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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: 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' potential receipt of milestone or other payments from existing partners, including Novartis Pharma AG and Rigel Pharmaceuticals, Inc. ("Rigel"); 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; the potential market opportunity for any of Arvinas' product candidates; 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 ("PSP"), Parkinson's disease and related diseases; Arvinas' plans with respect to initiation of clinical trials of ARV-102 in patients with PSP, pending regulatory feedback, and the timing thereof; that a PROTAC expanded polyglutamine androgen receptor degrader may eliminate the root cause of disease for spinal bulbar muscular atrophy; 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 with respect to a Phase 1/2 clinical trial of ARV-6723 as a monotherapy and in combination with pembrolizumab in advanced solid tumors; Arvinas' plans to out-license ARV-806 for any additional clinical trials; and Arvinas' plans, anticipated milestones, timing and potential impacts of such milestones in connection with ARV-102, ARV-027, ARV-393 and ARV-6723, including statements regarding sharing of data, types of data, initiation and enrollment of clinical trials, sharing or presenting data and any forums for doing so.

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-393, ARV-102 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 its other preclinical or clinical candidates, including ARV-6723, including whether Arvinas initiates and completes preclinical studies or clinical trials and receives results from such studies or trials on expected timelines, or at all; the potential therapeutic benefits or profile of any of Arvinas' product or preclinical candidates; the uncertainties inherent in research and development, including preclinical study or clinical trial results; risks related to the potential market opportunity for any of Arvinas' product candidates; risks related to obtaining marketing approval for any product candidates; Rigel's performance of its obligations under the license agreement with Arvinas, Pfizer and Rigel and whether Rigel will successfully commercialize VEPPANU, or conduct and complete further development of VEPPANU, or the current timeline expectations or at all; the potential demand and market potential and acceptance of, VEPPANU or any other product candidate, including estimates regarding the potential market opportunity; the competitive landscape for VEPPANU or any other product candidate; the risk that any regulatory approval may be subject to significant limitations on use or subject to withdrawal or other adverse actions by the applicable regulatory authority; 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' plans to seek an outlicense for further development of ARV-806; risks associated with Arvinas' collaboration and license 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 Arvinas 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.

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ARVINAS

IGNITING A

TRANSFORMATIVE CHANGE

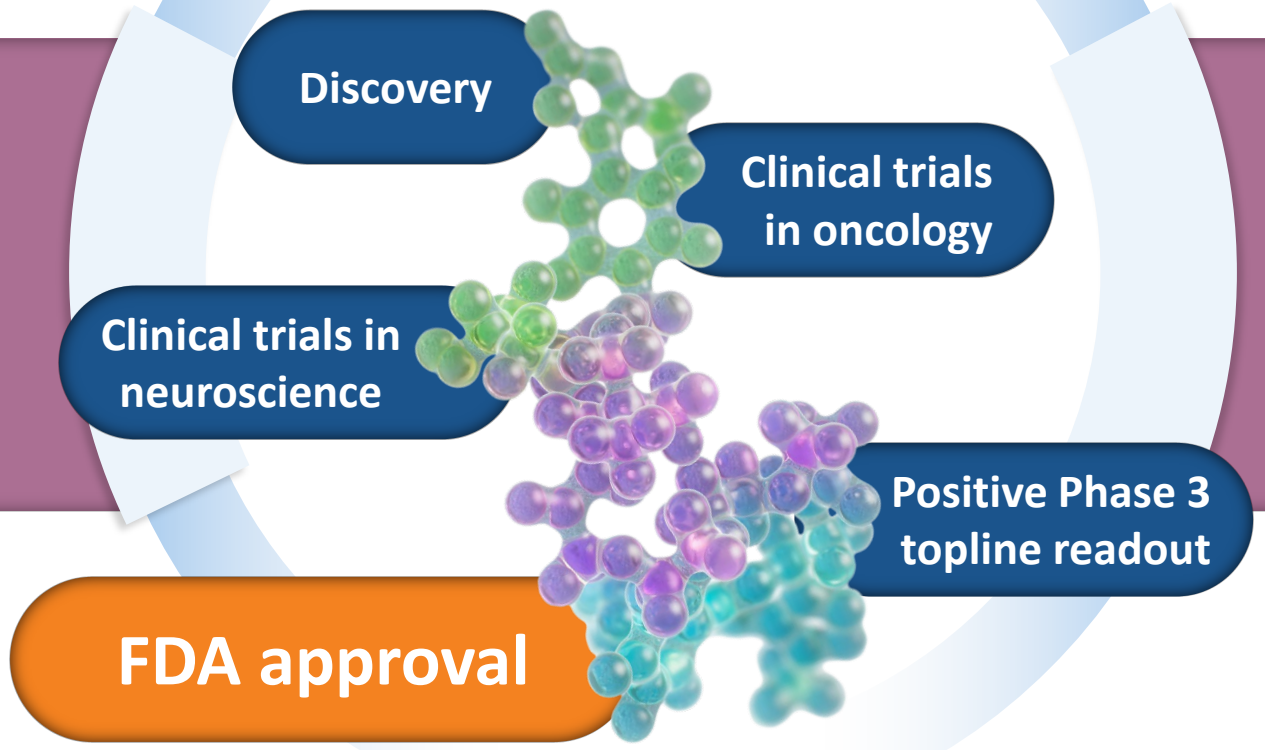
in the fight for patients with cancer and neurodegenerative diseases

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
- Global rights licensed to Rigel Pharmaceuticals in May 2026

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 three 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.

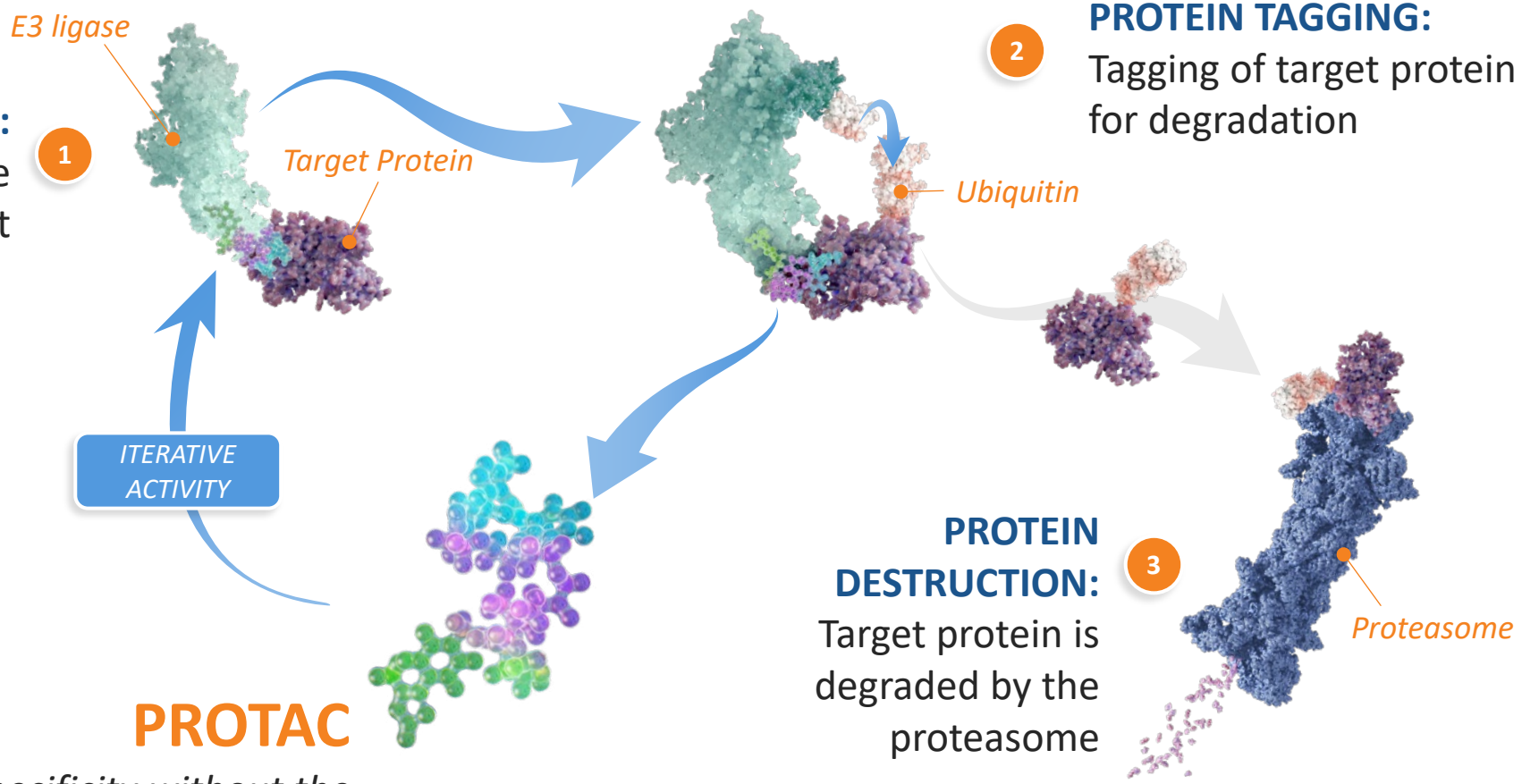
a. In 2021, Arvinas entered into a collaboration agreement with Pfizer to co-develop and co-commercialize vepdegestrant

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

ARVINAS

BENEFITS IN ONCOLOGY

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

By 2040, **30M new cancer cases per year** worldwide, leading to **15M cancer-related death per year**[1]

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

By 2040, neurodegenerative diseases are estimated to be **the #2 leading cause of death** in developed countries[2]

IM, intramuscular; IV, intravenous

1. Global Cancer Observatory: https://gco.iarc.fr/tomorrow/en/dataviz/isotype?years=2040; accessed 10/25/25. 2. Nature: https://doi.org/10.1038/nj7526-299a; accessed 10/25/25.

Arvinas' pipeline includes differentiated PROTAC degraders in neurology and oncology

PROGRAM*	INDICATION(S)	PRECLINICAL	PHASE 1/1B	PHASE 2	PHASE 3	APPROVED
ARV-102 (LRRK2)	PSP, Parkinson's Disease	*Planned initiation of additional clinical trials in 2027***	Phase 1 in HV/PD			
ARV-027 (polyQ-AR)	Spinal-Bulbar Muscular Atrophy	Phase 1 in HV/SBMA				
ARV-393 (BCL6)	Non-Hodgkin Lymphoma	Phase 1 monotherapy: NHL[1]	Phase 1 combination: DLBCL			
ARV-6723 (HPK1)	Advanced Solid Tumors	Phase 1 in advanced solid tumors *(planned initiation in 3Q 2026)*				
ARV-806 (KRAS G12D)	Solid tumors	Phase 1 in solid tumors harboring KRAS G12D mutations		*Enrollment in Phase 1 dose escalation cohort is complete; Arvinas plans to seek an out-licensing agreement for additional trials*		
VEPPANU™ (vepdegestrant)	ER+/HER2-, *ESR1*-Mutated Metastatic Breast Cancer	Phase 1/2 combination trials ongoing[2] Pfizer				FDA APPROVED Global rights licensed to rigel
Luxdegalutamide (ARV-766, JSB462; AR)	Prostate Cancer	Phase 2 trials in combination with PLUVICTO® (mCRPC), tulmimetostat (mCRPC) and abiraterone (mHSPC)			*Global rights licensed to* NOVARTIS	

AR, androgen receptor; BCL6, B-cell lymphoma 6; ER+, estrogen receptor positive; ESR1, estrogen receptor 1; DLBCL, diffuse large b-cell lymphoma; HER2-, human epidermal growth factor receptor 2-negative; HPK1, hematopoietic progenitor kinase 1; HV, healthy volunteers; 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; NHL, non-Hodgkin lymphoma; PD, Parkinson's disease; polyQ, expanded polyglutamine; PSP, progressive supranuclear palsy; SBMA, spinal-bulbar muscular atrophy.

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

*These agents, other than VEPPANU which has been approved by the FDA, are currently under investigation and their safety and effectiveness for these investigational uses have not been established; **Upon health authority clearance to proceed with clinical trials.

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

ARVINAS

Multiple Phase 1 PROTAC Programs with Near-Term Data

- Targeting LRRK2 for neurodegeneration, polyQ-AR for spinal and bulbar muscular atrophy, BCL6 for hematological malignancies and HPK1 for solid tumors
- 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

*Based on cash, cash equivalents, and marketable securities position as of June 30, 2026

CLINICAL PROGRAMS: Neurology

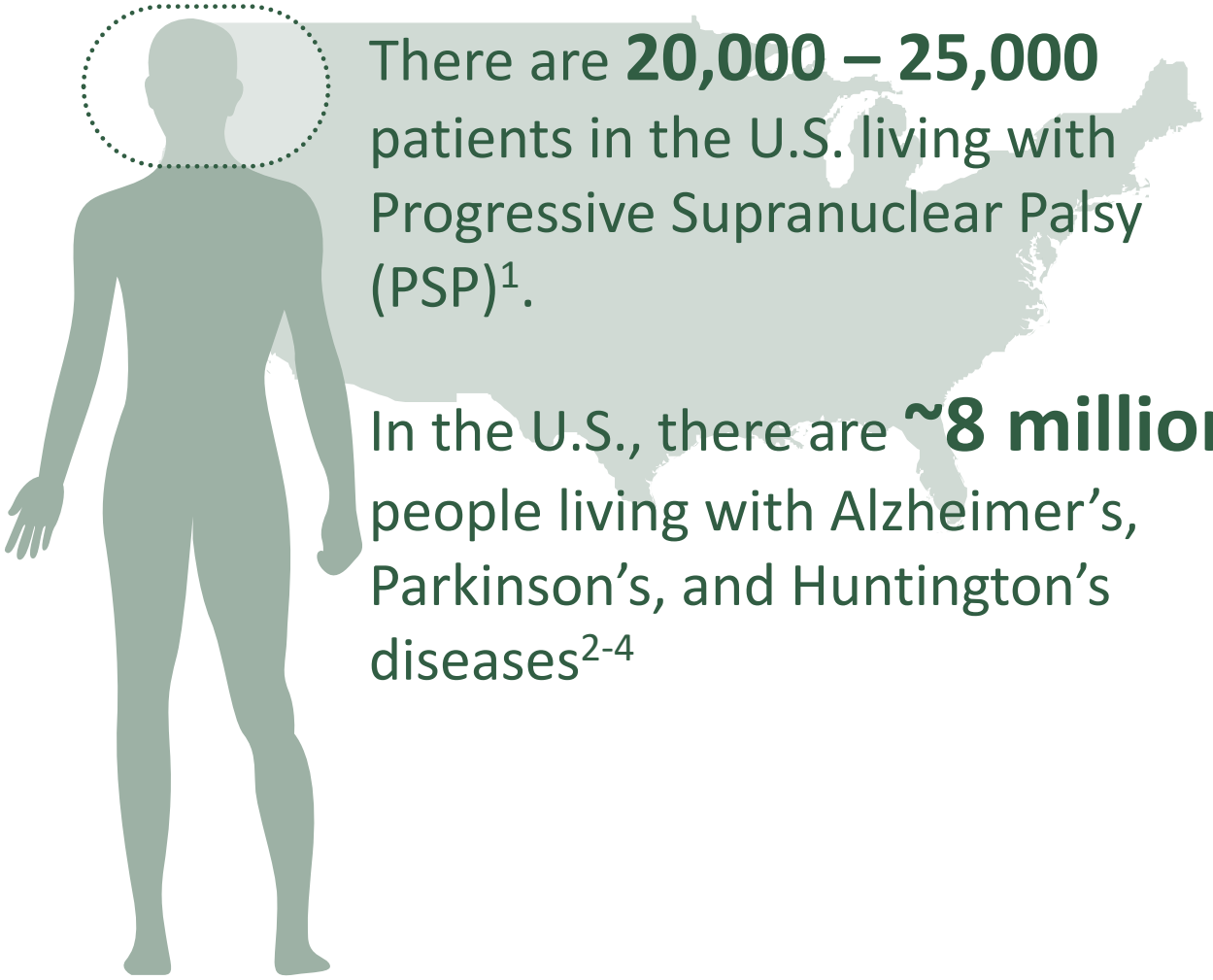
ARV-102

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].

