N=25)
Palbociclib 75 mg daily 3/1 schedule + vepdegestrant 200 mg daily in a 28-day cycle

Selection of palbociclib dose (100 or 75 mg) with 200 mg vepdegestrant

Randomize 1:1
Open Label

Investigational Arm
Vepdegestrant + palbociclib (N ≈ 565)
Vepdegestrant 200 mg in 28-day cycle + palbociclib at determined dose

Comparator Arm
Letrozole + palbociclib (N ≈ 565)
Palbociclib 125 mg daily 3/1 schedule + letrozole daily in a 28-day cycle

Key Exclusion Criteria	Primary Endpoint
• Prior adjuvant CDK 4/6i • Primary/secondary endocrine resistance • Visceral crisis	• Progression Free Survival (PFS) by Blinded Independent Central Review (BICR)

CDK, cyclin-dependent kinase

Results from Phase 1b trial with vepdegestrant + palbociclib presented at SABCS 2023

Efficacy benchmarks in CDK4/6i after CDK4/6i trials

Data below are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population and many other factors

	PACE[1] Palbo/fulvestrant after CDK4/6i	BioPER[2] Palbo/PC after CDK4/6i	MAINTAIN[3] Ribo/ET after CDK4/6i	PALMIRA[4] Palbo/ET after CDK4/6i	Vepdeg + palbo P1b
Prior CDK4/6i	100%	100%	100%	100%	87.0%
Prior chemo for mBC	14.4%	12.5%	6.7%	0%	45.7%
Prior fulvestrant	0%	43.8%	16.8%	11.8%	80.0%
Overall Response Rate (Evaluable)[a]	13.7% (n=73)	6.3% (n=32)	20.0% (n=35)	6.4% (n=94)	41.9% (n=31)
Clinical Benefit Rate (Evaluable)	32.4% (n=111)	34.4% (n=32)	42.9% (n=49)	41.9% (n=136)	63.0% (n=46)
Progression-Free Survival Median (95% CI), months	4.6 (3.6–5.9) (n=111)	2.6 (1.8–6.7) (n=32)	5.3 (3.0–8.1) (n=60)	4.9 (3.6–6.0) (n=136)	11.1 (8.2–NR) (n=46)

Data presented at SABCS2023

[a] Patients with measurable disease at baseline (two patients in the vepdeg + palbo P1b trial had an unknown ESR1 status and both were non-responders)

CDK, cyclin-dependent kinase; mBC, metastatic breast cancer; ET, endocrine therapy; NR, not reached; PC, physician's choice endocrine therapy;

[1.] Mayer E et al SABCS 2022. [2.] Albanell J et al. Clin Cancer Res 2023. [3.] Kalinsky K et al. J Clin Oncol 2023. [4.] Llombart-Cussac A et al. ASCO 2023.

Safety/tolerability in Phase 1b trial

- Safety was manageable, with standard on-label dose reductions of palbociclib resulting in a 72% decline in Grade 4 neutropenia in subsequent cycles
- **No febrile neutropenia,** low rates of discontinuation
  - Among 36 pts who had at least one palbociclib dose reduction, only 5 (13.9%) had Grade 4 neutropenia after last palbociclib dose reduction

Expanded clinical program designed to position vepdegestrant as a backbone ER-targeting therapy in breast cancer

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Pfizer

Adjuvant (Post-Surgical) Breast Cancer in US (~190K[1])

Metastatic Breast Cancer in US (~60K[1])

TACTIVE-N neoadjuvant trial
to inform potential adjuvant trial

First Line

VERITAC-3 combination
pivotal trial (SLI enrolling)
- vepdeg + palbo combo

Second/Third Line

VERITAC-2 monotherapy
pivotal trial

TACTIVE-E: in combination with everolimus

TACTIVE-K: in combination with CDK4i (PF-07220060)

TACTIVE-U: in combination with ribo/abema/CDK7i

Active Trials

Planned trials[a]

Pending further data and regulatory agreement:

Planned: *Pivotal*
Vepdeg+CDK4i (PF-7220060) combination

New

Planned: *Pivotal* Vepdeg combo with palbo and potentially other CDK4/6i

New

[a]Pending health authority feedback on potential pivotal trials
CDK, cyclin-dependent kinase; SLI, study lead-in
[1]. Kantar Cancer MPact Patient Metrics (accessed Nov. 2023)

CLINICAL PROGRAMS

ARV-766

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Arvinas' PROTAC® degraders eliminate the androgen receptor (AR), potentially surpassing the benefits of AR inhibitors

1 in 8 U.S. men will be diagnosed with prostate cancer during their lifetime[a]

Prostate cancer is the **2nd leading cause of cancer death** for men in the U.S.[a]

An AR-targeting PROTAC degrader may address the unmet needs of patients with prostate cancer across multiple stages of disease

AR is a critical target in prostate cancer, but tumors develop resistance to standard-of-care AR inhibitors

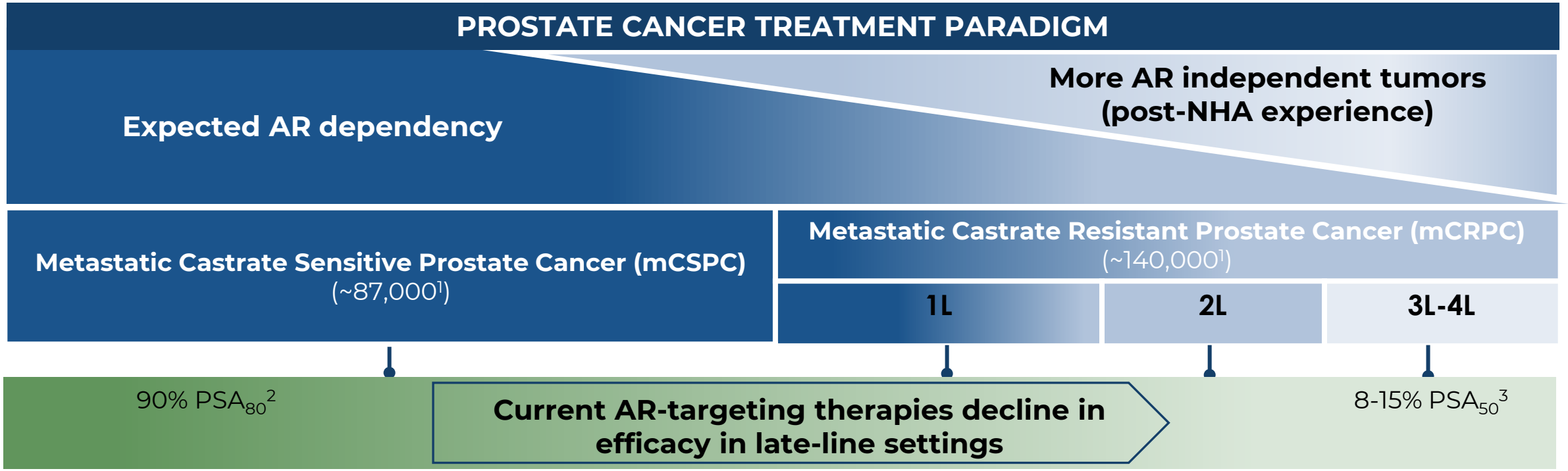
ARV-766, our second-generation PAN AR-targeting PROTAC degrader, has demonstrated an excellent tolerability profile and improved efficacy profile compared to our first-generation AR PROTAC degrader (bavdegalutamide)

