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: Arvinas' potential receipt of milestone or other payments from existing partners, including Novartis and Rigel; PROteolysis TAargeting Chimera ("PROTAC") protein degraders having potential benefits that may provide advantages over other modalities in oncology and neurology; whether Arvinas' product candidates will address two areas of significant unmet need for patients, oncology and neurology; Arvinas' plans and expectations related to its clinical trials and preclinical studies and the timings associated therewith with respect to initiation of trials or studies and presentation of data; Arvinas' assets' intended differentiation from other therapies; Arvinas' capitalization, and having cash runway into the second half of 2028; the continued potential for future partnerships to enhance the value of Arvinas' pipeline; Arvinas' novel PROTAC approach having first-in-class promise and potential to differentiate from existing and emerging modalities in, and potentially revolutionize the treatment of, neurodegenerative diseases; PROTAC-induced leucine-rich repeat kinase 2 ("LRRK2") degradation having the potential to differentiate from kinase inhibition; PROTAC-induced LRRK2 degradation as a potential treatment for progressive supranuclear palsy, Parkinson's disease and related diseases; that a PROTAC expanded polyglutamine androgen receptor degrader may eliminate the root cause of disease for spinal bulbar muscular atrophy; Arvinas' plans, anticipated milestones, timings and potential impacts of such milestones, related to its neurology pipeline candidates, including ARV-102 and ARV-027; the potential for ARV-806, Arvinas' novel PROTAC Kirsten rat sarcoma ("KRAS") G12D degrader, to be a best-in-class therapy for patients with KRAS G12D mutated cancers and to address high unmet need in solid tumors, such as pancreatic, colorectal and non-small cell lung cancer; the potential for a PROTAC B-cell lymphoma 6 ("BCL6") degrader to address substantial unmet needs for patients with non-Hodgkin Lymphoma ("NHL"); the potential for ARV-393 to become an attractive combination partner for development of novel treatment approaches for NHL, including all oral or chemotherapy-free options; the potential for ARV-6723, an oral hematopoietic progenitor kinase 1 ("HPK1") degrader, to offer sustained anti-tumor immune response as a single agent or in combination with standard of care therapies, and the potential to result in improved clinical benefits over standard of care across a wide range of cancers; Arvinas' plans, anticipated milestones, timing and potential impacts of such milestones, related to its oncology pipeline candidates, including ARV-393, ARV-806 and VEPPANU (vepdegestrant); and Arvinas' anticipated milestones in the first and second halves of 2026 in connection with ARV-102, ARV-393, ARV-806, ARV-027, VEPPANU (vepdegestrant) and its preclinical candidates.

The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "goal," "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. Arvinas may not actually achieve the plans, intentions or expectations disclosed in its forward-looking statements, and you should not place undue reliance on these forward-looking statements.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements Arvinas makes as a result of various risks and uncertainties, including but not limited to: whether Arvinas will be able to successfully conduct and complete development for its product candidates, including ARV-102, ARV-806, ARV-393 and ARV-027 including whether Arvinas initiates and completes clinical trials for its product candidates and receives results from its clinical trials on expected timelines, or at all; whether Arvinas will be able to successfully conduct and complete development for preclinical candidates, including ARV-6723 and its pan-KRAS degrader, including whether Arvinas initiates and completes preclinical studies and receives results from such studies on expected timelines, or at all; the potential therapeutic benefits or profile of any of Arvinas' product candidates; the results of clinical and preclinical research; the potential market opportunity for any of Arvinas' product candidates; risks related to obtaining marketing approval for any product candidates; the satisfaction or waiver of the closing conditions set forth in the license agreement with Rigel; each party's performance of its obligations under the license agreement; whether Rigel will be able to successfully commercialize VEPPANU, or conduct and complete further development of VEPPANU; whether VEPPANU will be commercially available when expected; the potential demand and market potential and acceptance of, VEPPANU, including estimates regarding the potential market opportunity; the competitive landscape for VEPPANU or any other product candidate; regulatory actions or delays or government regulation generally; Arvinas' ability to protect its intellectual property portfolio; risks associated with Arvinas' reliance on third parties; risks associated with Arvinas' collaboration agreements; whether Arvinas will be able to raise capital when needed; whether Arvinas' cash and cash equivalent resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors, any of which could cause Arvinas' actual results to differ from those contained in the forward-looking statements, discussed in the "Risk Factors" sections of Arvinas' quarterly and annual reports on file with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this presentation reflect Arvinas' current views as of the date of this presentation 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 Arvinas' views as of any date subsequent to the date of this presentation.

This presentation may also contain estimates and other statistical data made by independent parties and by Arvinas relating to market size and other data about the company's 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 the company's future performance and the future performance of the markets in which the company operates 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

IGNITING A

TRANSFORMATIVE CHANGE

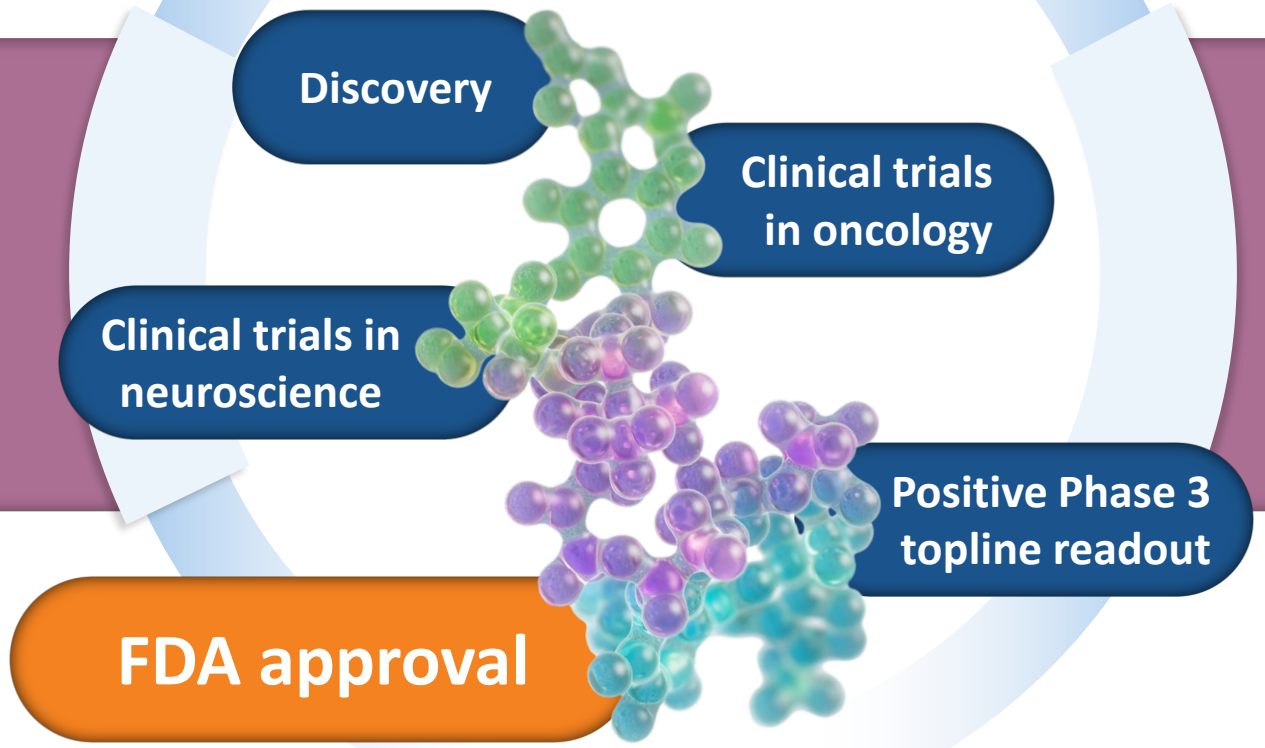
in the fight for patients with cancer and neurodegenerative diseases

Our experienced and talented team is advancing a new therapeutic modality for patients

Promising preclinical results are translating into the clinic

7 programs entered clinical trials in 5 years[a], targeting significant unmet needs for patients

History of FIRSTS with our novel PROTAC therapeutic modality:



Strong, experienced leadership team

Expertise from bench to commercialization

PROTAC:, proteolysis targeting chimera

a. vepdegestrant, bavdegalutamide, luxdegalutamide (JSB462), ARV-102, ARV-393, ARV-806, ARV-027

ER and AR degraders highlight Arvinas' ability to develop valuable PROTAC degraders

ER: VEPPANU[a]

FDA approved VEPPANU™ (vepdegestrant) on May 1, 2026

- VEPPANU is the first-and-only FDA-approved PROTAC, a type of heterobifunctional protein degrader
- Approved for adults with ER+/HER2-, *ESR1*-mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy

AR: luxdegalutamide

- Demonstrated signals of efficacy in late-line prostate cancer suggests potential for positive efficacy in earlier-line settings
- Out-licensed to Novartis in 2024 with potential for more than $1B in total deal value
- Novartis is currently evaluating luxdegalutamide in 3 Phase 2 combination trials in mCRPC and mHSPC

Strategic clinical-stage partnerships with Pfizer and Novartis have resulted in more than $800M in non-dilutive cash

AR, androgen receptor; ER, estrogen receptor; *ESR1*, estrogen receptor 1 gene; ER+/HER2-, estrogen receptor-positive/human epidermal growth factor receptor 2-negative; FDA, Food and Drug Administration; mCRC, metastatic castrate resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer. VEPPANU is a trademark of Arvinas Operations, Inc.

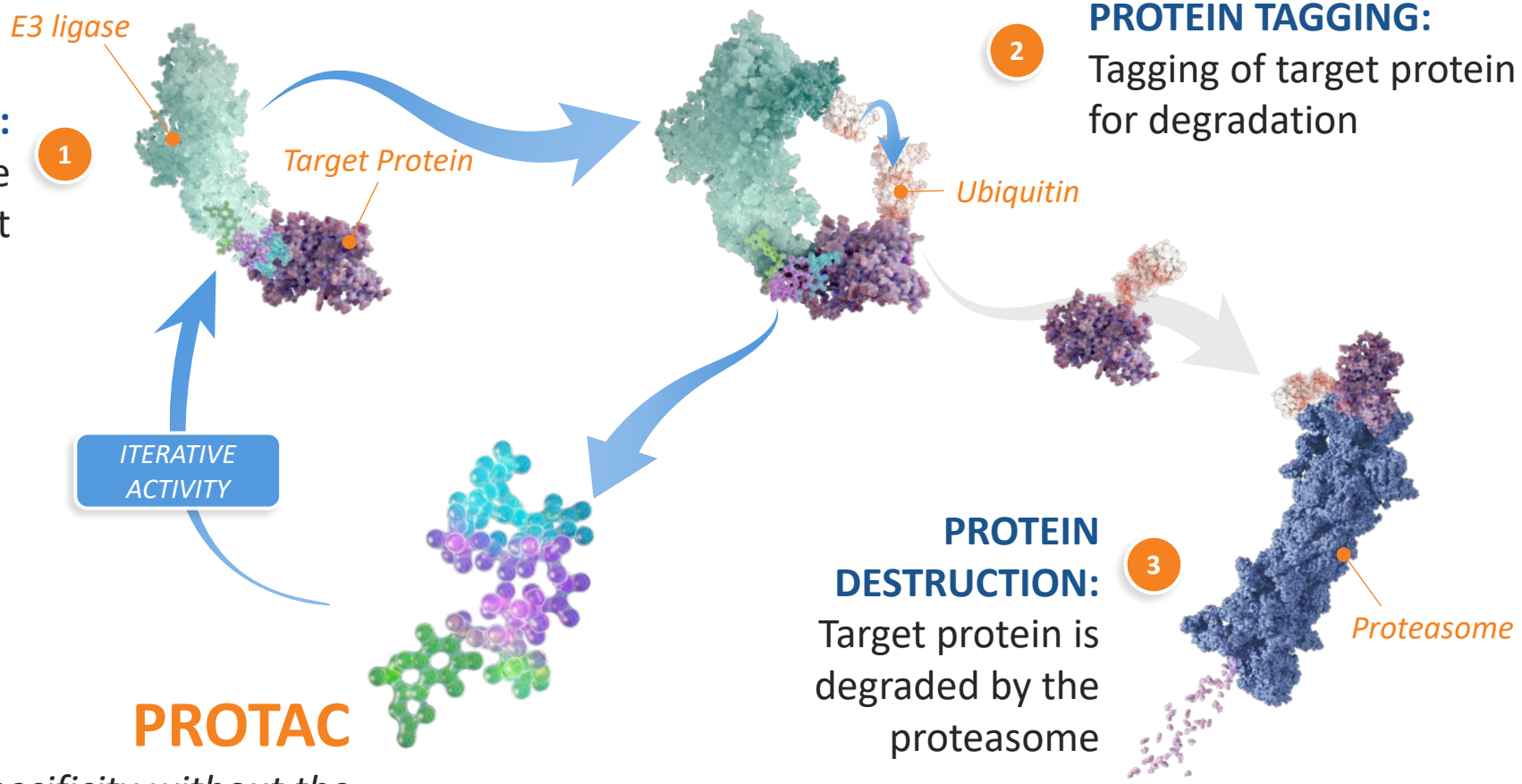
a. In 2021, Arvinas entered into a collaboration agreement with Pfizer to co-develop and co-commercialize vepdegestrant

PROTAC degraders harness the body's natural machinery to degrade, not simply inhibit, disease-causing proteins

ARVINAS

COMPLEX FORMATION:
Recognizing disease causing protein of interest

1



PROTEIN TAGGING:
Tagging of target protein for degradation

PROTEIN DESTRUCTION:
Target protein is degraded by the proteasome

PROTAC

High specificity without the requirement for strong binding

PROTAC degraders have potential benefits that may provide advantages over other modalities in oncology and neurology

BENEFITS IN
ONCOLOGY

- ✓ Ability to overcome evolving resistance mechanisms
- ✓ Targeting of classically "undruggable" proteins
- ✓ Therapies with potential to improve upon existing treatment options

BENEFITS OF
PROTAC
PROTEIN DEGRADERS

- ✓ Elimination (rather than inhibition) of disease-causing proteins
- ✓ Interruption of scaffolding functions of target proteins
- ✓ Iterative (catalytic) activity
- ✓ Oral delivery and broad tissue distribution
- ✓ Mutant and/or wild-type specificity
- ✓ Efficient manufacturing and routes of synthesis (versus biologics and cell therapies)

BENEFITS IN
NEUROLOGY

- ✓ Blood-brain barrier penetration
- ✓ Oral administration, avoiding IM, IV, or intrathecal dosing
- ✓ Biodistribution to deep-brain regions

IM, intramuscular; IV, intravenous

Seeking to address two of the largest areas of significant unmet need for patients

ARVINAS

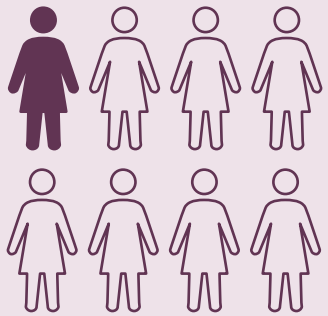
ONCOLOGY

By 2040

30M Leading to **15M**

New cancer cases per year worldwide[1]

Cancer-related deaths per year[1]



1 in 8

US women will develop breast cancer in their lifetime[2]

Despite progress, cancer remains one of the most common causes of death[3] **and new treatments are needed**

NEUROLOGY

By 2040

neurodegenerative diseases are estimated to be the

#2 LEADING CAUSE OF DEATH

in developed countries[4]

65-70 M+

people worldwide live with major tau-related neurodegenerative disorders[5]

Well-known, but poorly drugged targets represent **strong potential for effective treatments**

1. Global Cancer Observatory: https://gco.iarc.fr/tomorrow/en/dataviz/isotype?years=2040; accessed 10/25/25. 2. ACS: https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer; accessed 10/25/25. 3. World Health Organization: https://www.who.int/news-room/fact-sheets/detail/cancer; accessed 10/25/25. 4. Nature: https://doi.org/10.1038/nj7526-299a; accessed 10/25/25; 5. includes Alz. Disease (WHO 2025) + non-Alz. tauopathies (e.g., PSP) and Parkinson's disease (Parkinson's Foundation).

Arvinas pipeline includes differentiated PROTAC degraders in neurology and oncology

PROGRAM	INDICATION	PRECLINICAL	PHASE 1/1B	PHASE 2	PHASE 3	APPROVAL
ARV-102* (LRRK2)	PSP, Parkinson's Disease	*Planned initiation of Phase 1b/2 PSP trial in 2026***	Phase 1: Parkinson's disease			
ARV-027* (polyQ-AR)	Spinal Bulbar Muscular Atrophy	Phase 1: SBMA				
ARV-806* (KRAS G12D)	Pancreatic, colorectal, NSCLC cancers	Phase 1: Solid tumors harboring KRAS G12D mutations				
ARV-393* (BCL6)	Non-Hodgkin Lymphoma	Phase 1 monotherapy: NHL[a]				
ARV-6723* (HPK1)	Advanced Solid Tumors	I-O indications				
VEPPANU™ (vepdegestrant)	ER+/HER2-, *ESR1*-Mutated Metastatic Breast Cancer	Phase 1/2 combination trials ongoing[b] Pfizer				FDA APPROVED Out licensed† for commercialization to rigel
Luxdegalutamide* (ARV-766, JSB462; AR)	Prostate Cancer	Phase 2: mHSPC and mCRPC				*Global rights licensed to* NOVARTIS

AR, androgen receptor; BCL6, B-cell lymphoma 6; ER+, estrogen receptor positive; ESR1, estrogen receptor 1, HER2-, human epidermal growth factor receptor 2-negative, HPK1, hematopoietic progenitor kinase 1; I-O, immuno-oncology; KRAS, Kirsten rat sarcoma viral oncogene homolog; LRRK2, leucine-rich repeat kinase 2; mCRPC, metastatic castration resistant prostate cancer; mHSPC, metastatic hormone sensitive prostate cancer; NSCLC, non small cell lung cancer; NDA, new drug application; NHL, non-Hodgkin lymphoma; polyQ, expanded polyglutamine; PSP, progressive supranuclear palsy; SBMA, spinal bulbar muscular atrophy

a. Includes relapsed/refractory angioimmunoblastic T-cell lymphoma (AITL) and relapsed/refractory mature B cell NHL b. Phase 1/2 combination trials with palbociclib, atirmociclib, abemaciclib, ribociclib, samuraciclib, everolimus.

*These agents are currently under investigation; their safety and effectiveness for these investigational uses have not been established; **Upon submission of final chronic toxicology data in non-human primates and FDA clearance to proceed with the Phase 1b clinical trial; †Subject to Hart-Scott-Rodino Antitrust Improvement Act of 1976, as amended, and satisfaction of closing conditions.

Committed to bringing valuable treatments for patients and creating value for shareholders

ARVINAS

Four Phase 1 PROTAC Programs with Near-Term Data

- Targeting LRRK2 for neurodegeneration, KRAS G12D for solid tumors, BCL6 for hematological malignancies, and polyQ-AR for spinal and bulbar muscular atrophy
- Delivering innovative assets intended to differentiate from other therapies
- Committed to investing in highest value drivers across the pipeline

Pivotal Proof of Concept with Vepdegestrant

- First-and-only FDA-approved PROTAC, a type of heterobifunctional protein degrader
- Out licensed to Rigel Pharmaceuticals for commercialization and potential for future regulatory and commercial milestones and tiered royalites on net sales*

Strong Capitalization

- Cash runway into 2H 2028**
- Multiple value-inflecting milestones ahead, with potential to receive milestone payments from existing partners, including NOVARTIS for luxdegalutamide
- Potential for future partnerships to enhance the value of Arvinas' pipeline

ASCO, American Society of Clinical Oncology; BCL6, B-cell lymphoma 6; KRAS, Kirsten rat sarcoma viral oncogene homolog; LRRK2, leucine-rich repeat kinase 2; NDA, new drug application; polyQ-AR, polyglutamine androgen receptor

* Subject to Hart-Scott-Rodino Antitrust Improvement Act of 1976, as amended, and satisfaction of closing conditions; **Based on cash, cash equivalents, and marketable securities position as of March 31, 2026

CLINICAL PROGRAMS: Neurology

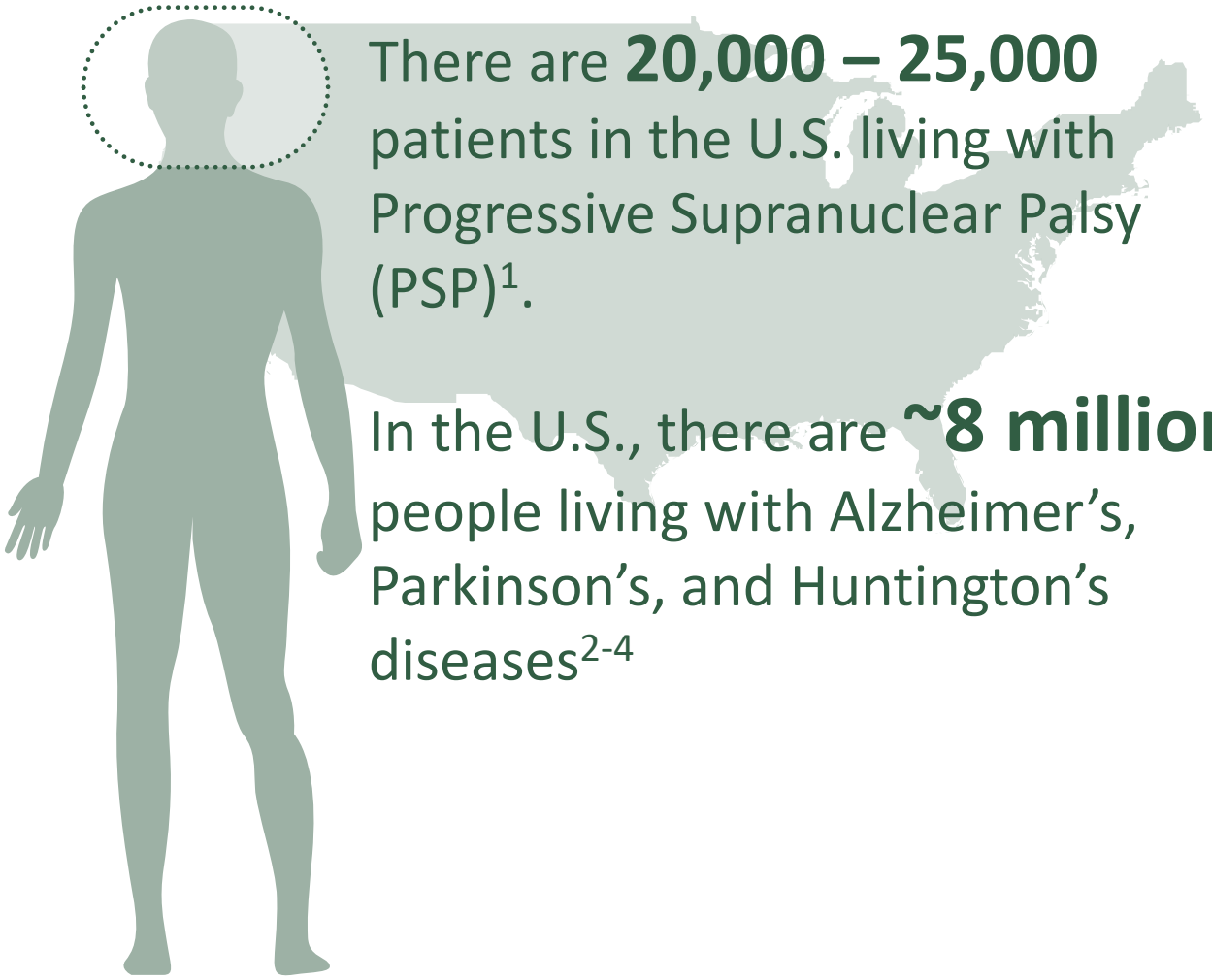
ARV-102

PROTAC LRRK2 degrader

ARVINAS

ARV-102 is an investigational compound. Its safety and effectiveness have not been established.

Neurodegenerative diseases: An area of tremendous unmet need



There are **20,000 – 25,000** patients in the U.S. living with Progressive Supranuclear Palsy (PSP)[1].

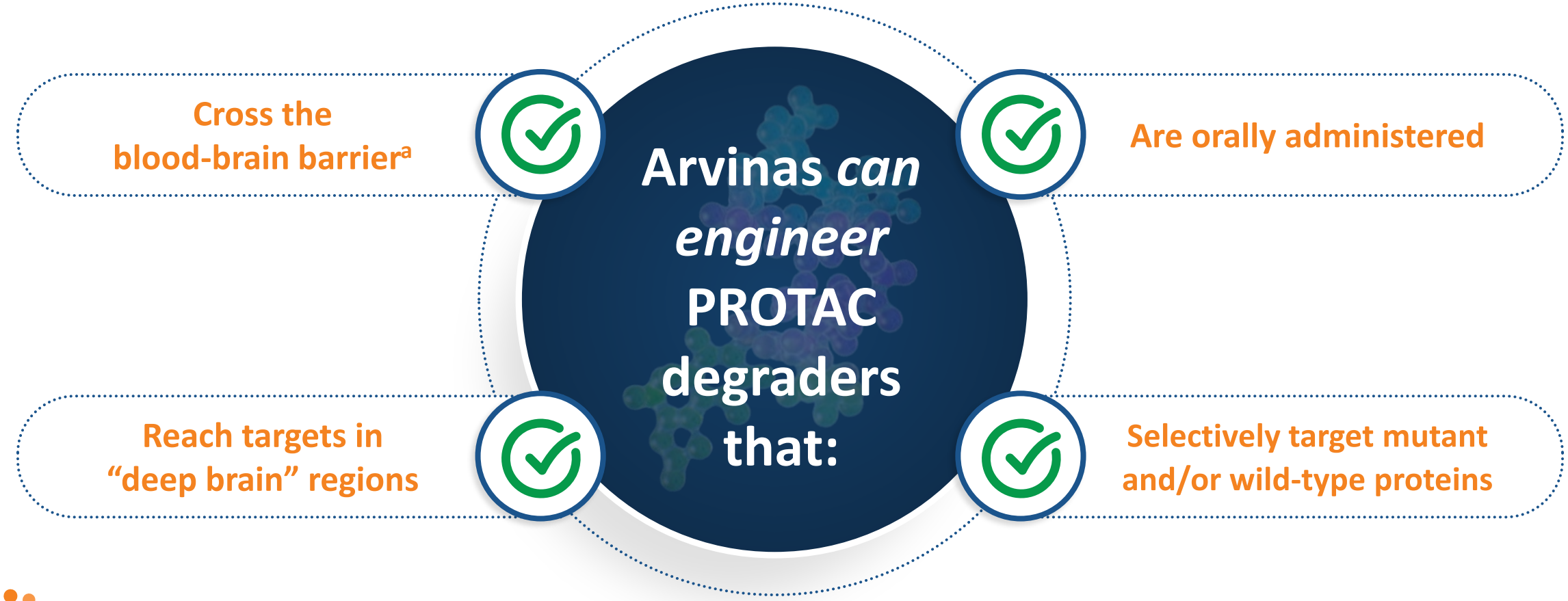
In the U.S., there are **~8 million** people living with Alzheimer's, Parkinson's, and Huntington's diseases[2-4]

Unmet need is high:

- No approved disease-modifying therapies for multiple important target proteins (e.g., LRRK2, tau, α-synuclein) implicated in the pathology of various neurodegenerative diseases[5]
- Blood-brain barrier penetration is a challenge for other modalities (e.g., antibodies and antisense oligonucleotides)
- Other existing and potential therapies have difficult routes of administration (e.g., intrathecal, intracerebral)

1. Cummings, J.L., Gonzalez, M.I., Pritchard, M.C. et al., Alz Res Therapy 15, 168 (2023); 2. Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures. Alzheimer's Dement 2024;20(5); 3. Willis et al., npj Parkinson's Dis. 2022; 4. Yohrling, et al., Neurology 2020; 5. Lyons S, et al. J Neurol. 270, 4451–4465 (2023) and Counsell CE, Swallow DMA, Zheng CS. Mov Disord Clin Pract. 9, 604–613 (2022)

PROTAC degraders could potentially revolutionize the treatment of neurodegenerative diseases



A novel PROTAC approach with first-in-class promise and potential to differentiate from existing and emerging modalities in neurodegenerative diseases

a. In preclinical and clinical studies, dose-dependent increases in exposure in cerebral spinal fluid after single and multiple doses of ARV-102 indicated brain penetration.