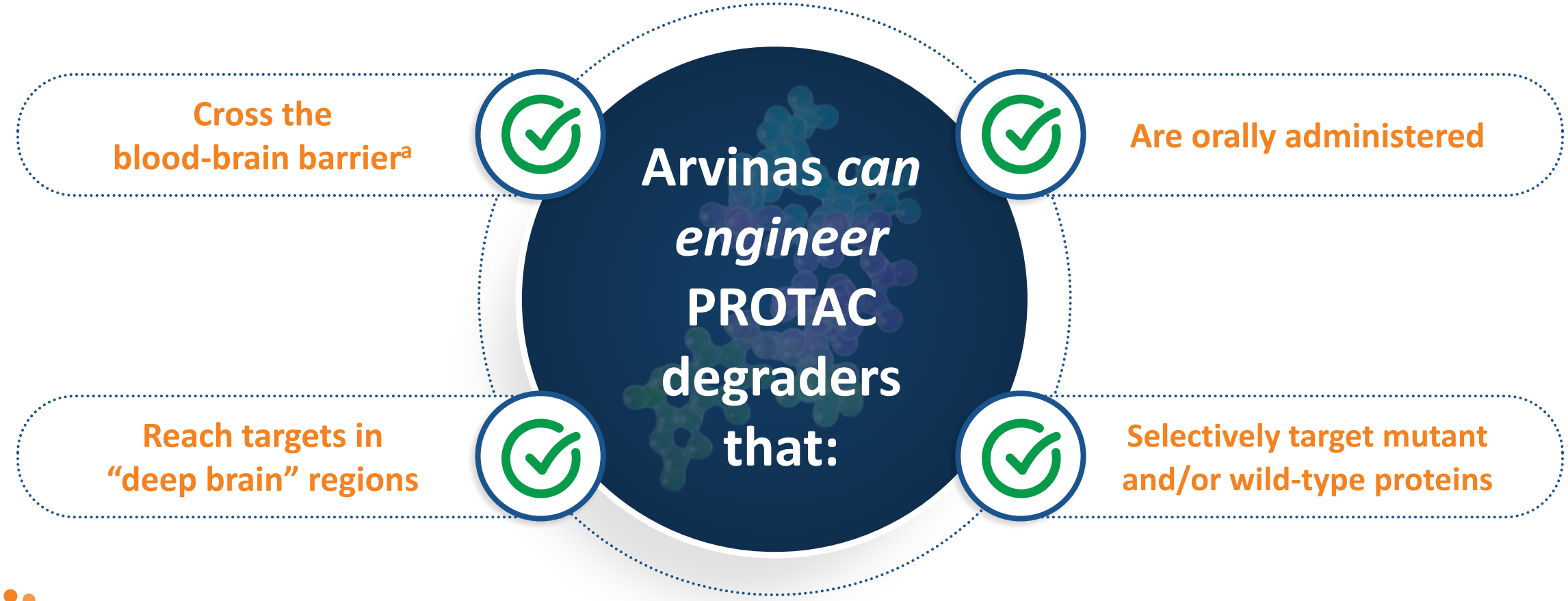
In the U.S., there are **~8 million** people living with Alzheimer's, Parkinson's, and Huntington's diseases[2-4]

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)[1]
- 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[2]
- Increased LRRK2 expression and activity contributes to neurodegeneration and pathogenesis of idiopathic PD,[2] 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

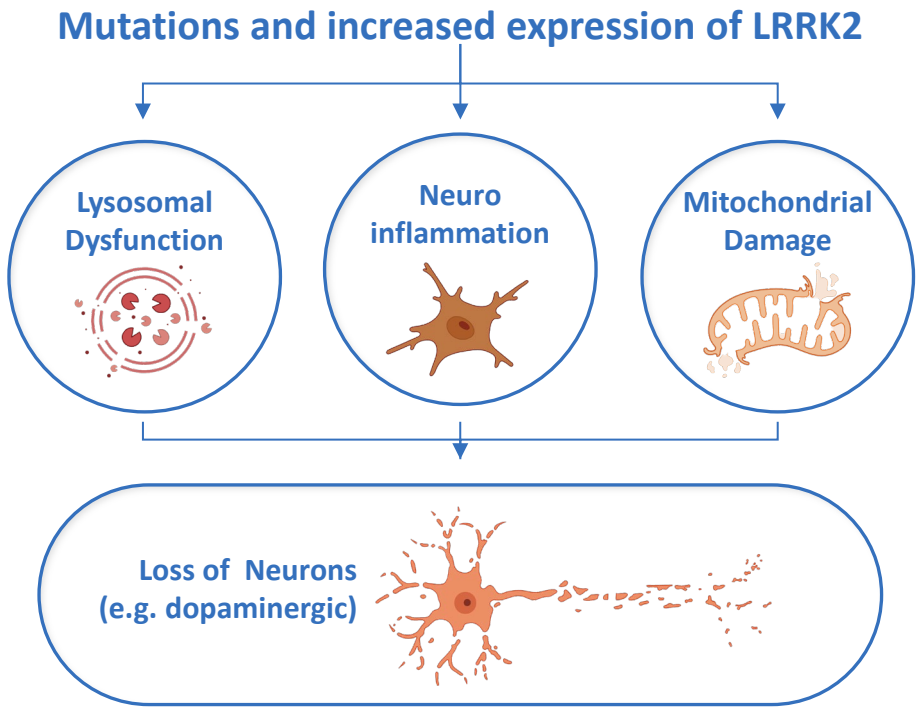
LRRK2, leucine-rich repeat kinase 2

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

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

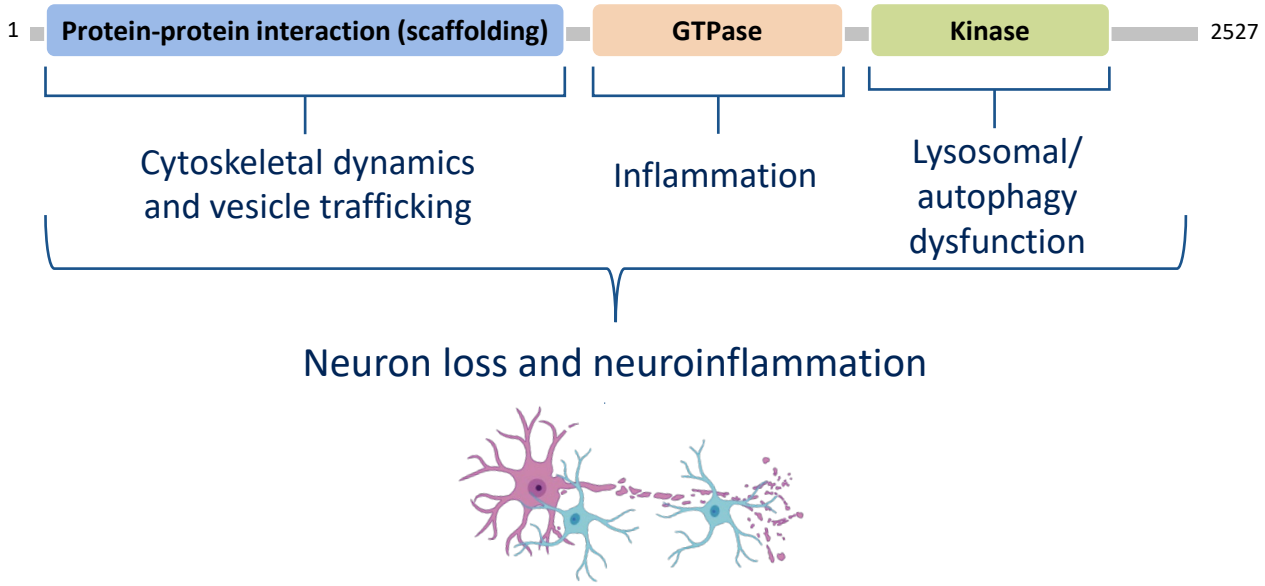
- Increased LRRK2 expression and activity contribute to neurodegeneration and pathogenesis of PD,[1] making it a rational therapeutic target
  - LRRK2 mutations are a common genetic cause of PD; variants have also been observed in idiopathic cases[12-14]
- LRRK2 levels are ~2x higher in CSF, microglia 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; 7. Herbst et al Clin Sci 2022; 8. Jabbari et al 2021; 9. Nielsen et al 2025; 10. Evans et al 2025; 11. Rocha EM, et al. Trends Neurosci. 2022;45(3):224-3612. 12. Kluss JH, et al. Biochem Soc Trans. 2019;47(2):651-661. 13. Di Fonzo A, et al Lancet. 2005;365(9457):412-5. 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]



ARV-102 degrades the entire LRRK protein and differentiates from inhibitors

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

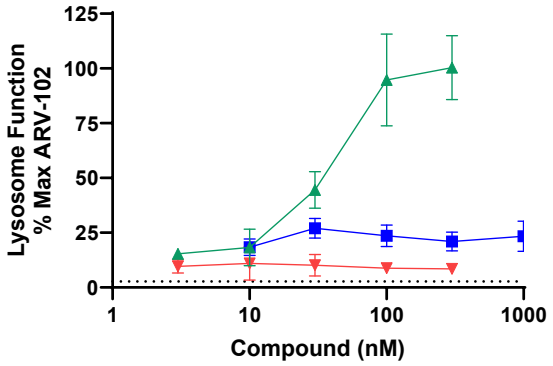
Increased activity and expression of LRRK2 have been linked with the development and progression of neurological diseases like progressive supranuclear palsy[4], or PSP, and Parkinson's disease[5].

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.

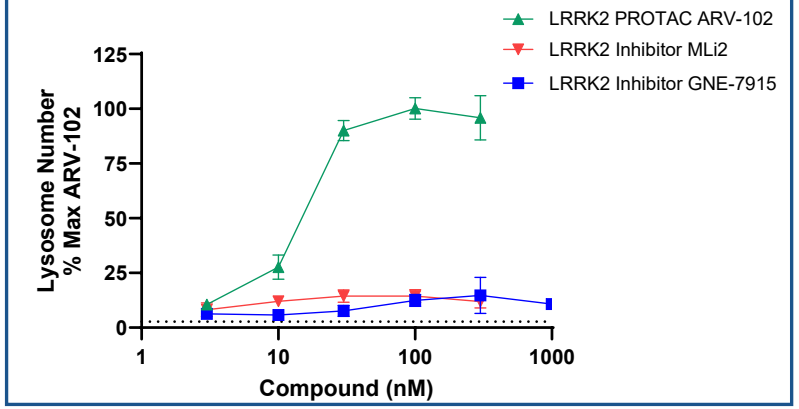
ARV-102 increases lysosome functional degradative capacity and number *in vitro*

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]

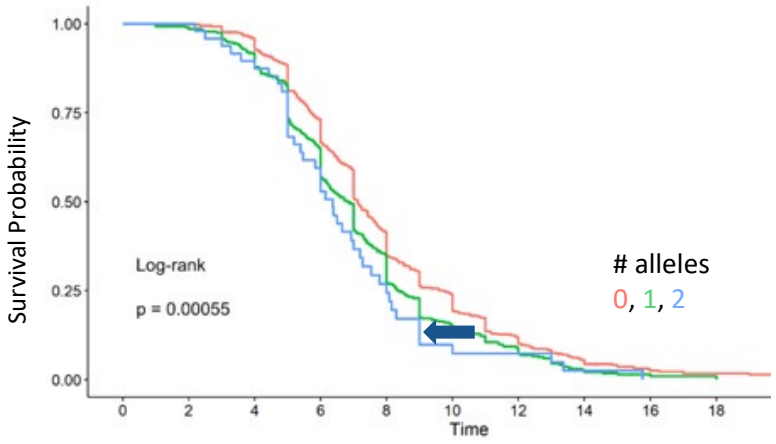
LRRK2, Leucine-rich repeat kinase 2; PD, Parkinson's disease; KO, genetic knock out; DQ-BSA, Dye Quenched-Bovine Serum Albumin

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

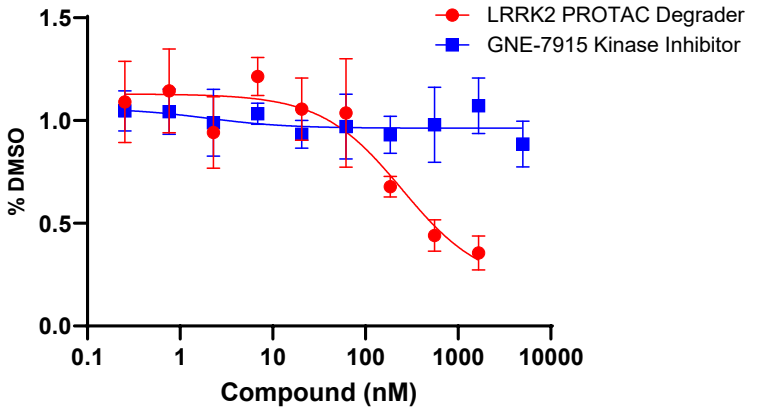
In vitro and *in vivo* data suggest that Arvinas' LRRK2 PROTAC degraders can reduce PSP-induced pathologic tau

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



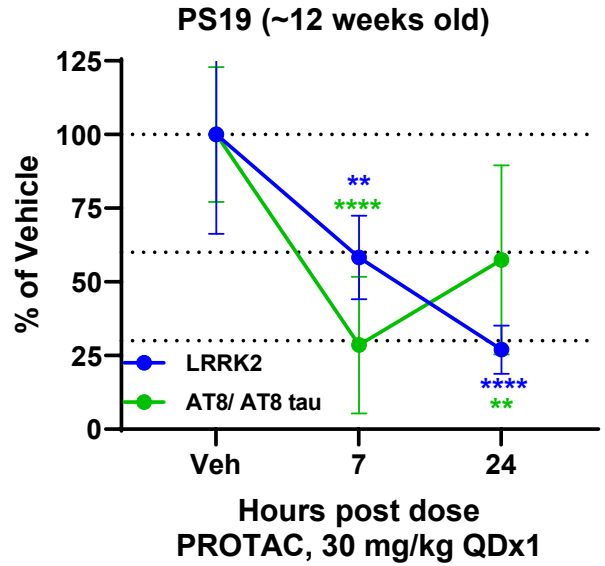
- Pooled analysis from 1239 PSP cases
- Arrow point to reduced survival for LRRK2 SNP rs2242367 – potentially via increased LRRK2 expression