ARV-766's activity in late-line settings suggests additional potential benefit in earlier-line, less-pretreated patients

[a] "Key Statistics for Prostate Cancer," American Cancer Society, www.cancer.org/cancer/prostate-cancer/about/key-statistics.html, accessed 01/06/24

AR, androgen receptor

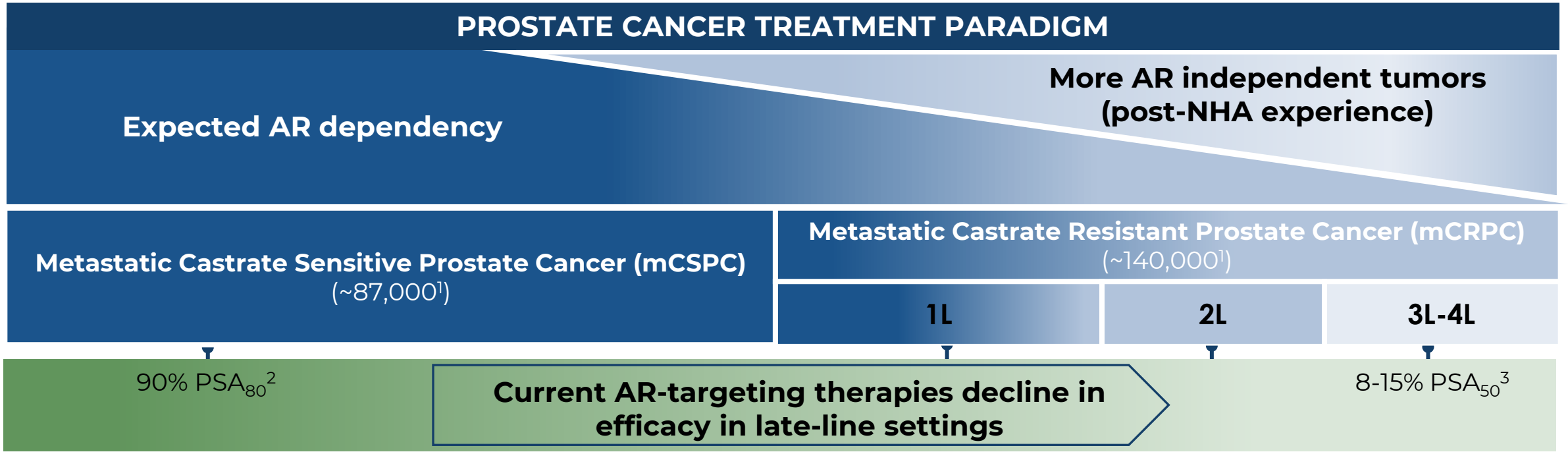
AR-targeting PROTAC® degrader could meet the substantial unmet need across the prostate cancer treatment paradigm



Unmet need remains for **well-tolerated therapies** that **overcome resistance mechanisms, extend survival** and provide **durable responses**

AR, androgen receptor; NHA, novel hormonal agent; PSA, prostate-specific antigen; PSA_{80}, best PSA decline ≥ 80%; PSA_{50}, best PSA decline ≥ 50%
[1] Kantar 2023 Epidemiology Database; includes US, EU4, UK, and Japan. [2] Tombal, Lancet Oncology 2014; [3] deWit R N Engl J Med. 2019; Hussain, ESMO 2019

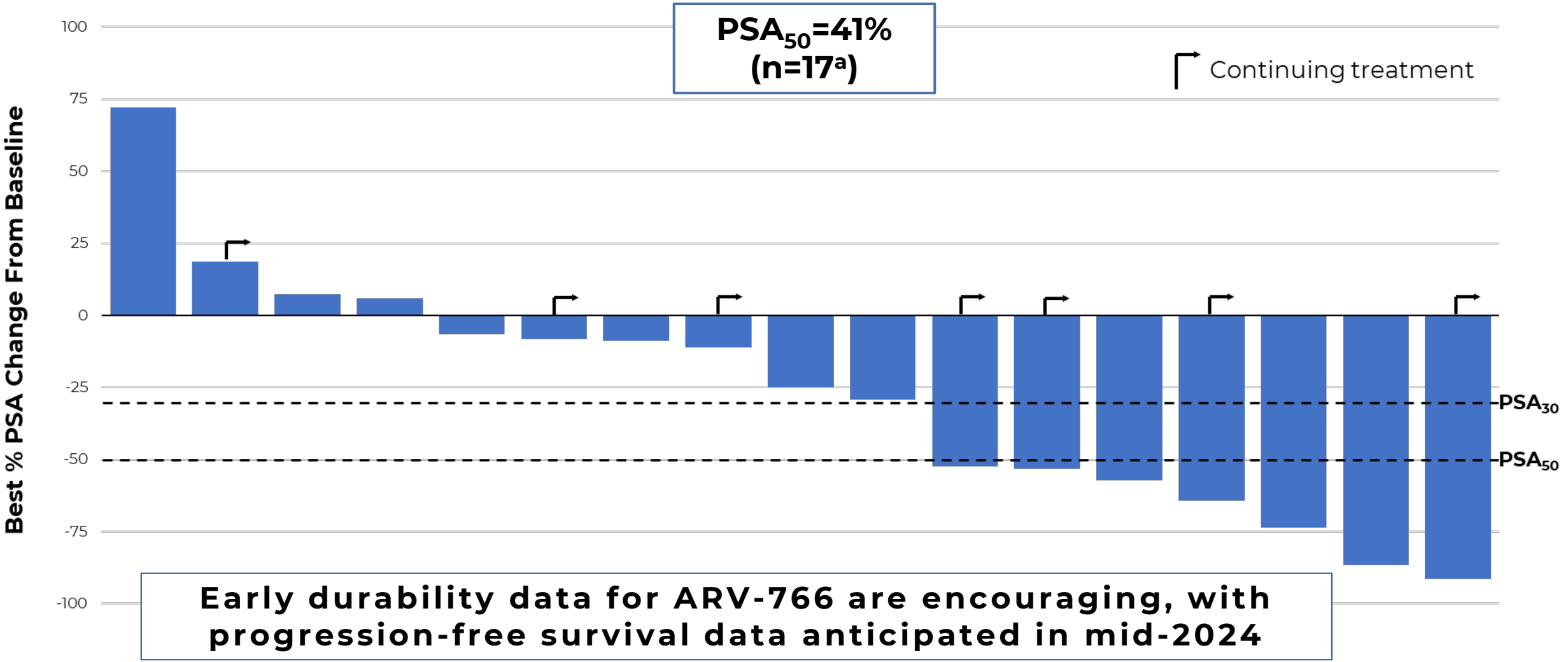
AR-targeting PROTAC® degrader could meet the substantial unmet need across the prostate cancer treatment paradigm



- Our *first generation* PROTAC® AR degrader (bavdegalutamide) demonstrated **strong antitumor activity in 3L+ patients with T878/H875 AR LBD mutations (11.1 month rPFS)**
- Arvinas has selected our ***second generation* PROTAC® AR degrader ARV-766** to advance into Phase 3 trials due to a **broader efficacy profile** and **better tolerability** vs. bavdegalutamide, making it well suited for both mCRPC and mCSPC patients.