LRRK2 is implicated in both in progressive supranuclear palsy and Parkinson's disease

Progressive Supranuclear Palsy (PSP)

- Rare progressive neurological disease that affects movement, balance, and cognitive function
- Characterized by tauopathy (accumulation of abnormal forms of the microtubule-associated protein tau)[2]
- Preclinical data indicate that LRRK2 mutations are associated with tau pathology resembling PSP[2]
- Genetic variations in LRRK2 are associated with PSP progression, highlighting the potential importance of LRRK2 in tauopathies[2]

No approved disease-modifying therapies exist for patients with PSP or PD

Parkinson's Disease (PD)

- Neurodegenerative disease that affects movement, balance, and coordination
- Mutations in the LRRK2 gene are one of the most common genetic causes of PD; variants have also been observed in idiopathic cases[1]
- Increased LRRK2 expression and activity contributes to neurodegeneration and pathogenesis of idiopathic PD,[1] making it a rational therapeutic target

Given its role in neurodegeneration, Arvinas is exploring LRRK2-targeting PROTAC degraders as possible treatments for PSP, PD, and related diseases

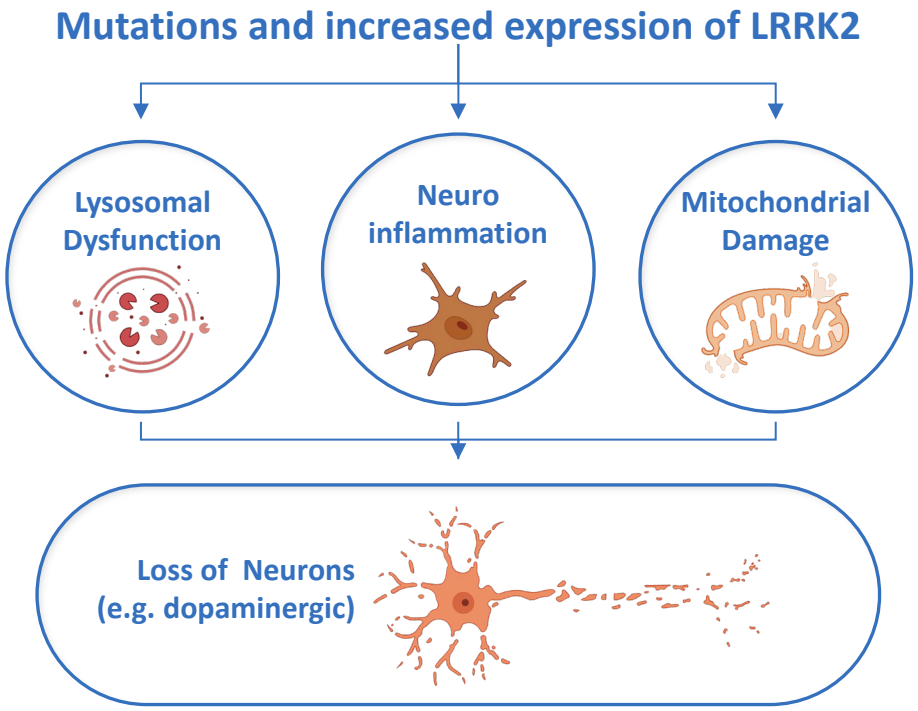
LRRK2, leucine-rich repeat kinase 2

1. Kluss et al. Biochem Soc Trans. 2019;47:651-61. 2. Herbst et al. Clin Sci 2022;136:1071-1079.

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

Progressive supranuclear palsy (PSP) is a tauopathy with rapid progression to death within 5-7 years

- LRRK2 SNPs and variants are associated with tau pathology resembling PSP[1]
  - LRRK2 genetic variants with elevated expression accelerates disease progression[(2,8-10)]
- Increased LRRK2 expression is associated with PSP progression, highlighting the potential importance of LRRK2 in tauopathies[1]
  - Increased LRRK2 levels or activity drives tau accumulation, neurotoxicity, and cGAS/STING-mediated neuroinflammation [(2-6)]
- Reducing LRRK2 protein or kinase activity limits pathological tau and its spread in animal models and human neurons [(4-6, 11)]



Parkinson's disease (PD) is the second-largest tauopathy

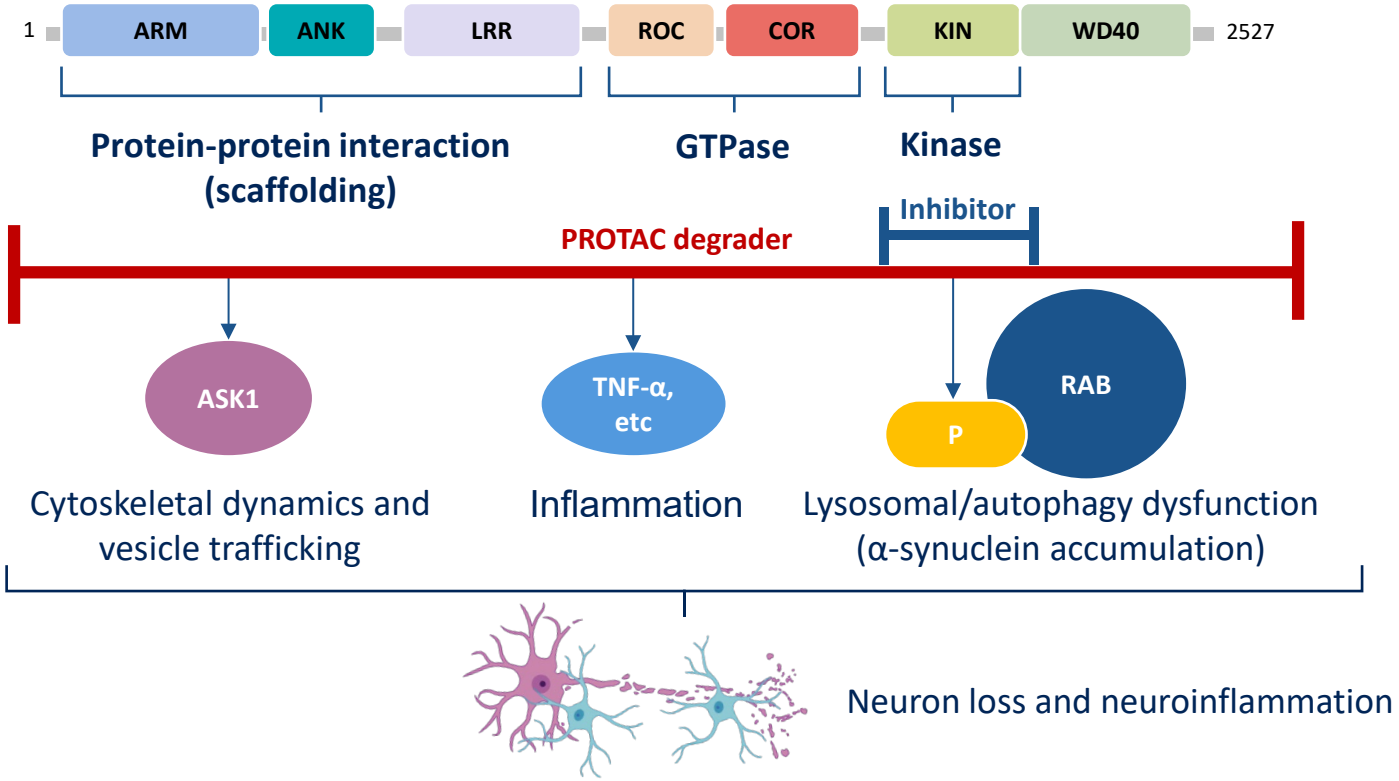
- Increased LRRK2 expression and activity contribute to neurodegeneration and pathogenesis of PD,[1] making it a rational therapeutic target
  - LRRK2 mutations are a common genetic cause of PD; variants have also been observed in idiopathic cases[12-14]
- LRRK2 levels are ~2x higher in CSF, microglia in idiopathic PD, reducing LRRK2 by ~50% improves pathology, α-synuclein, neuronal death, & dysfunction in models [(3-6, 14-15)]

cGAS/STING, cyclic GMP-AMP synthase/stimulator of interferon genes; CSF, cerebral spinal fluid; LRRK2, leucine-rich repeat kinase 2; SNP, single nucleotide polymorphism.

1 . Jabbari E, et al. Lancet Neurol. 2021;20(2):107-116; 2.West et al 2007; 3. Wang et al 2021; 4. Ujiie et al 2012; 5. Nguyen et al 2018; 6. Lubben et al 2024; 8. Herbst et al Clin Sci 2022; 9. Jabbari et al 2021; 10. Nielsen et al 2025; 11. Evans et al 2025; 12. Rocha EM, et al. Trends Neurosci. 2022;45(3):224-3612. 13. Kluss JH, et al. Biochem Soc Trans. 2019;47(2):651-661. 14. Di Fonzo A, et al Lancet. 2005;365(9457):412-5. 14. Jabbari E, et al. Lancet Neurol. 2021;20(2):107-116; 14. Zhao et al 2017; 15. Bieri et al 2019

PROTAC-induced LRRK2 degradation has the potential to differentiate from kinase inhibition

LRRK2 is a large multidomain scaffolding kinase[1-3]



PROTAC LRRK2 degrader differentiates from inhibitors

LRRK2	Inhibitor	PROTAC
Kinase activity	✓	✓
GTPase activity	✗	✓
Protein-protein interaction (scaffolding)	✗	✓

Increased activity and expression of LRRK2 have been linked with the development and progression of neurological diseases like progressive supranuclear palsy[4], or PSP, and Parkinson's disease[5].

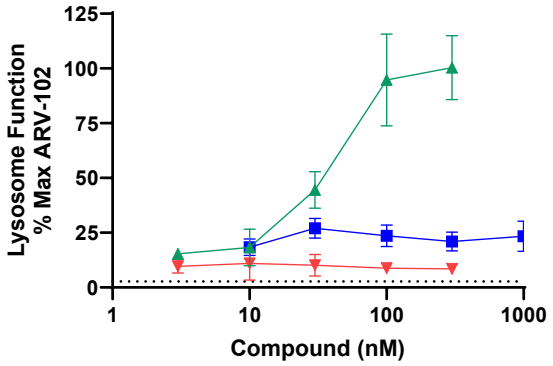
ARM, armadillo; ANK, ankyrin; ASK1, apoptosis signal-regulating kinase 1; COR, C-terminal of ROC; KIN, kinase; LRR, leucine-rich repeat; LRRK2, leucine-rich repeat kinase 2; ROC, Ras of complex; TNF-α, tumor necrosis factor α; WD40, WD domain, G-beta repeat

1. Rocha EM, et al. Trends Neurosci. 2022;45(3):224-36. 2. Kluss JH, et al. Biochem Soc Trans. 2019;47(2):651-661. 3. Di Fonzo A, et al Lancet. 2005;365(9457):412-5; 4. Jabbari et al., 2021; 5.Langston et al. 2022.

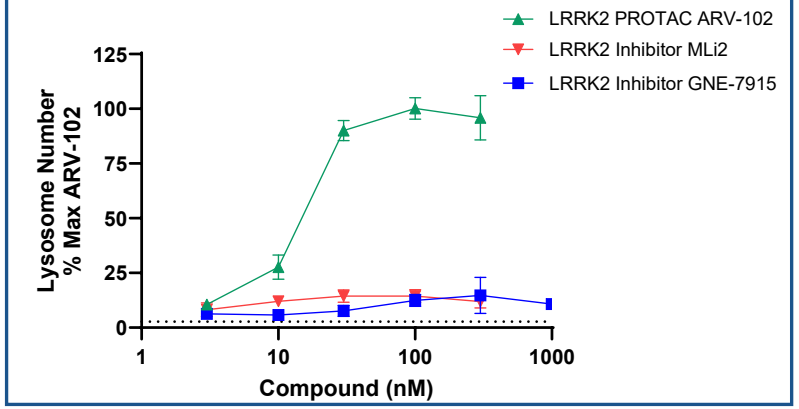
ARV-102 increases lysosome functional degradative capacity and number *in vitro*

Lysosome function and number are reduced preclinically and in patients with PD[a]; ARV-102 dose-dependently increased degradation efficiency and lysosome number vs kinase inhibitors

ARV-102 increases lysosome ***degradation*** in A549 cells



ARV-102 increases lysosome ***number*** in A549 cells



- Mutant familial PD and increased LRRK2 expression 'puts the brakes' on lysosomal clearance system
- Autophagy (clearance dependent on lysosome) is reduced with increased LRRK2 expression, LRRK2 familial mutation (G2019S), and LRRK2 activity/levels in rodent neurons[b]
- LRRK2 PROTAC activity is consistent with literature showing an increase in lysotracker spot count observed in LRRK2 KO astrocytes[c]

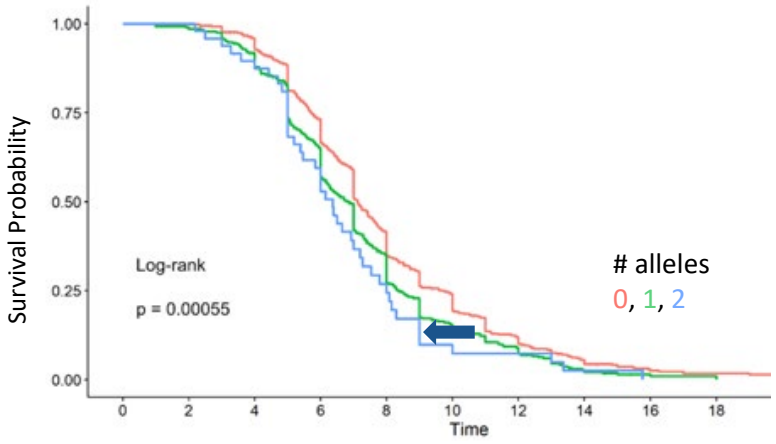
LRRK2, Leucine-rich repeat kinase 2; PD, Parkinson's disease; KO, genetic knock out; DQ-BSA, Dye Quenched-Bovine Serum Albumin

a. Dehey et al., 2013. Lysosomal impairment in Parkinson's disease; b. R. Wallings et al., 2019; c. Henry et al., 2015

Data presented at 2023 Keystone Summit: Autophagy and Neurodegeneration

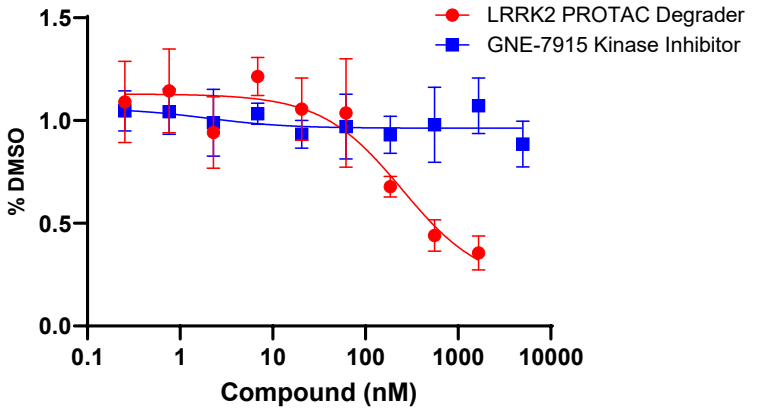
In vitro and *in vivo* data suggest that Arvinas' LRRK2 PROTAC degraders can reduce PSP-induced pathologic tau

LRRK2 SNP accelerated time to death by 1 year in PSP[1]



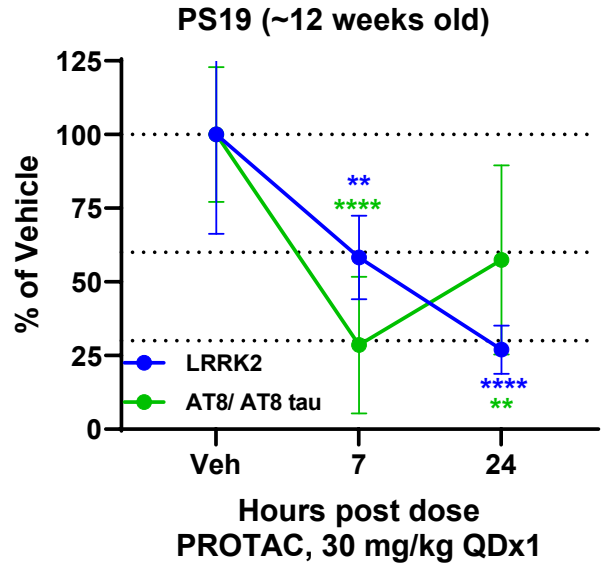
- Pooled analysis from 1239 PSP cases
- Arrow point to reduced survival for LRRK2 SNP rs2242367 – potentially via increased LRRK2 expression

LRRK2 PROTAC reduced PSP induced pathologic AT8-tau, *in vitro*



Reduction of pathologic (AT8) Tau induced by LRRK2 PROTAC but not LRRK2 kinase inhibitor

LRRK2 PROTAC degraders reduced pathologic tau protein *in vivo*



Reductions of soluble AT8+ tau aggregates occur as early as 7 hours post dose in both Tg4510 (data not shown) and PS19 mouse brain tissue

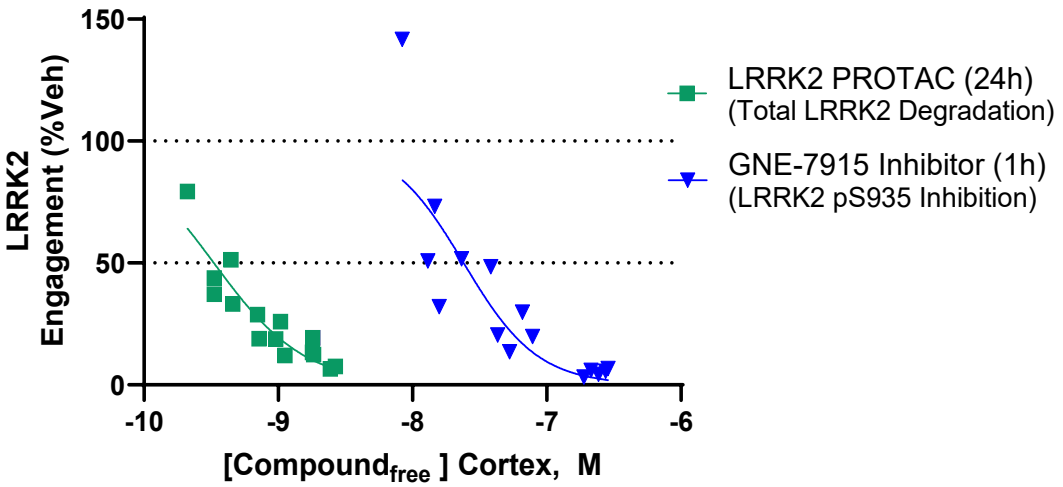
LRRK2, Leucine-rich repeat kinase 2; PSP, Progressive Supranuclear Palsy; SNP, single nucleotide polymorphism;

1. Jabbari et al., 2021

ARV-102 shows 50x greater target and pathway engagement, with enhanced potency, versus a LRRK2 inhibitor in preclinical model

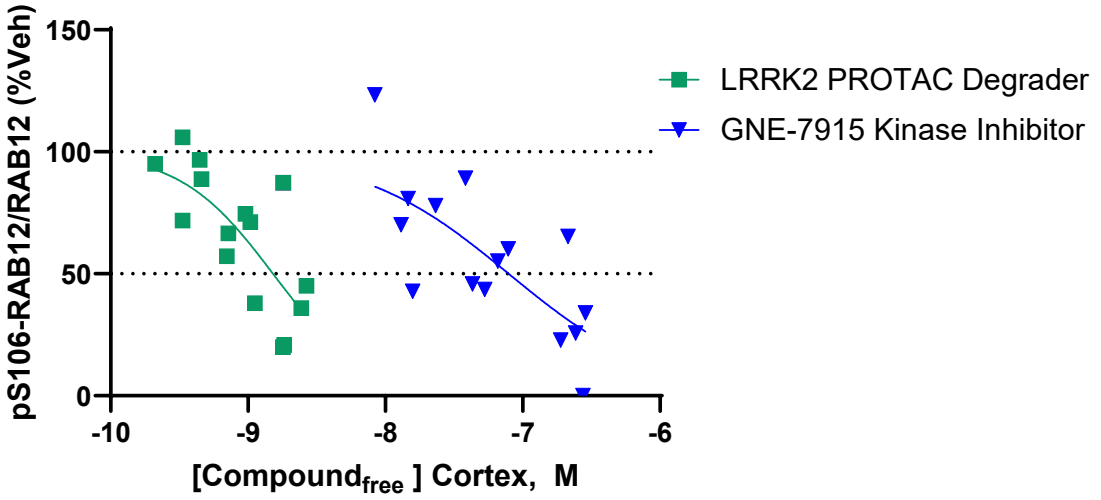
Iterative and catalytic PROTAC advantage results in stronger LRRK2 reduction and RAB pathway engagement versus a LRRK2 kinase inhibitor[a]

LRRK2 Target Engagement
LRRK2 PROTAC vs. Kinase inhibitor at Tmax



50x greater *target* engagement with ARV-102

RAB Pathway Engagement (pS106 Rab12)
(LRRK2 PROTAC vs. Inhibitor)



50x greater *pathway* engagement with ARV-102

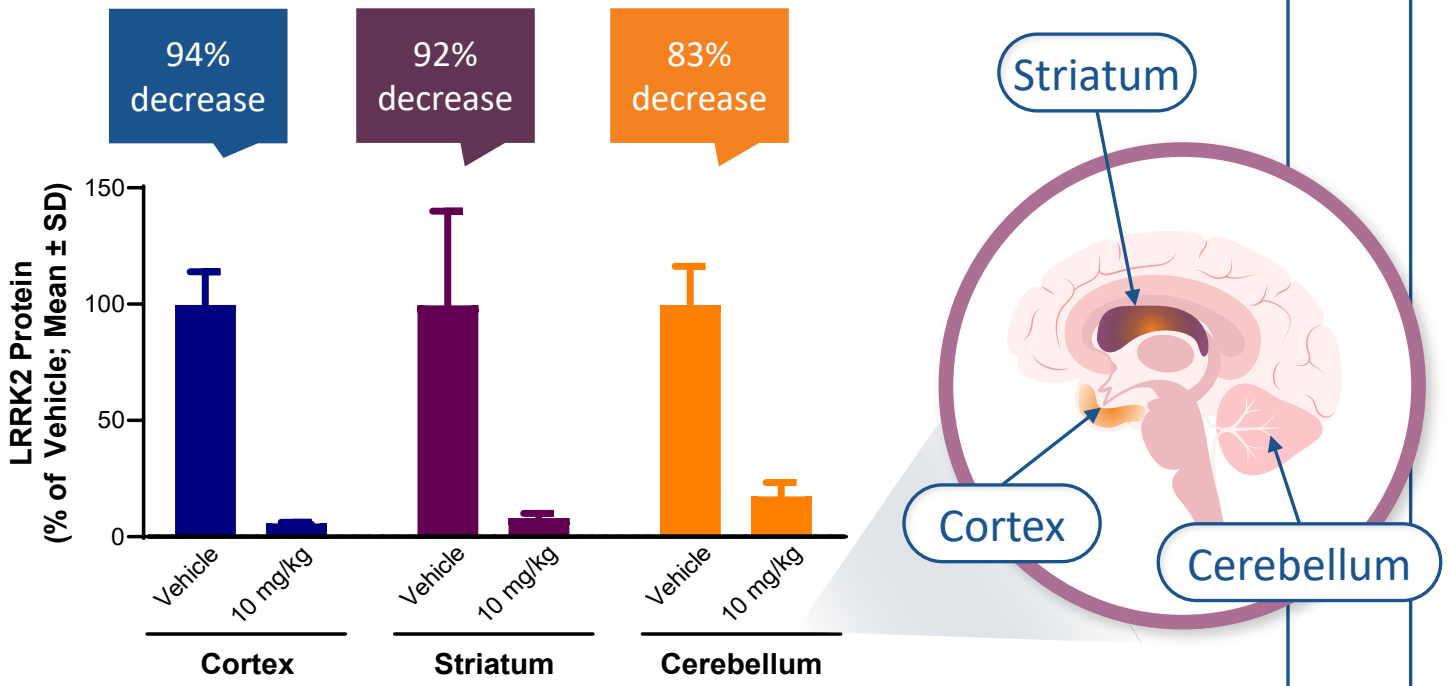
LRRK2, Leucine-rich repeat kinase 2

a. G2019S familial Parkinson's Disease mouse model.

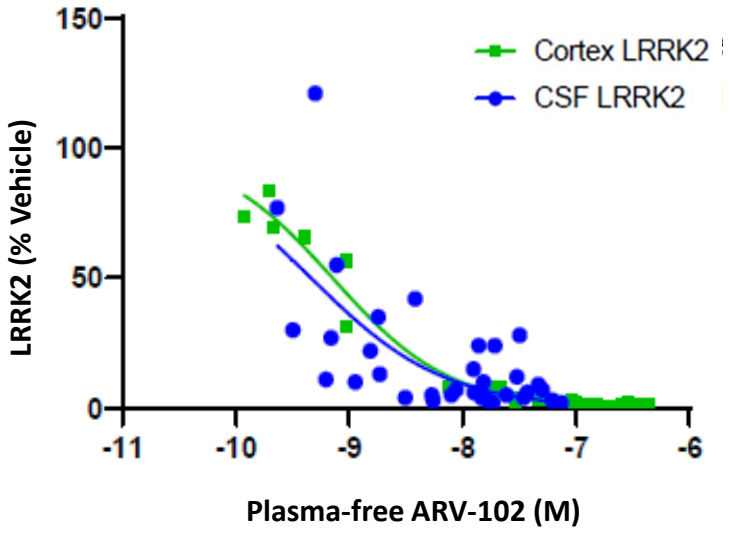
Data presented at 2023 Keystone Summit: Autophagy and Neurodegeneration.

ARV-102 degrades LRRK2 in NHP deep-brain regions in non-human primates

Orally dosed ARV-102 reaches multiple “deep brain” regions in non-human primates (NHPs) and **degrades** LRRK2 up to 94%



In NHPs, CSF levels of LRRK2 can be used to indicate levels of LRRK2 in cortex

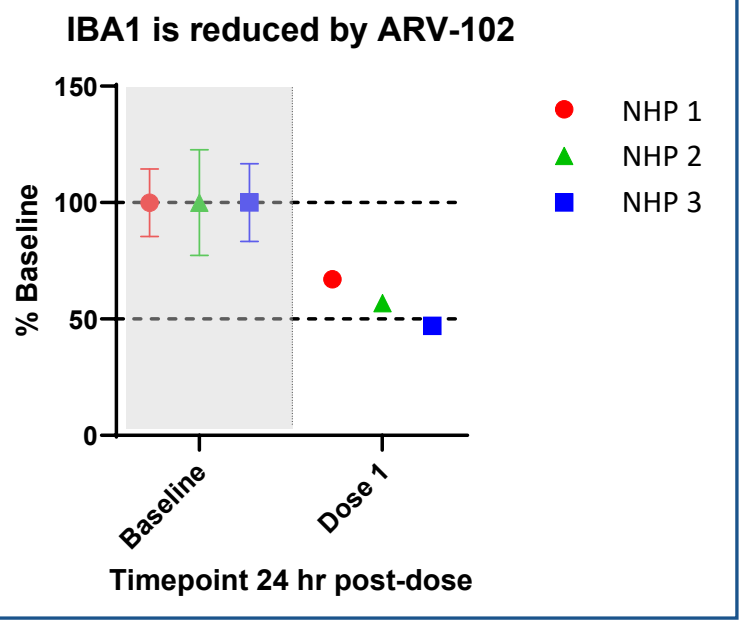


CSF, cerebrospinal fluid; LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate

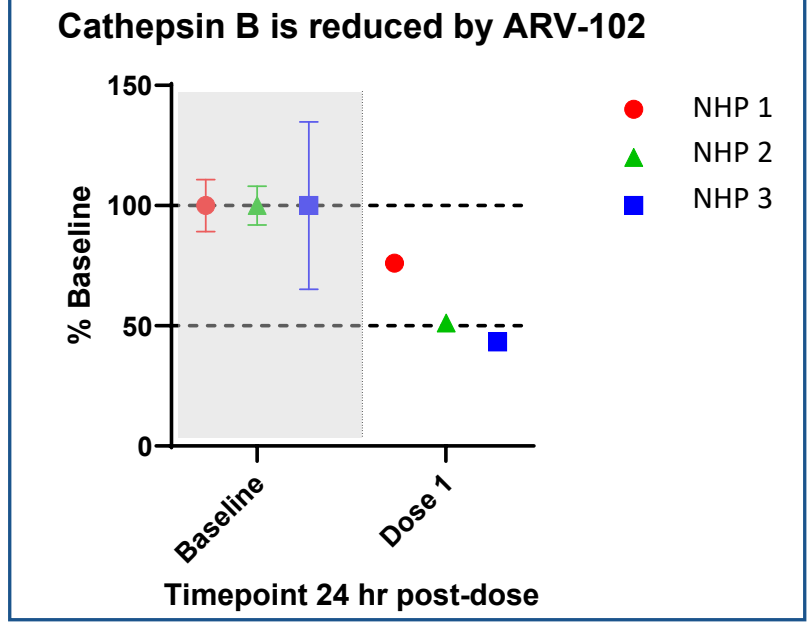
Putative LRRK2 biomarkers associated with disease are reduced in non-human primate CSF after dosing with ARV-102

ARVINAS

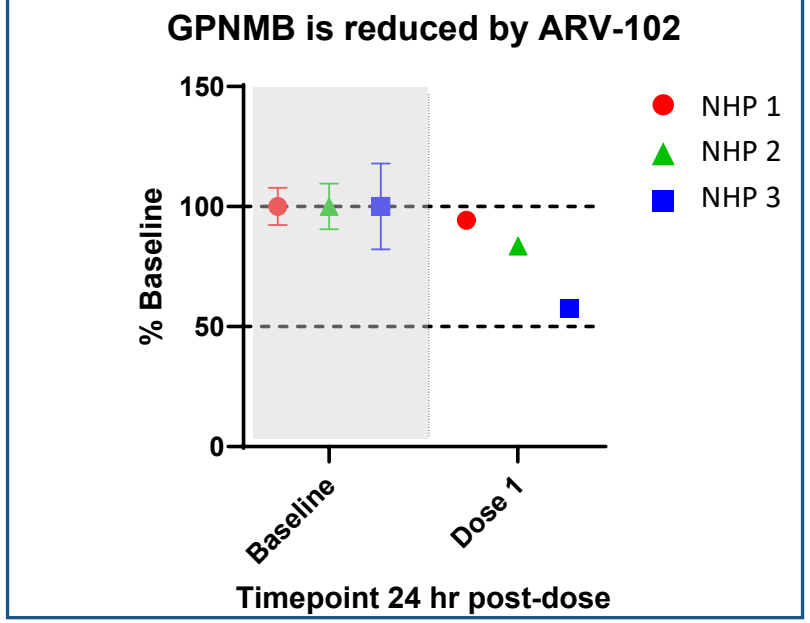
Marker of pathologic neuroinflammation



Lysosomal hydrolase implicated in Parkinson's disease



Lysosomal marker increased in glia in neuroinflammation



The Parkinson's Progression Marker Initiative identified proteins enriched in pathways related to neuroinflammatory response and lysosomal function

- IBA1, Cathepsin B, and GPNMB were identified as LRRK2-dependent pathway biomarkers that concord with LRRK2 protein levels in NHP CSF

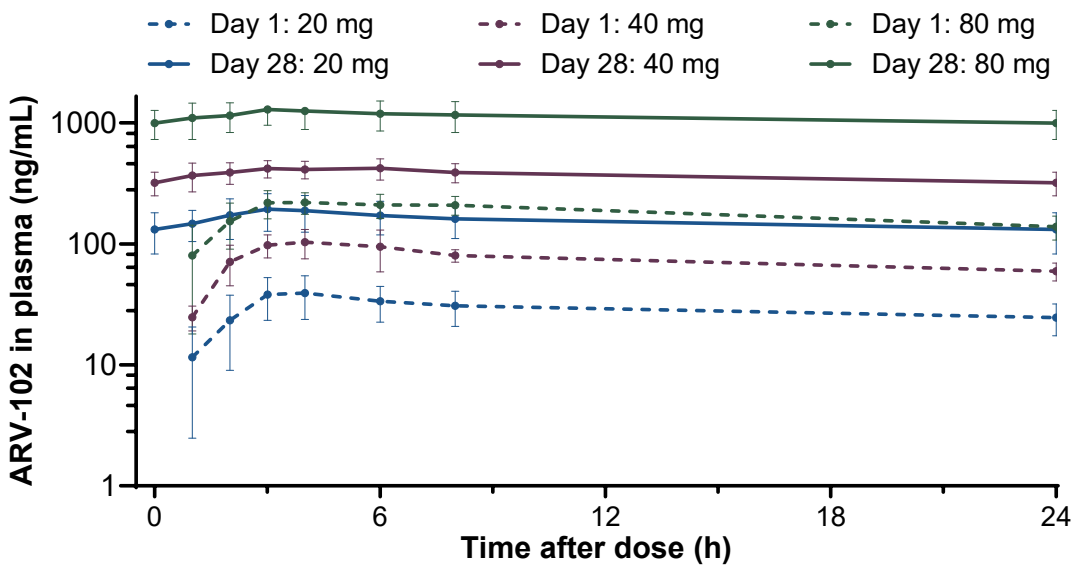
CSF, cerebrospinal fluid; GPNMB, transmembrane glycoprotein identified as a "Damage-associated Microglia" neurodegenerative protein; IBA1, microglia marker, also known as "Allograft Inflammatory Factor 1 (AIF-1); LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate

In patients with Parkinson's disease, exposure of ARV-102 in plasma and CSF increased in a dose-dependent manner, indicating brain penetration

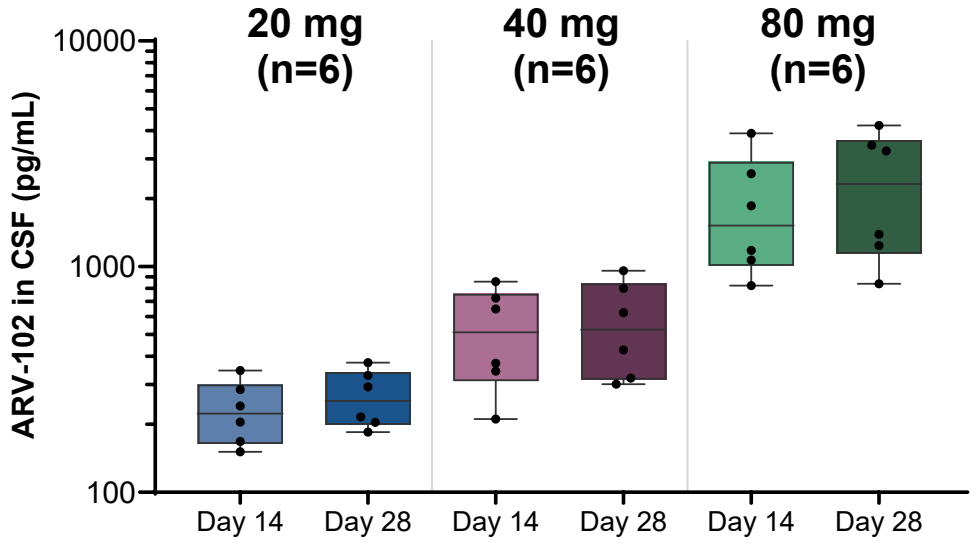
ARVINAS

ARV-102 exposure (AUC_{inf} and C_{max}) increased in a dose-dependent manner in plasma and in CSF

Plasma



CSF



Lower limit of quantification was 0.25 ng/mL.