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

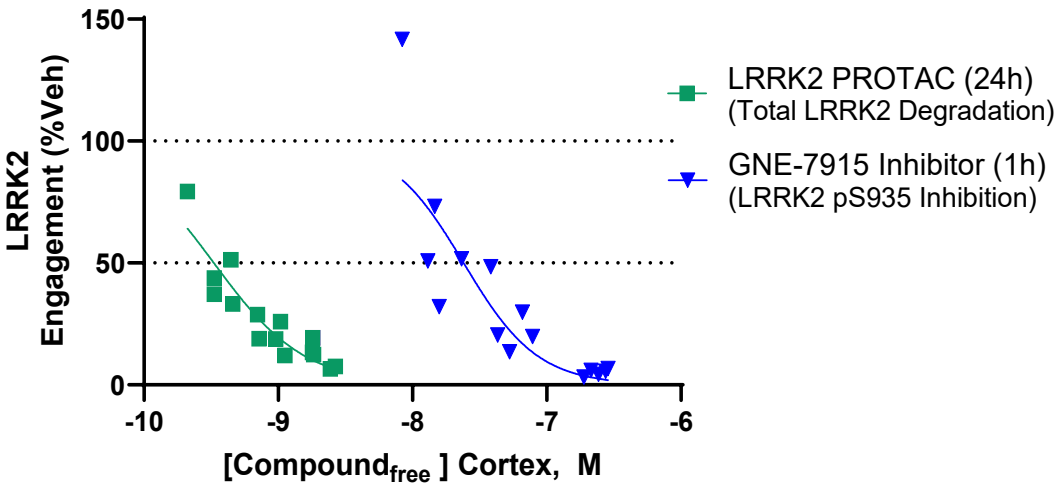
LRRK2, Leucine-rich repeat kinase 2; PSP, Progressive Supranuclear Palsy; SNP, single nucleotide polymorphism;

1. Jabbari et al., 2021

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

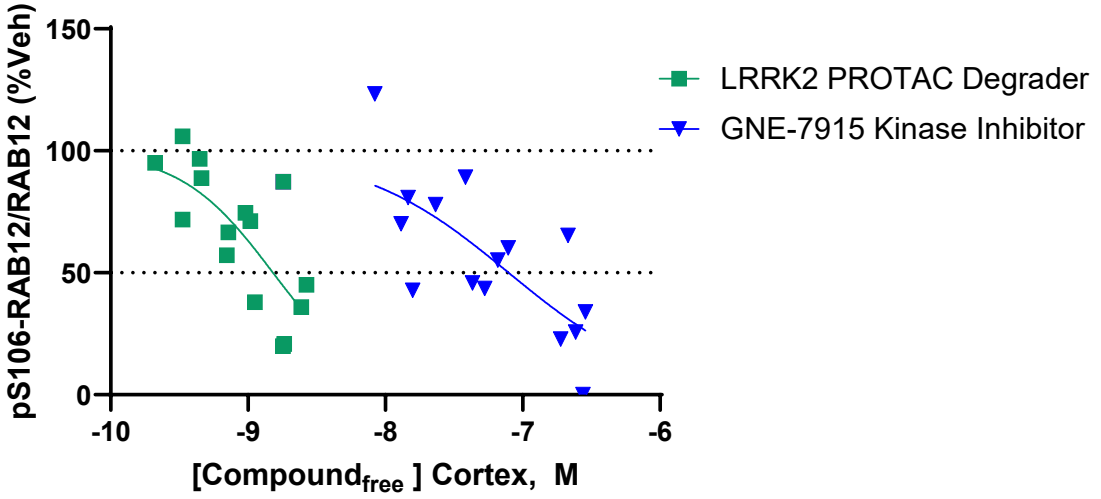
Iterative and catalytic PROTAC advantage results in stronger LRRK2 reduction and RAB pathway engagement versus a LRRK2 kinase inhibitor[a]

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

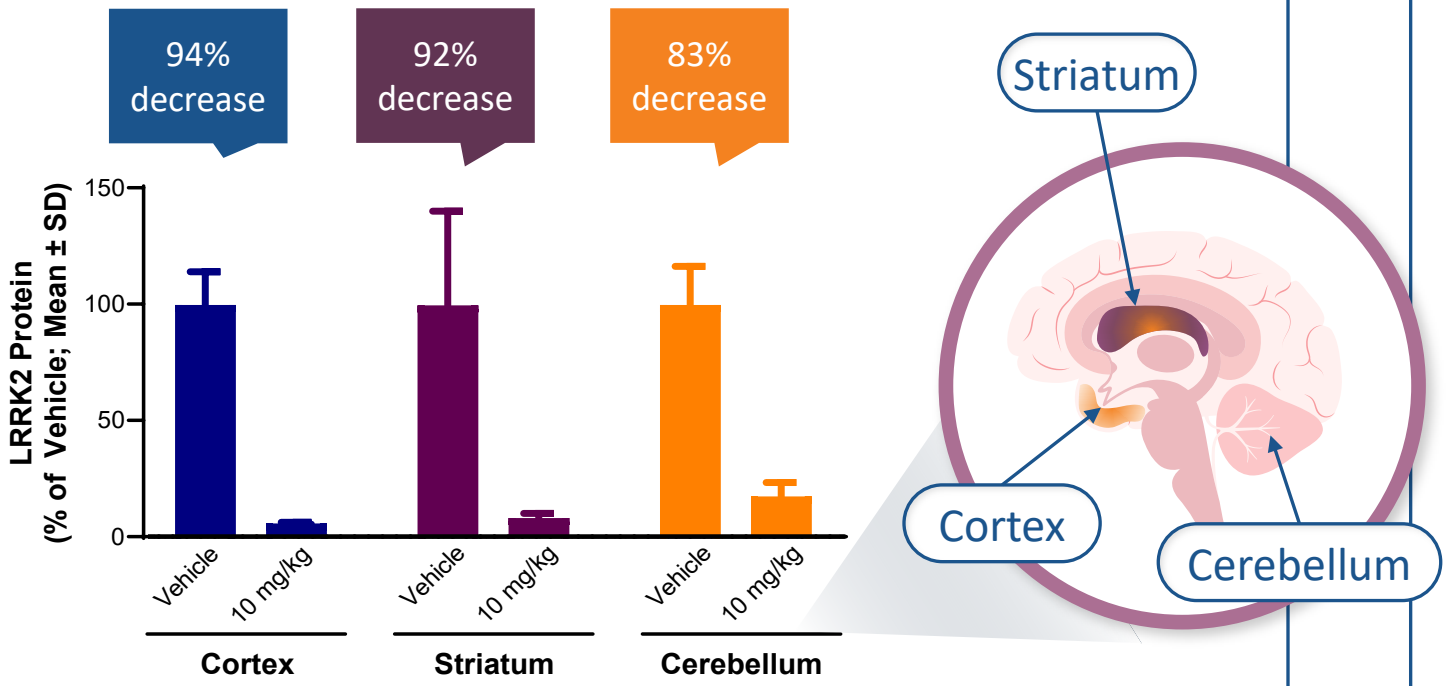
LRRK2, Leucine-rich repeat kinase 2

a. G2019S familial Parkinson's Disease mouse model.

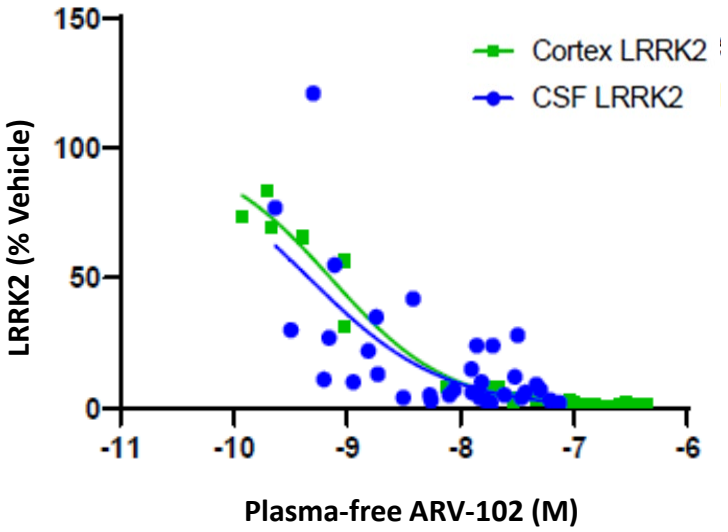
Data presented at 2023 Keystone Summit: Autophagy and Neurodegeneration.

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

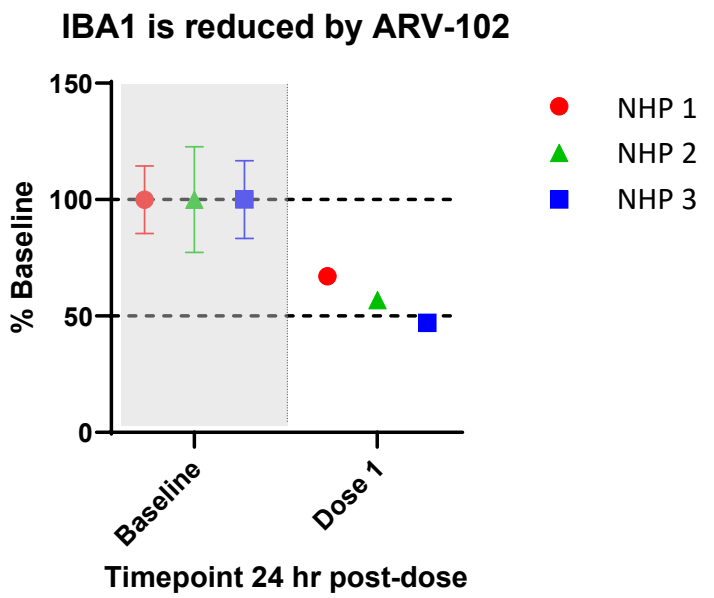


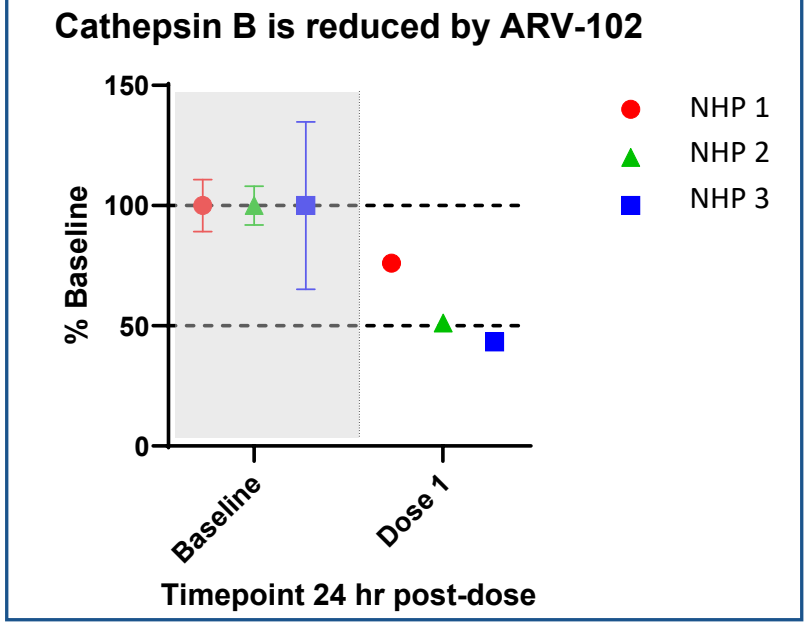
CSF, cerebrospinal fluid; LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate

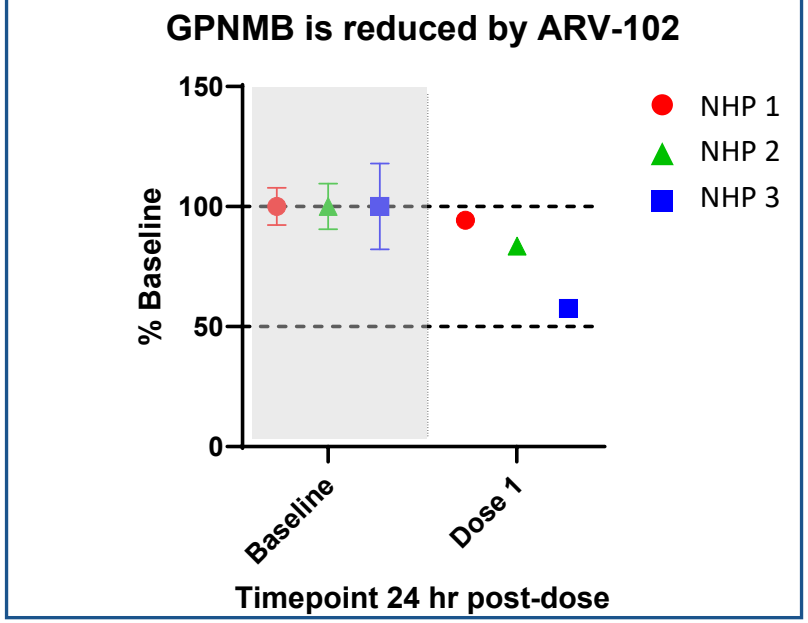
Putative LRRK2 biomarkers associated with disease are reduced in non-human primate CSF after dosing with ARV-102

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

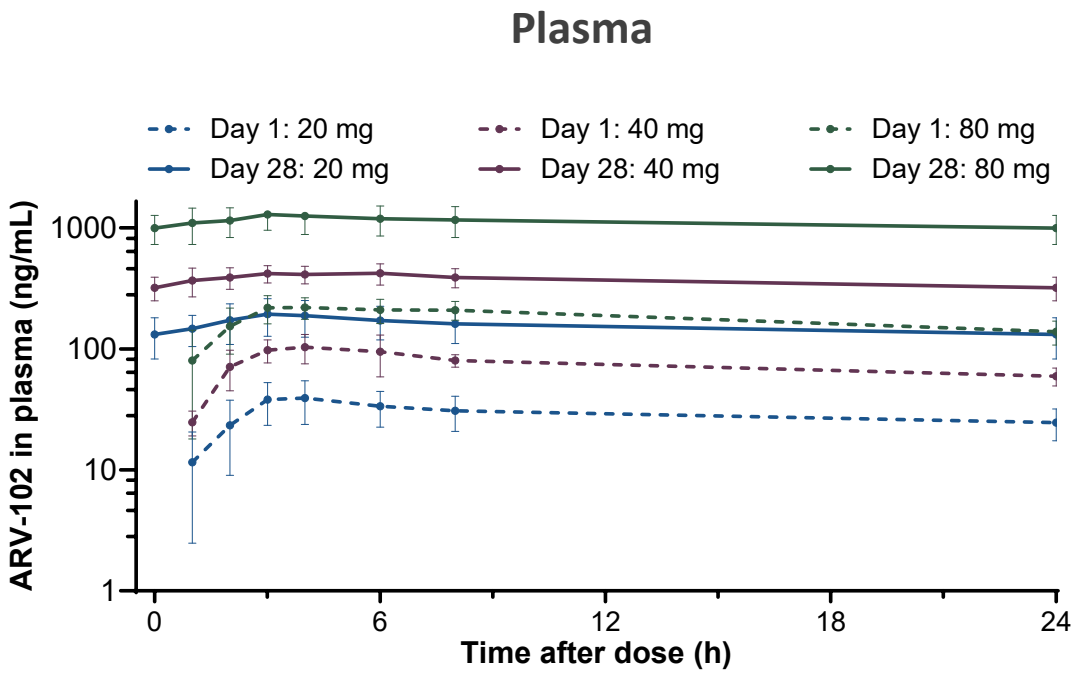
- IBA1, Cathepsin B, and GPNMB were identified as LRRK2-dependent pathway biomarkers that concord with LRRK2 protein levels in NHP CSF

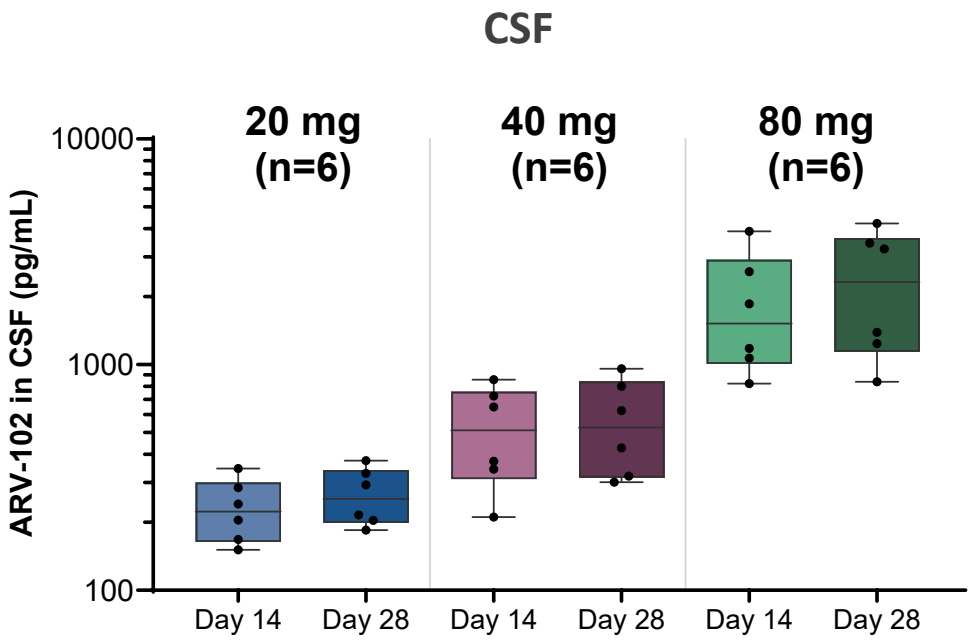
CSF, cerebrospinal fluid; GPNMB, transmembrane glycoprotein identified as a "Damage-associated Microglia" neurodegenerative protein; IBA1, microglia marker, also known as "Allograft Inflammatory Factor 1 (AIF-1); LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate

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





Lower limit of quantification was 0.25 ng/mL.