AR, androgen receptor; LBD, ligand binding domain; NHA, novel hormonal agent; PSA, prostate-specific antigen; PSA_{80}, best PSA decline ≥ 80%; PSA_{50}, best PSA decline ≥ 50%
[1] Kantar 2023 Epidemiology Database; includes US, EU4, UK, and Japan; [2] Tombal, Lancet Oncology 2014; [3] deWit R N Engl J Med. 2019; Hussain, ESMO 2019

ARV-766 shows promising efficacy signals in heavily pretreated mCRPC patients with AR LBD mutations who have progressed on a prior NHA



[a] 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
mCRPC, metastatic castrate-resistant prostate cancer; AR, androgen receptor; LBD, ligand-binding domain; PSA, prostate-specific antigen; PSA_{30}, best PSA declines ≥30%; PSA_{50}, best PSA declines ≥50%; NHA, novel hormonal agent

ARV-766's excellent tolerability profile is well-suited for both late-and early-line settings

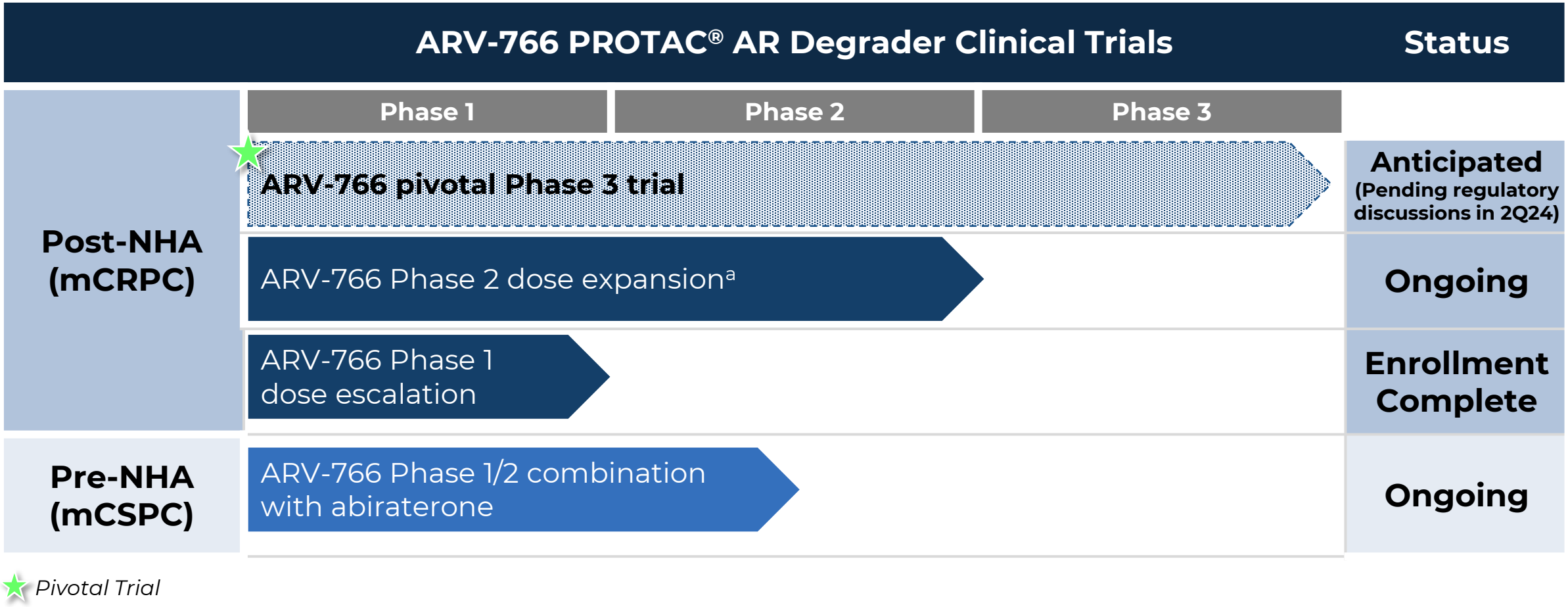
ARV-766 has been well tolerated to date

- Majority of treatment related adverse events (TRAEs) are Grade 1 or 2, with no Grade ≥4 TRAEs
- Low rates of discontinuation or dose reduction

TRAE ≥10% n (%)	ARV-766 (N=84[a])	
	Any Grade	Grade 3+
Any TRAE	55 (66)	7 (8)
Fatigue	24 (29)	2 (2)
Nausea	12 (14)	0 (0)
Diarrhea	9 (11)	1 (1)
Vomiting	9 (11)	0 (0)
Decreased appetite	9 (11)	0 (0)
Alopecia	8 (10)	0 (0)
Any TRAE leading to discontinuation	3 (4)	

[a] As of August 23, 2023

Ongoing clinical development program for ARV-766 in the post-and pre-NHA settings



[a] Progression free survival data anticipated in 2024

NHA, novel hormonal agent; AR, androgen receptor; mCSPC, metastatic castrate-sensitive prostate cancer; mCRPC, metastatic castrate-resistant prostate cancer

Preclinical Programs

ARVINAS

Advancing an industry leading preclinical pipeline of PROTAC® degraders

We have the **deepest and most diverse pipeline** of any protein degradation company

The capabilities of our PROTAC® **platform remain unmatched**

Arvinas' pipeline is differentiated and sustainable

Initiating two new first-in-human trials in 1H 2024

- ***LRRK2*-targeting PROTAC *ARV-102* reaches and degrades in deep brain regions (Phase 1 trial enrolling)**
- ***BCL6*-targeting PROTAC *ARV-393* addresses a historically undruggable target (IND cleared)**

LRRK2, Leucine-rich repeat kinase 2; BCL6, B-cell lymphoma 6

We expect ARV-393, our BCL6 PROTAC® degrader, to be a first-in-class potential therapy for non-Hodgkin Lymphoma

BCL6 is genetically mutated in up to 85% of DLBCL[1], a subset of Non-Hodgkin Lymphoma