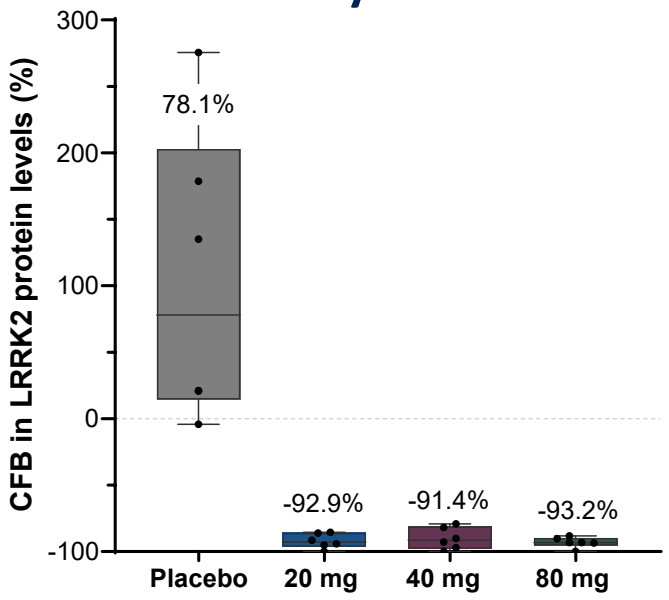
Data presented at 2026 International Conference on Alzheimer's and Parkinson's Disease and Related Neurological Disorders (AD/PD)

As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

Robust reductions of LRRK2 levels in PBMCs and BMP levels in urine were observed following multiple doses of ARV-102 treatment

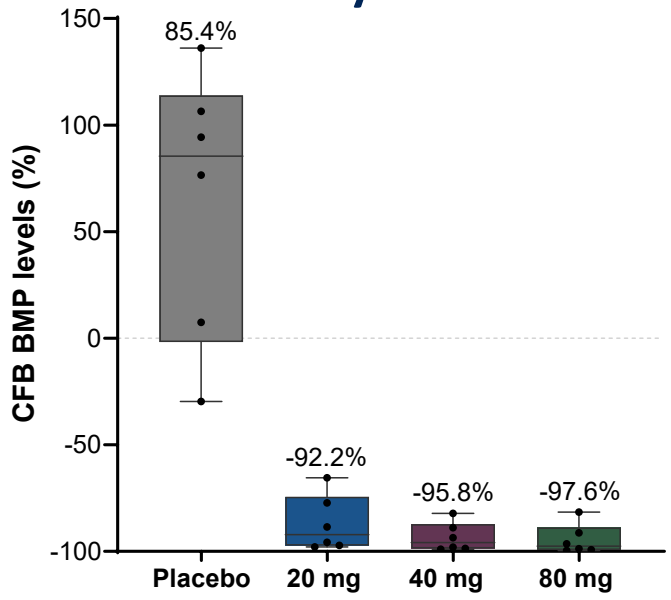
PBMC LRRK2

Day 28

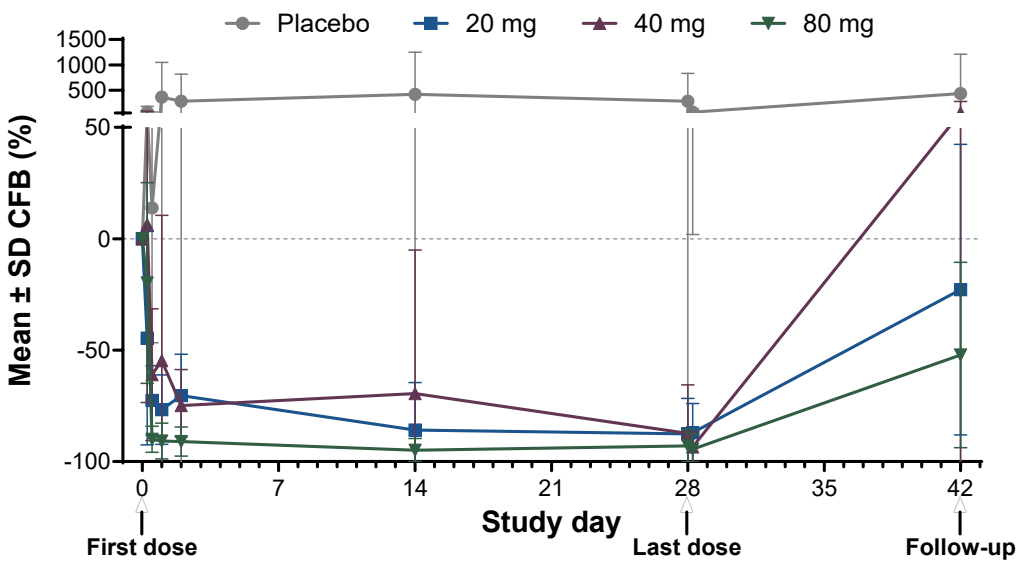


Urine BMP

Day 28



Time course



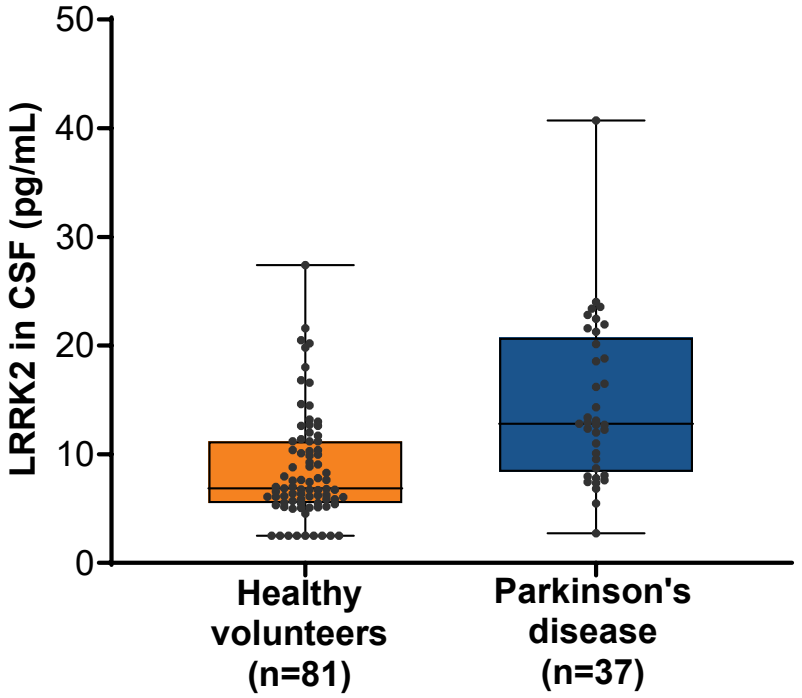
- Robust reductions of LRRK2 levels in PBMCs and BMP levels in urine were observed following multiple doses of ARV-102 treatment, with BMP levels returning towards baseline after 2 weeks of follow-up
- Peripheral pharmacodynamic biomarker results in participants with Parkinson's disease were consistent with those observed in the study of ARV-102 in healthy volunteers[1,2]

As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY
International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

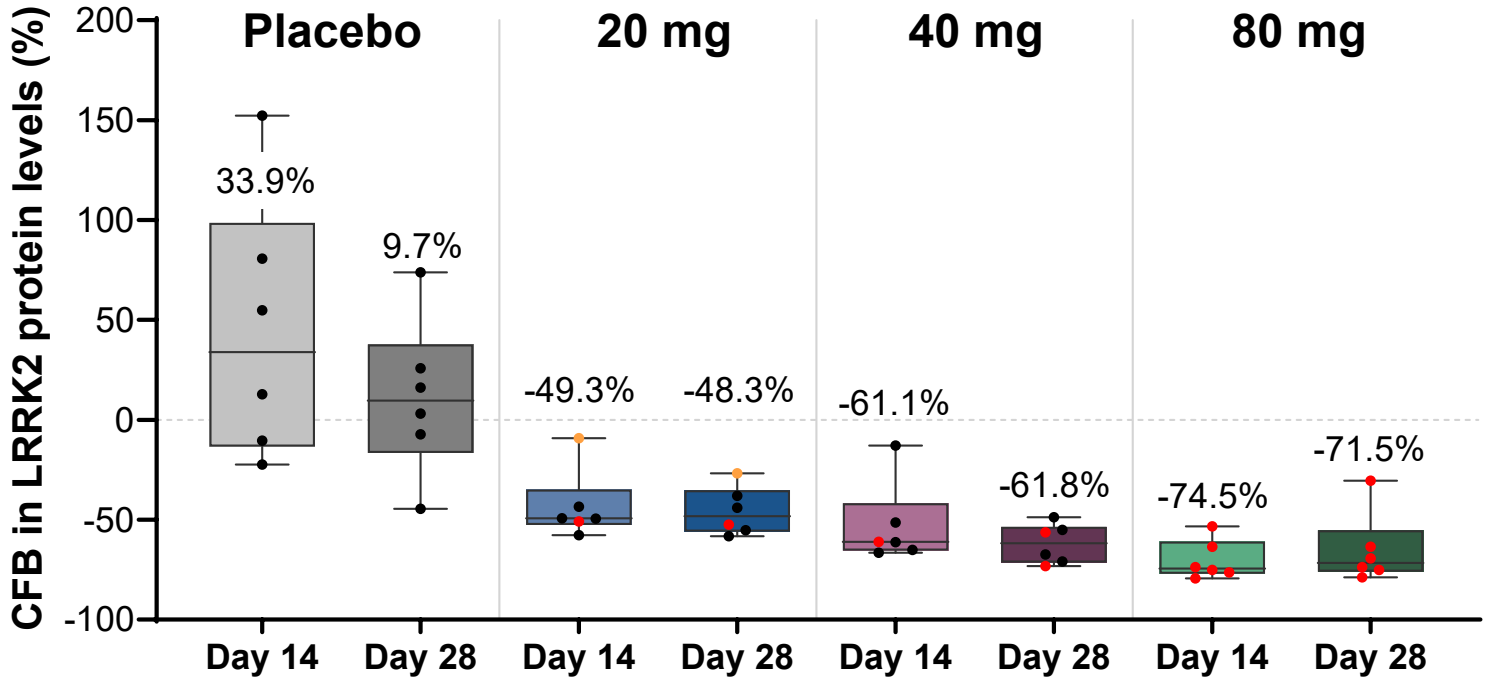
BMP, bis(monoacylglycerol)phosphate; LRRK2, leucine-rich repeat kinase 2; PBMC, peripheral blood mononuclear cell.
1. Smits L, et al. Oral presentation at International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD) 2025. 2. Smits L, et al. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders (MDS) 2025; Poster #904.

ARV-102 achieved more than ~50% LRRK2 degradation in the CNS at all dose levels

Baseline LRRK2 in CSF[a]



Change in participants with Parkinson's disease[b]



- Baseline levels of LRRK2 in CSF were higher in participants with Parkinson's disease than in healthy volunteers
- Median LRRK2 reductions of ~50% or greater were achieved in participants with Parkinson's disease starting at daily ARV-102 doses of 20 mg

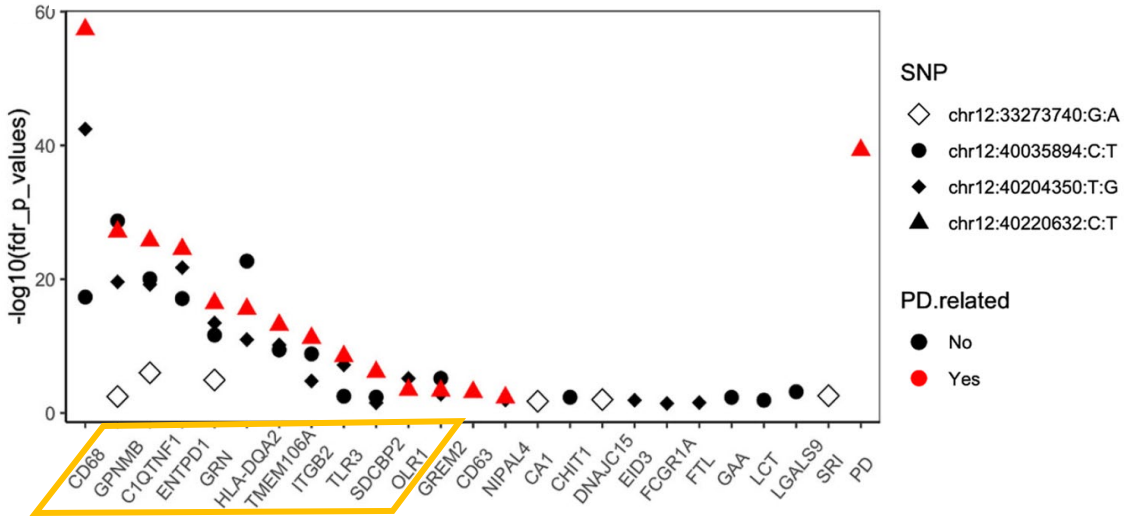
CFB, change from baseline; CSF, cerebrospinal fluid; LLD, lower limit of detection; LLOQ, lower limit of quantification; LRRK2, leucine-rich repeat kinase 2; QD, once daily.
Box plots show median and 25%/75% quartiles with whiskers to the minimum and maximum values. Circles indicate individual participant values.
aPlot shows baseline total LRRK2 levels in CSF from all participants in the single- and multiple-dose arms of the phase 1 studies in healthy volunteers and participants with Parkinson's disease.
bRed circles denote values that were <4 pg/mL (LLOQ) post baseline, which were calculated using one half of the LLOQ. Orange circles denote values that were below the LLOQ, but above the LLD (2 pg/mL); reported values were used to calculate CFB for these data points.

As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

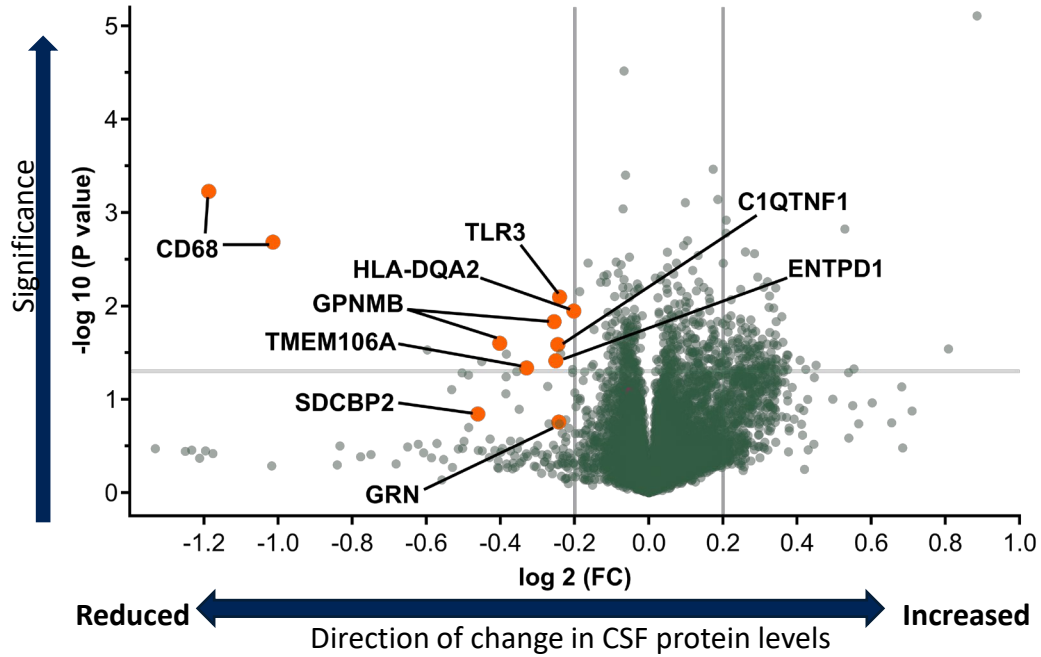
ARV-102 reduced endolysosomal and neuroinflammatory pathway proteins that are elevated in LRRK2-related Parkinson's disease[1]

- Multi-cohort CSF proteomics analysis identified lysosomal and microglial proteins associated with LRRK2 variants[1] that are also reduced with ARV-102 treatment in healthy volunteers[2]
- A prespecified panel of these proteins were evaluated in this study of ARV-102 in participants with Parkinson's disease; aggregate protein reductions in this panel were observed with LRRK2 degradation (*P*=0.024)[a]

Proteins associated with *LRRK2* variants in Parkinson's disease[b]



ARV-102 80 mg in participants with Parkinson's disease (day 28)



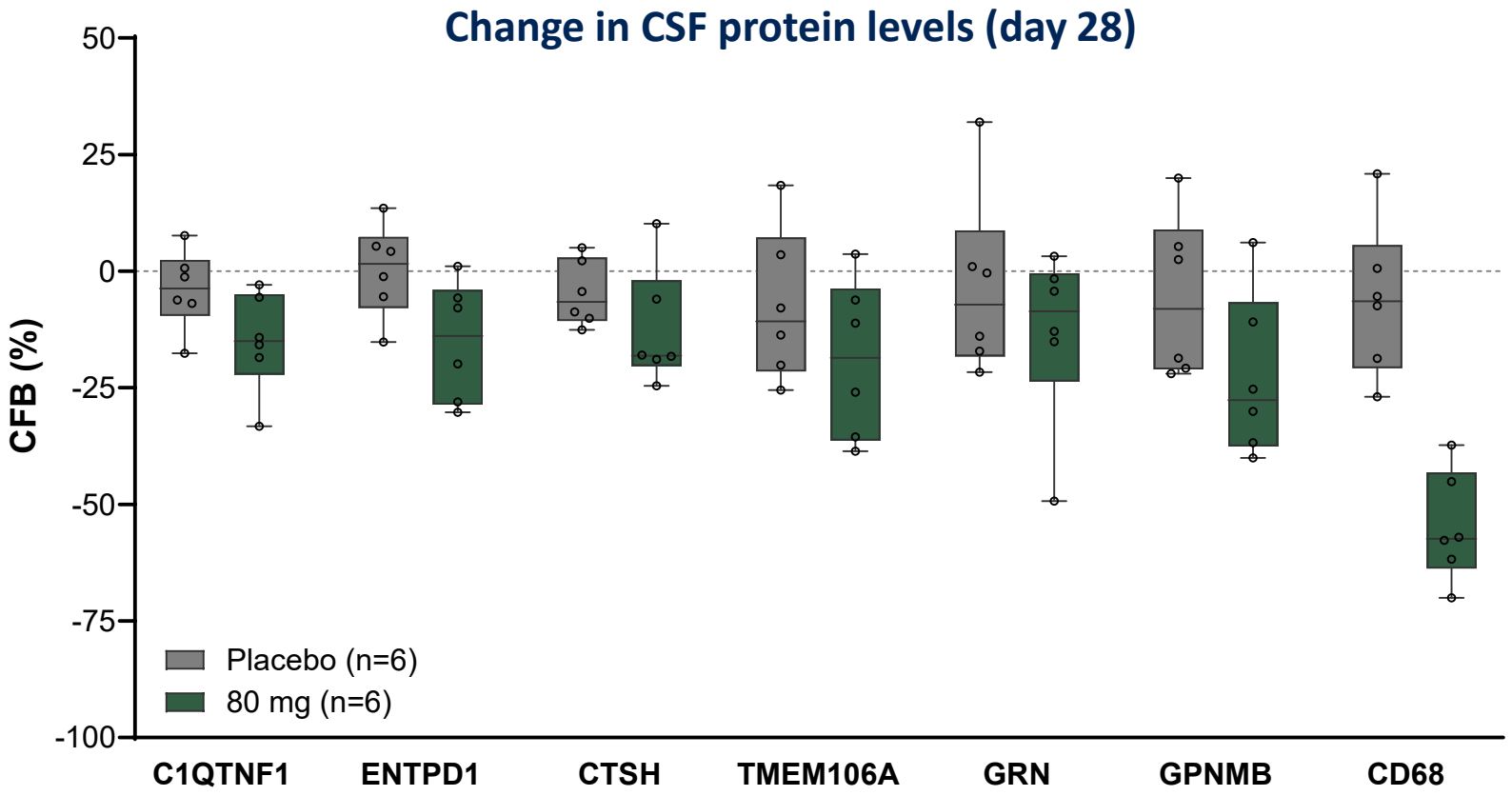
C1QTNF1, complement C1q tumor necrosis factor-related protein 1; CD68, cluster of differentiation 68; CSF, cerebrospinal fluid; ENTPD1, ectonucleoside triphosphate diphosphohydrolase 1; FC, fold change; GRN, granulin precursor; GPNMB, glycoprotein non-metastatic melanoma protein B; HLA-DQA2, major histocompatibility complex, class II, DQ alpha 2; ITGB2, integrin subunit beta 2; LRRK2, leucine-rich repeat kinase 2; PheWAS, protein phenome-wide association studies; PPMI, Parkinson's Progression Markers Initiative; SDCBP2, syndecan binding protein 2; TLR3, Toll-like receptor 3; TMEM106A, transmembrane protein 106A.

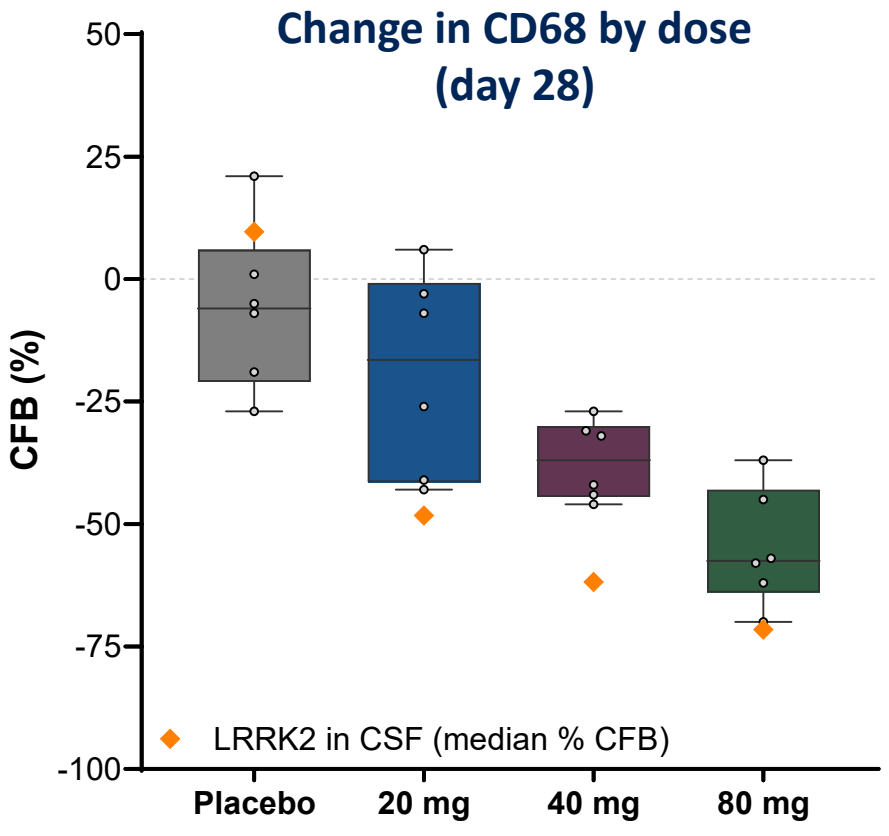
a, .Global O'Brien's statistical test was utilized to evaluate aggregate change in top 10 proteins related to LRRK2 variants. b. Figure adapted from Phillips et al. (2023). NPJ Parkinson's Disease.

1. Phillips B, et al. NPJ Parkinsons Dis. 2023;9(1):107. 2. Smits L, et al. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders (MDS) 2025; Poster #LBA 22.

As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

ARV-102 at 80 mg QD led to consistent reductions from baseline across the predefined panel of CSF proteins





As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

C1QTNF1, complement C1q tumor necrosis factor-related protein 1; CD68, cluster of differentiation 68; CFB, change from baseline; CTSH, cathepsin H; CSF, cerebrospinal fluid; ENTPD1, ectonucleoside triphosphate diphosphohydrolase 1; GRN, granulin precursor; GPNMB, glycoprotein non-metastatic melanoma protein B; LRRK2, leucine-rich repeat kinase 2; QD, once daily; TMEM106A, transmembrane protein 106A.

Development plan for ARV-102 includes clinical trials in patients with progressive supranuclear palsy and Parkinson's disease

Status of ARVINAS Trials with ARV-102

OBJECTIVES: Safety, Tolerability, PK, and PD

Phase 1: Healthy Volunteers (Complete)

Single Ascending Dose (Part A) Multiple Ascending Dose (Part B)

- ✓ First-in-human data presented during oral presentation at AD/PD (Q2 2025)
- ✓ Final data from HV SAD/MAD cohorts presented at MDS (Q3 2025)

Phase 1: Parkinson's Disease (Complete)

Single Ascending (Part A) and Multiple Dose (Part B)

- ✓ Presented initial single ascending dose data at (MDS Q3 2025)
- ✓ Presented multi-dose cohort during oral presentation at AD/PD (Q1 2026)

Planned trials in 2026 (pending regulatory feedback)*

Phase 1b/2: Progressive Supranuclear Palsy

Phase 1b: Multiple dose

- Initiate multi-site Phase 1b multi-dose cohort in patients with progressive supranuclear palsy (2H 2026)

Phase 2: Potential for registrational pathway

- Initiate multi-site Phase 2 trial in patients with progressive supranuclear palsy (2H 2026)
  - Potential for registrational pathway

AD/PD, International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders; MDS, Movement Disorders Society; PK; Pharmacokinetics; PD, pharmacodynamics; PSP, progressive supranuclear palsy

*Upon submission of final chronic toxicology data in non-human primates and FDA clearance to proceed with the Phase 1b trial

CLINICAL PROGRAMS: Neurology

ARV-027

PROTAC polyQ-AR degrader

ARVINAS

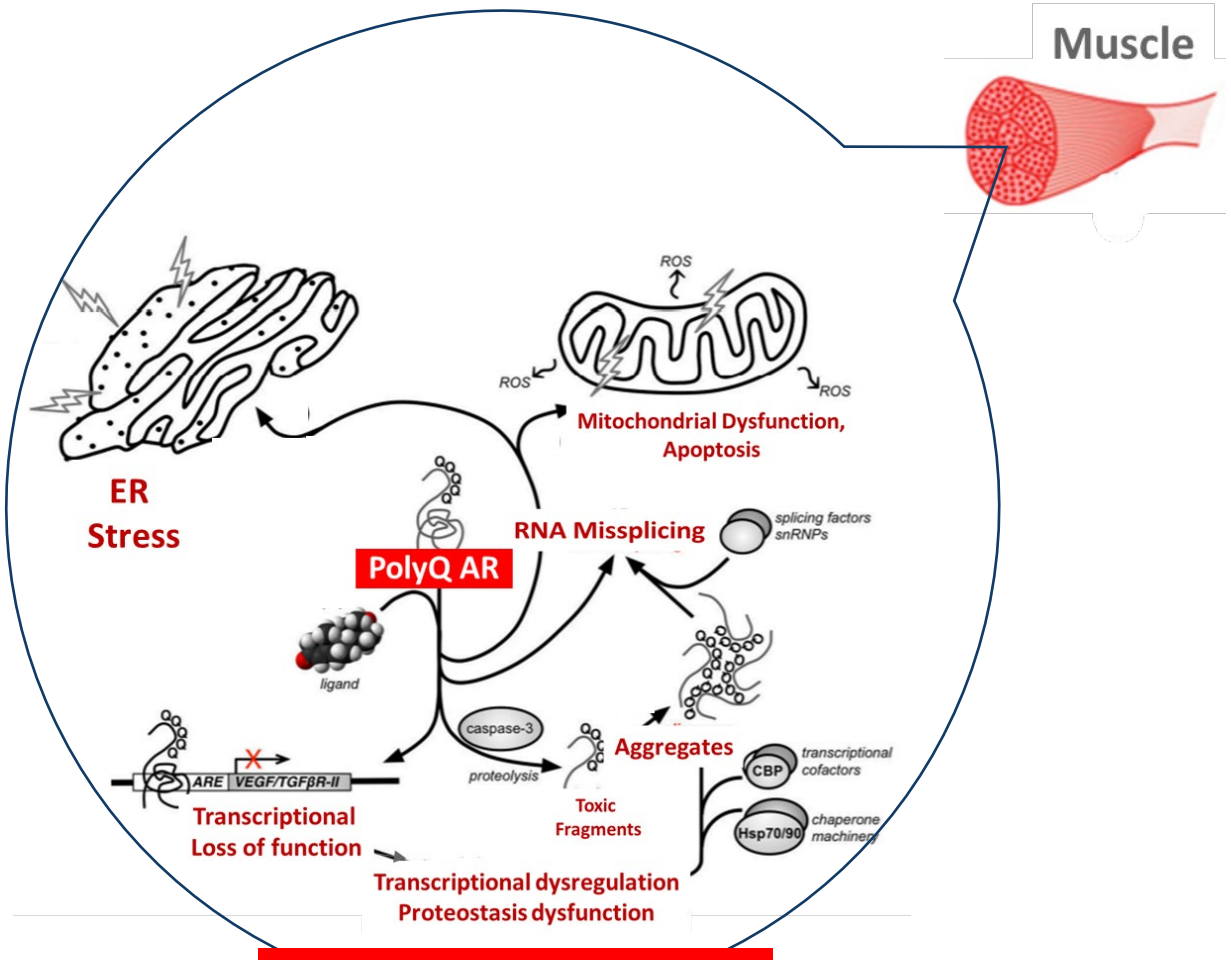
ARV-027 is an investigational compound. Its safety and effectiveness have not been established.