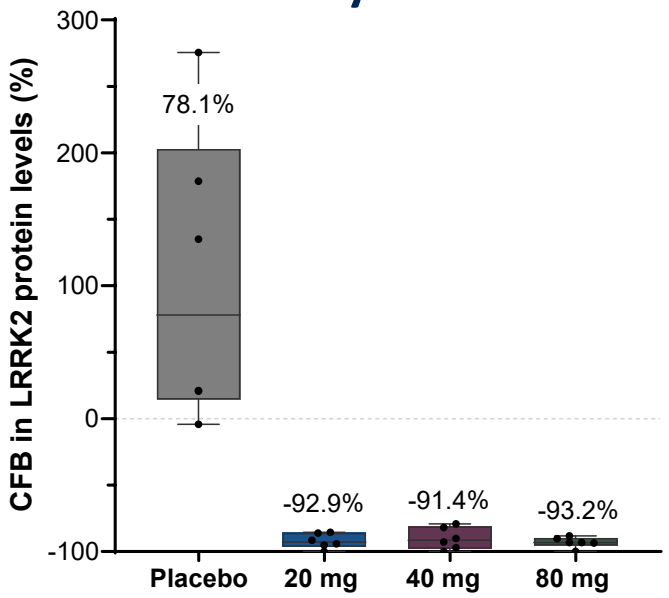
Data presented at 2026 International Conference on Alzheimer's and Parkinson's Disease and Related Neurological Disorders (AD/PD)

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

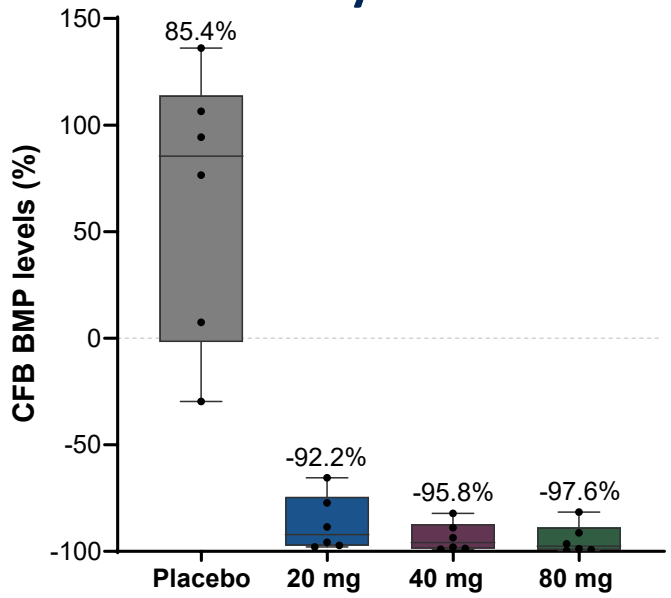
PBMC LRRK2

Day 28

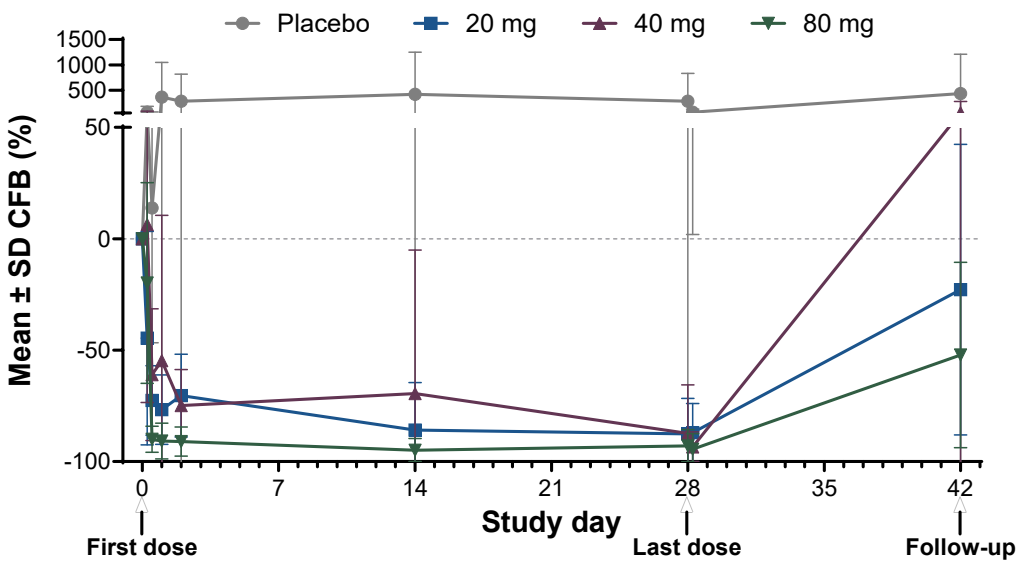


Urine BMP

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]

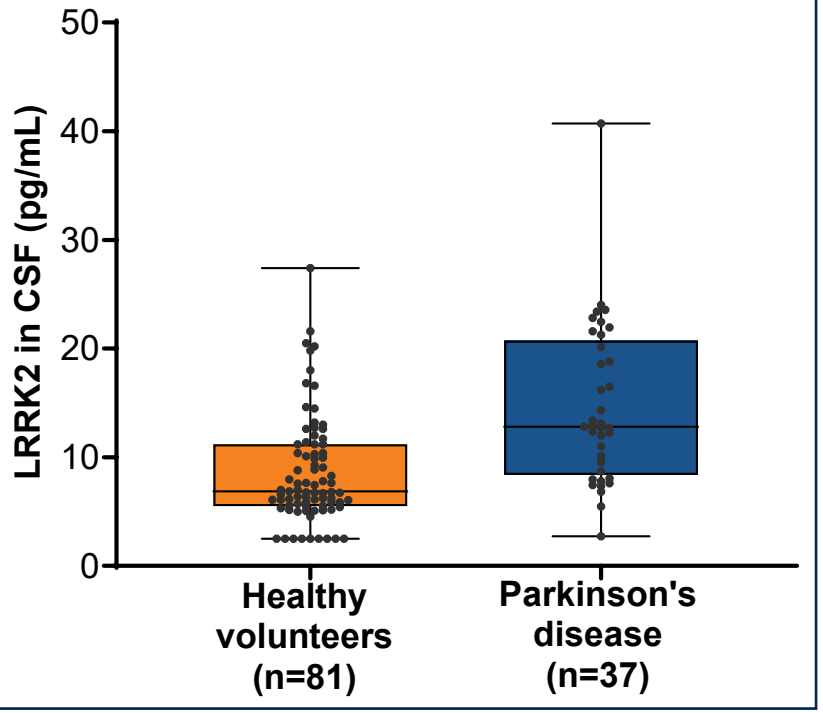
As presented at AD/PD 2026 ADVANCES IN SCIENCE & THERAPY
International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

BMP, bis(monoacylglycerol)phosphate; LRRK2, leucine-rich repeat kinase 2; PBMC, peripheral blood mononuclear cell.

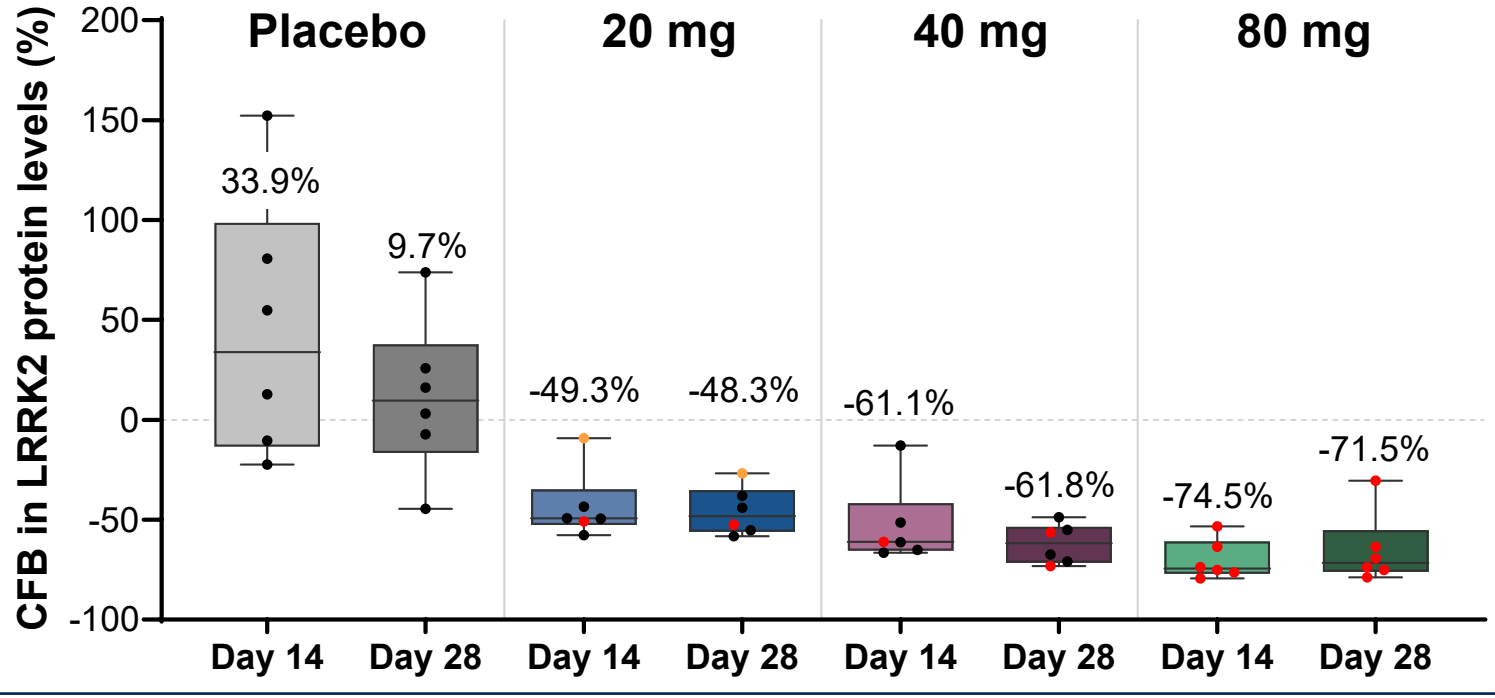
1. Smits L, et al. Oral presentation at International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD) 2025. 2. Smits L, et al. Poster presented at the International Congress of Parkinson's Disease and Movement Disorders (MDS) 2025; Poster #904.

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

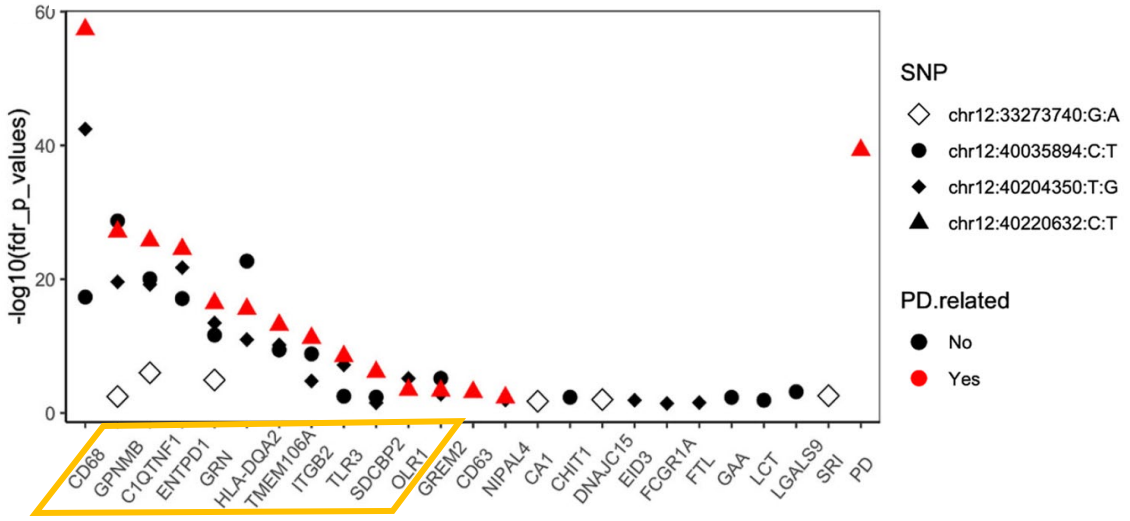
CFB, change from baseline; CSF, cerebrospinal fluid; LLD, lower limit of detection; LLOQ, lower limit of quantification; LRRK2, leucine-rich repeat kinase 2; QD, once daily.
Box plots show median and 25%/75% quartiles with whiskers to the minimum and maximum values. Circles indicate individual participant 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
March 17-21, 2026 | Copenhagen, Denmark