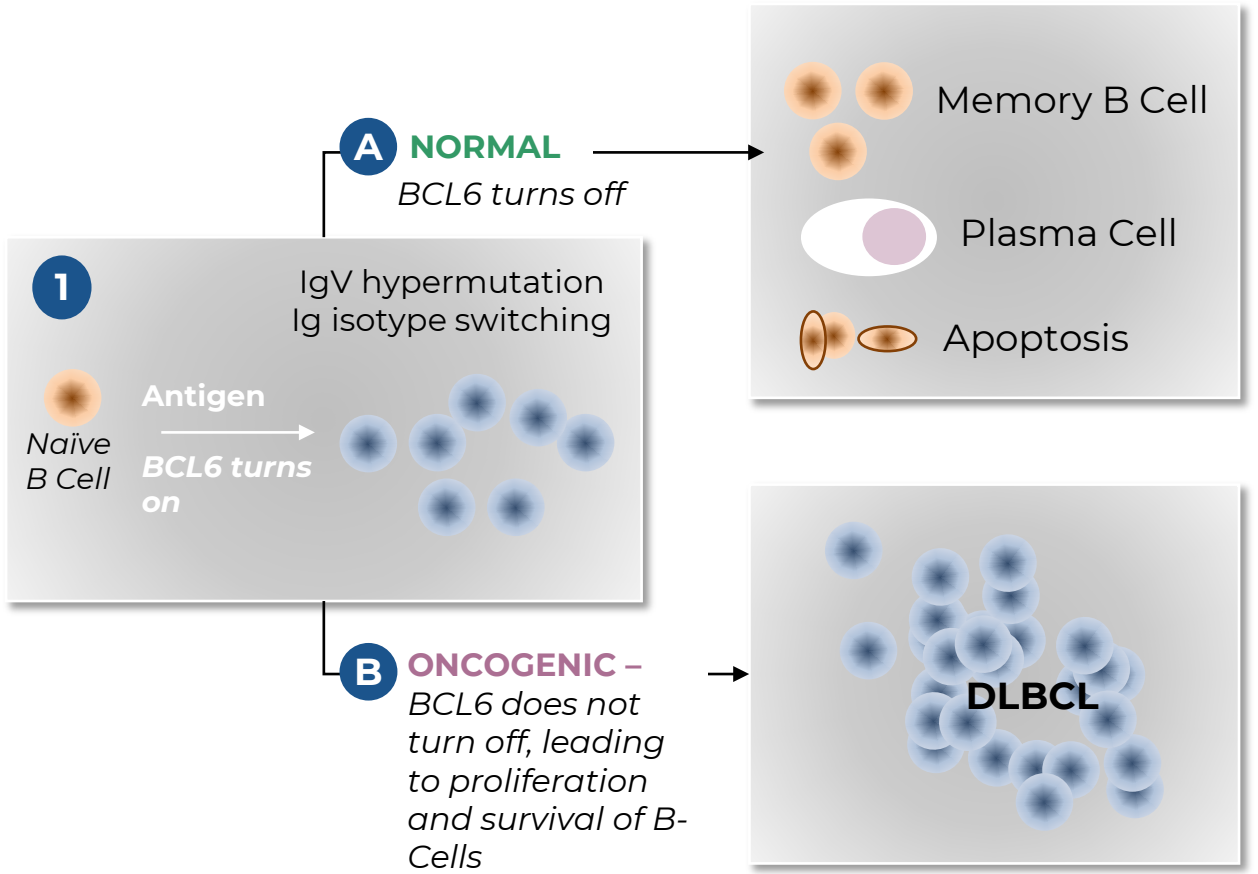
More than 74,000 people are diagnosed with DLBCL each year[2]

DLBCL is largely devoid of oral options; no BCL6-targeted therapy on the market

Additional opportunities for a BCL6 degrader exist in Burkitt's Lymphoma, Follicular Lymphoma, Angioimmunoblastic T-cell lymphoma, and solid tumors

IND cleared for ARV-393
Phase 1 trial initiation anticipated in 1H24

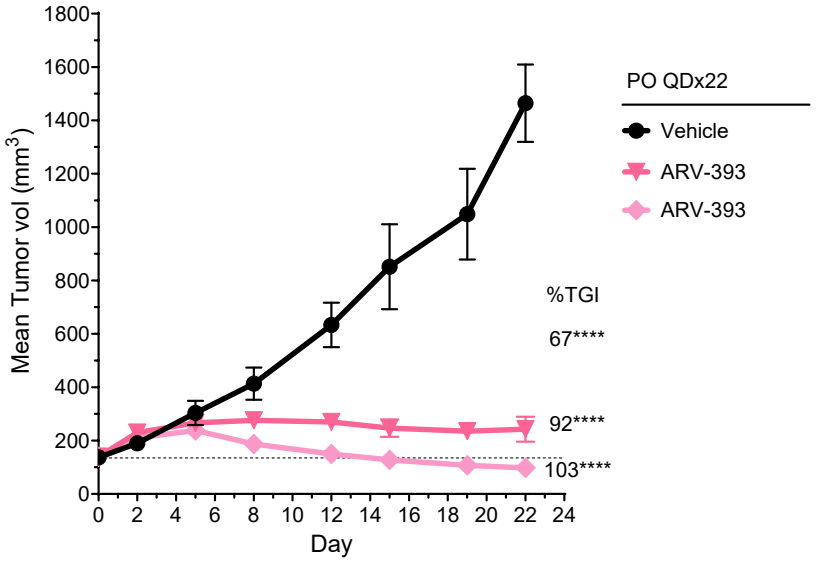
The role of BCL6 in driving DLBCL[3]



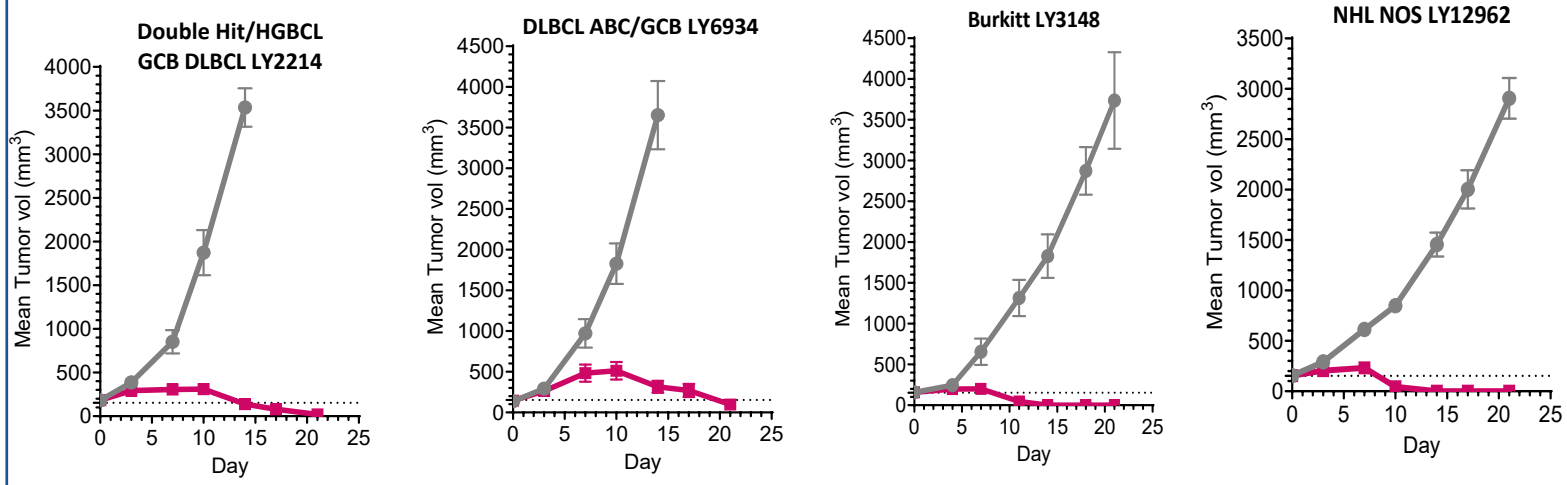
BCL6, B-cell lymphoma 6; DLBCL, diffuse large B cell lymphoma; Ig, immunoglobulin; IND, investigational new drug application
[1]. J Iqba et. al., 2007; [2].2023 Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia Disease Landscape & Forecast Report from Decision Resources; includes US, EU4, UK, and Japan
[3]. Figure adapted from Pasqualucci et. al., 2003 (figure at bit.ly/3Q8IGHH)

ARV-393 shows robust tumor inhibition in a DLBCL model and in models of multiple subtypes of Non-Hodgkin's Lymphoma