Spinal bulbar muscular atrophy is caused by a trinucleotide CAG repeat expansion in the androgen receptor

Spinal bulbar muscular atrophy (SBMA) is a rare, genetically defined, neuromuscular disease

- X-linked inheritance pattern and caused by a polyglutamine (polyQ) expansion in the androgen receptor (AR)
- Clinical features result from both the loss of normal androgen signaling and gain of toxic properties due to the polyQ-expansion
- PolyQ-AR ultimately causes death of myofibers by apoptosis, leading to progressive muscle weakness and loss of motor neurons
- SBMA prevalence is estimated between 5.5-20K patients in the U.S.[1]

Muscle is heavily impacted in SBMA



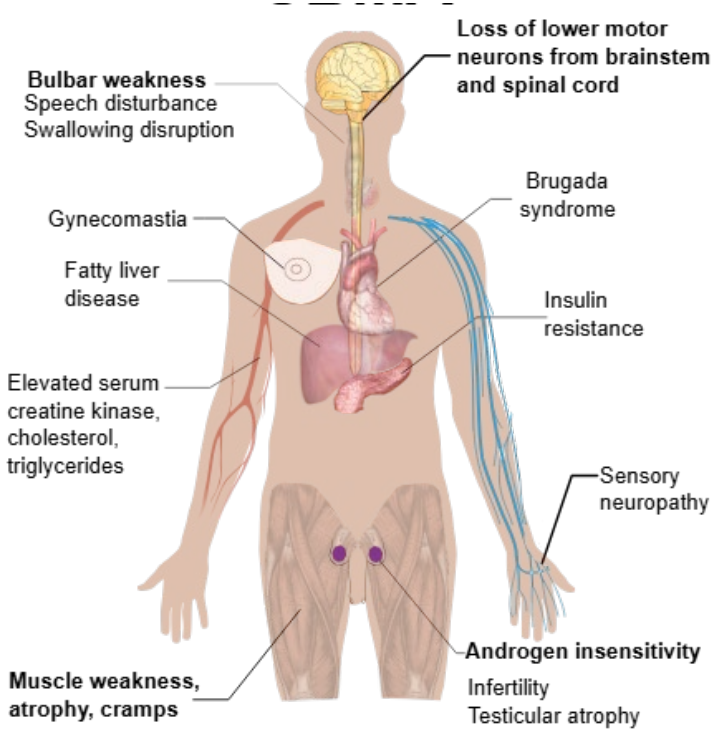
PROTAC PolyQ-AR degrader may eliminate the root cause of disease

Figure adopted from Chua J, et. al, CNS Neurol Disord Drug Targets. 2013. https://pubmed.ncbi.nlm.nih.gov/24040817

1. Zanovello et al., 2023

SBMA is a multisystemic disease and patients suffer from progressive debilitating neuromuscular symptoms[1]

SBMA Disease Overview



SBMA Natural History and Treatment Options

Onset typically occurs between 35 – 55 years old, with hand tremors and limb weakness being the most common initial manifestations

- Symptom Onset
- Diagnosis
- Dysphagia
- Cane Use
- Wheelchair Use
- Death

Life expectancy is modestly impacted (brugada / aspiration pneumonia), but disability severely impacts patients

There are no approved therapies for SBMA in the U.S.

Current treatment focuses on symptom management only, including physical therapy and rehabilitation

High unmet need for disease-modifying therapy to slow down the disease progression or reverse disease biology

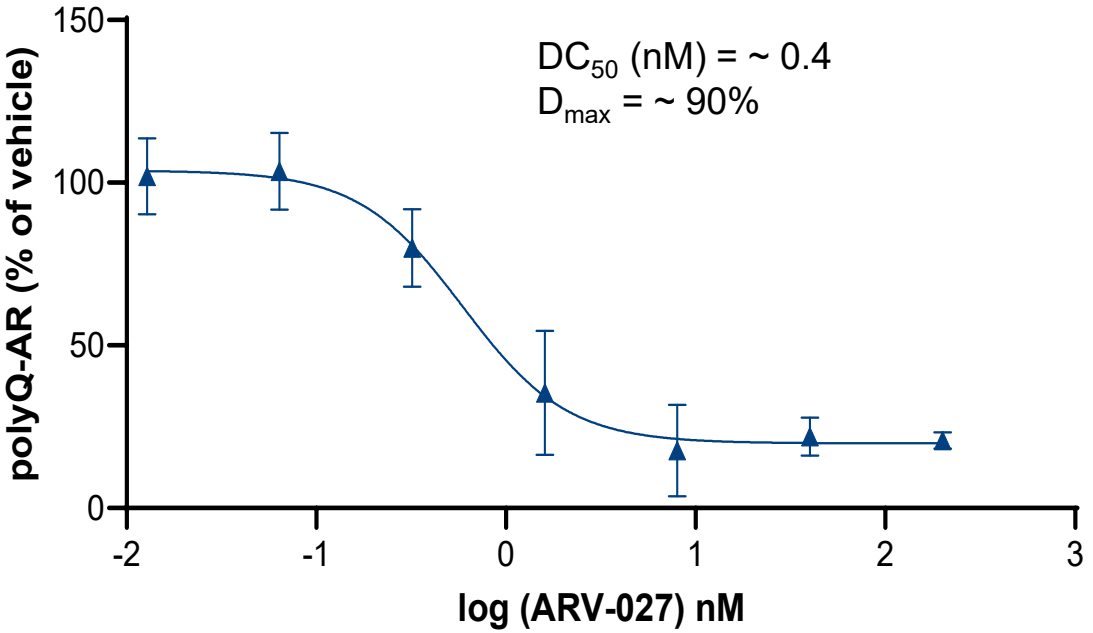
SBMA, spinal bulbar muscular atrophy

[1] Grunseich et al. Curr Opin Neurol 2020; 33(5):629-634

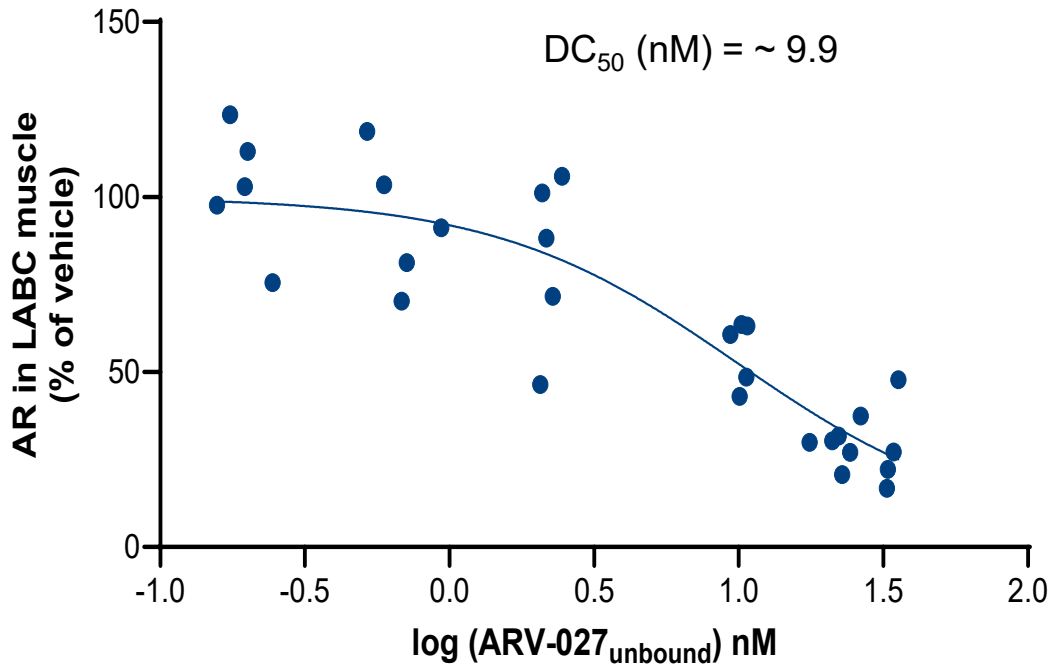
ARV-027 is a potent *in vitro* and *in vivo* PROTAC degrader of polyQ-AR, the root cause of SBMA[1]

ARVINAS

ARV-027 induces degradation of polyQ-AR in myotubes derived from SBMA patient induced pluripotent stem cells



ARV-027 induces degradation of AR in muscle tissue from male mice



The mechanism of the polyQ-AR degradation was confirmed to be E3 ligase and proteosome dependent (data not shown)

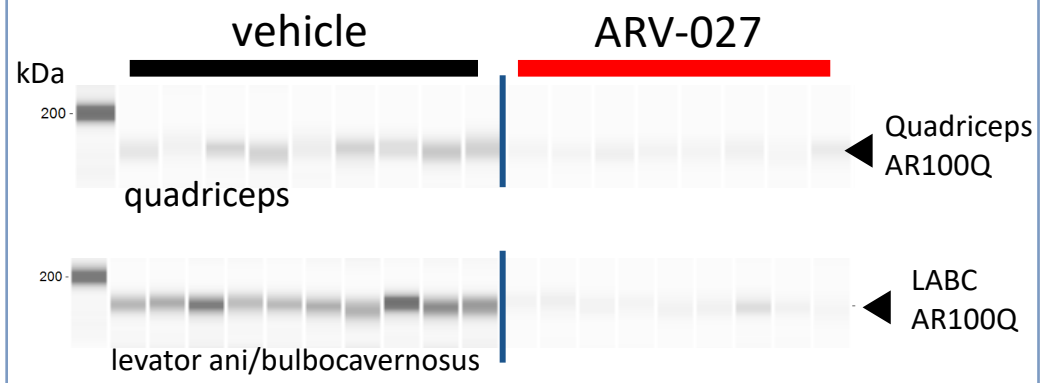
polyQ-AR, polyglutamine-expanded (polyQ) androgen receptor (AR); SBMA, spinal bulbar muscular atrophy

[1] Young J, et al. JNEUROSCI.4072-08.2009

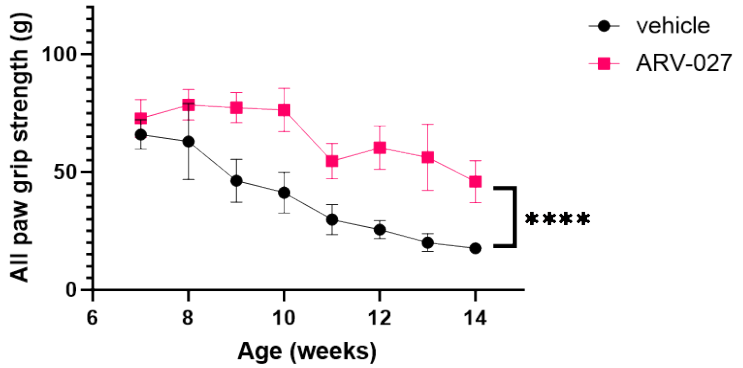
Gregory J et al., International Congress of the World Muscle Society (WMS), Poster 718LBP. Presented October 10, 2025

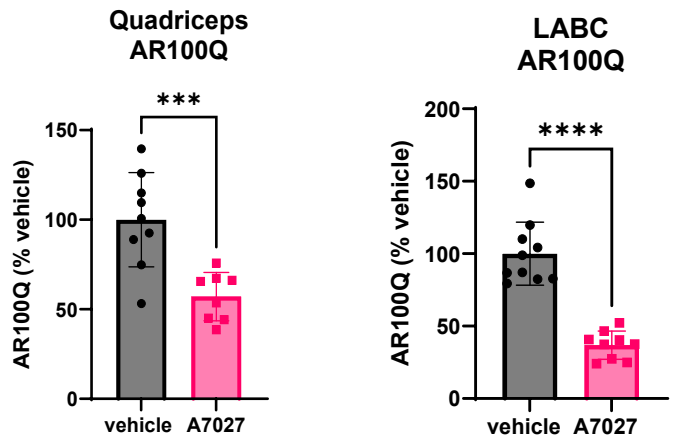
In preclinical models, ARV-027 induced polyQ-AR degradation in muscle tissues and rescued strength and endurance

Monomeric polyQ-AR[a]



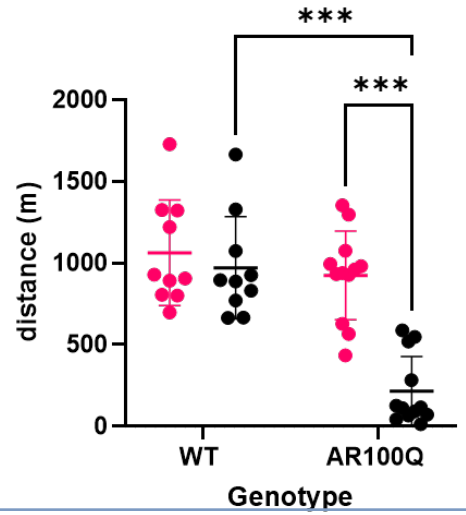
All Paw Grip Strength[a]





Degradation of monomeric polyQ-AR ranged from 43-63%[a]

Endurance (Distance on Treadmill)[a]



polyQ-AR, polyglutamine-expanded (polyQ) androgen receptor (AR); SBMA, spinal bulbar muscular atrophy

a. AR100Q mice

Gregory J et al., International Congress of the World Muscle Society (WMS), Poster 718LBP. Presented October 10, 2025

A first-in-human Phase 1 clinical trial of ARV-027 is currently enrolling healthy volunteers

Status of ARVINAS Trials with ARV-027

OBJECTIVES: Safety, Tolerability, PK, and PD

ARV-027 Phase 1 trial

SINGLE ASCENDING DOSE in healthy volunteers	**MULTIPLE ASCENDING DOSE** in healthy volunteers	**MULTIPLE ASCENDING DOSE** in patients with SBMA
Ongoing: Part A ✓ Single ascending dose cohorts in healthy volunteers	*Planned: Part B* • Multiple ascending dose cohorts in healthy volunteers	*Planned: Part C* • Multiple doses in patients with SBMA

PK; Pharmacokinetics; PD, pharmacodynamics; SBMA; spinal bulbar muscular atrophy

CLINICAL PROGRAMS: Oncology

ARV-806

PROTAC KRAS G12D degrader

ARVINAS

ARV-806 is an investigational compound. Its safety and effectiveness have not been established.

ARV-806 is a novel PROTAC KRAS G12D degrader with the potential to be a best-in-class therapy

ARVINAS

KRAS is one of the most frequently mutated human oncogenes and G12D is the most common mutation of the KRAS protein. ARV-806 has the potential to address high unmet need in solid tumors, such as pancreatic, colorectal, and non-small cell lung cancer.

KRAS G12D

ARV-806 is a novel, investigational PROTAC **degrader** that is designed to target both the ON and OFF forms of the KRAS G12D protein.

There are no approved drugs for KRAS G12D mutated cancers, where patients have high unmet need and poor survival outcomes.

ARV-806 is differentiated from other G12D targeting agents in development and has potential to be a best-in-class therapy for KRAS G12D mutated cancers due to:

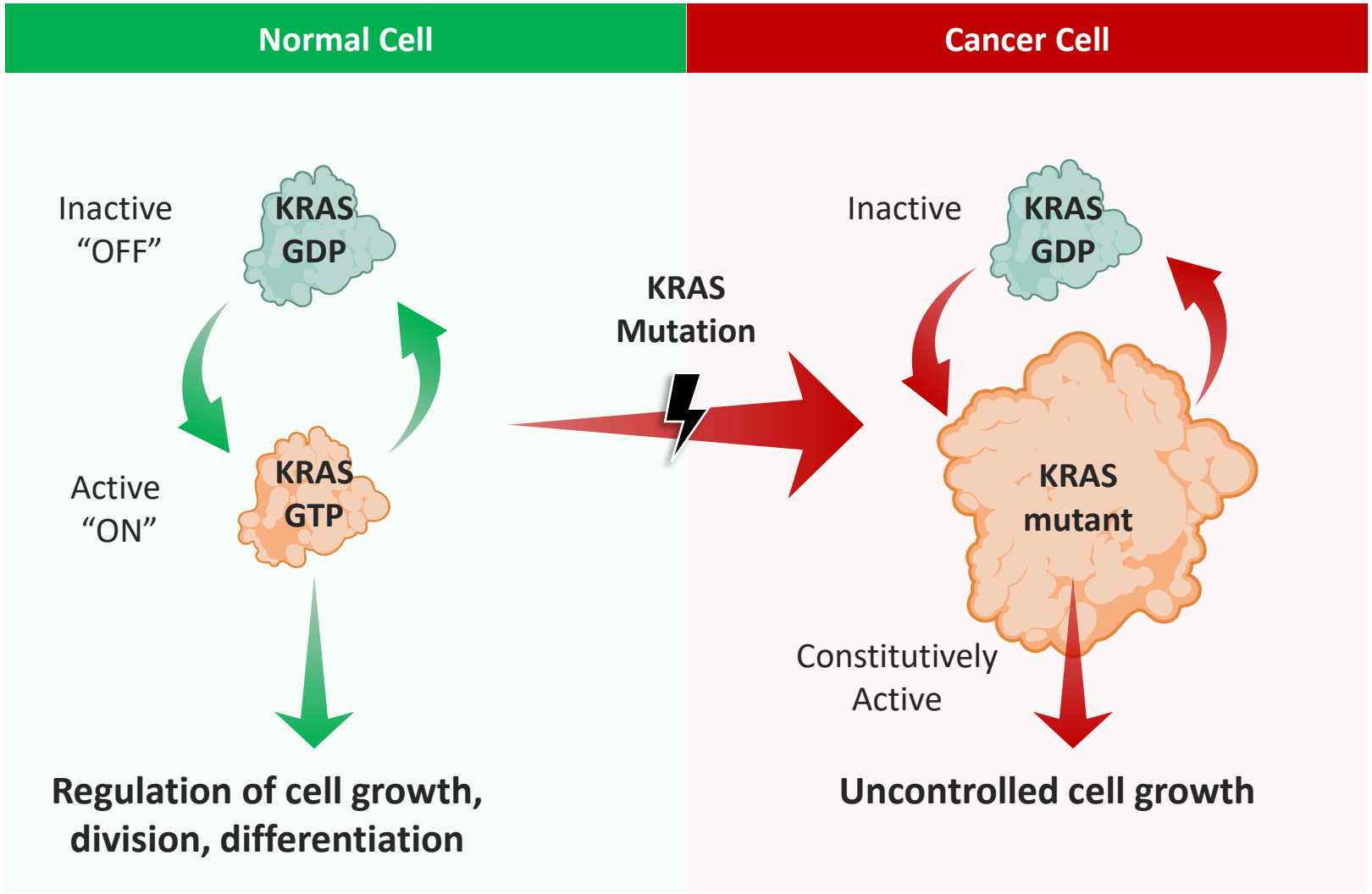
- Catalytic activity (overcomes upregulation, a common mechanism of resistance to inhibitor treatment)
- Preclinically, ARV-806 demonstrated >40-fold higher potency in degrading KRAS G12D protein vs the comparable clinical-stage G12D degrader
- Preclinically, ARV-806 demonstrated >25-fold greater potency in reducing cancer cell proliferation compared with clinical-stage KRAS G12D ON and OFF inhibitors and a clinical-stage G12D degrader

A Phase 1 clinical trial is currently enrolling patients with advanced solid tumors harboring KRAS G12D mutations (NCT07023731)

G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

1. Zeissig, Mara N. et al., Trends in Cancer, https://www.cell.com/trends/cancer/fulltext/S2405-8033(23)00137-1.

KRAS is a key regulator of cell growth, and KRAS mutations lead to cancer

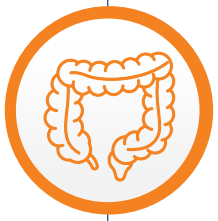
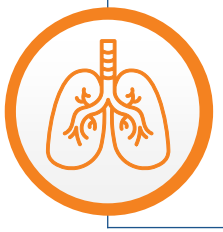


Role of KRAS G12D in Cancer[1,2]

- KRAS is a GTPase that alternates between inactive and active states, regulating several critical signaling pathways
- Mutations in KRAS, such as G12D, lock the protein in the active "ON" state, leading to uncontrolled cell growth and cancer development
- KRAS G12D is the most frequent KRAS mutation and one of the most common mutations across various cancer types

1. Huang, L., Guo, Z., Wang, F. et al., Sig Transduct Target Ther 6, 386 (2021). https://doi.org/10.1038/s41392-021-00780-4.
2. Lee et al., NPJ Precis. Oncol., 2022; Cox et al., Nat Rev Drug Dis, 2014. Vasan et al., 2014, Clin Cancer Res.

Patients with metastatic cancers harboring KRAS G12D mutations have poor survival outcomes with no approved KRAS G12D-targeted therapy

Key Tumors Harboring KRAS G12D Mutations	5-year Survival Rate for Metastatic Setting[1]	Newly Diagnosed Patients Per Year in the US (2025)[2]	Prevalence of KRAS G12D Mutations
 **Pancreatic ductal adenocarcinoma**	~3%	~60,000	~35 - 40%[3,4]
 **Colorectal carcinoma**	~16%	~158,000	~12 - 15%[3,4]
 **Non-small cell lung cancer**	~10%*	~195,000	~3 - 4%[3,4,5]

G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

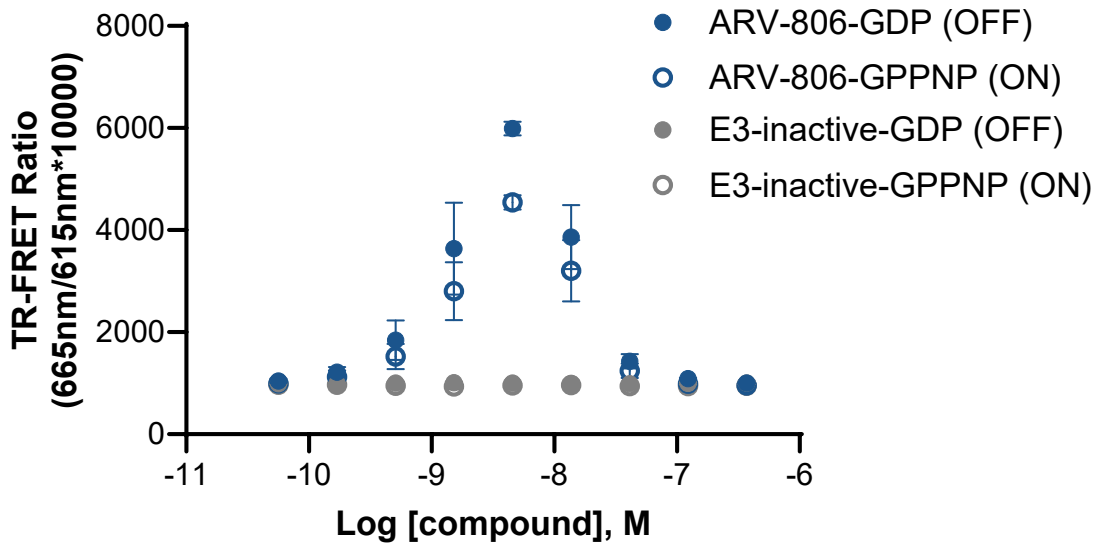
1. Surveillance, Epidemiology, and End Results (SEER) Program Data, Cancer Stat Facts; 2. The American Cancer Society's Cancer Facts & Figures 2026; 3 Lee et al., NPJ Precis. Oncol., 2022, 4 AACR Project Genie (Genomics Evidence Neoplasia Information Exchange); 5 Acker et al., Frontiers in Oncol., 2021

*Reported for combined non-small cell lung cancer and small-cell lung cancer

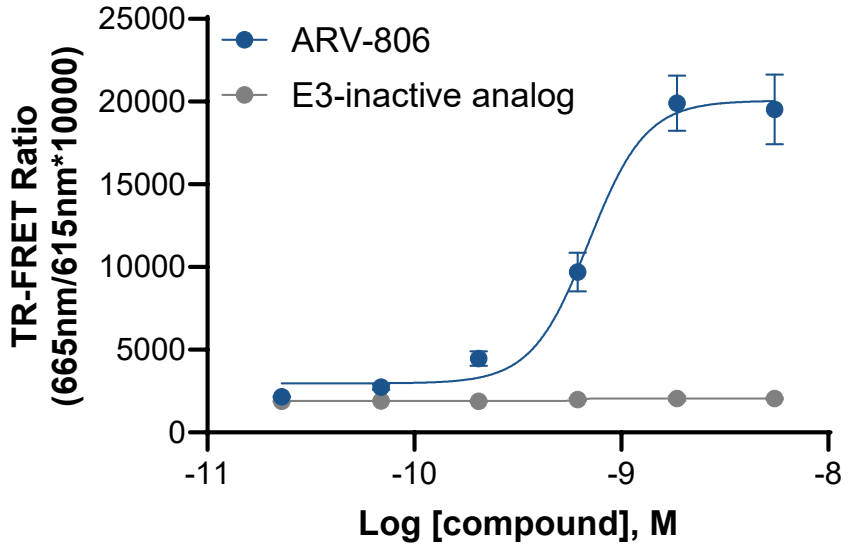
ARV-806 targets both ON and OFF forms of KRAS G12D

- ARV-806 forms a ternary complex with **both** OFF (GDP-bound) and ON (GTP-bound) KRAS G12D
  - Targeting both OFF and ON KRAS G12D allows ARV-806 to **eliminate** this oncogenic protein from the cell
- ARV-806 treatment directly leads to ubiquitination of KRAS G12D protein

Ternary Complex Formation



Ubiquitination of KRAS G12D Protein



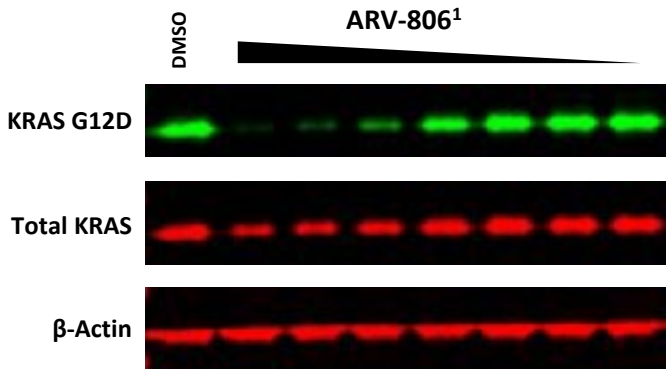
G12D, mutations in codon 12 on KRAS oncogene; GPPNP is a non-hydrolysable analog of GTP; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston

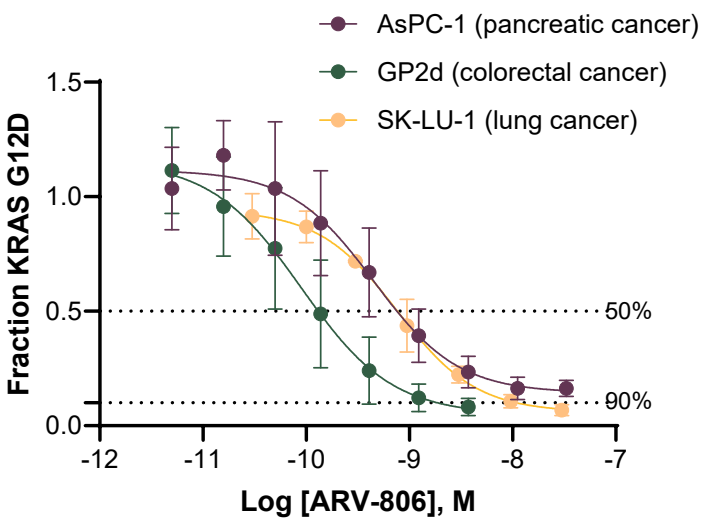
Preclinical data show ARV-806 is a highly potent, selective degrader of KRAS G12D