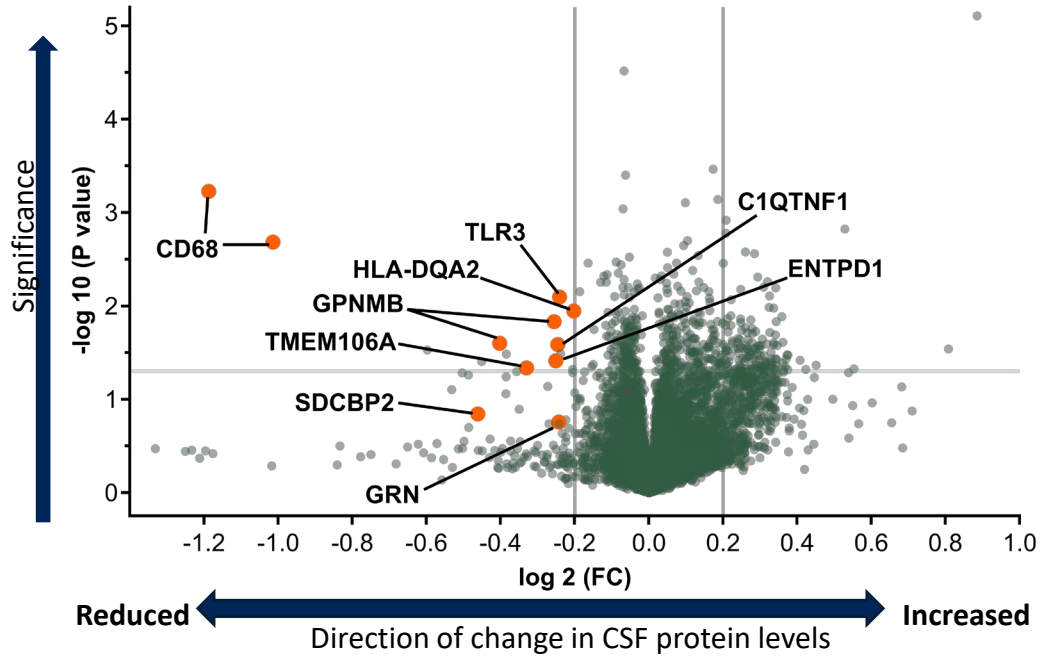
ARV-102 reduced endolysosomal and neuroinflammatory pathway proteins that are elevated in LRRK2-related Parkinson's disease[1]

- 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)



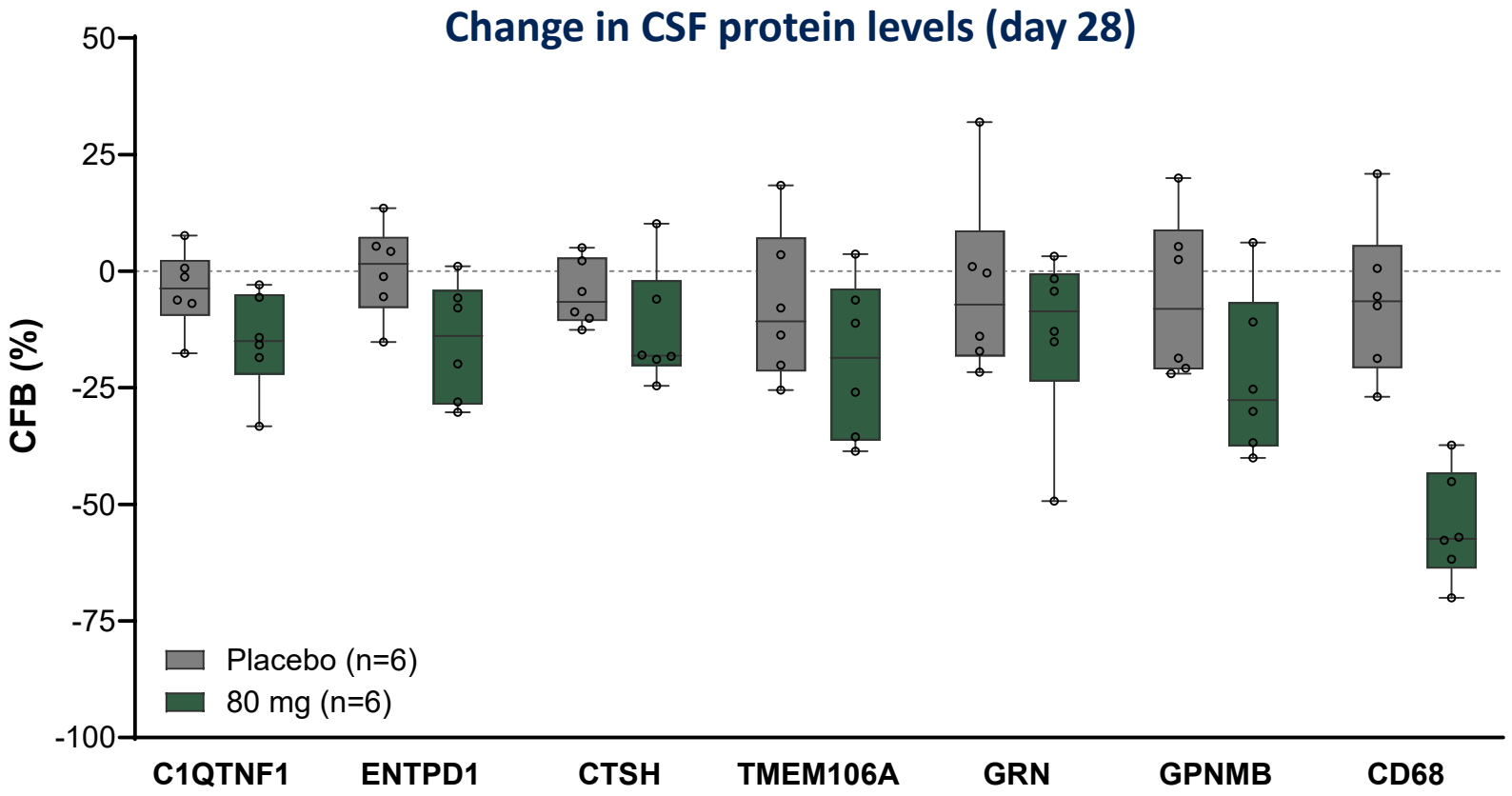
C1QTNF1, complement C1q tumor necrosis factor-related protein 1; CD68, cluster of differentiation 68; CSF, cerebrospinal fluid; ENTPD1, ectonucleoside triphosphate diphosphohydrolase 1; FC, fold change; GRN, granulin precursor; GPNMB, glycoprotein non-metastatic melanoma protein B; HLA-DQA2, major histocompatibility 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.

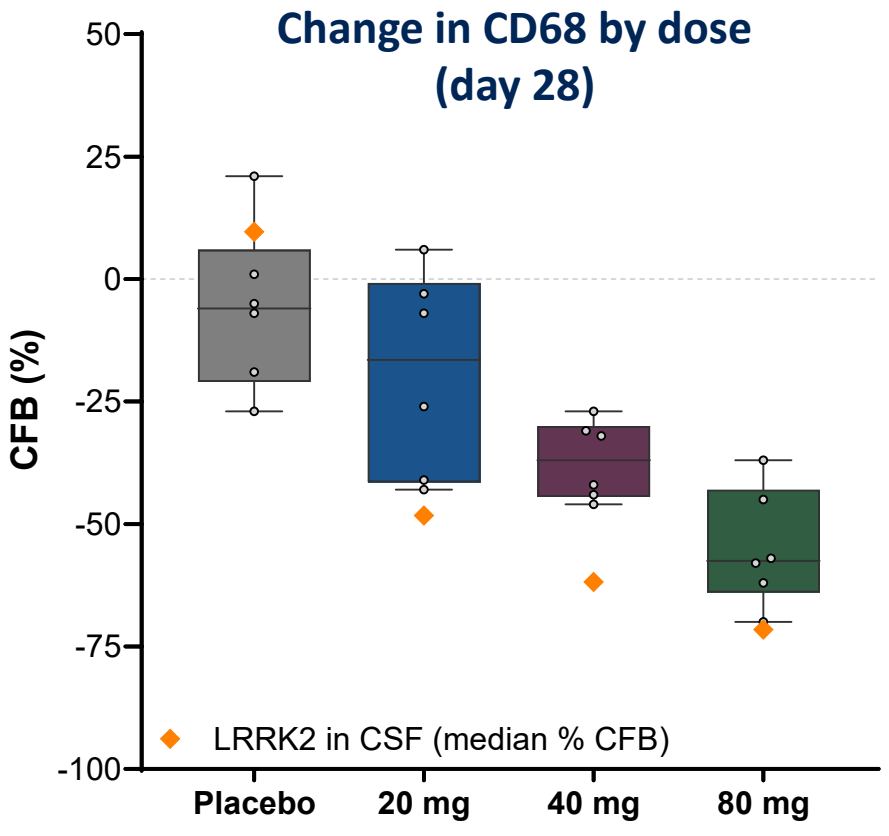
a, .Global O'Brien's statistical test was utilized to evaluate aggregate change in top 10 proteins related to LRRK2 variants. b. Figure adapted from Phillips et al. (2023). NPJ Parkinson's Disease.

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 2027 (pending regulatory feedback)*

Progressive Supranuclear Palsy

Phase 1b: Multiple dose

- Initiate Phase 1b multi-dose cohort in patients with progressive supranuclear palsy

Global registrational trial

- Initiate global multi-site registrational trial in patients with progressive supranuclear palsy

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

*Discussions with health authorities are ongoing and Arvinas plans to initiate clinical trials in 2027.

CLINICAL PROGRAMS: Neurology

ARV-027

PROTAC polyQ-AR degrader

ARVINAS

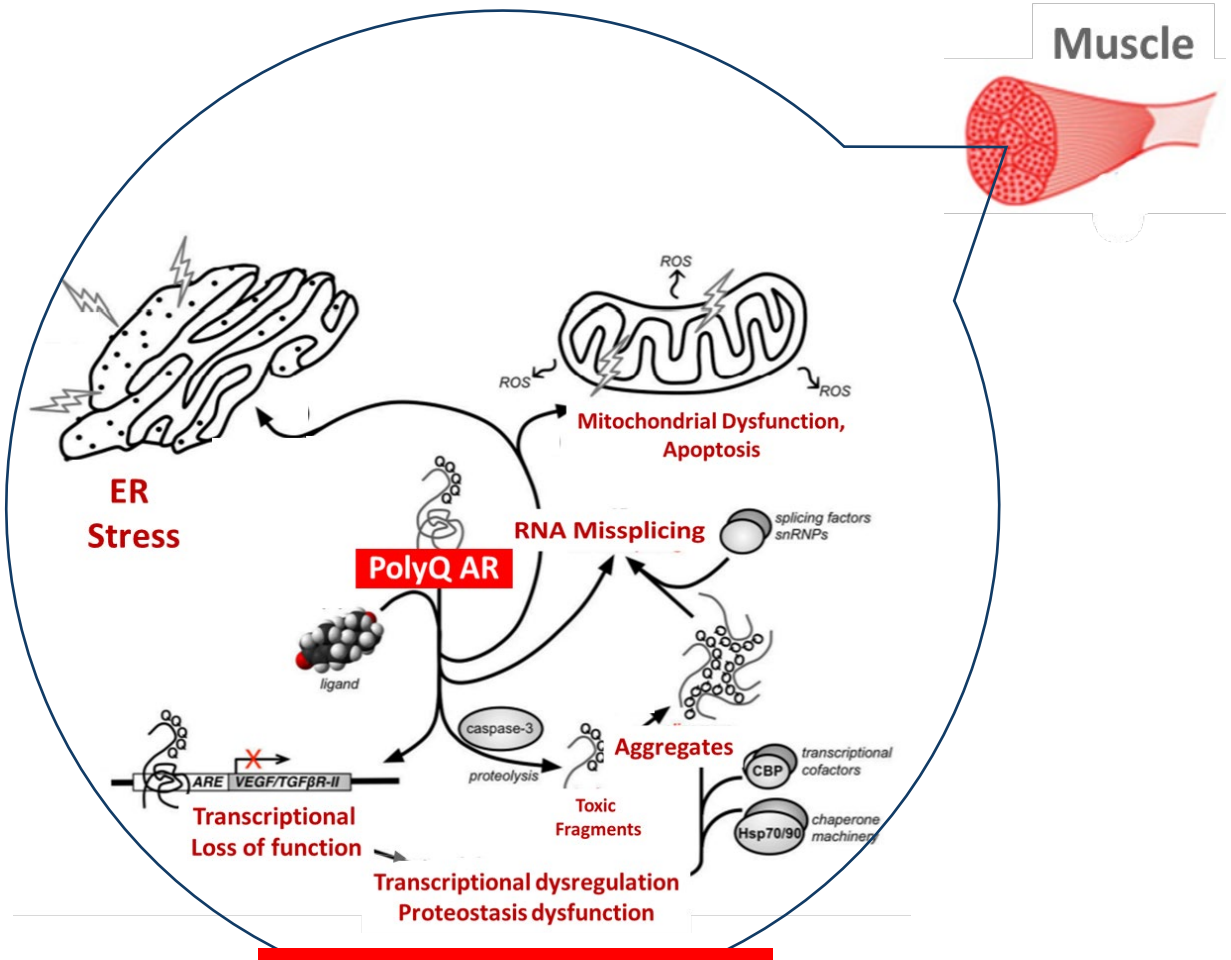
ARV-027 is an investigational compound. Its safety and effectiveness have not been established.

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



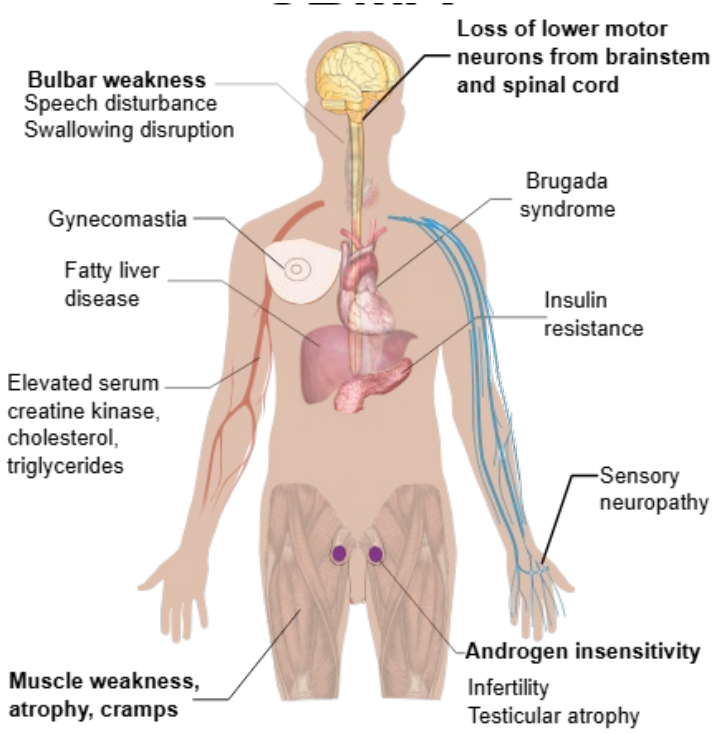
PROTAC PolyQ-AR degrader may eliminate the root cause of disease