Cell line-derived xenograft (CDX) model
OCI-LY1 GCB DLBCL



Breadth of efficacy beyond DLBCL demonstrated in multiple patient-derived xenograft (PDX) models with no body weight loss[a]



4 mice/group, PO QDx21
Vehicle
ARV-393

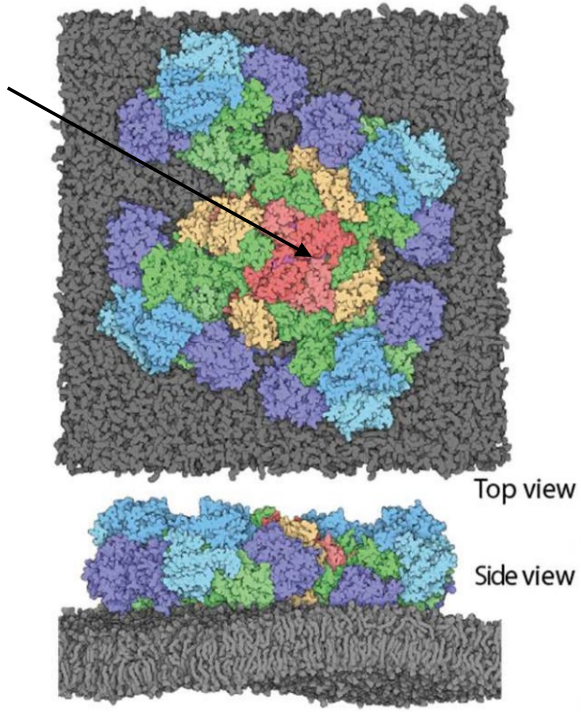
[a] Body weights not shown
NHL, non-Hodgkin's lymphoma; NOS, not otherwise specified; DLBCL, diffuse large B-cell lymphoma; HGBCL, high grade B-cell lymphoma; GCB, germinal center B-cell; ABC, activated B-cell; TGI, tumor growth inhibition

KRAS-targeting PROTAC® may provide a significant advance in treatment for multiple cancers

- KRAS has few druggable “pockets,” challenging traditional inhibitors
- KRAS also exists in a multi-protein (scaffolding) complex, limiting access to drugs
- KRAS mutations are highly prevalent in pancreatic (~90%), colorectal (~35%), and non-small cell lung cancers (~25%)[1-4]

KRAS G12D-targeted PROTAC degrader currently in IND-enabling studies

KRAS (in red) is surrounded by other proteins (other colors), and binding is often occluded



Mysore et al., BioRxiv, 2020

KRAS, frequently mutated oncogene in cancers; G12D, mutations in codon 12 on KRAS oncogene

[1]Lee, *et al.* npj Precis. Onc. 2022. [2]Cook *et al.* Nat Comm 2021. [3]Prior *et al.* Cancer Research 2020. [4]NIH TCGA: https://www.cbioportal.org

KRAS G12D-targeting PROTAC® demonstrates robust tumor growth inhibition with every other week dosing

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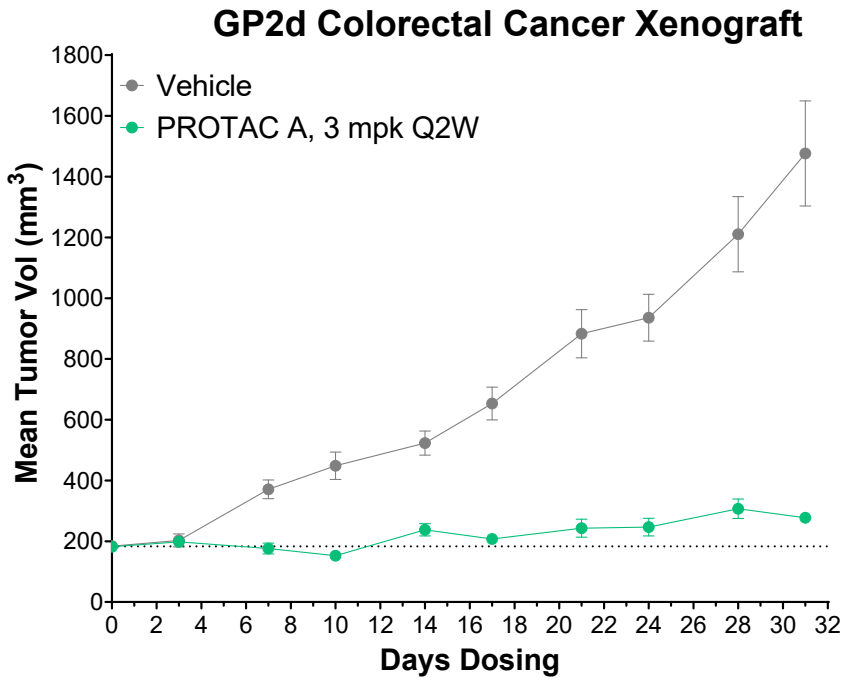
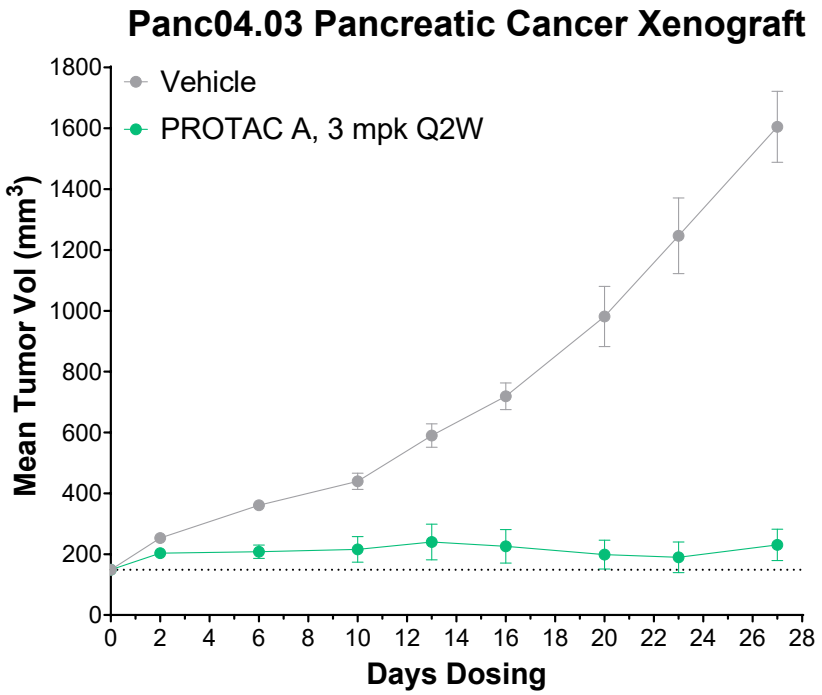
Colorectal cancer xenograft model