ARV-806 degrades KRAS G12D with picomolar potency

Degradation of KRAS G12D in GP2d Colorectal Cancer Cells



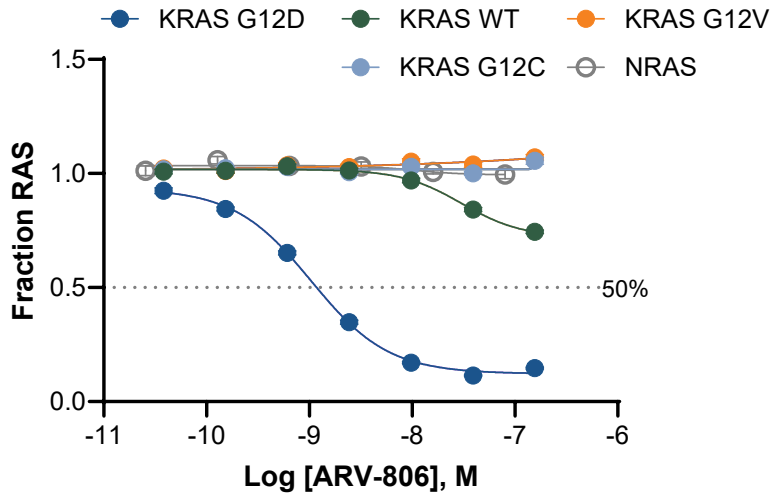
Degradation of KRAS G12D Multiple Cancer Cell Lines[2]



ARV-806 effectively eliminates KRAS G12D from cancer cells

ARV-806 is selective for KRAS G12D

Degradation of RAS Measured by HiBit Signal[3]



ARV-806 demonstrates exquisite selectivity for KRAS G12D, indicating a robust therapeutic index

G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); RAS, rat sarcoma

1. Concentrations of ARV-806: 3 nM – 3 pM; 2. Data from western blot of endogenous KRAS G12D levels; 3. Cell lines bearing HiBit-tagged variants of KRAS and NRAS were assessed for degradation when treated with ARV-806

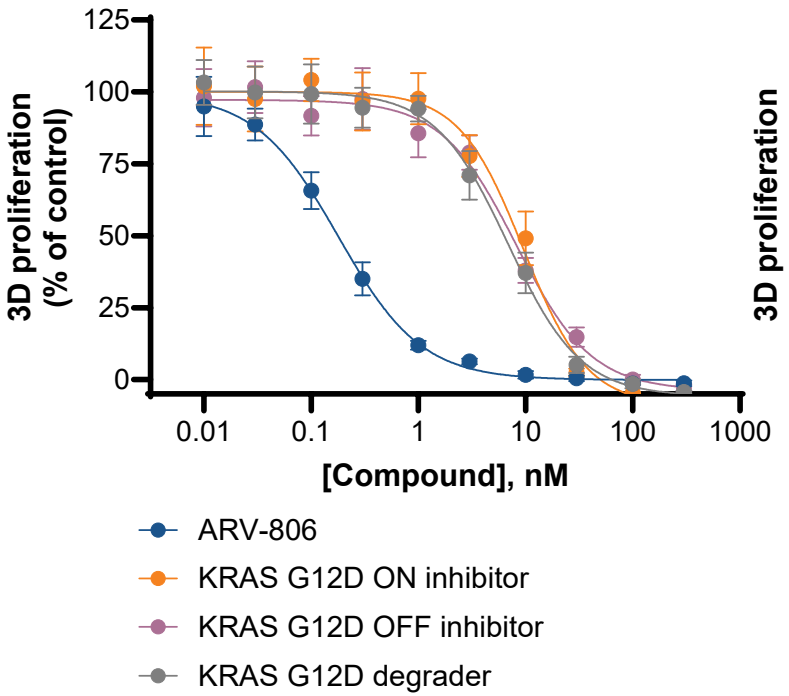
Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston

Preclinically, ARV-806 demonstrates anti-proliferative activity 25-40-fold greater than KRAS inhibitors and the leading clinical-stage degrader

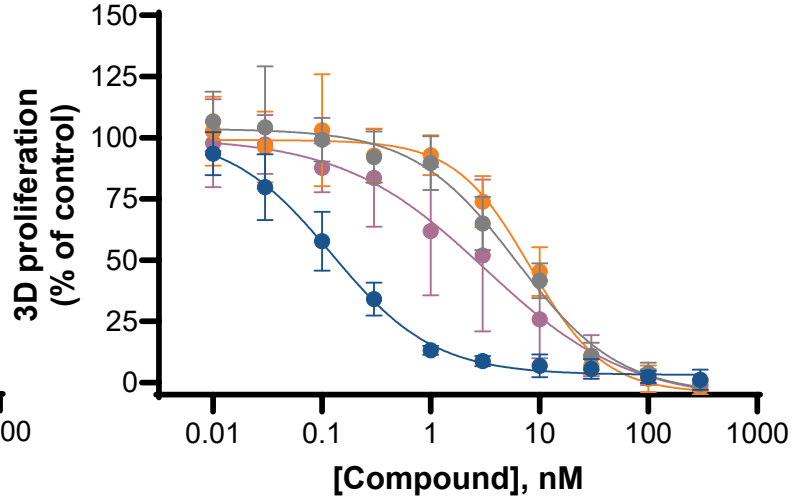
Proliferation

ARV-806 >**25-fold** more potent than all G12D-targeting competitors

AsPC-1 Pancreatic Cancer Cells[1]



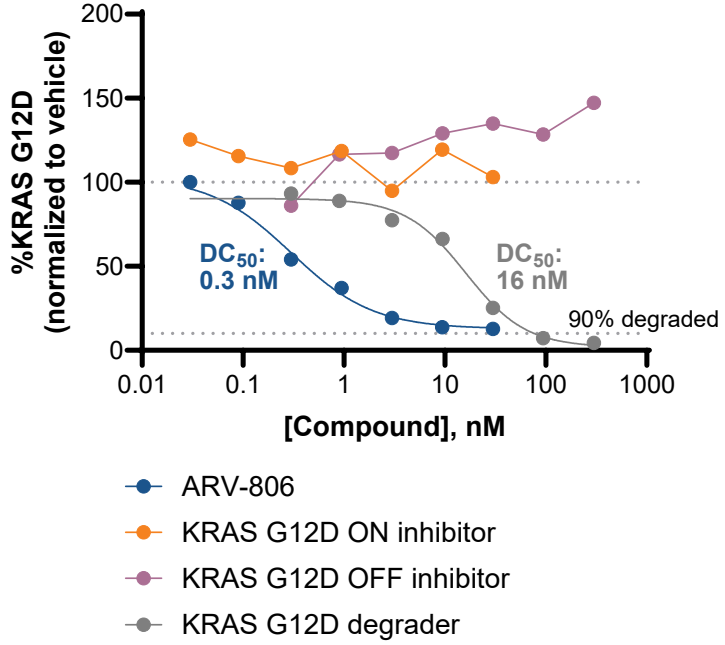
GP2d Colorectal Cancer Cells[2]



KRAS G12D Levels

ARV-806 >**40-fold** more potent

KRAS G12D Levels AsPC-1 Pancreatic Cancer Cells[3]



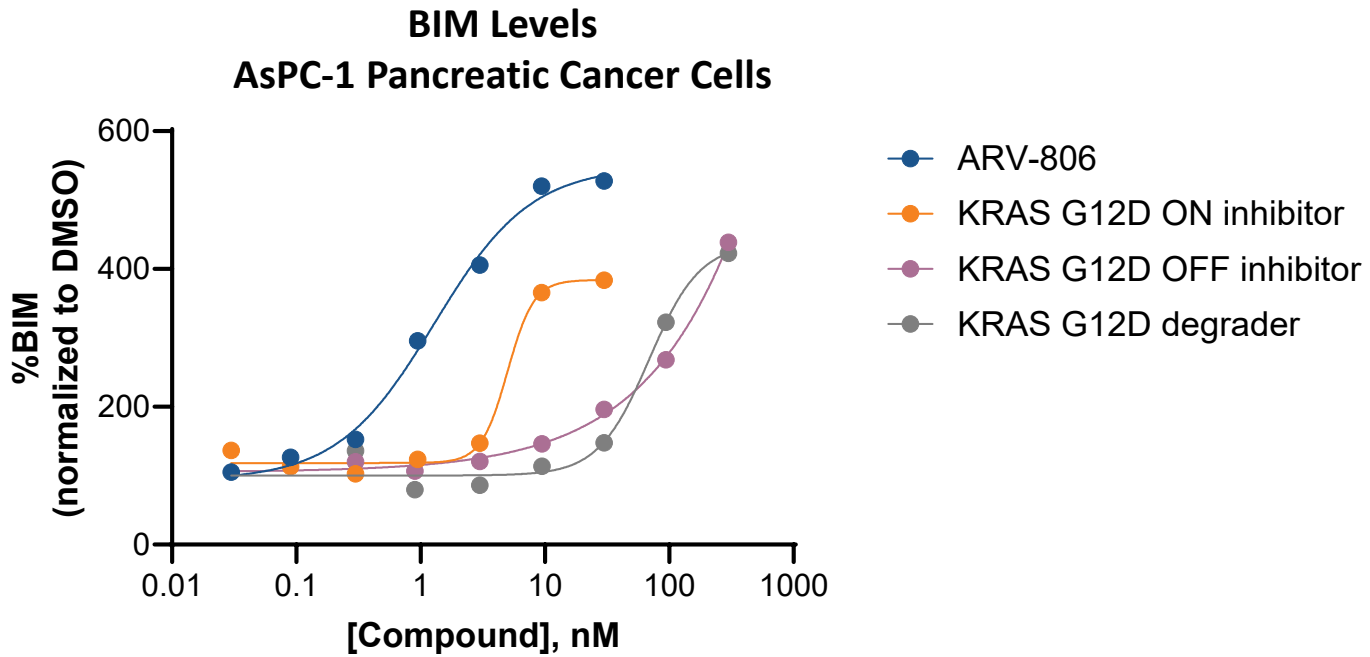
G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

1. AsPC-1 (G12D/G12D) pancreatic cancer cells treated for 5 days; 2. GP2d (G12D/WT) colorectal cancer cells treated for 5 days 3. Treatment for 24 hours;

Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston

ARV-806 more potently induces pancreatic cancer cell death *in vitro* relative to clinical-stage inhibitors and degrader

ARV-806 more potently increases apoptosis (cell death)

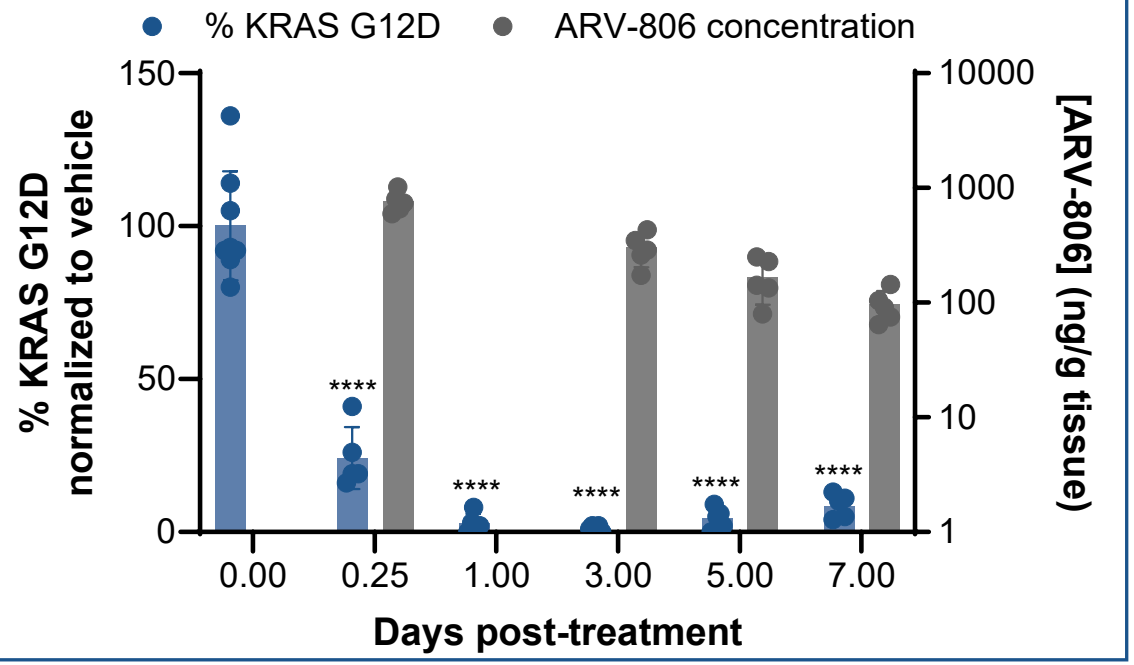


- Similar pharmacology observed for caspase 3/7 activity

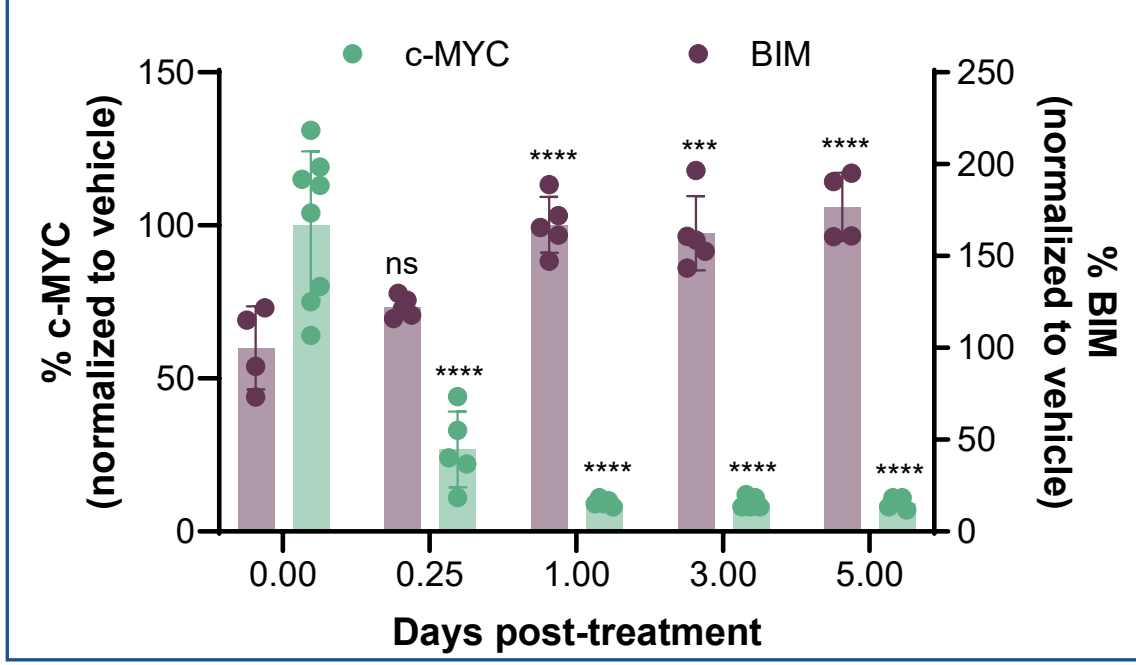
BIM, Bcl-2-interacting mediator of cell death (a pro-apoptotic factor); G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)
Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston
Treatments were for 24 hours

ARV-806 leads to robust and extended degradation and signaling suppression *in vivo*

KRAS G12D reduced >90% for 7 days[a]



Proliferative marker (c-MYC) suppressed and pro-apoptotic marker (BIM) increased for 5 days[a]



G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

a. Single IV dose of 3 mpk ARV-806 administered to mice bearing colorectal cancer tumors (GP2d xenograft model)

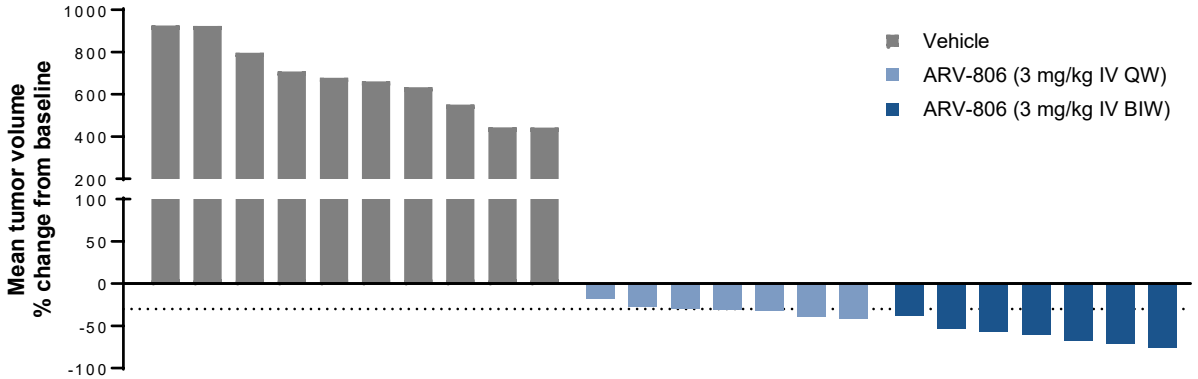
Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston

ARV-806 demonstrated robust responses at low doses in models of colorectal, pancreatic, and non-small cell lung cancers

≥30% tumor volume reductions in pancreatic and colorectal CDX models and a patient-derived xenograft (PDX) model of lung cancer

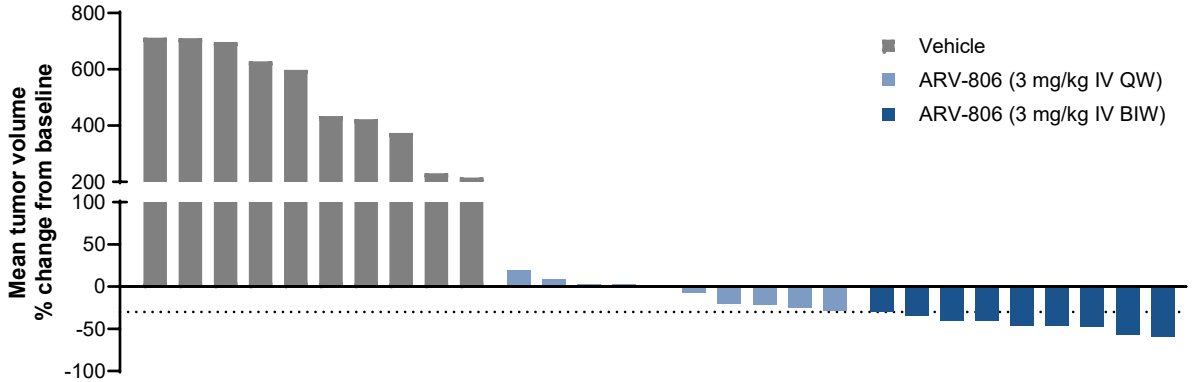
Pancreatic Cancer

SW1990 KRAS G12D Xenograft Model



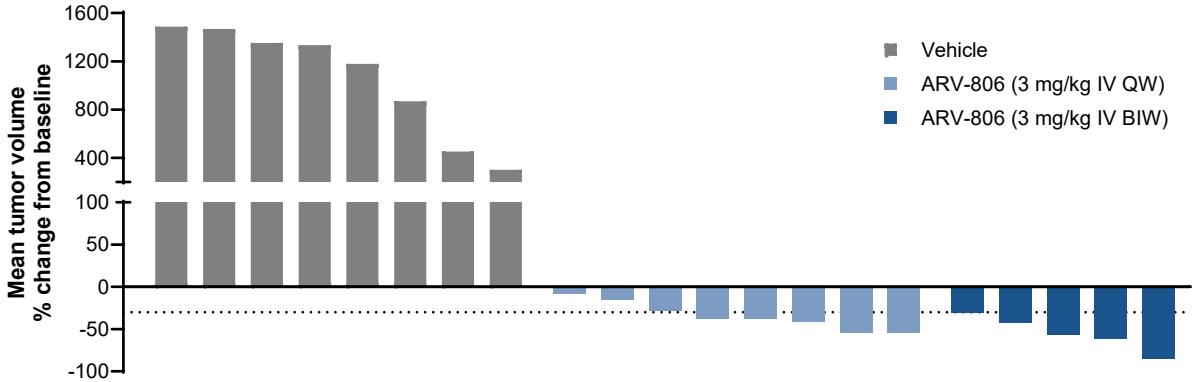
Colorectal Cancer

GP2d KRAS G12D Xenograft Model



Lung Cancer

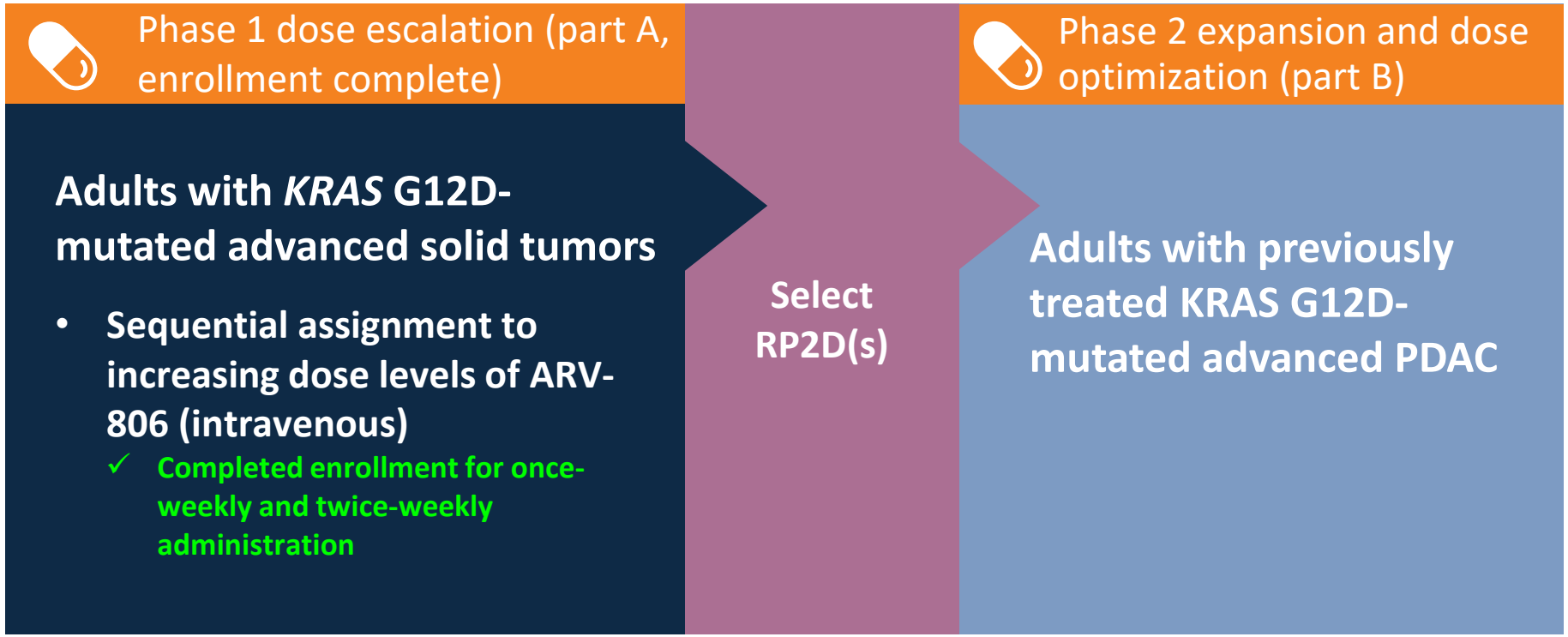
CTG-2803 KRAS G12D PDX Model



CDX, cell-derived xenograft; G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers)

Smith K et al., AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (AACR-NCI-EORTC) Poster B107. Presented October 24, 2025, Boston

A Phase 1/2 clinical trial of ARV-806 in KRAS G12D-mutated advanced solid tumors is currently enrolling



ARV-806 is being evaluated in an open-label, first-in-human Phase 1/2 clinical trial to assess its safety, tolerability, pharmacokinetics (PK), and preliminary antitumor activity in adult patients with KRAS G12D-mutated advanced solid tumors (NCT: 07023731)

G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); PDAC, pancreatic ductal adenocarcinoma; PK, pharmacokinetics; RP2D, recommended Phase 2 doses

CLINICAL PROGRAMS: Hematology-Oncology

ARV-393

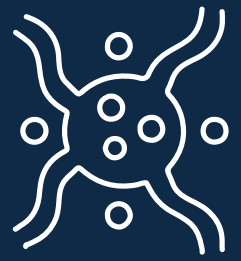
PROTAC BCL6 degrader

ARVINAS

ARV-393 is an investigational compound. Its safety and effectiveness have not been established.

A PROTAC BCL6 degrader has the potential to address substantial unmet needs for patients with non-Hodgkin lymphoma (NHL)

ARVINAS



Key Unmet Needs for Patients with Non-Hodgkin Lymphomas

Need for **safe and effective oral alternatives** to chemotherapy or immuno-chemotherapy SOC regimens

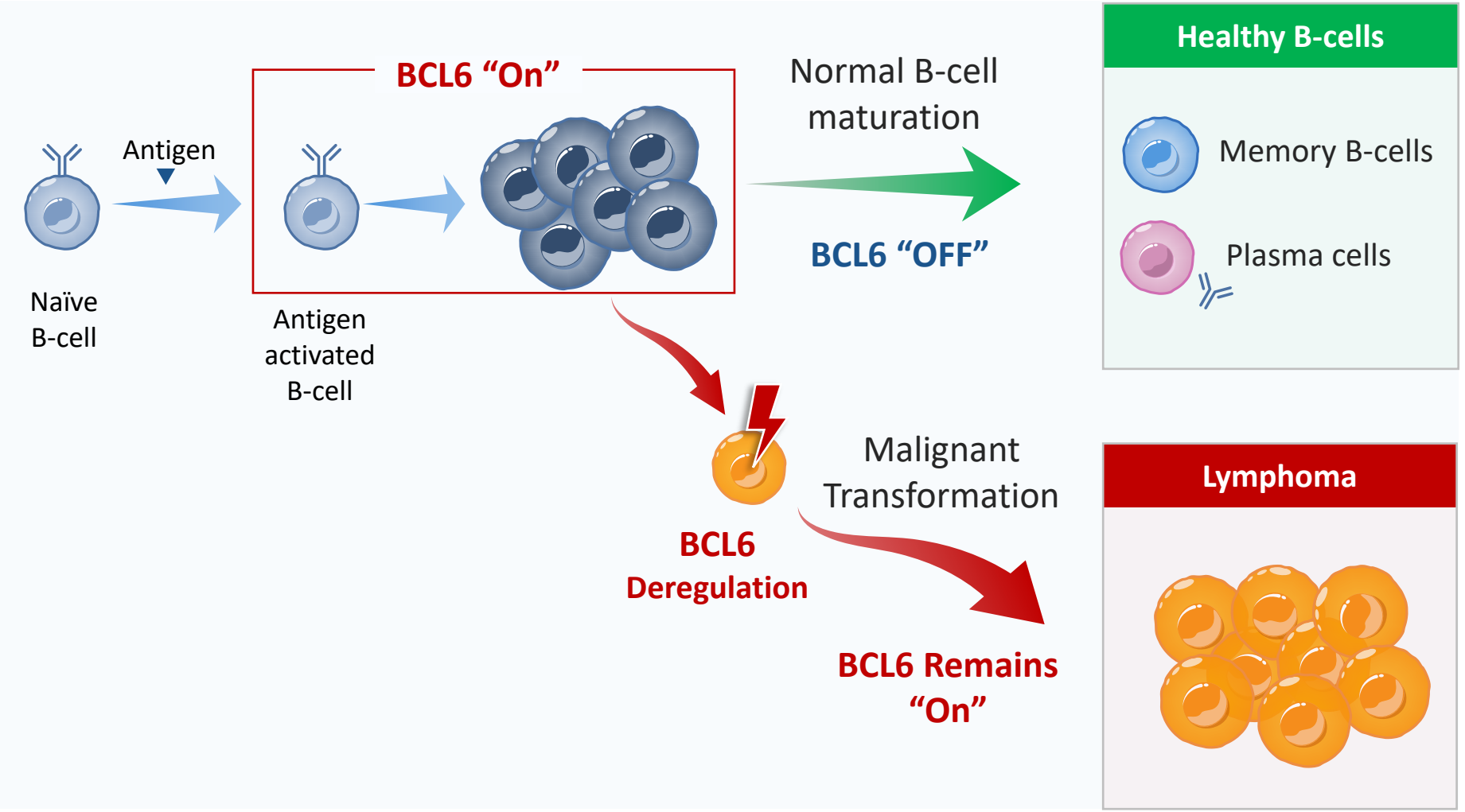
Need for patients with relapsed or high-risk disease, and particularly older adults

Large B-Cell Lymphoma (LBCL)	• Although a high proportion of patients achieve complete remission, therapy resistance or relapse still occurs in 30-40% of patients, thus evidencing a need for new therapeutic options[1] • Deregulation of BCL6 expression and/or functions are common in B-cell lymphomas[2]
Follicular Lymphoma (FL)	• Lack of effective options for patients who experience rapid disease progression within 2 years of initial therapy (POD24) • In ~15% of patients, indolent FL transforms into clinically aggressive lymphoma with rapid progression of disease and poor prognosis[3] • BCL6 mutation is associated with the transformation of FL
Other Subtypes of NHL	• T-cell lymphomas dependent on BCL6 (family of nodal T-follicular helper cell Lymphomas, nTFHL[4]) • nTFHL-AI (nTFHL, angioimmunoblastic type[4]), also known as AITL, is a rare and aggressive disease with no dedicated approved therapies and high levels of BCL6 expression[5]

AITL, angioimmunoblastic T-cell lymphoma; FL, Follicular Lymphoma; LBCL, Large B-Cell Lymphoma; NHL, non-Hodgkin lymphoma; nTFHL, nodal T-Follicular Helper Cell Lymphoma; nTFHL–AI, nodal T-Follicular Helper Cell Lymphoma angioimmunoblastic-type

1. Sehn and Salles NEJM 2021, 384(9):842. 2. Pasqualucci et al., Blood 2003;101 (8). 3. Conconi Br J Haematol 2012, 157(2):188-96. 4.De Level Die Pathologie 2023. 5. Nishizawa et al., Int J Hematol, 2017, 105(4):465.