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. or EU

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

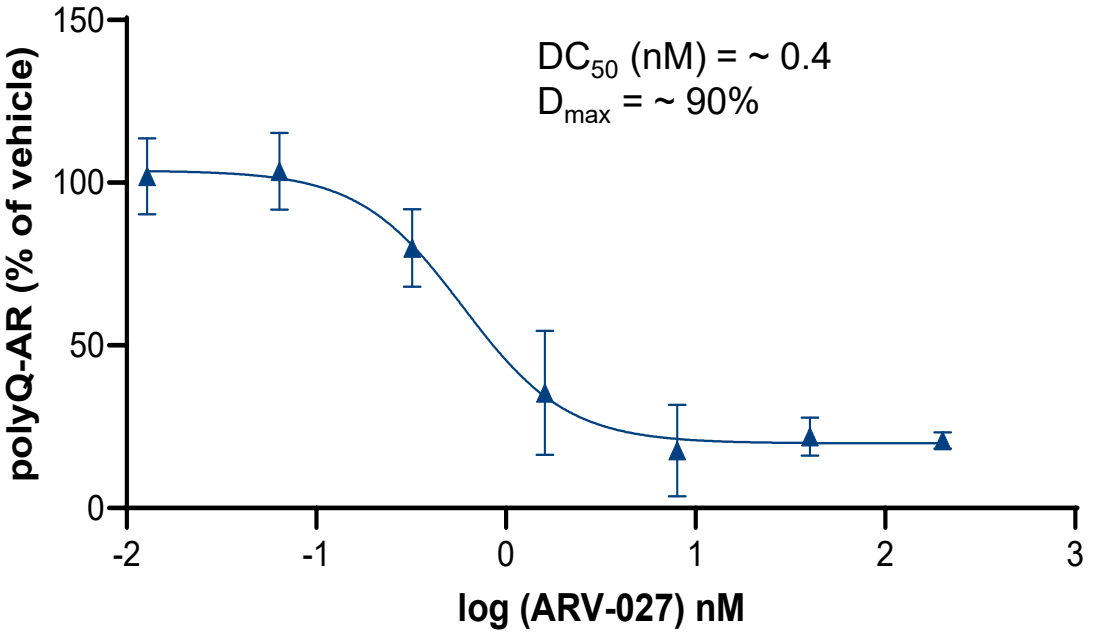
SBMA, spinal bulbar muscular atrophy

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

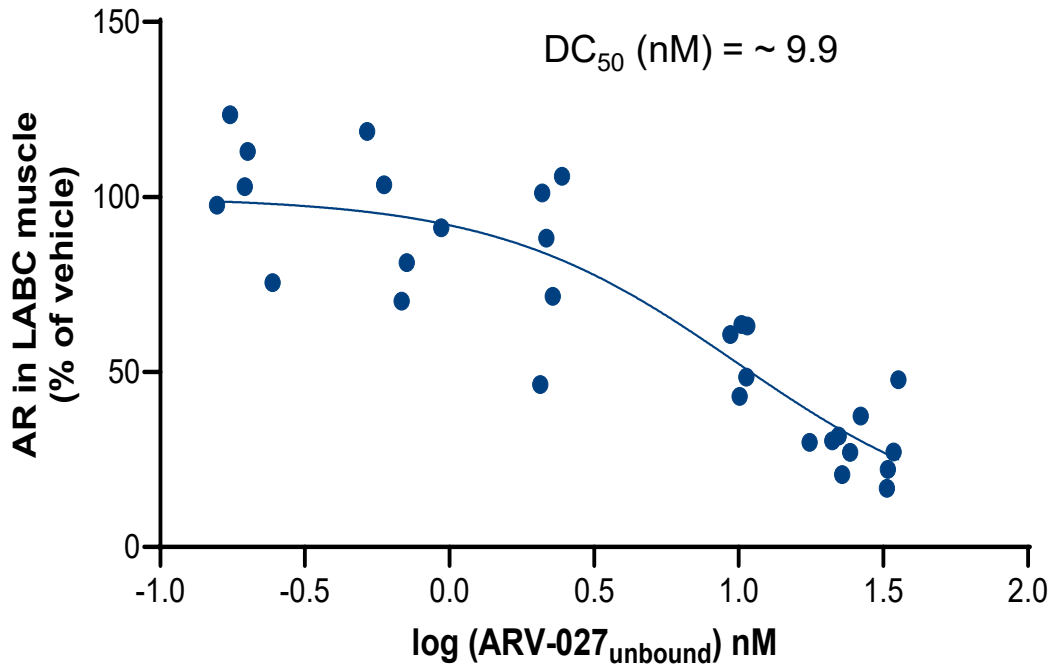
ARV-027 is a potent *in vitro* and *in vivo* PROTAC degrader of polyQ-AR, the root cause of SBMA[1]

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)

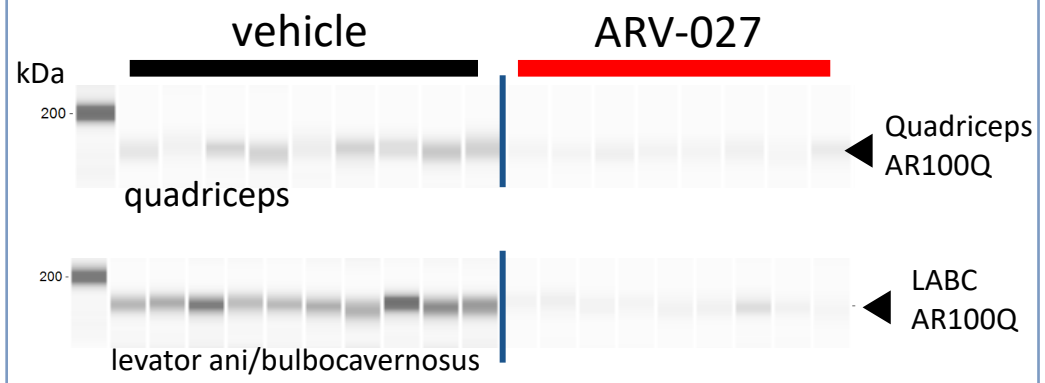
polyQ-AR, polyglutamine-expanded (polyQ) androgen receptor (AR); SBMA, spinal bulbar muscular atrophy

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

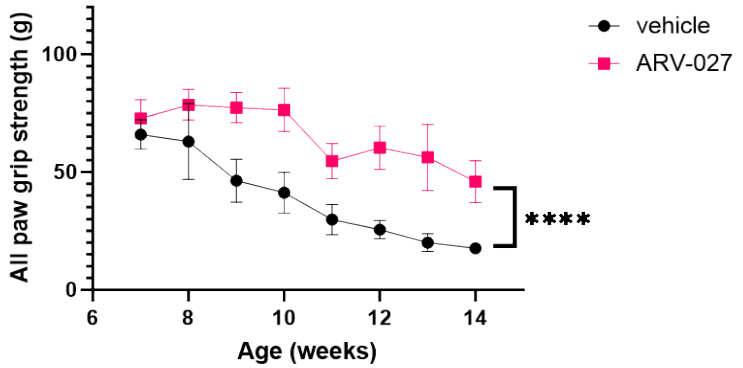
Gregory J et al., International Congress of the World Muscle Society (WMS), Poster 718LBP. Presented October 10, 2025

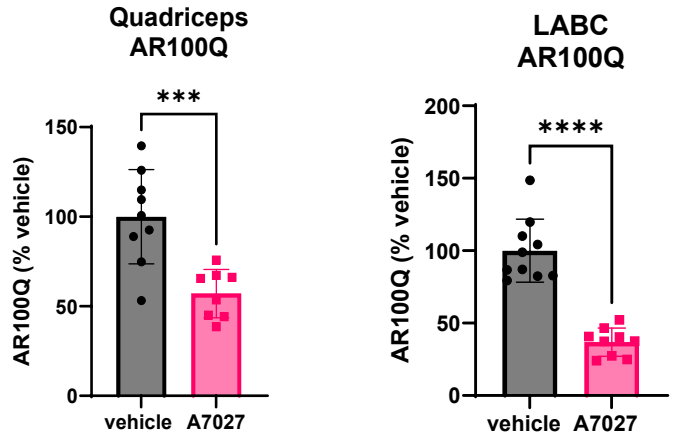
In preclinical models, ARV-027 induced polyQ-AR degradation in muscle tissues and rescued strength and endurance

Monomeric polyQ-AR[a]



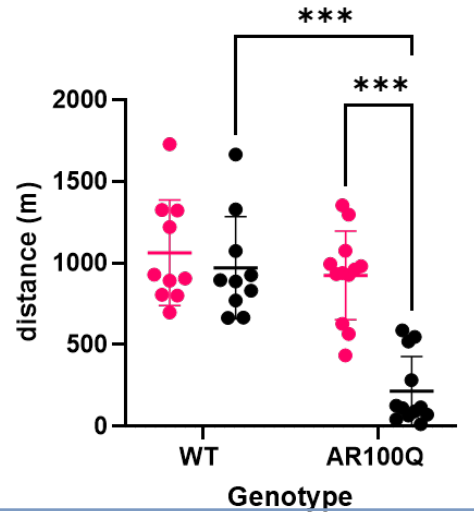
All Paw Grip Strength[a]





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 DOSE** in healthy volunteers	**MULTIPLE DOSE** in patients with SBMA
Complete: Part A ✓ Single ascending dose cohorts in healthy volunteers	Ongoing: Part B ✓ Multiple 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: Hematology-Oncology

ARV-393

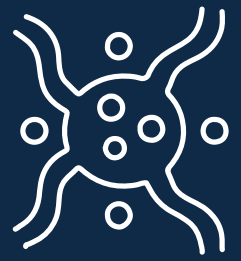
PROTAC BCL6 degrader

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

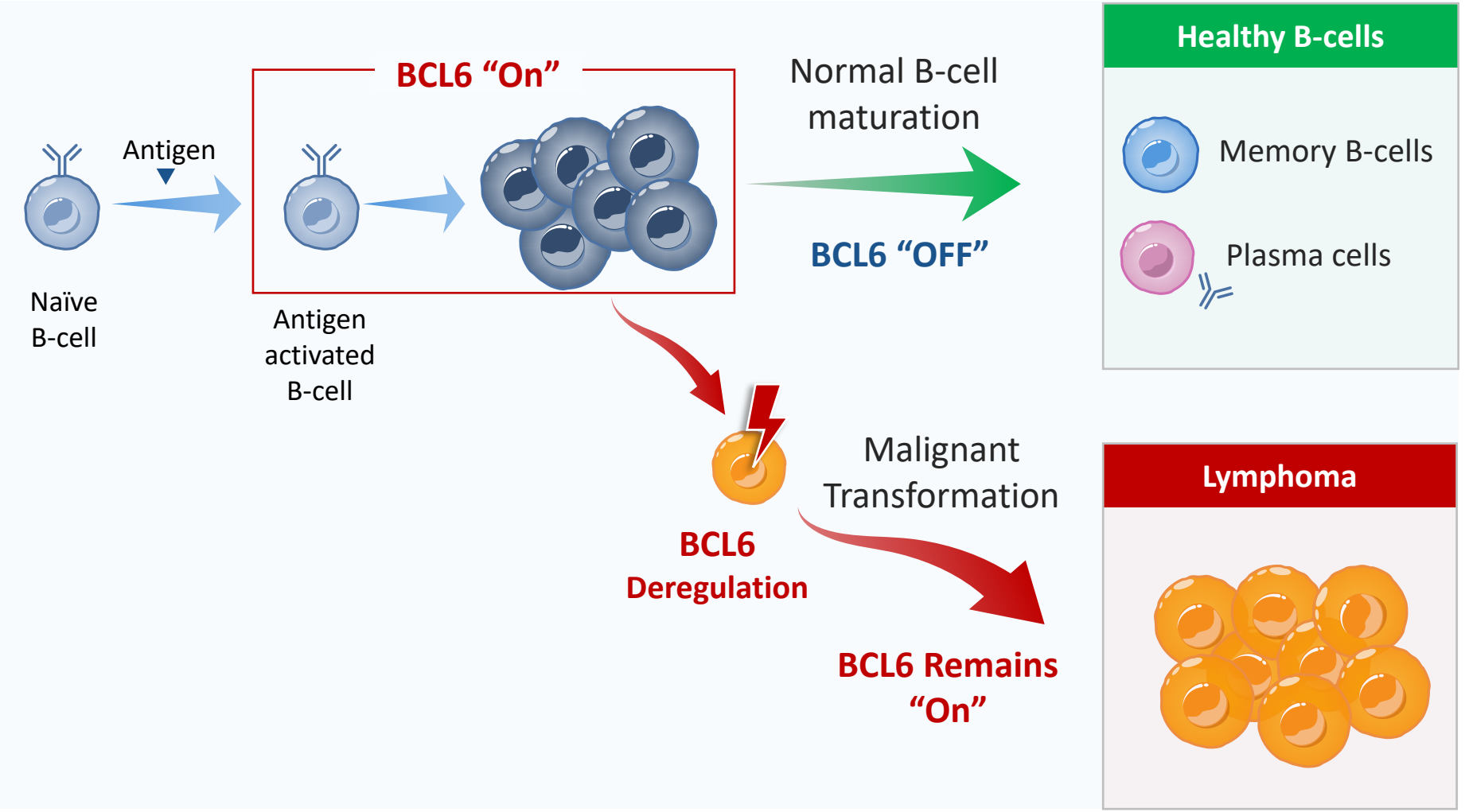
Need for patients with relapsed or high-risk disease, and particularly older adults

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**

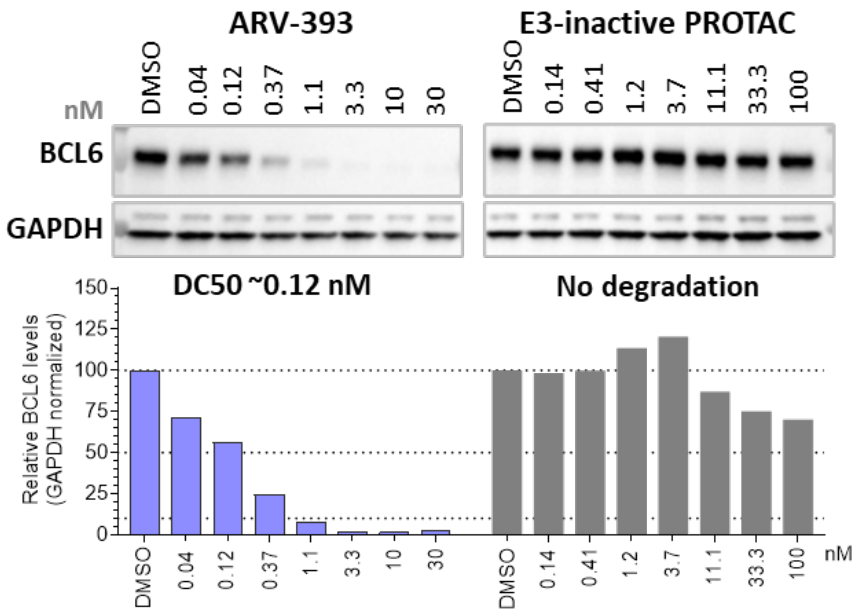
Phase 1 dose escalation trial of ARV-393 as monotherapy, and in combination with glofitamab, is currently enrolling patients with relapsed/refractory NHL (NCT06393738)

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

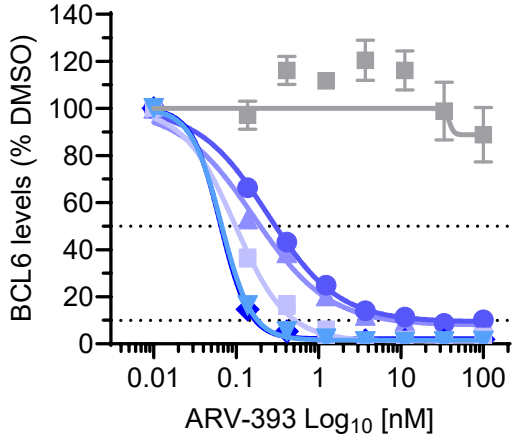
ARV-393, but not its E3-inactive analogue, robustly degrades BCL6 in the OCI-Ly1 model of DLBCL