Pancreatic cancer xenograft model

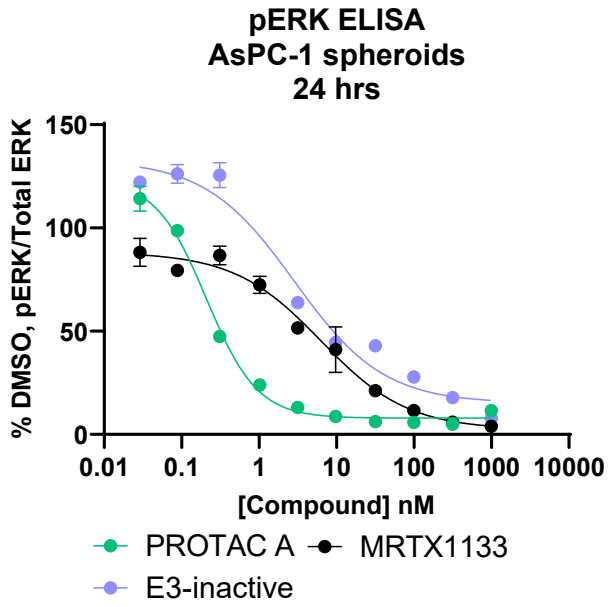


KRAS, frequently mutated oncogene in cancers; G12D, mutations in codon 12 on KRAS oncogene; mpk, milligrams per kilogram; Q2W, once every 2 weeks

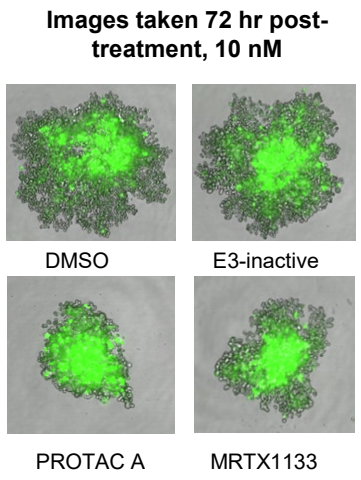
KRAS G12D-targeting PROTAC® potently suppresses signaling and proliferation versus an inhibitor

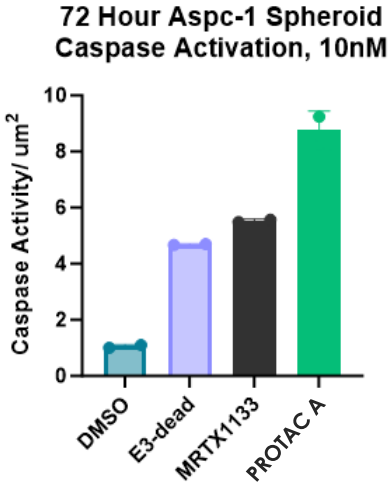
KRAS G12D-targeting PROTAC demonstrated potent outcomes in multiple measures of cancer cell inhibition while inducing cell apoptosis

MAPK Signaling
PROTAC **30-fold** more potent

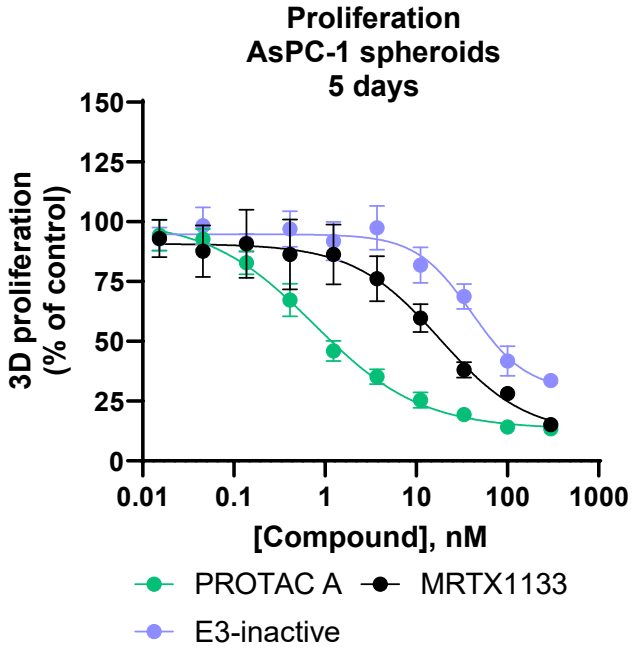


Spheroid size reduction and apoptosis induction





Proliferation
PROTAC **30-fold** more potent



KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); G12D, mutations in codon 12 on KRAS oncogene; MAPK, Mitogen-activated protein kinase

PROTAC® degraders could revolutionize the treatment of patients with neurological diseases

Arvinas can engineer oral PROTAC® degraders that:

- ✓ **Cross the blood-brain barrier**
- ✓ **Reach targets in "deep brain" regions**
- ✓ **Degrade disease-causing proteins inside cells**
- ✓ **Differentiate between mutant and wild-type proteins, e.g., mutant huntingtin**

Currently enrolling Phase 1 trial with ARV-102, the first oral PROTAC® in development to treat neurodegenerative diseases

LRRK2, Leucine-rich repeat kinase 2; CTA, clinical trial application

PROTAC®-induced LRRK2 degradation as a potential treatment for idiopathic Parkinson's Disease and Progressive Supranuclear Palsy

ARVINAS

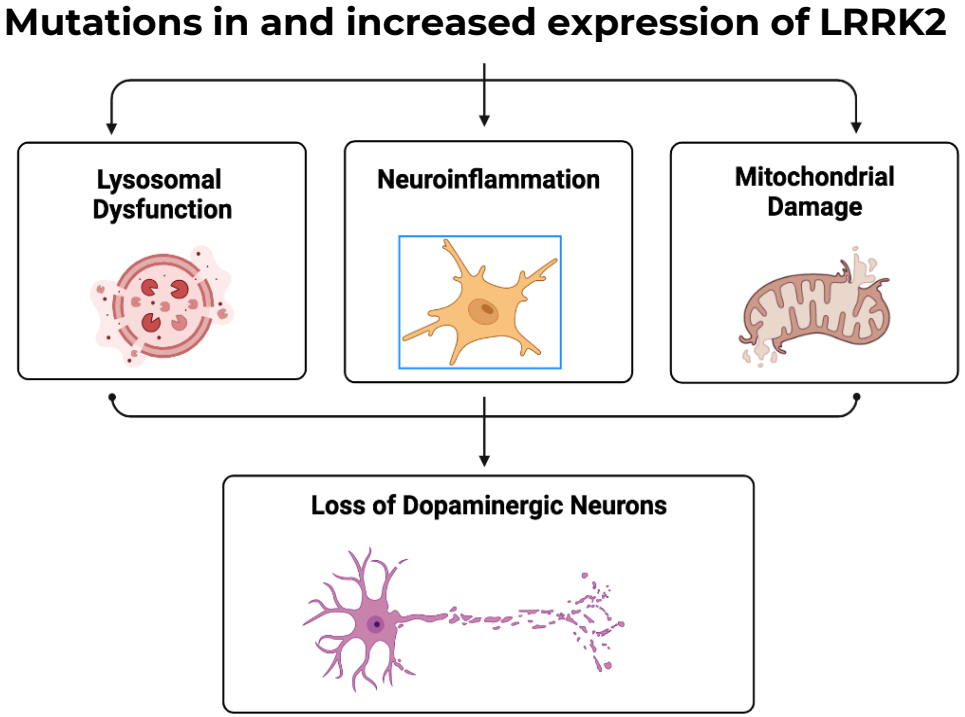
Human genetics and biology create a strong rationale for differential biology of PROTAC® LRRK2 degraders

- **LRRK2 is a large multidomain scaffolding kinase**

- **Parkinson's Disease (PD)** has a diagnosed prevalence of ~1M in the US, with more than 10M worldwide[1]
  - No approved disease-modifying therapies for PD
  - Familial mutations and sporadic variants implicate LRRK2 in PD