Uncontrolled activation of BCL6 is implicated in development of B-cell lymphomas



The Importance of BCL6 in Lymphoma

- **Master Regulator –** BCL6 represses genes that control cell proliferation, survival, and apoptosis during B-cell maturation
- **Disrupts B-Cell Function –** Deregulated BCL6 alters cell signaling and cycle control, preventing proper B-cell differentiation
- **Drives Malignant Transformation –** Abnormal BCL6 activity enables B-cells to evade regulatory mechanisms, leading to lymphoma

Pasqualucci et al., Blood 2003;101 (8); Cattoretti et al., Cancer Cell 2005; 7, p445; Green et al., Nat Comm 2014; Lossos et al., Leukemia 2002 16; Lossos et al., Blood 2000, 96.

ARV-393 is an investigational oral PROTAC degrader that degrades BCL6, a classic “undruggable” protein

ARV-393

Potent, orally bioavailable PROTAC small molecule degrader of BCL6[1]

Degrades BCL6, a target that has long been considered “undruggable”

Differentiated preclinical profile. ARV-393 **potently and rapidly degrades** BCL6 protein and has iterative activity, which is critical to overcoming BCL6’s rapid resynthesis rate and sustaining antitumor activity

Demonstrated significant anti-tumor single-agent activity[1] and broad combinability with complete tumor regressions in combination with SOC biologics and investigational small molecule agents in numerous preclinical *in vivo* models of NHL[2], with potential to become an **attractive combination partner** for development of novel treatment approaches for NHL including **all oral or chemotherapy-free options**

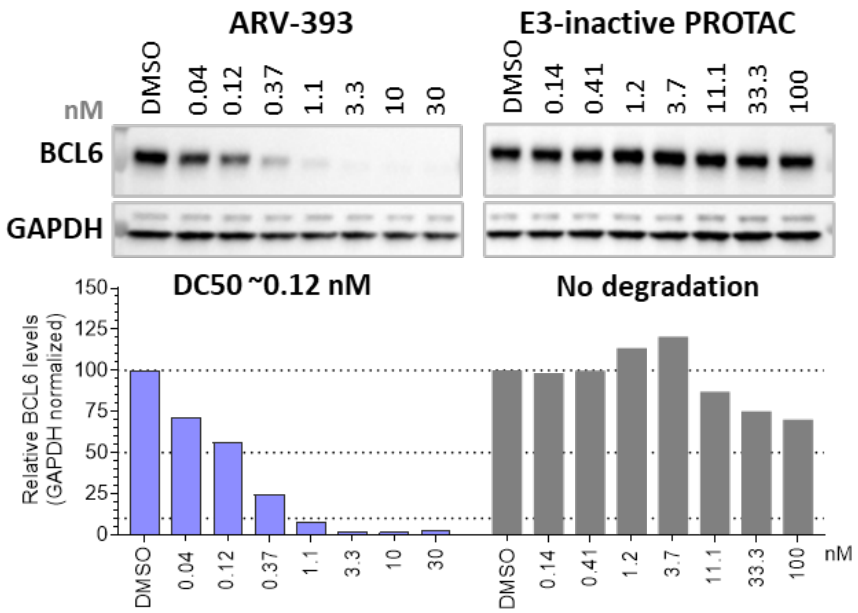
Phase 1 dose escalation trial of ARV-393 as monotherapy and in combination with glofitamab is currently enrolling patients with relapsed/refractory NHL (NCT06393738)

BCL6, B cell lymphoma 6; NHL, non-Hodgkin lymphoma; SOC, standard of care

1. Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain. 2. Van Acker et al., American Association for Cancer Research (AACR) Poster 1655/15. April 2025, Chicago.

ARV-393 potently degrades BCL6 in human lymphoma cell lines

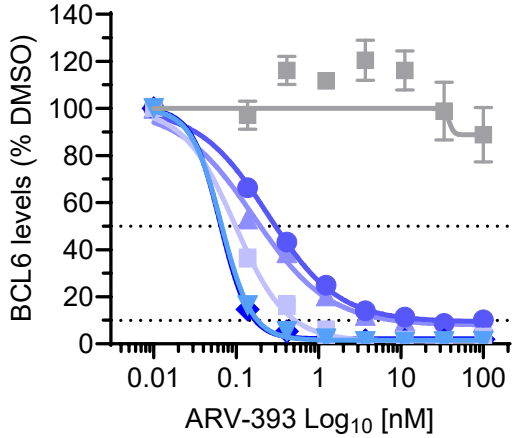
ARV-393, but not its E3-inactive analogue, robustly degrades BCL6 in the OCI-Ly1 model of DLBCL



Semi-quantitative western blot of BCL6 degradation by ARV-393

The E3-inactive analogue of ARV-393 cannot engage the E3 ligase and does not degrade BCL6, confirming ARV-393 degradation is mediated by PROTAC mechanism

ARV-393 exhibits picomolar degradation potency in quantitative immunocapture assay in multiple DLBCL cell lines



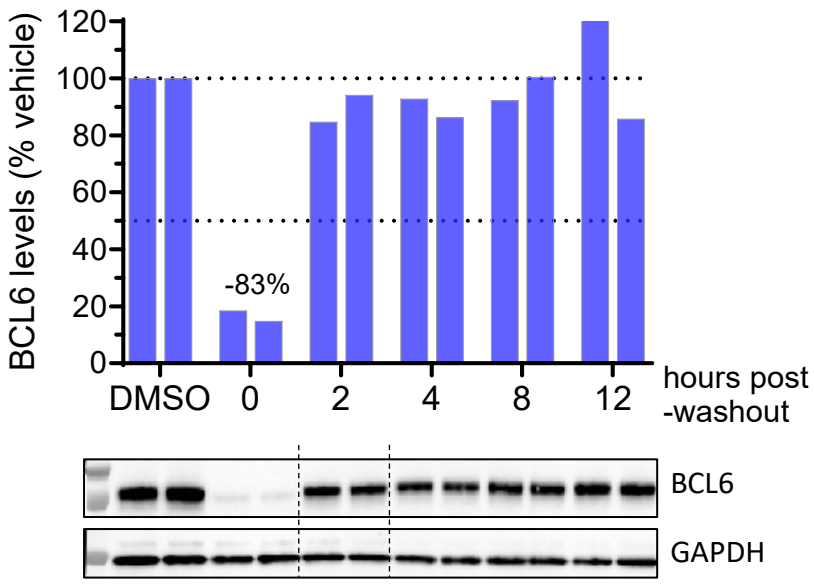
	DC_{50} [nM]	D_{max}
OCI-Ly1	0.07	99%
Farage	0.06	98%
SU-DHL-4	0.33	91%
SU-DHL-6	0.21	92%
OCI-Ly7	0.10	99%
OCI-Ly1 (E3-inactive ARV-393 analogue)	-	-

BCL6, B cell lymphoma 6; DLBCL, diffuse large b-cell lymphoma

Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain.

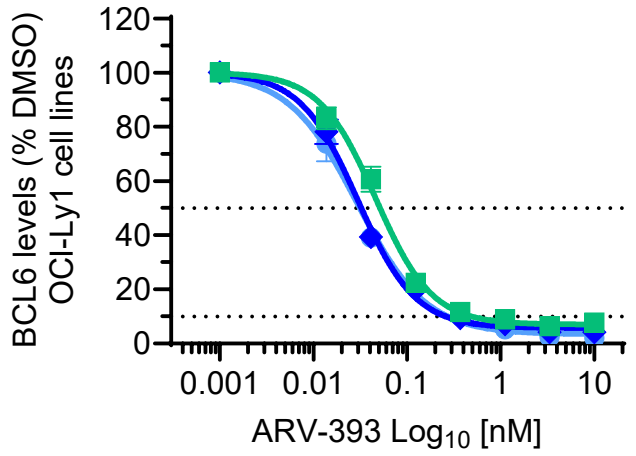
Preclinically, ARV-393 rapidly degrades BCL6 and overcomes its high resynthesis rate that drives tumor cell growth

BCL6 protein is resynthesized rapidly – nearly back to baseline levels at 2 hours post-ARV-393 washout



OCI-Ly1 cells were treated with 1.5 nM ARV-393 for 4 hours. Duplicate samples are shown following ARV-393 washout and addition of cereblon ligand (to block residual ARV-393)

ARV-393 rapidly degrades >90% of BCL6 within 2 hours - degrading BCL6 faster than the cell can resynthesize it



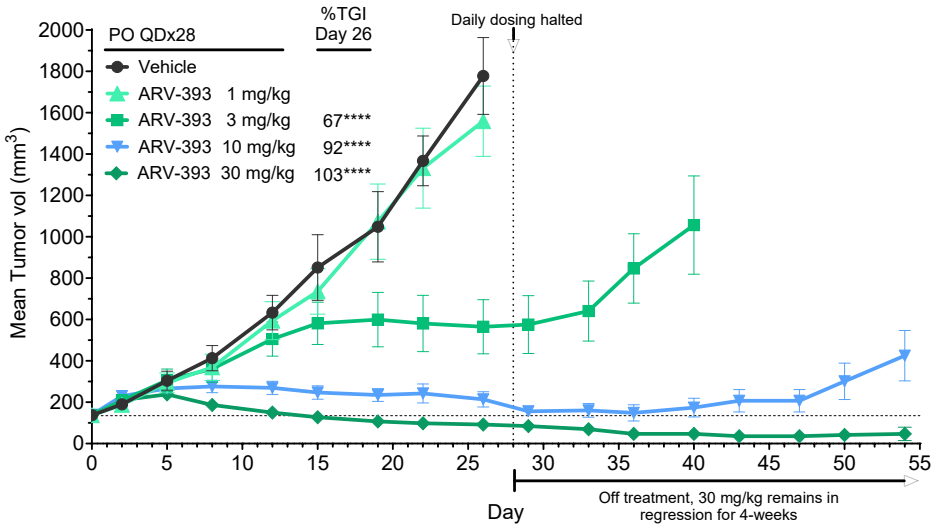
	DC_{50} [nM]	D_{max}
2 hours	0.05	93%
4 hours	0.03	94%
24 hours	0.03	97%

BCL6, B cell lymphoma 6

Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain.

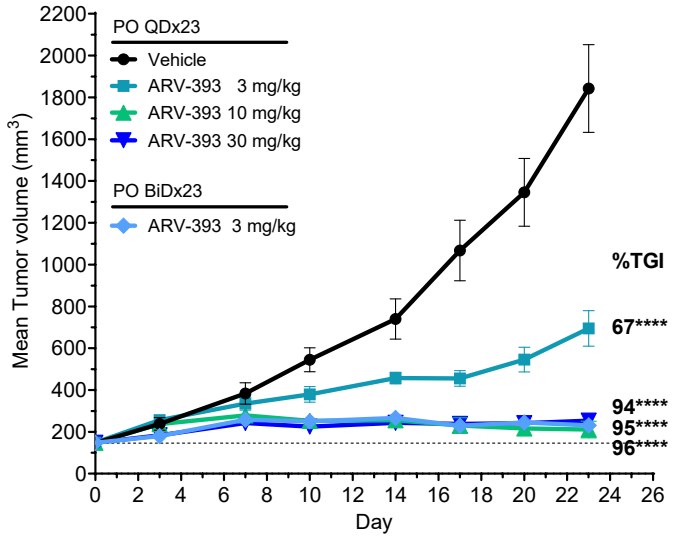
ARV-393 induces dose-dependent and sustained tumor growth inhibition and regressions *in vivo*

ARV-393 induces dose-dependent and sustained TGI in OCI-Ly1 DLBCL CDX model



- Tumor regression at 30 mg/kg dosed once per day (QD)
- No adverse impact on animal health/body weight (body weight not shown)

ARV-393 demonstrated >90% TGI

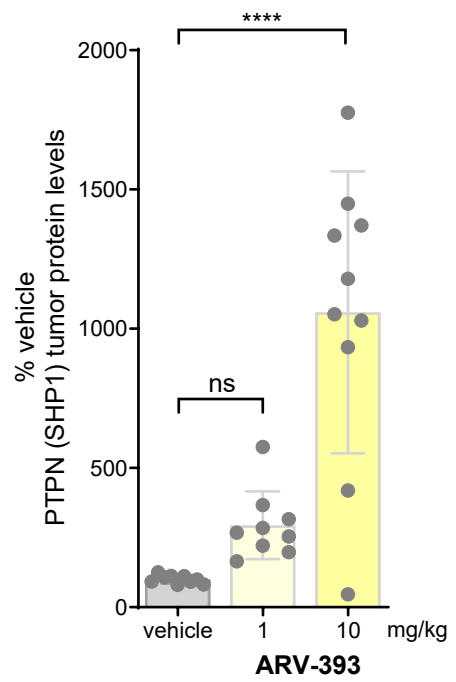


- TGI assessment of different dosing regimens of ARV-393 in the OCI-Ly1 CDX model demonstrate tumor growth inhibition >90% after 22 days at 10 and 30 mg/kg dosing

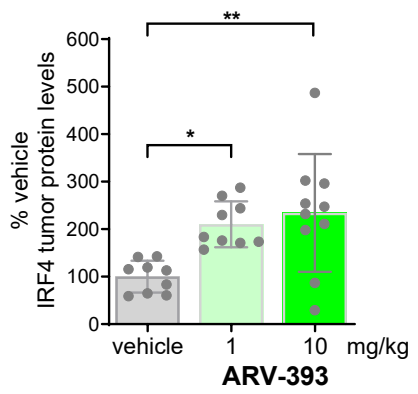
CDX, cell line derived xenograft model; DLBCL, Diffuse Large B-Cell Lymphoma; TGI, Tumor Growth Inhibition
Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain.
Statistical analyses were performed using two-way ANOVA, QD, Once daily; BID, Twice daily; ****p<0.0001.

Preclinically, BCL6 degradation by ARV-393 drives antitumor activity by increasing gene expression normally repressed by BCL6

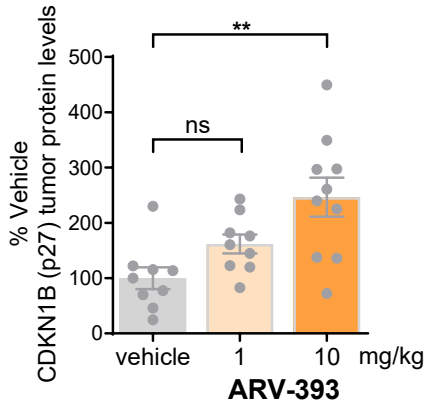
Signal Transduction PTPN6 (SHP1)	B-cell Differentiation IRF4	Cell cycle CDKN1B (p27)



****p<0.0001, one-way ANOVA



*p<0.05, **p<0.01, one-way ANOVA



**p<0.01, one-way ANOVA

OCI-Ly1 CDX tumor lysates from mice dosed twice daily at 1 and 10 mg/kg

- **BCL6 Repression** – BCL6 is a transcriptional repressor and expression of PTPN6, IRF4, and CDKN1B are repressed by it
- **Pathway Activation** – Treatment with ARV-393 increased the expression of PTPN6, IRF4, and CDKN1B, indicating BCL6 pathway engagement, collectively driving antitumor effects

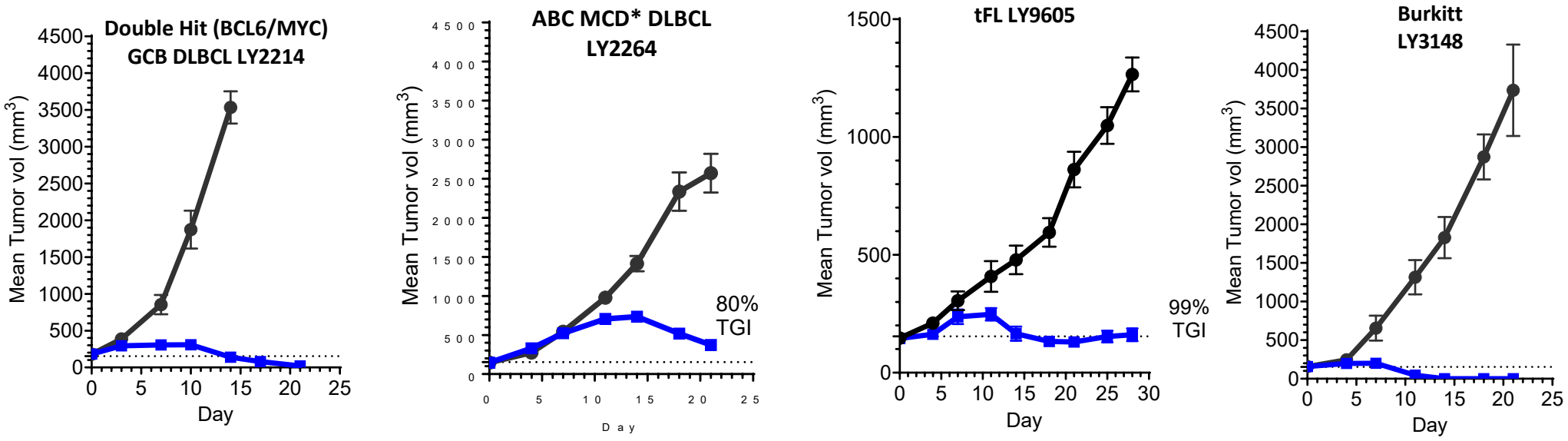
BCL6, B cell lymphoma 6; CDKN1B, Cyclin Dependent Kinase Inhibitor 1B; CDX, cell derived xenograft; IRF4, Interferon Regulatory Factor 4; PTPN6, Protein Tyrosine Phosphatase Non-Receptor Type 6

Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain.

Statistics performed using one-way ANOVA with Dunnett's multiple comparison test.

Single agent ARV-393 induces tumor growth inhibition in PDX models of various non-Hodgkin lymphoma subtypes

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



Similar results seen in fifteen PDX models of various NHL subtypes

ABC, activated B cell-like; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B cell-like; NHL, non-Hodgkin's lymphoma; PDX, patient derived xenograft model; tFL, transformed follicular lymphoma; TGI, tumor growth inhibition

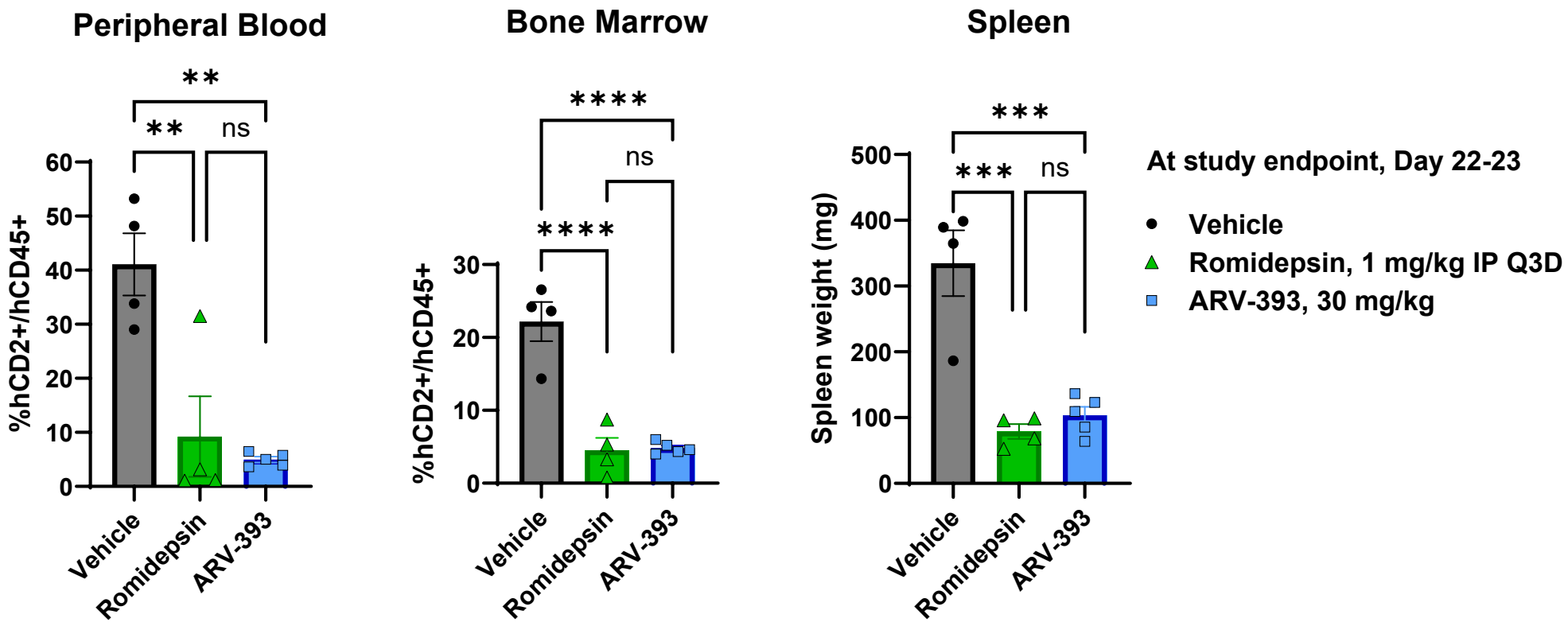
a. Body weight not shown.

*molecular classification according to LymphGen analysis, Wright et al., 2020. Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain. Van Acker et al., European Hematology Association (EHA) Poster PF1000. June 2025, Milan Italy.

First preclinical evidence of efficacy with a BCL6-targeted degrader in a patient-derived model of a rare T-cell lymphoma with a high unmet need

ARVINAS

ARV-393 demonstrates evidence of significant efficacy (comparable to SOC romidepsin) in a chemo (CHOP) relapsed AITL PDX model



AITL, angioimmunoblastic T-cell lymphoma, also known as nodal T-follicular helper cell lymphoma, angioimmunoblastic-type; BCL6, B cell lymphoma 6; CHOP, Cyclophosphamide, hydroxydaunorubicin, vincristine sulfate, and prednisone; ns, not significant; SOC, standard of care; PDX, patient-derived xenograft

Van Acker et al., European Hematology Association (EHA) Poster PF1000. June 2025, Milan Italy.

**P<0.01; ***P<0.005; ****P<0.0001

ARV-393 has the potential to be an attractive combination partner for development of novel treatment options for non-Hodgkin lymphoma

ARVINAS

CHEMOTHERAPY-FREE AND IMPROVED CHEMOTHERAPY OPTIONS

- **Standard of Care Chemotherapy**
  - R-CHOP
- **Standard of Care Biologics**
  - CD19 (tafasitamab)
  - CD79b (polatuzumab vedotin)
  - CD20 (rituximab)
  - CD20xCD3 (glofitamab)

ARV-393 Combinations

In Vivo DLBCL models

CHEMOTHERAPY-FREE AND ALL ORAL OPTIONS

Small molecule inhibitors

- BTK (acalabrutinib)
- BCL2 (venetoclax)
- EZH2 (tazemetostat)

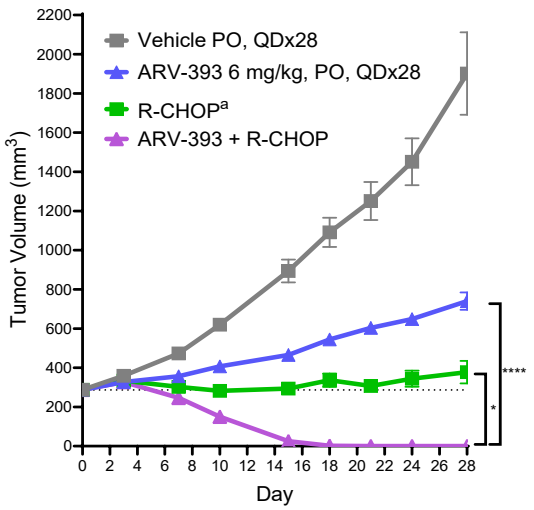
In preclinical models of aggressive DLBCL, ARV-393 demonstrated broad combinability, with tumor regressions observed in combination with SOC chemotherapy, SOC biologics, and investigational oral small molecule inhibitors targeting clinically validated oncogenic drivers of lymphoma

DLBCL, diffuse large B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine sulfate, and prednisone; SOC, standard of care

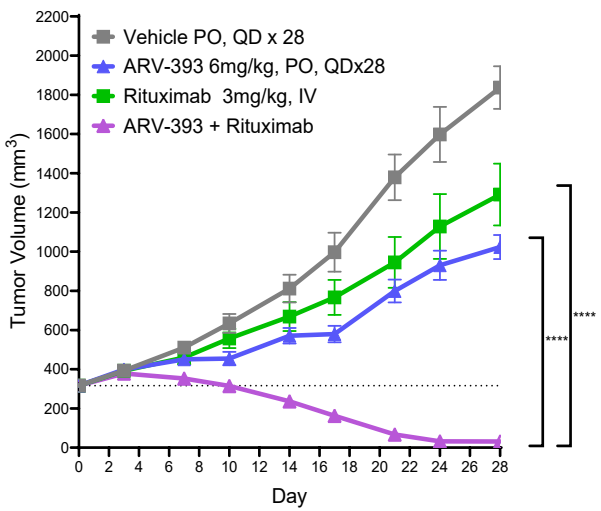
Acker et al., American Association for Cancer Research (AACR) Poster 1655/15. April 2025, Chicago.

ARV-393 demonstrates activity in combination with SOC chemotherapy/ biologics and drives tumor regressions, including complete responses, in a preclinical model of aggressive DLBCL

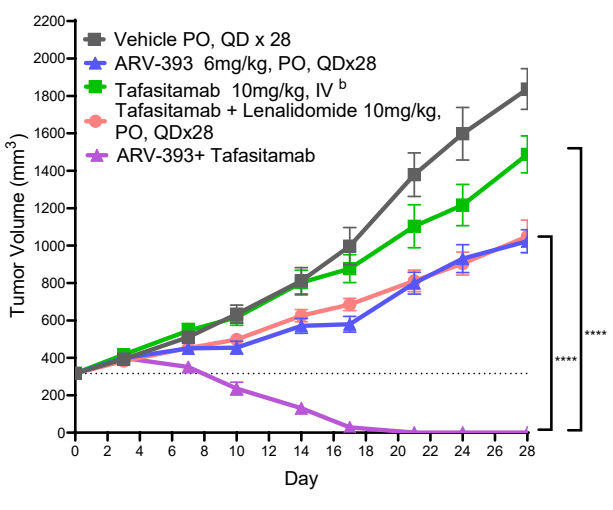
R-CHOP



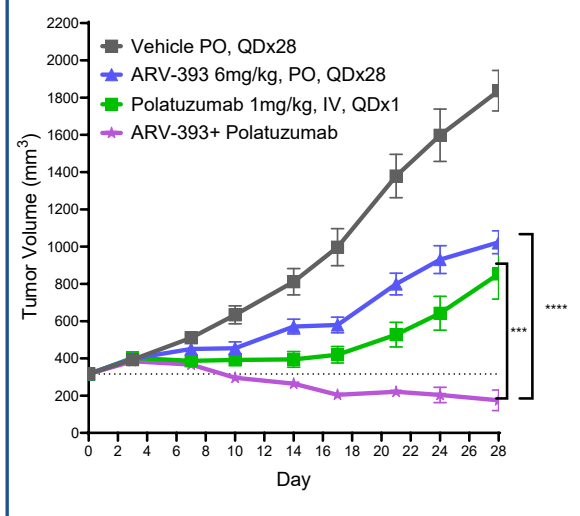
Rituximab



Tafasitamab



Polatuzumab vedotin



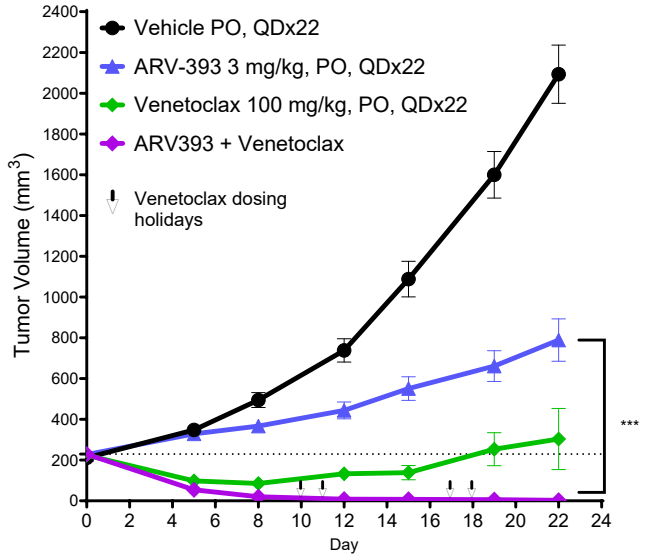
All data is in SU-DHL-4 high grade (triple hit) CDX model of diffuse large B-cell lymphoma

CDX, cell-derived xenograft; DLBCL, diffuse large B-cell lymphoma; IV, Intravenous; PO, oral; QD, once a day; R-CHOP, rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine sulfate, and prednisone; SOC, standard of care

a. Rituximab 3 mg/kg was administered intravenously (IV) on days 1, 8, 15, and 22; CHOP (30:2.475:0.375:0.15 mg/kg) was given IV on day 1 (prednisone was given PO QD on days 1–5). b. Tafasitamab was administered IV on days 1, 4, 8, 15 and 22. *P<0.05; ***P<0.005; ****P<0.0001 (one-way ANOVA, Tukey's multiple comparisons); Acker et al., American Association for Cancer Research (AACR) Poster 1655/15. April 2025, Chicago.