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



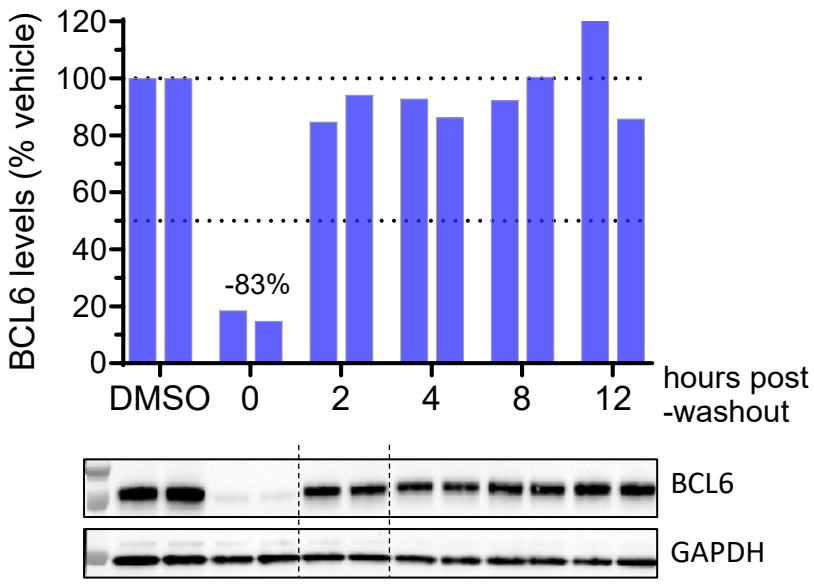
	DC_{50} [nM]	D_{max}
OCI-Ly1	0.07	99%
Farage	0.06	98%
SU-DHL-4	0.33	91%
SU-DHL-6	0.21	92%
OCI-Ly7	0.10	99%
OCI-Ly1 (E3-inactive ARV-393 analogue)	-	-

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

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

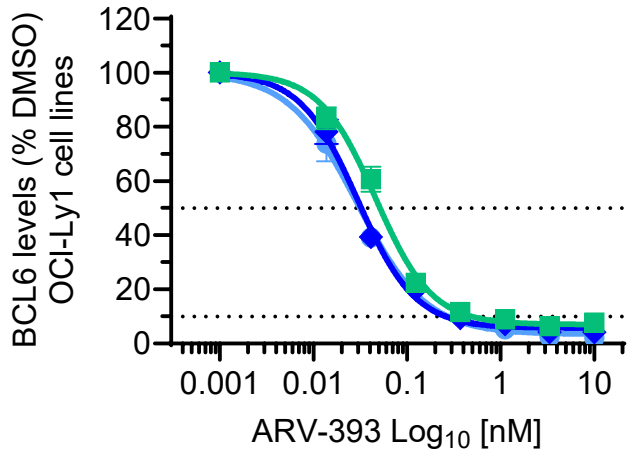
Preclinically, ARV-393 rapidly degrades BCL6 and overcomes its high resynthesis rate that drives tumor cell growth

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



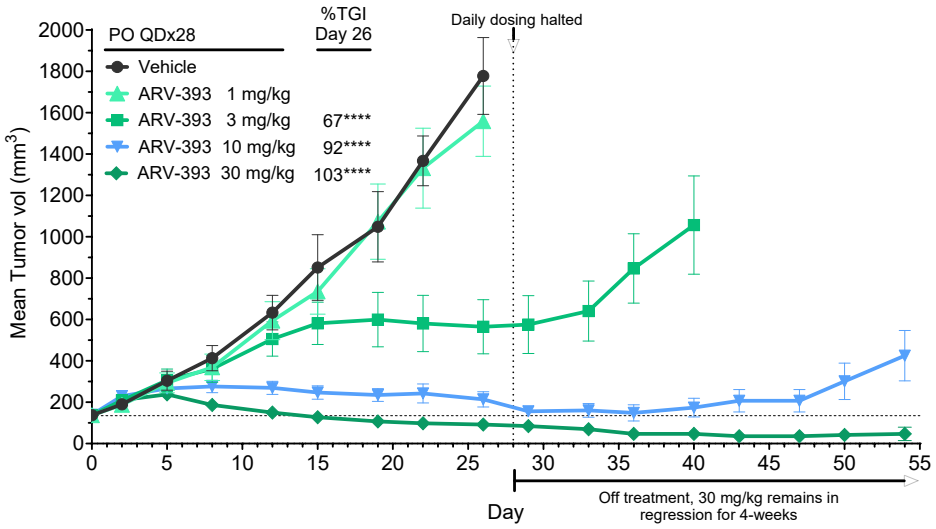
	DC_{50} [nM]	D_{max}
2 hours	0.05	93%
4 hours	0.03	94%
24 hours	0.03	97%

BCL6, B cell lymphoma 6

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

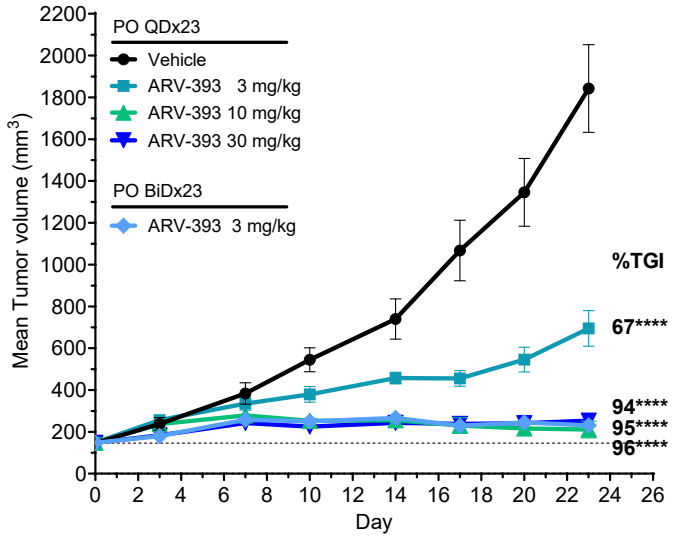
ARV-393 induces dose-dependent and sustained tumor growth inhibition and regressions *in vivo*

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

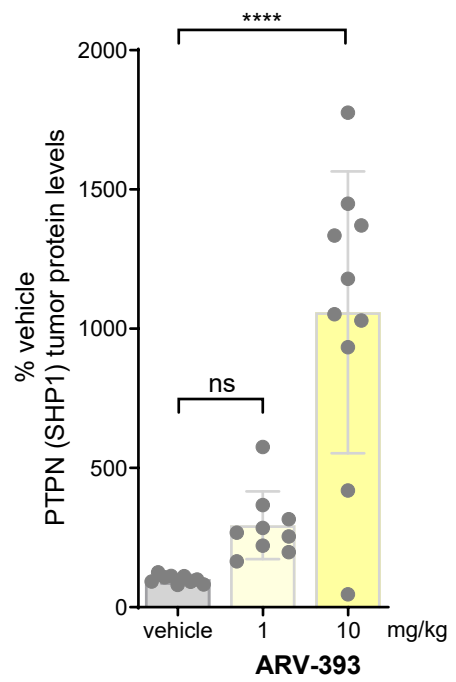


- TGI assessment of different dosing regimens of ARV-393 in the OCI-Ly1 CDX model demonstrate tumor growth inhibition >90% after 22 days at 10 and 30 mg/kg dosing

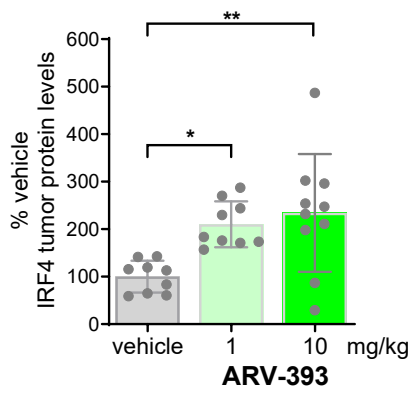
CDX, cell line derived xenograft model; DLBCL, Diffuse Large B-Cell Lymphoma; TGI, Tumor Growth Inhibition
Gough et al., European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain.
Statistical analyses were performed using two-way ANOVA, QD, Once daily; BID, Twice daily; ****p<0.0001.

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

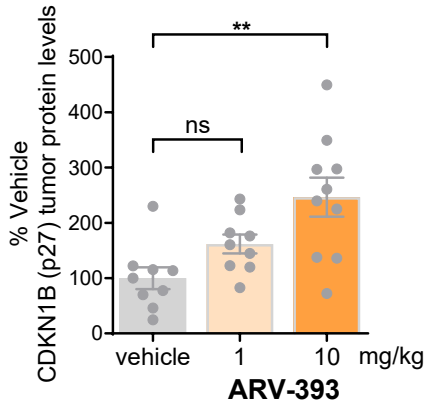
Signal Transduction PTPN6 (SHP1)	B-cell Differentiation IRF4	Cell cycle CDKN1B (p27)



****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

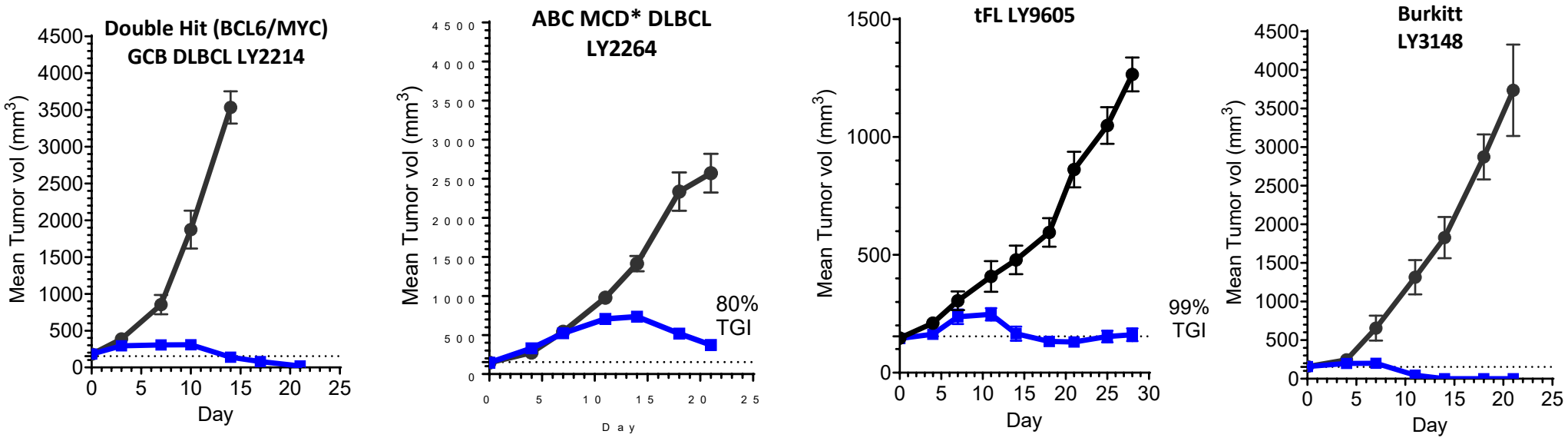
BCL6, B cell lymphoma 6; CDKN1B, Cyclin Dependent Kinase Inhibitor 1B; CDX, cell derived xenograft; IRF4, Interferon Regulatory Factor 4; PTPN6, Protein Tyrosine Phosphatase Non-Receptor Type 6

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

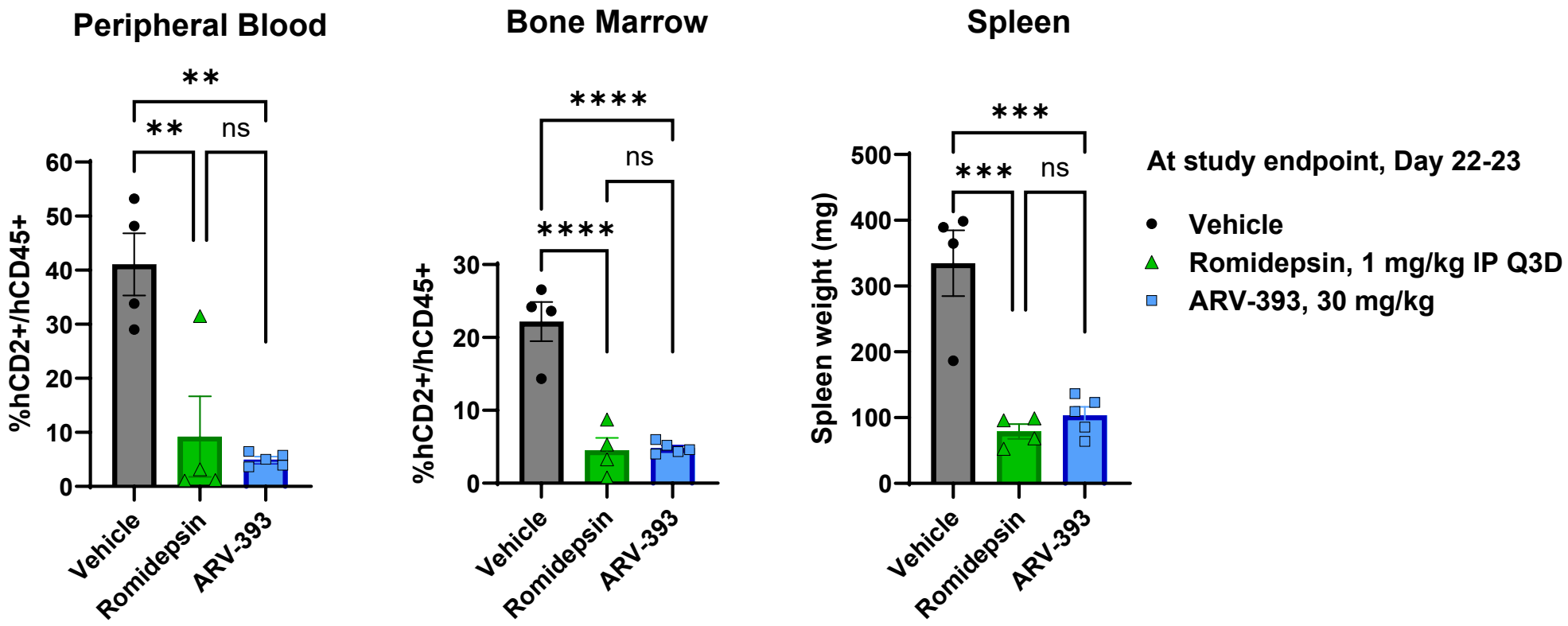
ABC, activated B cell-like; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B cell-like; NHL, non-Hodgkin's lymphoma; PDX, patient derived xenograft model; tFL, transformed follicular lymphoma; TGI, tumor growth inhibition

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

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

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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)

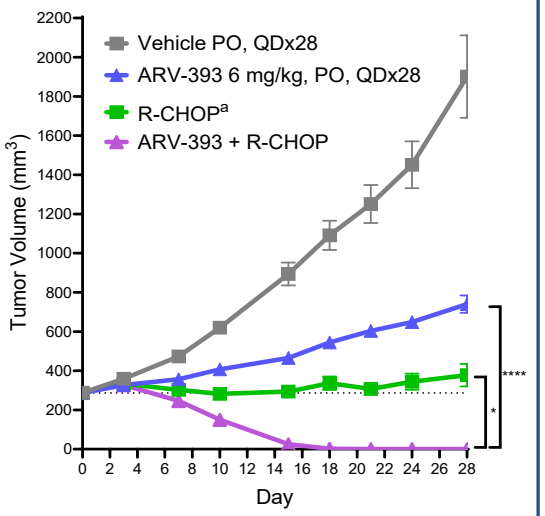
In preclinical models of aggressive DLBCL, ARV-393 demonstrated broad combinability, with tumor regressions observed in combination with SOC chemotherapy, SOC biologics, and investigational oral small molecule inhibitors targeting clinically validated oncogenic drivers of lymphoma

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

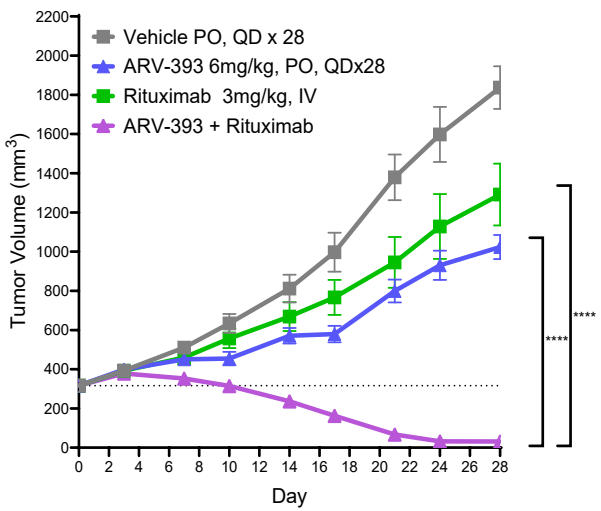
Acker et al., American Association for Cancer Research (AACR) Poster 1655/15. April 2025, Chicago.