- **Progressive Supranuclear Palsy (PSP)** is a pure tauopathy with rapid progression to death within 5-7 years
  - No approved therapies for PSP
  - LRRK2 genetic variants associated with accelerated progression time to death

- LRRK2 kinase inhibitors and an ASO in clinical trials



LRRK2, Leucine-rich repeat kinase, ASO, antisense oligonucleotide

[1] Parkinson's Foundation. *Who has Parkinson's?* https://www.parkinson.org/understanding-parkinsons/statistics, accessed 01/06/24

Arvinas' oral PROTAC® LRRK2 degrader reaches multiple "deep brain" regions in non-human primates and degrades LRRK2

Arvinas PROTAC degraders can be engineered to reach multiple regions of the brain

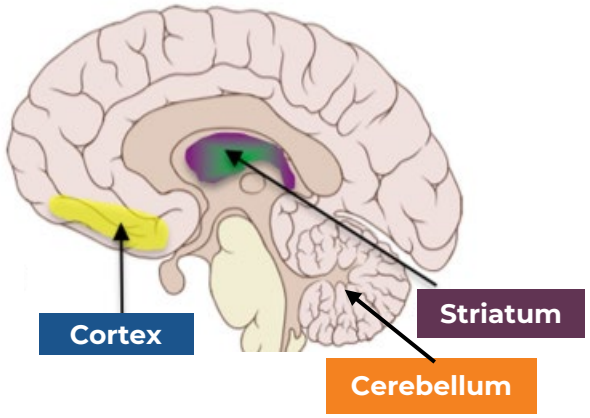
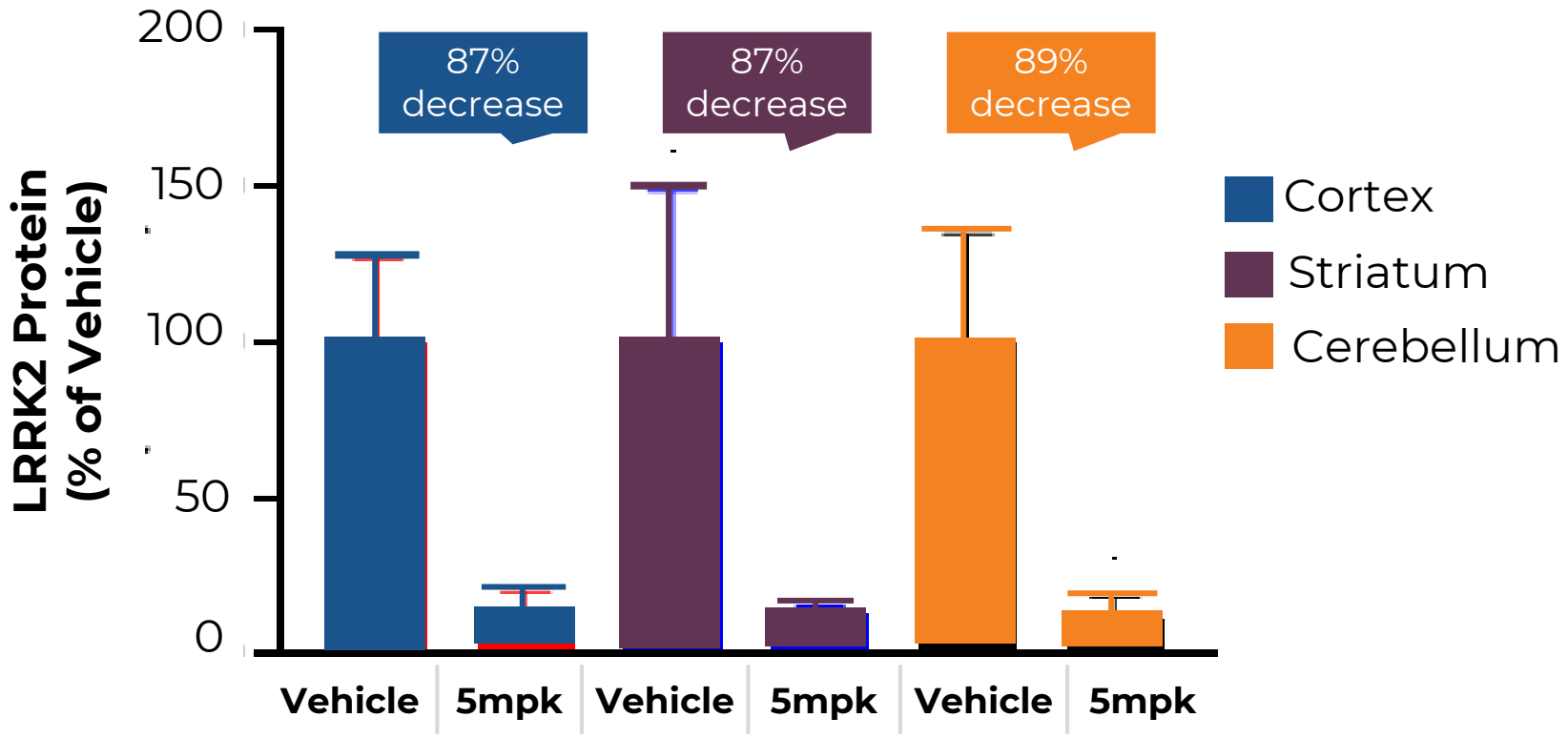


Figure modified from Beuriat et al. 2022

>85% LRRK2 degradation in deep brain regions of cynomolgus monkeys after oral dosing



LRRK2, leucine-rich repeat kinase 2; mpk, milligrams per kilogram

PROTAC® LRRK2 degrader shows better target engagement, enhanced potency and pathway engagement versus a LRRK2 inhibitor