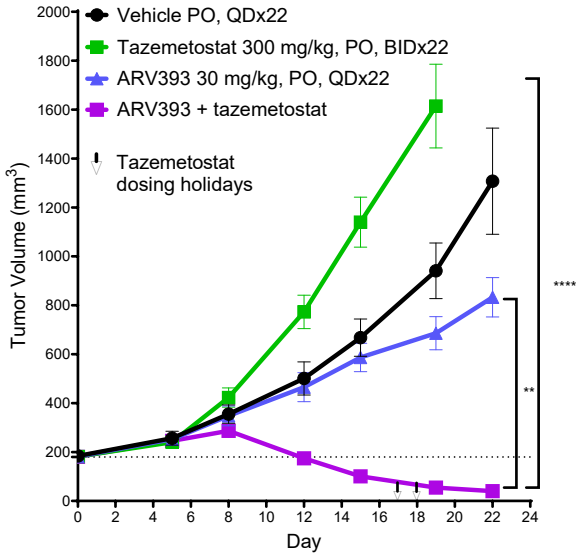
ARV-393 demonstrates activity in combination with small molecule inhibitors and drives tumor regressions, including complete responses, in a preclinical model of aggressive DLBCL

Venetoclax



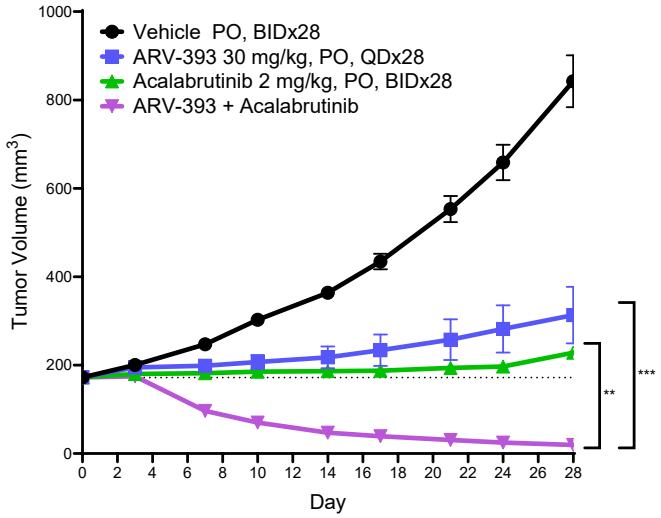
OCI-Ly1 GCB DLBCL CDX

Tazemetostat



SU-DHL-6 high grade (triple hit) DLBCL CDX

Acalabrutinib



OCI-Ly10 ABC DLBCL CDX

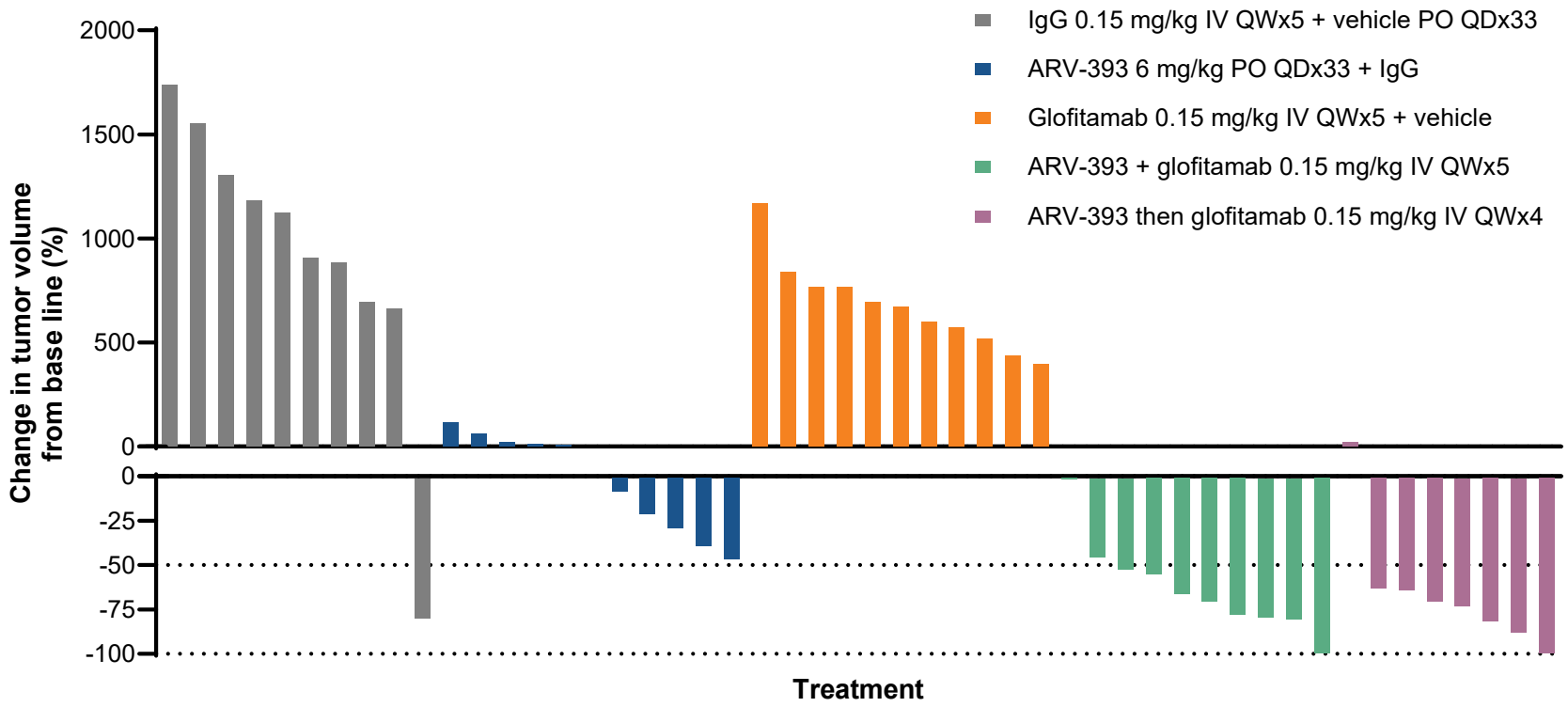
ABC, activated B-cell; BID, twice a day; CDX, cell-derived xenograft; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B-cell; IV, Intravenous; PO, oral; QD, once a daily

Van Acker et al., American Association for Cancer Research (AACR) Poster 1655/15. April 2025, Chicago; Van Acker et al., European Hematology Association (EHA) Poster PF1000. June 2025, Milan Italy.

**P<0.01; ***P<0.005; ****P<0.0001 (one-way ANOVA, Tukey's multiple comparisons)

Preclinical data support ARV-393 in combination with glofitamab as a chemotherapy-free combination approach in DLBCL*

Change in tumor volume at endpoint (day 34)



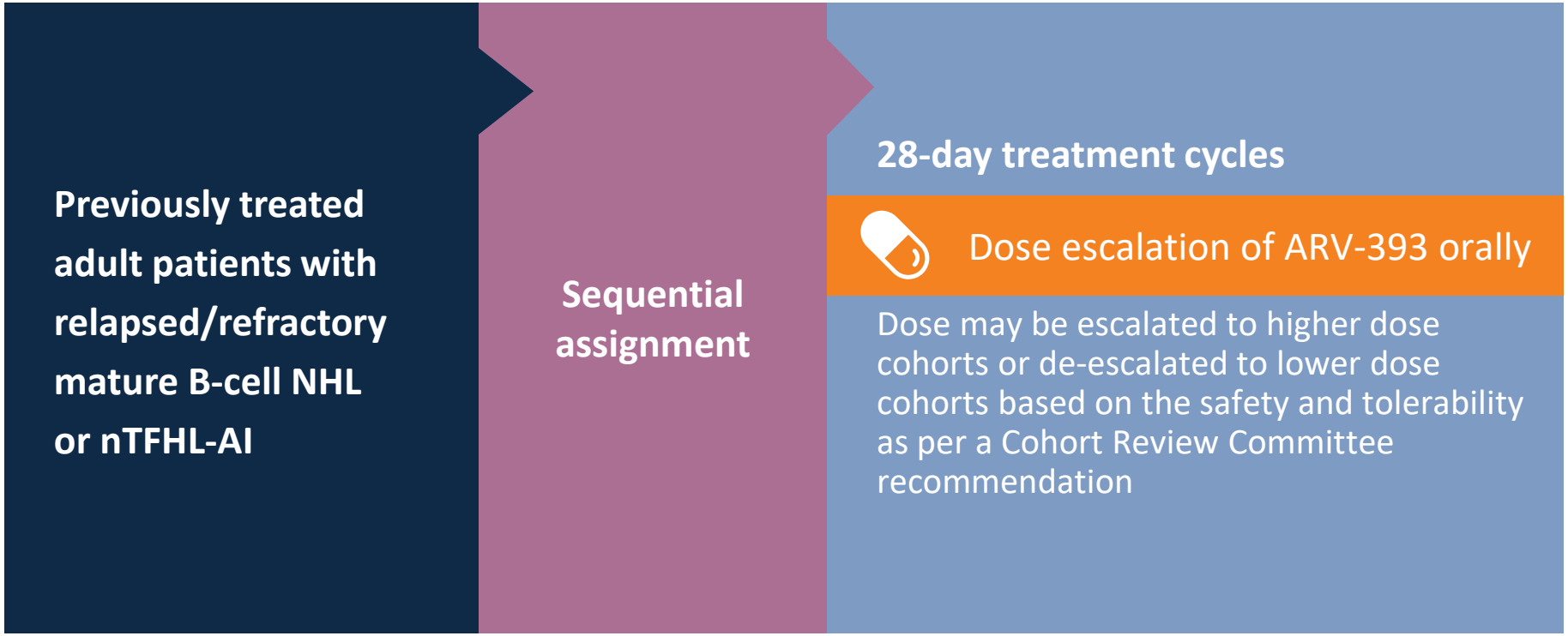
Increased tumor regressions observed with concomitant (10/10 mice) and sequential dosing (7/8 mice) vs single-agent ARV-393 (5/11 mice) or glofitamab (0/11 mice)

*Humanized WSU-DLCL2 HGBCL CDX model. Waterfall plot of individual tumor volume changes from baseline to final measurement.

CDX, cell line–derived xenograft; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; IgG, immunoglobulin G; IV, intravenously; PO, orally; QD, once daily; QW, once weekly

Van Acker et al., American Society of Hematology (ASH) Annual Meeting and Exposition 2025, Poster P1520.

Arvinas is currently enrolling a Phase 1 clinical trial of ARV-393 in relapsed/refractory non-Hodgkin lymphoma



Combination with glofitamab initiated in 1H 2026

- **ARV-393 is being evaluated in an open-label, first-in-human Phase 1 dose escalation study to assess its safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary antitumor activity in adult patients with relapsed/refractory NHL (NCT: 06393738)**
  - **Monotherapy and in combination with glofitamab**

NHL, non-Hodgkin lymphoma; nTFHL-AI, nodal T-follicular helper cell lymphoma, angioimmunoblastic-type

PRECLINICAL PROGRAMS: Oncology

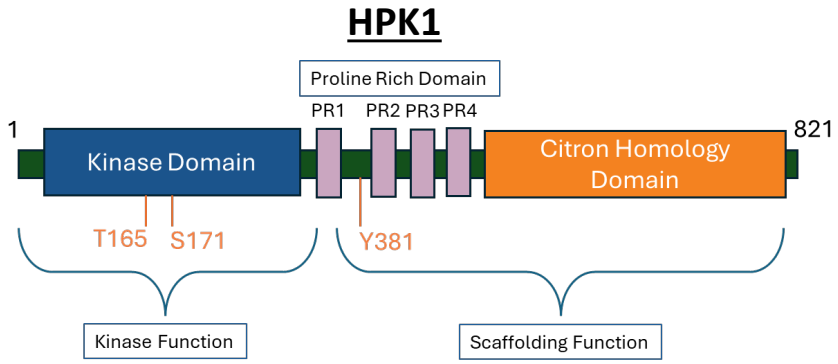
ARV-6723

PROTAC HPK1 degrader

ARVINAS

ARV-6723 is an investigational compound. Its safety and effectiveness have not been established.

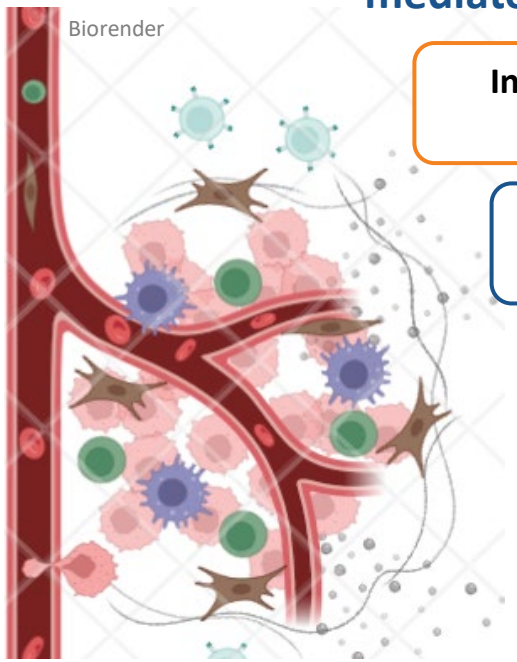
ARV-6723 is a potent PROTAC degrader of hematopoietic progenitor kinase 1 (HPK1), a central regulator of immune suppression



HPK1, a scaffolding protein kinase expressed exclusively in the hematopoietic compartment (T/B/dendritic/NK cells), has 2 functional domains:

- Kinase domain: drives catalytic immune suppression through adaptive immune pathways.
- Scaffolding domain: broad immunosuppressive regulation through innate immune pathways.

HPK1 degradation destroys both kinase and scaffold-mediated signaling, and may lead to:



Tumor Microenvironment (TME)

Increase immune function (T/dendritic cells) and immune attack (T/NK cells)

Counter activation of T cell exhaustion

Block suppressive TME (PGE_2, Adenosine)

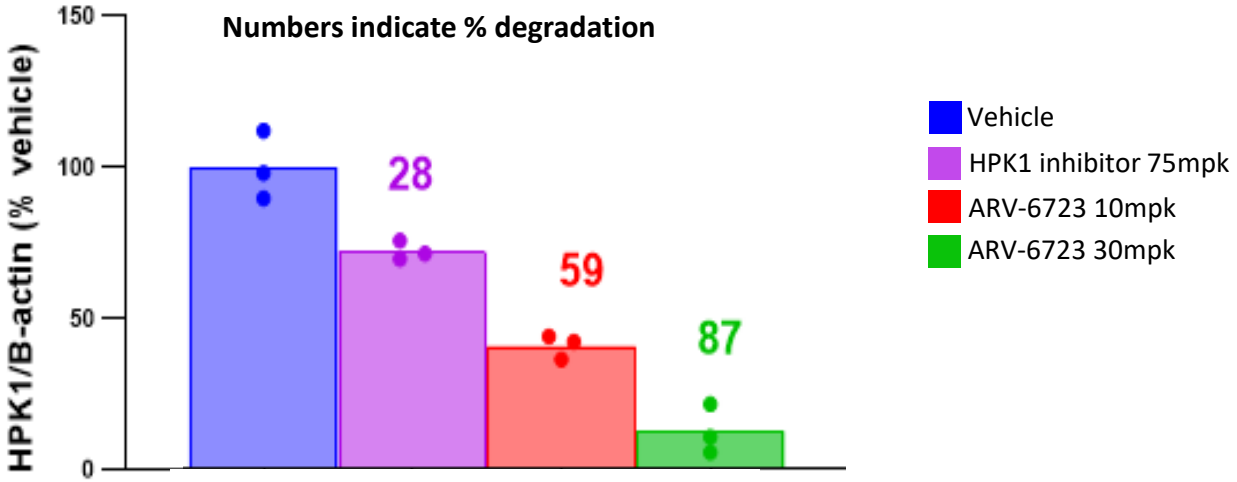
Reprogram the TME to unleash immune Response

ARV-6723, an oral HPK1 degrader, could offer sustained anti-tumor immune response as a single agent or in combination with SoC (e.g., anti-PD1, chemotherapy), resulting in improved clinical benefits over SoC across a wide range of cancers

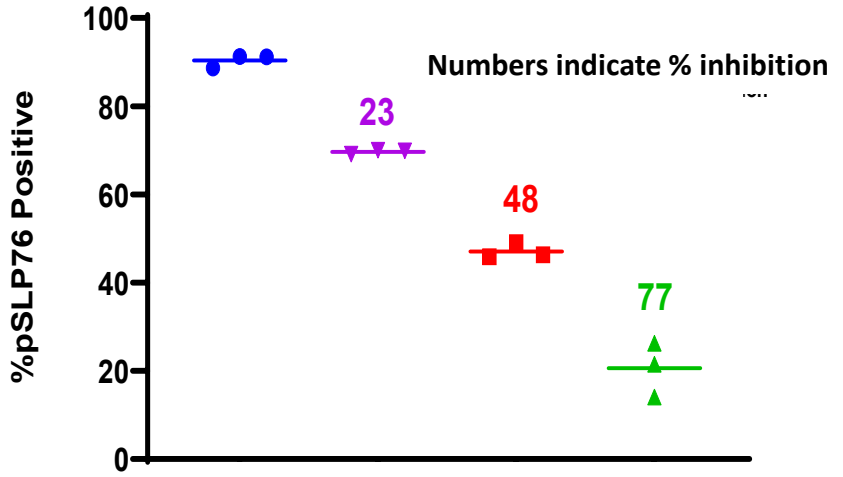
NK, natural killer; PGE_2, prostaglandin E2; SoC, standard of care;

Single dose of oral ARV-6723 showed profound and sustained target degradation and durable pathway engagement

HPK1 Degradation



Downstream Pathway Inhibition (pSLP76)



24h post oral dose

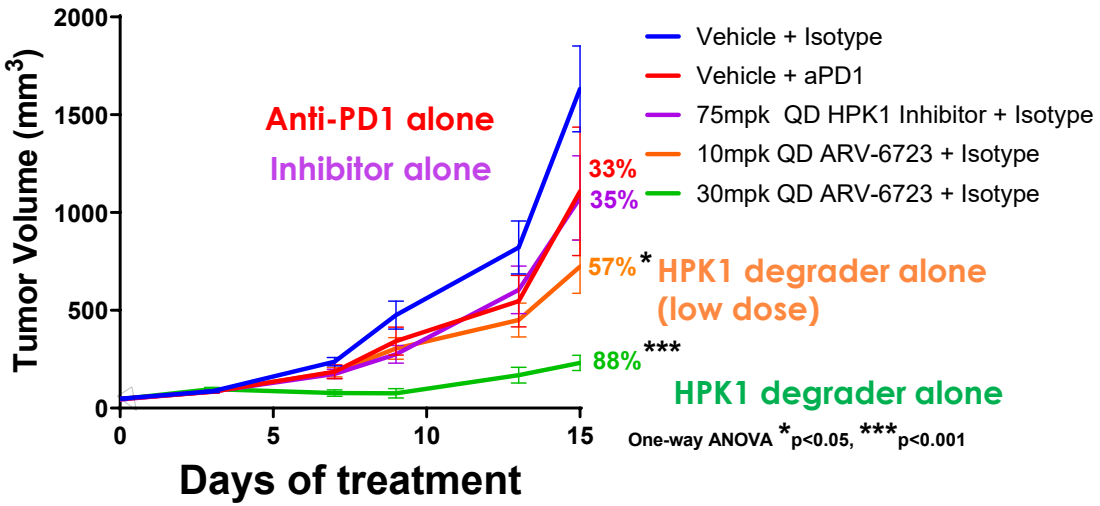
- ARV-6723 is a potent single-digit nanomolar degrader of HPK1, leading to sustained downstream pathway inhibition (via pSLP76) and induction of IL-2 release (data on file)
- This enhanced PK/PD profile results in more complete *in vivo* pathway suppression that recapitulates a genetic KO phenotype upon repeated PROTAC dosing

As presented at

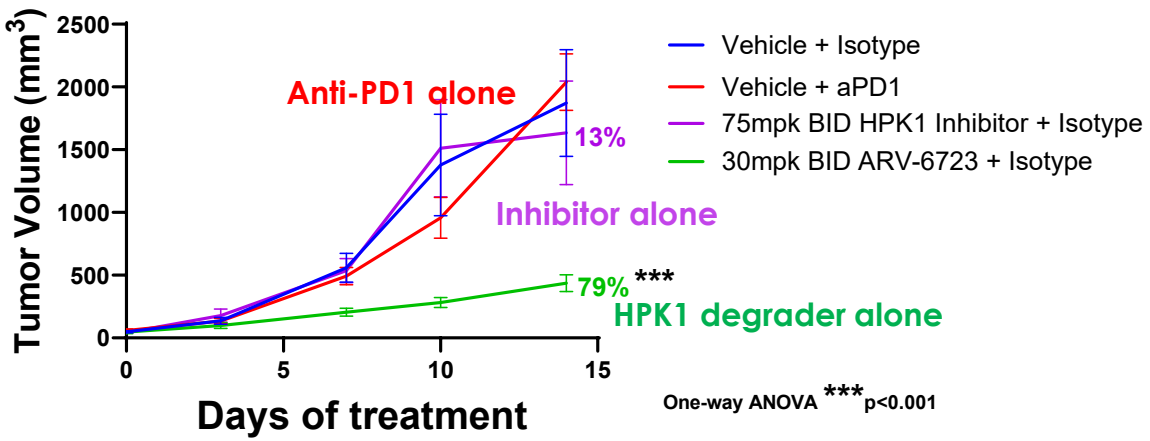
HPK1 , hematopoietic progenitor kinase 1; KO, knock out; mpk, milligrams per kilogram; PK/PD, pharmacokinetic/pharmacodynamic; pSLP76, SH2 domain-containing leukocyte protein of 76 kDa, phosphorylated.

ARV-6723 shows superior TGI compared to either anti-PD1 or HPK1 inhibitor in both high and low immunogenic tumor model

CT26 Model (Highly immunogenic)



B16F10 Model (Low immunogenic)



- ARV-6723 showed superior single-agent activity compared to a clinical HPK1 inhibitor or anti-PD-1 antibody
- ARV-6723 combined with anti-PD1 further enhanced efficacy and drive immunogenic tumor rejections (i.e., rechallenge protection)*
- HPK1 PROTACs have yielded strong single-agent efficacy in other highly immunogenic syngeneic tumor models (EMT6, MC38)*

- HPK1 PROTAC elicited strong TGI as a single agent in B16F10 (low immunogenic, 'cold') model, compared to limited activity with clinical HPK1 inhibitor or anti-PD-1 antibody

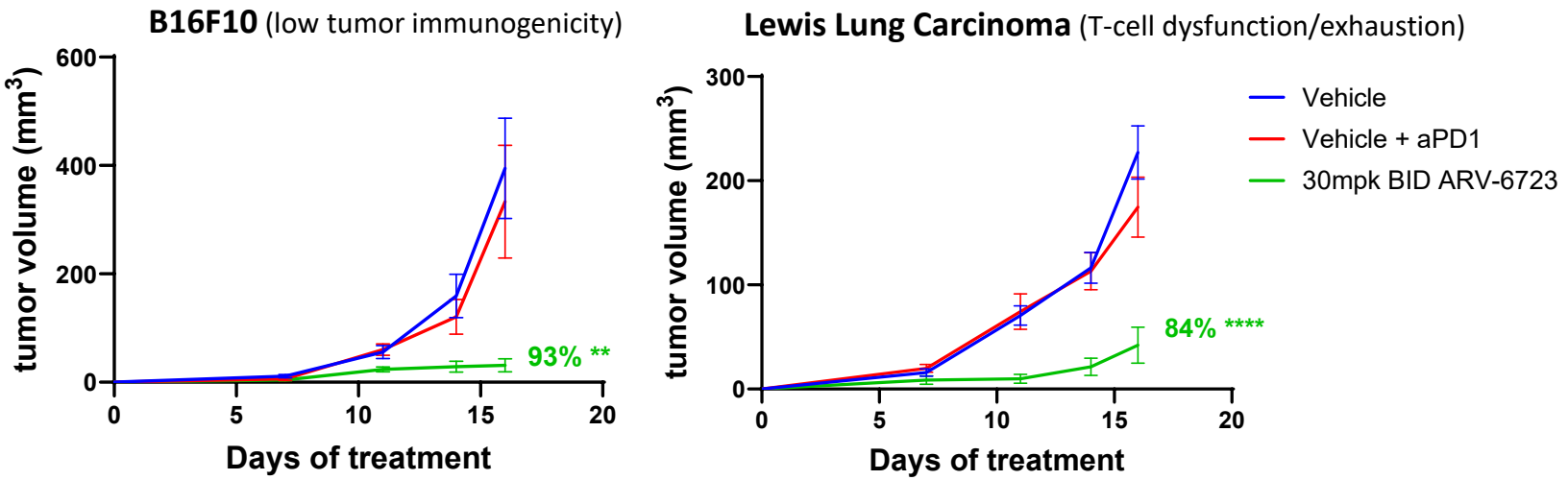
As presented at

HPK1 , hematopoietic progenitor kinase 1; TGI, tumor growth inhibition

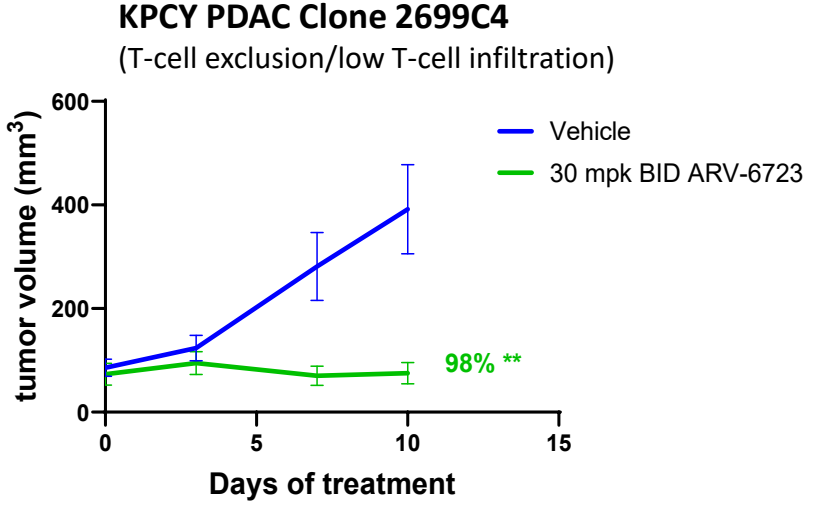
*Data on file

ARV-6723 efficacy signals across models of IO resistance demonstrates clear differential response vs. anti-PD1

IFNγ Resistant Tumor Lines



KPCY PDAC Low Immunogenic Clone



ARV-6723 demonstrated significant TGI in multiple IO-resistance models that represent a broad range of potential clinically relevant responses, including:

- Low tumor immunogenicity
- T-cell dysfunction/exhaustion
- T-cell exclusion/low T-cell infiltration

As presented at

BID, twice-daily dosing; HPK1, hematopoietic progenitor kinase 1; IFNγ, Interferon-gamma; I/O, immuno-oncology; PDAC, pancreatic ductal adenocarcinoma; TGI, tumor growth inhibition

CLINICAL PROGRAMS: Oncology

VEPPANU™ (vepdegestrant)

Heterobifunctional protein degrader

Approved by U.S. FDA on May 1, 2026

ARVINAS

Pfizer

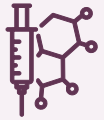
Unmet need in ER+/HER2- metastatic breast cancer

ER+/HER2- breast cancer accounts for approximately

70%

of all breast cancer cases and is driven in part by the ER signaling pathway.[1]

ER pathway mediates the transcription of genes that promote tumor cell growth, proliferation, and survival[2]



First-line treatments for ER+/HER2- advanced or metastatic breast cancer are typically endocrine therapies combined with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor[3]

No clear standard of care in the second-line-plus (2L+) setting; new treatment options are needed

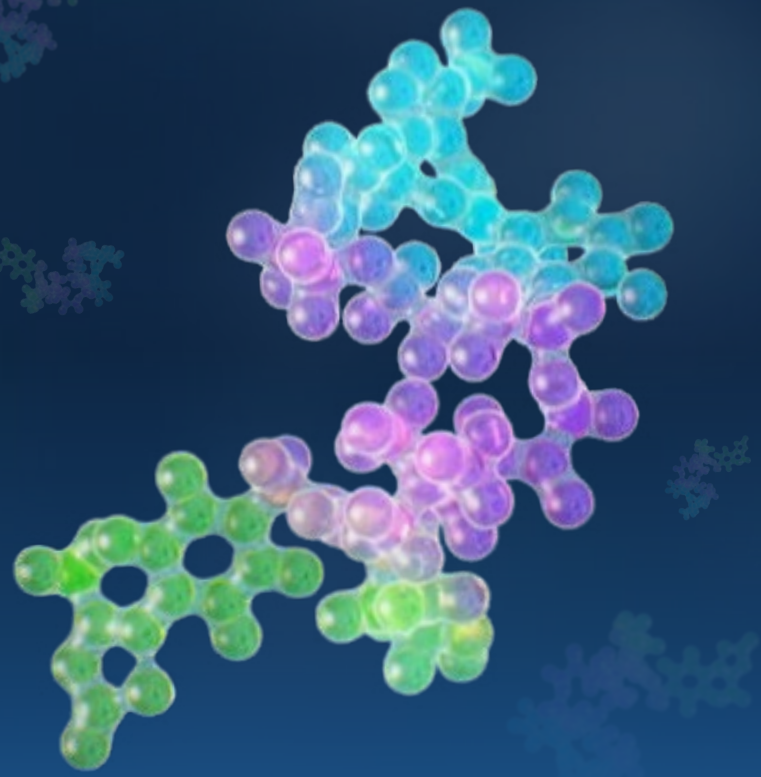
Despite clinical improvements with these first-line therapies, patients often experience treatment resistance and disease progression.[4]

1. Surveillance, Epidemiology, and End Results Program Data, https://seer.cancer.gov/statfacts/html/breast-subtypes.html. 2. Chen P (2022) Role of estrogen receptors in health and disease. Front. Endocrinol. 13:839005. doi: 10.3389/fendo.2022.839005. 3. ESMO Guidelines, https://www.annalsofoncology.org/article/S0923-7534(21)04498-7/pdf Citation: Gennari A, et al., Ann Oncol. 2021(32). 4. American Association for Cancer Research, https://aacrjournals.org/cancerdiscovery/article/10/8/1174/2810/The-Genomic-Landscape-of-Intrinsic-and-Acquired. doi: 10.1158/2159-8290.CD-19-1390.