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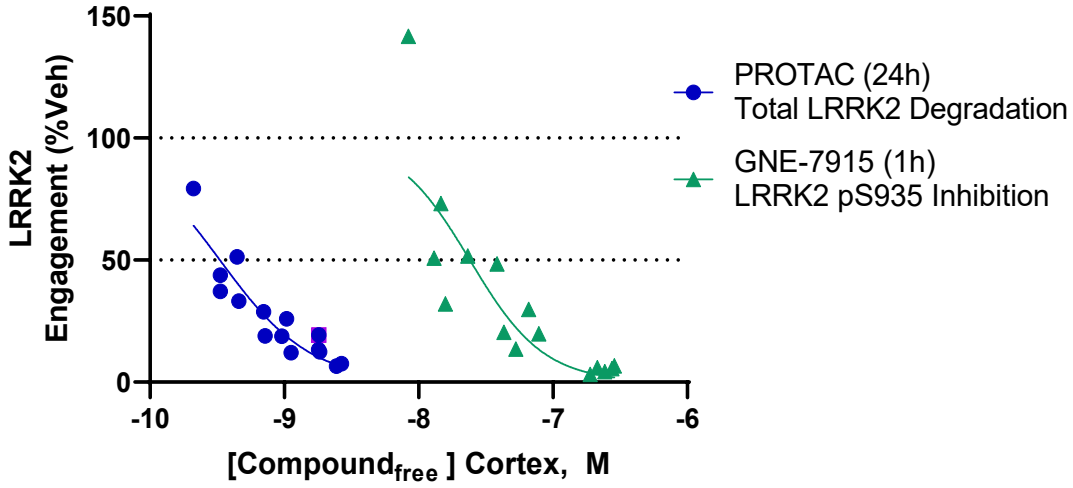
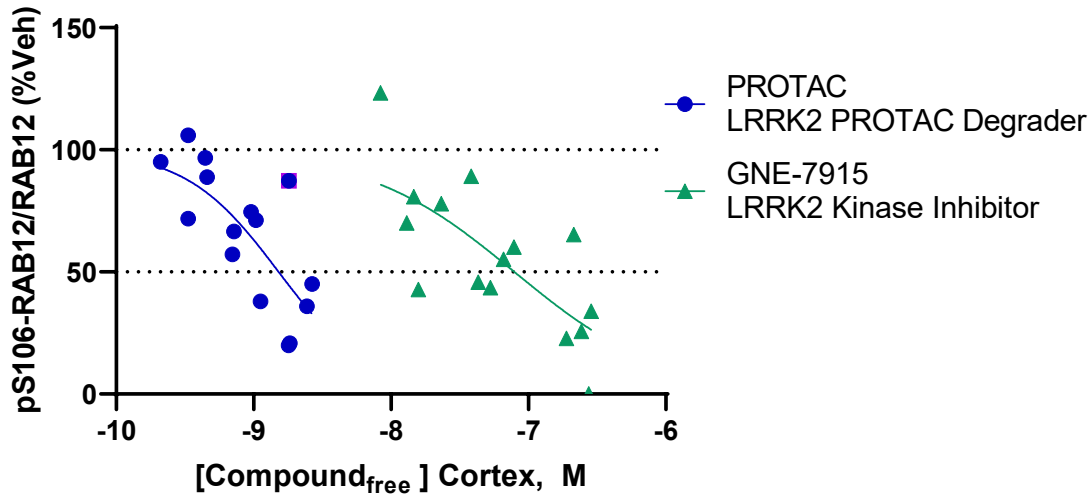
Iterative (catalytic) PROTAC® advantage results stronger LRRK2 and lysosomal pathway engagement vs. a LRRK2 inhibitor[a]

LRRK2 PROTAC vs. Kinase inhibitor (Tmax)



Lysosomal Pathway Engagement (LRRK2 PROTAC vs. Inhibitor)

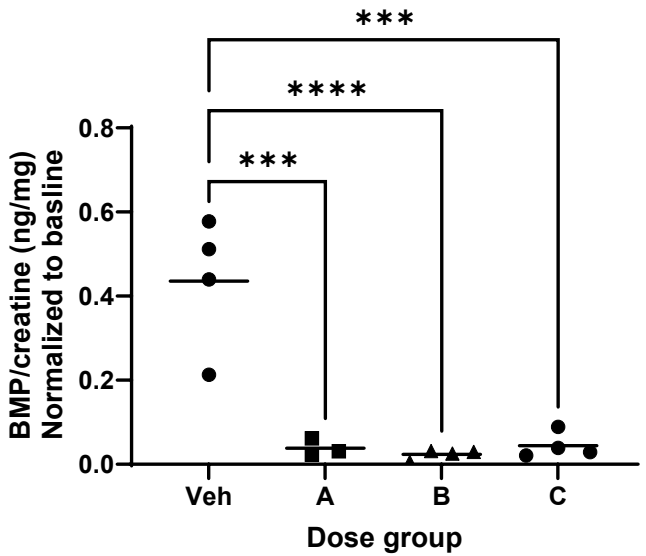


[a] G2019S familial Parkinson's Disease mouse model
LRRK2, Leucine-rich repeat kinase 2

Our LRRK2 degrader induces biomarker changes that reinforce confidence in the PROTAC® MoA in the brain and periphery

PROTAC-induced reductions observed in key lysosomal marker in cynomolgus monkey

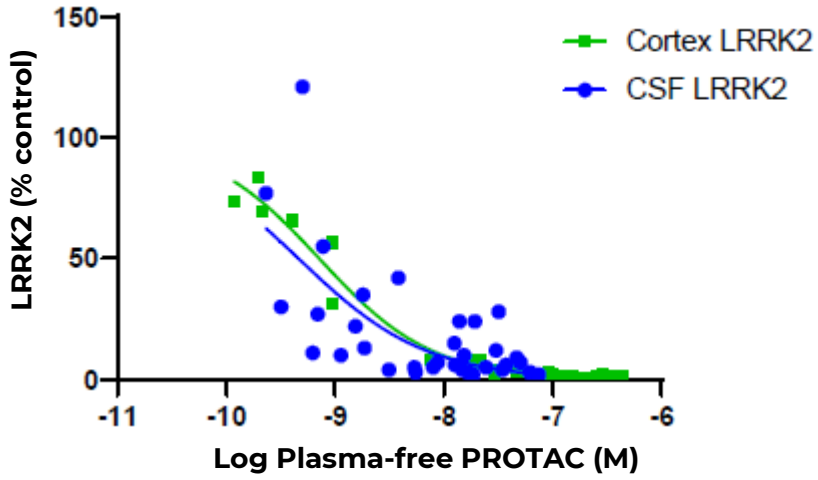
BMP reductions in cynomolgus monkeys



BMP levels were measured by UPLC-MS/MS and normalized to creatinine and then expressed relative to baseline.

PK/PD of LRRK2 reduction in cortex and CSF following oral dosing in cynos

CSF LRRK2 reductions in cynomolgus monkeys; surrogate compartment for brain



Equivalent PK/PD supports the utility of measuring CSF LRRK2 as a surrogate for monitoring LRRK2 reductions in the brain.

LRRK2, Leucine-rich repeat kinase 2; PK/PD, pharmacokinetic-pharmacodynamic; CSF, cerebrospinal fluid; BMP, basic metabolic panel; ULPC, ultra high-performance liquid-chromatography; MS, mass spectrometry

Strategically positioned to benefit patients in the years ahead across multiple areas of unmet need

ARVINAS

Vepdegestrant provides a path to multiple potential launches

- ✓ VERITAC-2 Ph3 2L+ monotherapy trial on track to complete enrollment in 2H24 (topline data dependent on event rate)
- ✓ Ph3 1L combo with palbociclib dose selection expected in 2H24
- ✓ Ph3 2L combination trial (pending HA feedback)
- ✓ Ph3 1L combination with CDK4i (pending HA feedback)

Strengthened by a best-in-class R&D engine

- ✓ Initiation of ARV-766 mCRPC Ph 3 trial (following HA feedback)
- ✓ Enrolling Ph1 trial with ARV-102, first PROTAC in development for neurodegenerative diseases
- ✓ Initiation of BCL6 Ph1 dose escalation study expected in 1H2024
- ✓ KRAS G12D-targeted PROTAC degrader currently in IND-enabling studies
- ✓ Goal to nominate 1 clinical candidate per year

Strong capital position

- ✓ Cash runway into 2027
- ✓ $350M PIPE financing (oversubscribed) announced November 2023
- ✓ ~$1.3B cash on hand[a]
- ✓ Key program catalysts expected in 2024 and 2025

[a] Cash, cash equivalents, and marketable securities as of December 31, 2023
HA, health authority; CDK, cyclin-dependent kinase; mCRPC, metastatic castrate-resistant prostate cancer; IND, investigational new drug application

Thank You

For More Information

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