VEPPANU™

(vepdegestrant)

First and only approved PROTAC, a type of heterobifunctional protein degrader



VEPPANU was approved by U.S. FDA on May 1, 2026 for treatment of adults with ER+/HER2-, *ESR1*-mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy

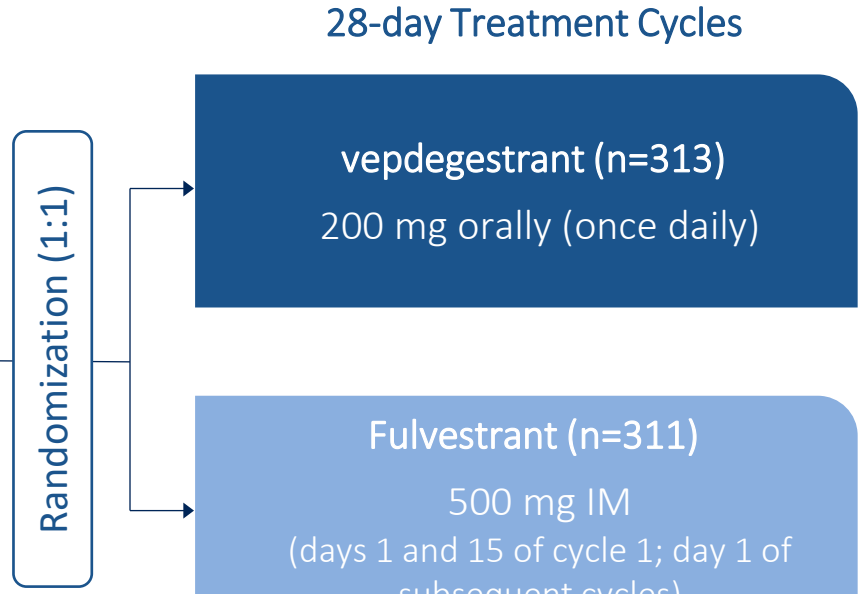
- Vepdegestrant is the first PROTAC to be evaluated in a Phase 3 pivotal study, VERITAC-2, and VEPPANU is the first FDA-approved PROTAC, a type of heterobifunctional protein degrader
- VERITAC-2 data supporting FDA approval, and published in the *New England Journal of Medicine,* showed:
  - Vepdegestrant was well tolerated, with low rates of discontinuation
  - Vepdegestrant met its primary endpoint of improvement in progression-free survival versus the standard of care, fulvestrant, in previously-treated patients with *ESR1m*, ER+/HER2- advanced breast cancer
- More than 1,000 patients and healthy volunteers have been treated with vepdegestrant across the clinical program

ASCO, American Society of Clinical Oncology, *ESR1,* estrogen receptor 1 gene; *ESR1m*, estrogen receptor 1 mutant; ER+/HER2-, estrogen receptor-positive/human epidermal growth factor receptor 2-negative; FDA, Food and Drug Administration

VERITAC-2: Global Phase 3 clinical trial of VEPPANU™ (vepdegestrant)

Key Eligibility Criteria

- Age ≥18 years old
- ER+/HER2- advanced or metastatic breast cancer
- Prior therapy:
  - 1 line of CDK4/6i + ET
  - ≤1 additional ET
  - Most recent ET for ≥6 months
  - No prior SERD (eg, fulvestrant, elacestrant)
  - No prior chemotherapy for advanced or metastatic disease
- Radiological progression during or after the last line of therapy



Primary Endpoints:

- PFS by BICR in
  - *ESR1*m population
  - All patients

Secondary Endpoints:

- OS (key secondary)
- CBR and ORR by BICR
- AEs

Data cutoff date: Jan 31, 2025
Clinicaltrials.gov: NCT05654623

AE, adverse event; BICR, blinded independent central review; CBR, clinical benefit rate; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ER, estrogen receptor; *ESR1*, estrogen receptor 1 gene; *ESR1*m, estrogen receptor 1 gene mutation; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IM, intramuscularly; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SERD, selective estrogen receptor degrader

a. *ESR1*m status was assessed in ctDNA by Foundation Medicine, except in China, where Origmed testing was used.

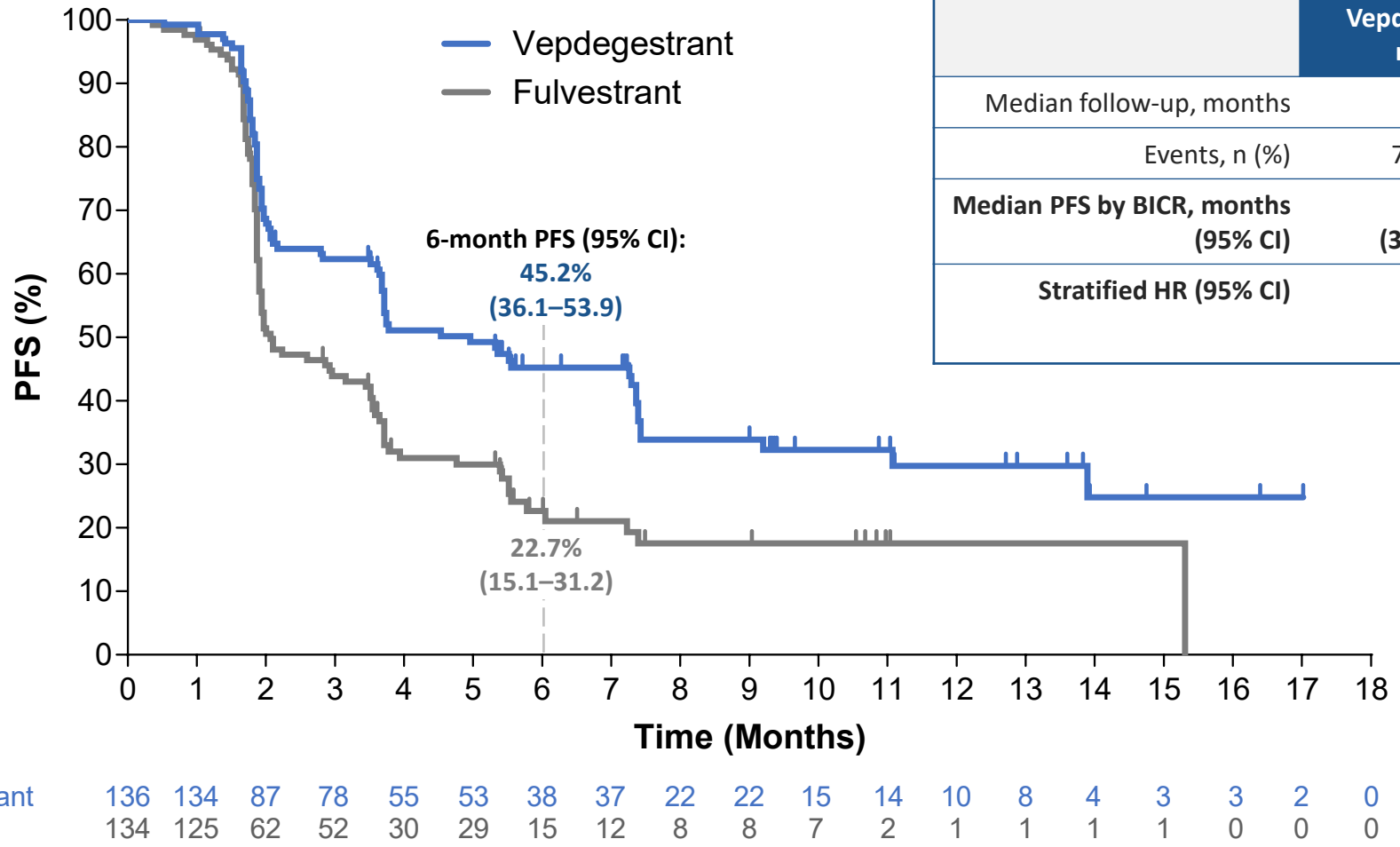
Baseline characteristics of the VERITAC-2 population representative of the real-world second-line setting in the U.S.

Characteristic	Patients With *ESR1*m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Median age (range), y	60 (26–87)	60 (34–85)	60 (26–89)	60 (28–85)
Female, %	99	100	99	100
Postmenopausal, %	79	79	78	78
Race, %				
White	43	51	47	46
Black or African American	3	4	2	2
Asian	45	37	39	41
Unknown/NR	9	7	12	9
ECOG PS, %				
0	57	57	61	64
1	43	43	39	36
*ESR1*m, %[a]	100	100	43	43
Sites of disease, %				
Visceral disease	68	68	63	63
Liver metastasis	46	44	40	36
Bone-only disease	18	18	18	20

Characteristic, %	Patients With *ESR1*m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Measurable disease[b]	71	75	71	71
Prior lines of therapy in advanced/metastatic setting[c]				
1	82	80	82	76
2	18	20	18[d]	23[d]
Prior endocrine therapy	100	100	100	100[e]
Aromatase inhibitor	99	100	99	99
SERM	15	16	16	20
Prior CDK4/6 inhibitor	100	100	100	100
Palbociclib	50	54	46	52
Ribociclib	38	28	36	31
Abemaciclib	16	25	20	21
Other[f]	1	5	4	4

CDK4/6, cyclin-dependent kinase 4/6; ECOG PS, Eastern Cooperative Oncology Group performance status; *ESR1*m, estrogen receptor 1 gene mutation; NR, not reported; SERD, selective estrogen receptor degrader; SERM, selective estrogen receptor modulator
a. *ESR1*m status was assessed in pretreatment circulating tumor DNA; b. measurable disease assessed by blinded independent central review using Response Evaluation Criteria for Solid Tumors v1.1; c. disease progression during or within 12 months from the end of adjuvant therapy was counted as a line of therapy in the advanced/metastatic setting; d. one additional patient in the vepdegestrant group and 3 additional patients in the fulvestrant group received 3 prior lines of therapy; e. one patient received a prior SERD. f. other CDK4/6 inhibitors included birociclib, dalpiciclib, lerociclib

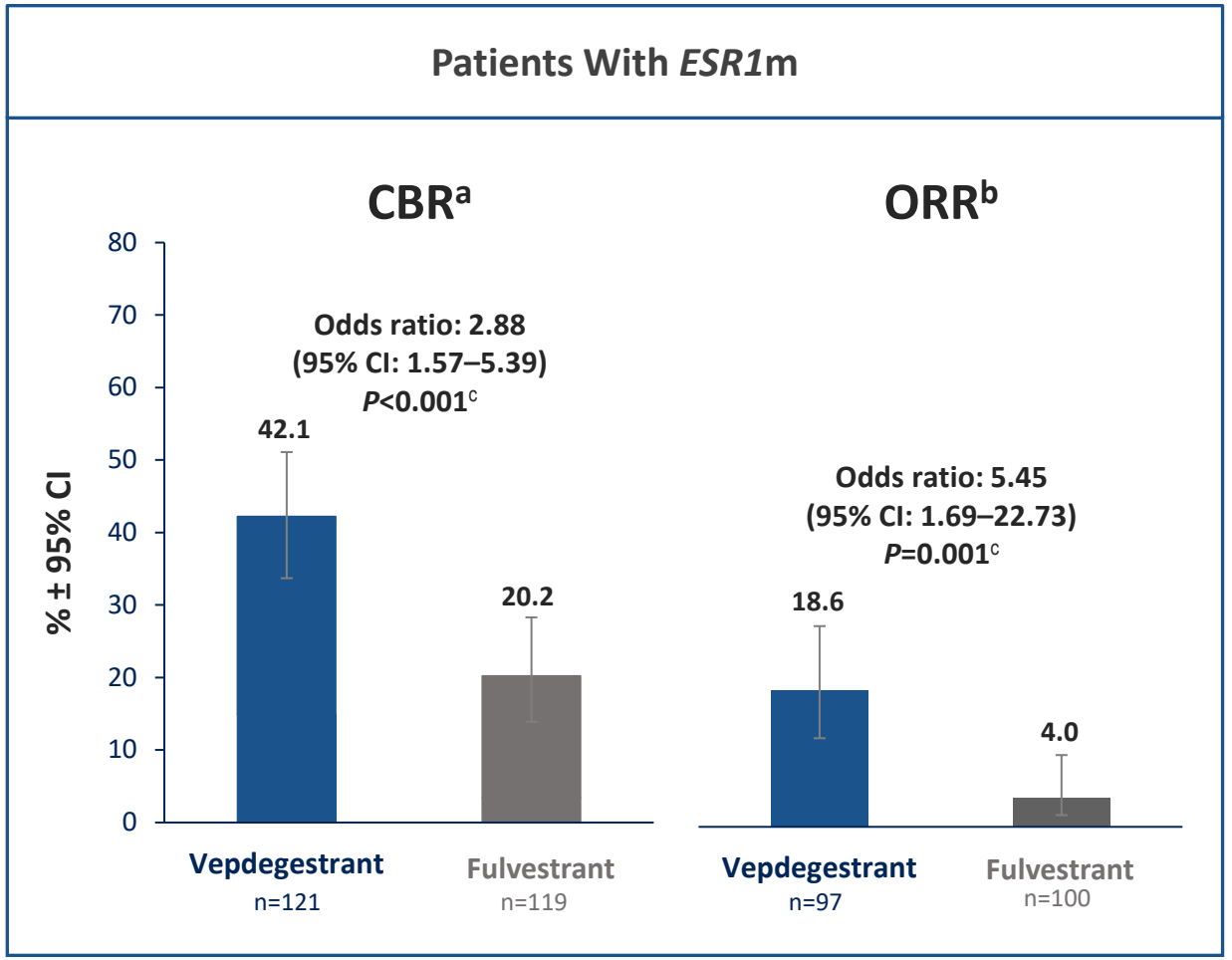
VEPPANU™ (vepdegestrant) met the primary endpoint with a ~3-month mPFS improvement in patients with tumors harboring *ESR1* mutations



	Vepdegestrant n=136	Fulvestrant n=134
Median follow-up, months	7.4	6.0
Events, n (%)	79 (58)	95 (71)
Median PFS by BICR, months (95% CI)	**5.0 (3.7–7.4)**	**2.1 (1.9–3.5)**
Stratified HR (95% CI)	**0.57 (0.42–0.77)**	
	2-sided *P*<0.001	

BICR, blinded independent central review; *ESR1m*, estrogen receptor 1 gene mutation; HR, hazard ratio; mPFS, median progression-free survival

VEPPANU™ (vepdegestrant) showed statistically significant improvements in CBR and ORR in the *ESR1* mutant population



BICR, blinded independent central review; CBR, clinical benefit rate; CR, complete response; *ESR1*m, estrogen receptor gene 1 mutation; ORR, objective response rate; PR, partial response; SD, stable disease

a. CBR was defined as the rate of confirmed CR or PR at any time, or SD, non-CR, or non-progressive disease for ≥24 weeks and was estimated in CBR-evaluable patients (those enrolled for ≥24 weeks prior to data cutoff or those with confirmed CR or PR). b. ORR was defined as the rate of confirmed CR or PR and was estimated in patients with measurable disease at baseline. c. Nominal p-value.

VEPPANU™ (vepdegestrant) was generally well-tolerated, with low rates of discontinuation and dose reductions; majority of TRAEs Gr 1/2

Overview

TEAEs, %	Vepdegestrant (n=312)	Fulvestrant (n=307)
Any grade	87	81
Grade ≥3	23	18
Serious	10	9
Leading to treatment discontinuation	3	1
Leading to dose reduction	2	NA
TRAEs, %		
Any grade	57	40
Grade ≥3	8	3

QT prolongation

- TEAEs: vepdegestrant,10%; fulvestrant, 1%
- A QT interval sub-study (n=88) confirmed a mild increase (11.1 ms) from baseline in mean QTcF, with upper 90% CI (13.7 ms) <20 ms,[f]

TEAEs in >10% of Patients in Either Group

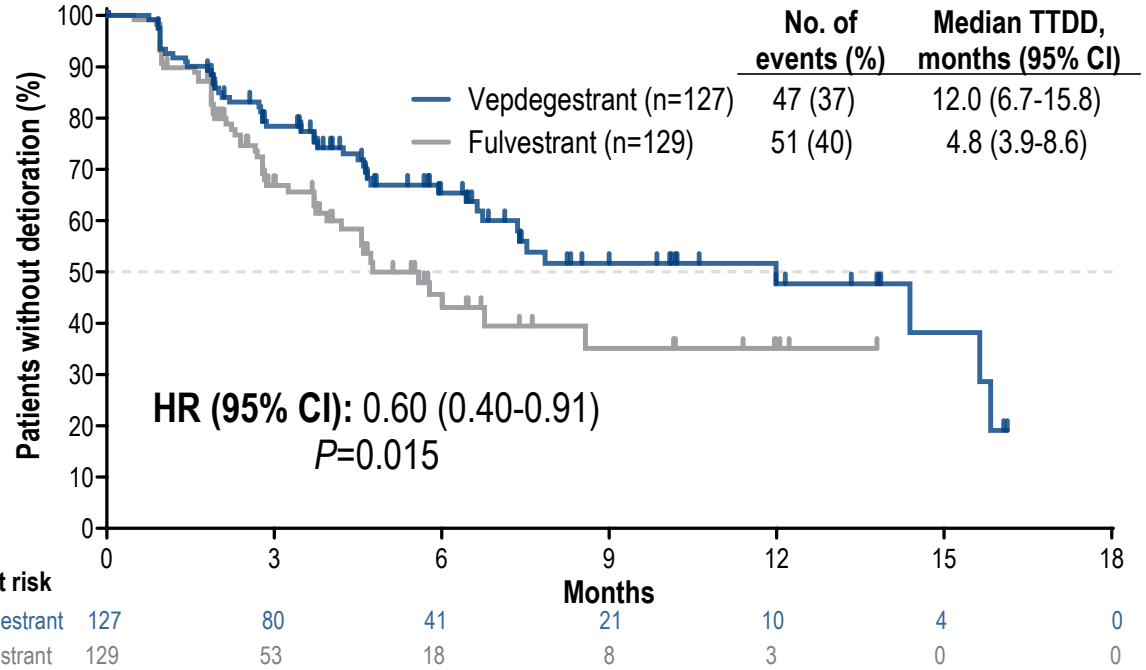
TEAE, %	Vepdegestrant (n = 312)		Fulvestrant (n = 307)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Fatigue[a]	27	1	16	1
ALT increased[b]	14	1	10	1
AST increased[b]	14	1	10	3
Nausea	13	0	9	1
Anemia[b, c]	12	2	8	3
Neutropenia[d]	12	2[e]	5	1[e]
Back pain	11	1	7	<1
Arthralgia	11	1	11	0
Decreased appetite	11	<1	5	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GI, gastrointestinal; QTcF, corrected QT interval using Fridericia's method; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event
a. Includes fatigue and asthenia. b. No between-group differences were observed for ALT/AST increases or anemia based on laboratory values. c. Includes anemia, hemoglobin decreased, and iron deficiency anemia. d. Includes neutropenia and neutrophil count decreased. No events led to dose reductions or treatment discontinuation in either treatment group. There were no events of febrile neutropenia in the vepdegestrant group and 1 event of grade 2 febrile neutropenia in the fulvestrant group. e. One patient with grade 4 event. f. Based on a concentration-QTc population modeling analysis.

VEPPANU™ (vepdegestrant) significantly reduced risk of clinically meaningful definitive deterioration in measures of overall health status compared to fulvestrant in patients with *ESR1* mutations

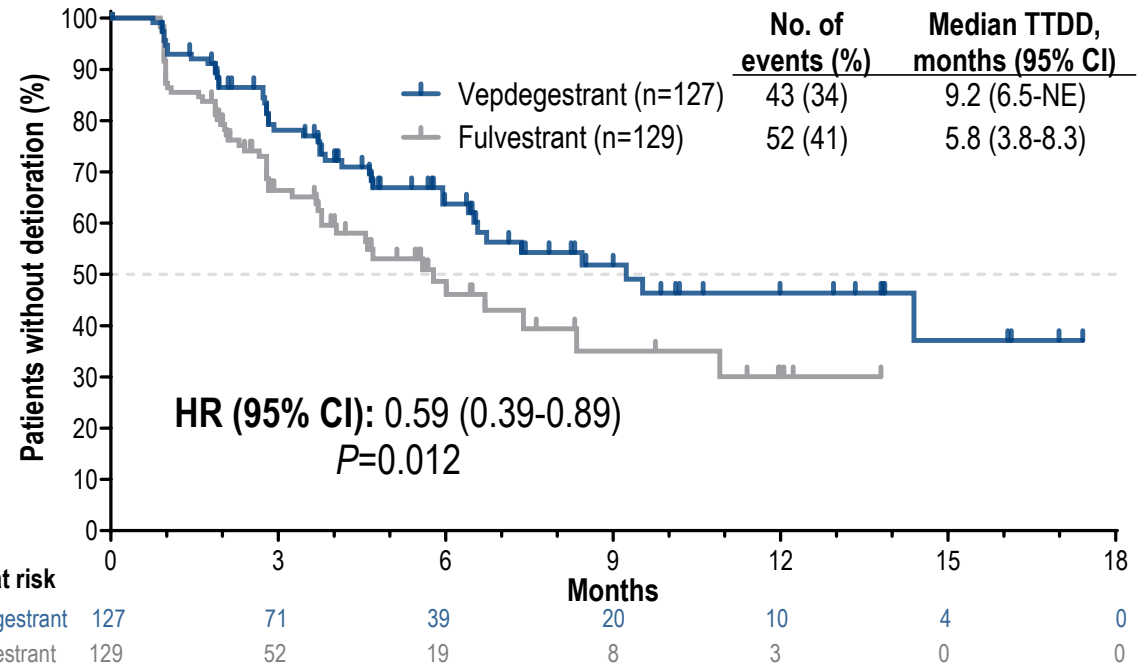
VERITAC-2: Patient Reported Outcomes in patients with *ESR1* mutations

TTDD in EORTC QLQ-C30 GHS/QoL



No. at risk							
Vepdegestrant	127	80	41	21	10	4	0
Fulvestrant	129	53	18	8	3	0	0

TTDD in EQ-5D-5L VAS



No. at risk							
Vepdegestrant	127	71	39	20	10	4	0
Fulvestrant	129	52	19	8	3	0	0

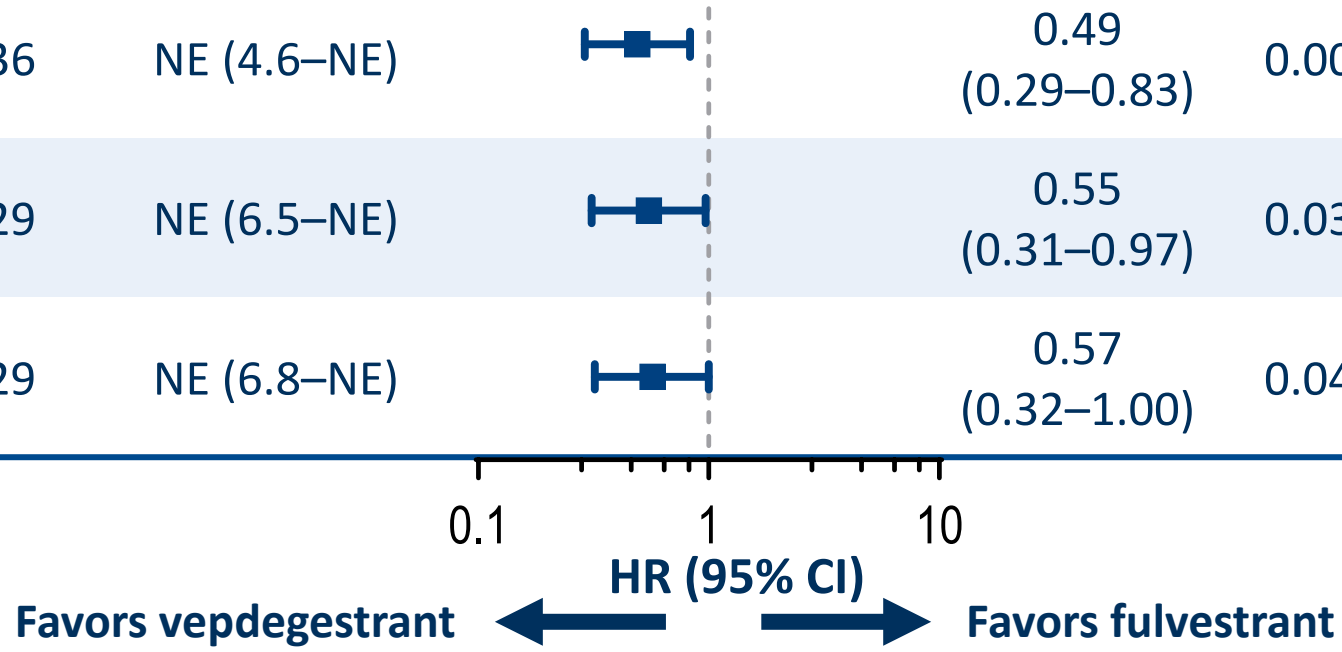
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D-5L= EuroQoL 5-dimension, 5-level; GHS, global health status; HR, hazard ratio; QoL, quality of life; TTDD, time to definitive clinically meaningful deterioration; VAS, visual analog scale.

HRs and their 95% CIs were calculated using a Cox regression model stratified by visceral disease status at baseline (yes/no), with fulvestrant as a reference. P values were calculated using a stratified log-rank test that accounted for the stratification by visceral disease status.

The risk of clinically meaningful deterioration in pain was significantly lower with VEPPANU™ (vepdegestrant) compared to fulvestrant across all pain measures evaluated in patients with *ESR1* mutations

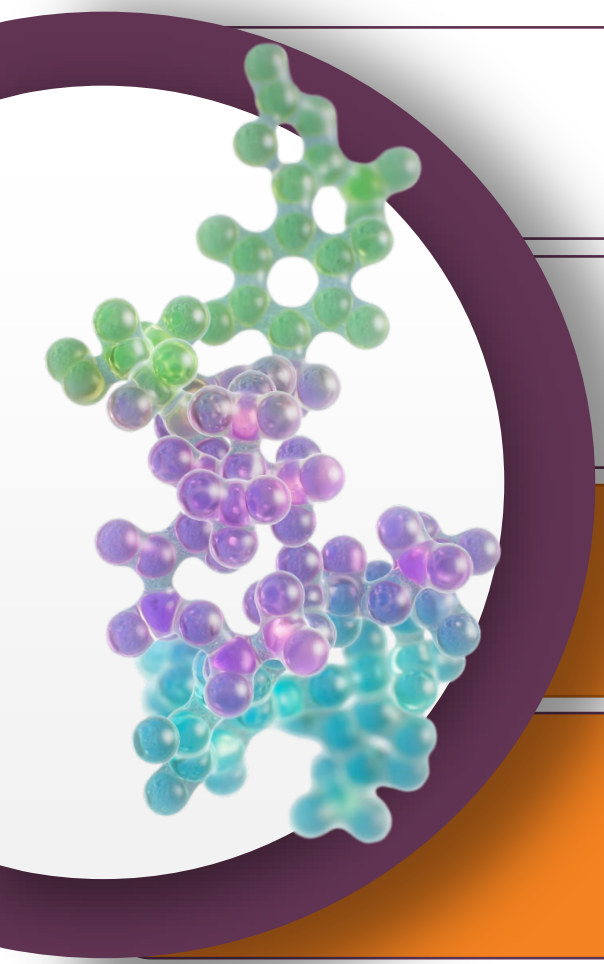
VERITAC-2: Patient Reported Outcomes in patients with *ESR1* mutations

BPI-SF Domain	Vepdegestrant (n = 127) Events (n)	Vepdegestrant (n = 127) Median TTDD, months (95% CI)	Fulvestrant (n=129) Events (n)	Fulvestrant (n=129) Median TTDD, months (95% CI)	HR (95% CI)[a]	*P* value[b]
Item 3 “worst pain"	25	NE (14.4–NE)	36	NE (4.6–NE)	0.49 (0.29–0.83)	0.007
Pain severity	22	NE (NE–NE)	29	NE (6.5–NE)	0.55 (0.31–0.97)	0.036
Pain interference	24	14.4 (14.0–NE)	29	NE (6.8–NE)	0.57 (0.32–1.00)	0.048



BPI-SF, Brief Pain Inventory Short Form; HR, hazard ratio; NE, not estimable; TTDD, time to definitive deterioration.
a. HRs and their 95% CIs were calculated using a Cox regression model stratified by visceral disease status at baseline (yes/no), with fulvestrant as a reference; b. P values were calculated using a stratified log-rank test that accounted for the stratification by visceral disease status.

Positive results from VERITAC-2 Phase 3 clinical trial supported U.S. FDA approval



VEPPANU (vepdegestrant) showed a clinically meaningful median PFS benefit over fulvestrant, a current standard of care, in patients with *ESR1* mutations

VEPPANU's safety and tolerability provided further evidence of a potential best-in-class profile

The U.S. Food and Drug Administration approved VEPPANU on May 1, 2026

Arvinas and Pfizer entered into a transaction with Rigel Pharmaceuticals for the exclusive global rights of VEPPANU on May 11, 2026

2L+, second-line plus; *ESR1*, estrogen receptor 1 gene; FDA, Food and Drug Administration; PFS, progression free survival
VEPPANU (vepdegestrant) is for the treatment of adults with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-), estrogen receptor 1 (ESR1)-mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy.

Arvinas is a leader in developing PROTAC degraders with potential best-in-class profiles, with multiple upcoming value-driving milestones

PROTAC degraders designed to provide advantages over other modalities in oncology and neurology

	2H 2025 Anticipated Milestones	1H 2026 Anticipated Milestones	2H 2026 Anticipated Milestones
ARV-102* LRRK2 degrader	✓ Initial Phase 1 SAD data in PD ✓ Initiate multiple dose cohort in PD	✓ Phase 1 MAD data in PD	Initiate Phase 1b in PSP** Initiate Phase 2 in PSP
ARV-806* KRAS G12D degrader	✓ Preclinical data	Initial Phase 1 data (2026)	
ARV-393* BCL6 degrader	✓ Phase 1 mono trial update ✓ Preclinical combination data	✓ Initiate Phase 1 combo with glofit	Phase 1 dose escalation data (mono)
ARV-027* polyQ-AR degrader		✓ Initiate Phase first-in-human P1	
VEPPANU™ (vepdegestrant)	✓ File NDA	✓ Select 3rd party to commercialize ✓ Approved by U.S. FDA	
Preclinical		Initiate Phase 1: ARV-6723 (HPK1; advanced solid tumors) mid-2026 ✓ Pan-KRAS: preclinical data	

Strong capital position with ~$615M cash on hand[a] and runway into second half 2028

BCL6, B-cell lymphoma 6; G12D, mutations in codon 12 on KRAS oncogene; glofit, glofitamab; HPK1, hematopoietic progenitor kinase 1; KRAS, Kirsten rat sarcoma; LRRK2, leucine-rich repeat kinase 2; NDA, new drug application; SAD, single ascending dose; MAD, multiple ascending dose, PD, Parkinson's disease; PDUFA, Prescription Drug User Fee Act; polyQ-AR, polyglutamine-expanded (polyQ) androgen receptor (AR); PSP, progressive supranuclear palsy; SBMA, spinal bulbar muscular atrophy.

a. Cash, cash equivalents, and marketable securities position as of March 31, 2026.

*The agents listed on this slide are investigational. Their safety and effectiveness for these investigational uses have not been established; **Upon submission of final chronic toxicology data in non-human primates and FDA clearance to proceed with the Phase 1b clinical trial