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

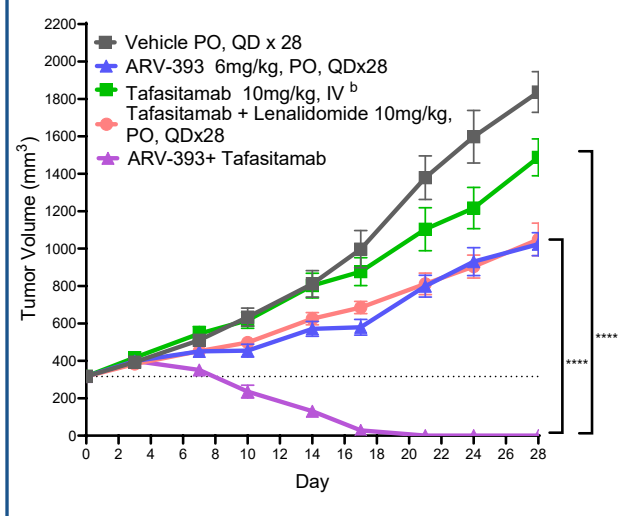
R-CHOP



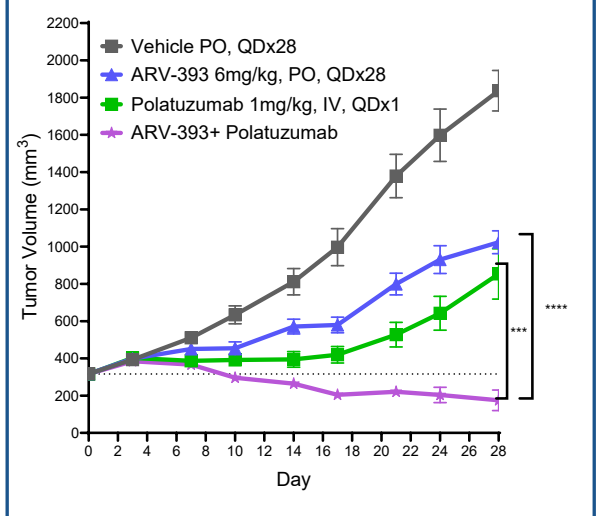
Rituximab



Tafasitamab



Polatuzumab vedotin



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

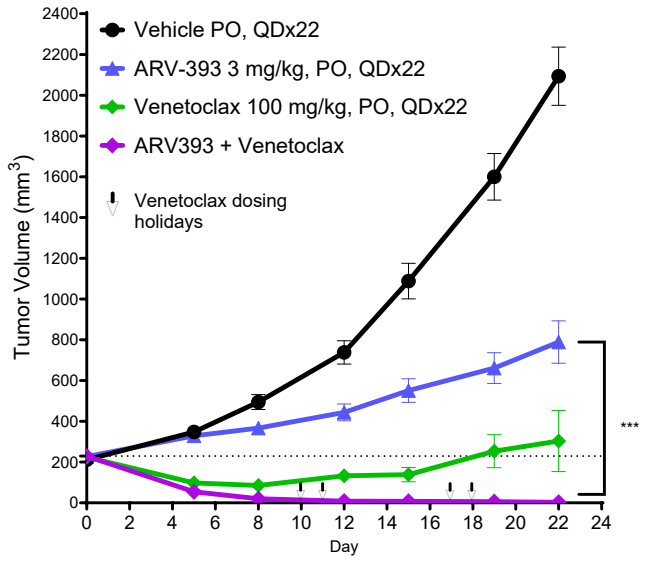
CDX, cell-derived xenograft; DLBCL, diffuse large B-cell lymphoma; IV, Intravenous; PO, oral; QD, once a day; R-CHOP, rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine sulfate, and prednisone; SOC, standard of care

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.

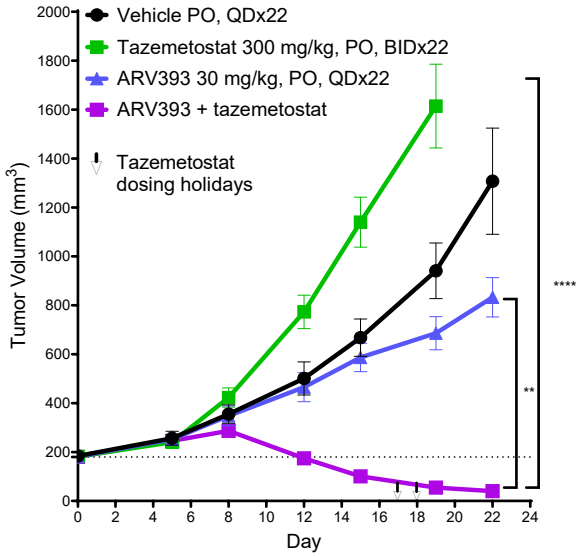
ARV-393, in combination with small molecule inhibitors, drives tumor regressions, including complete responses, in a preclinical model of aggressive DLBCL

Venetoclax



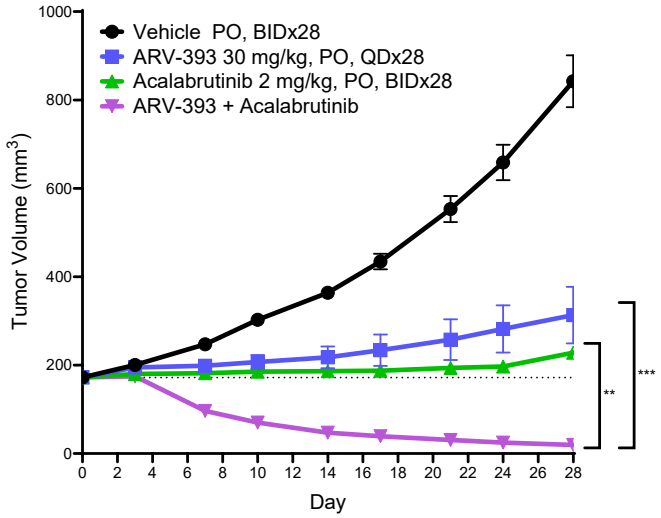
OCI-Ly1 GCB DLBCL CDX

Tazemetostat



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

Acalabrutinib



OCI-Ly10 ABC DLBCL CDX

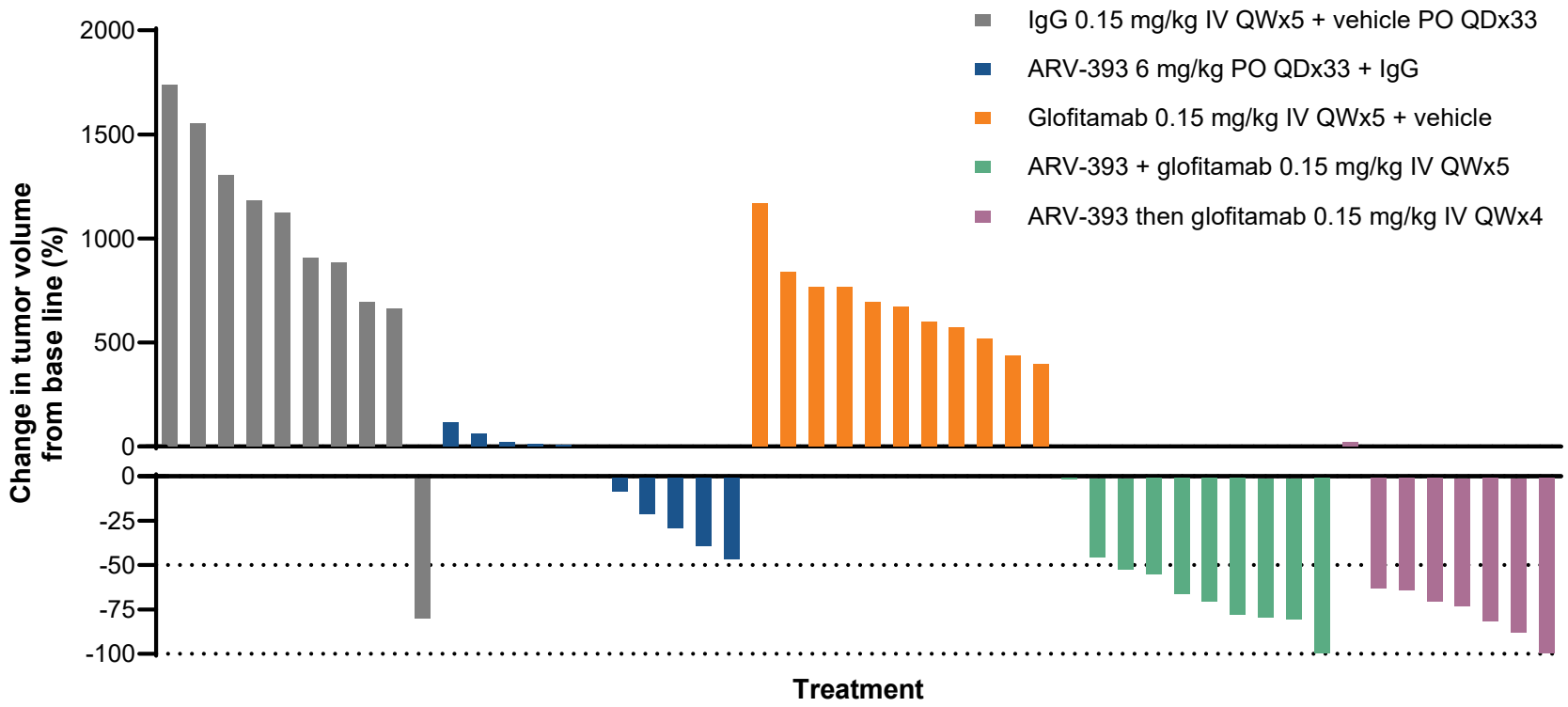
ABC, activated B-cell; BID, twice a day; CDX, cell-derived xenograft; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B-cell; IV, Intravenous; PO, oral; QD, once a daily

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)



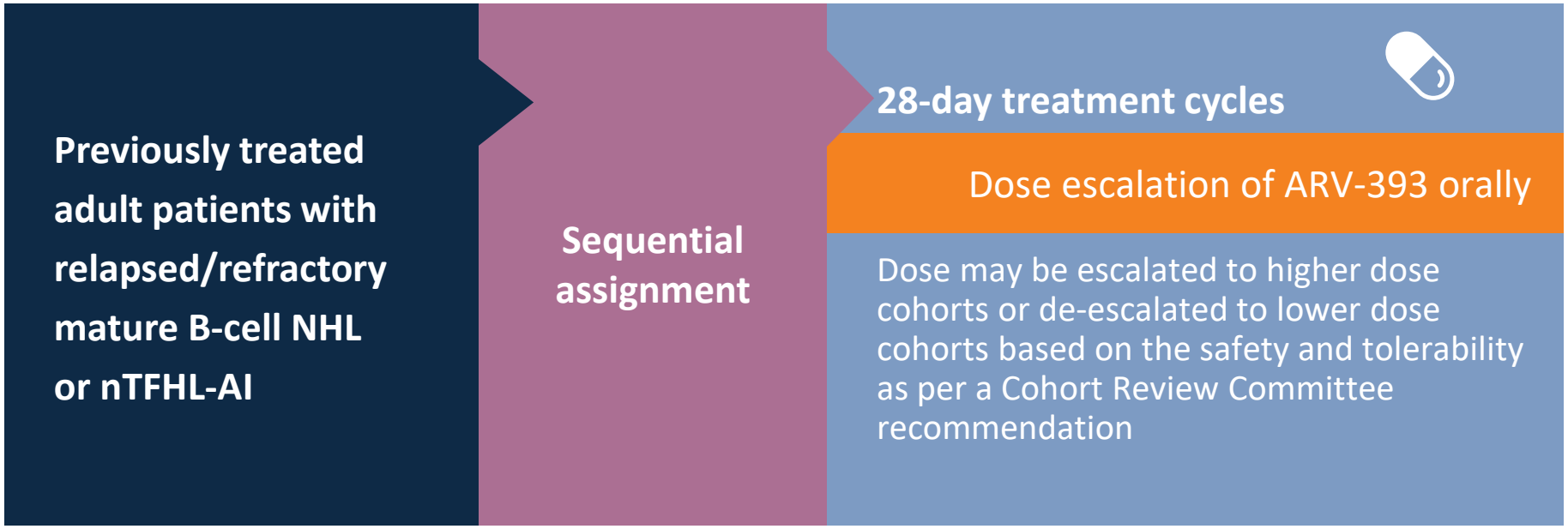
Increased tumor regressions observed with concomitant (10/10 mice) and sequential dosing (7/8 mice) vs single-agent ARV-393 (5/11 mice) or glofitamab (0/11 mice)

*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



Phase 1 monotherapy dose escalation data disclosure from early cohorts in 2H 2026

Phase 1 monotherapy dose escalation data in B- and T-cell lymphomas, and combination data with glofitamab, in mid-2027

- **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

CLINICAL PROGRAMS: Oncology

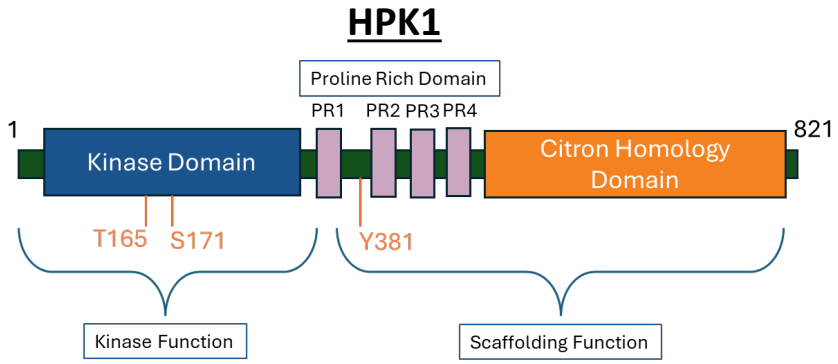
ARV-6723

PROTAC HPK1 degrader

ARVINAS

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

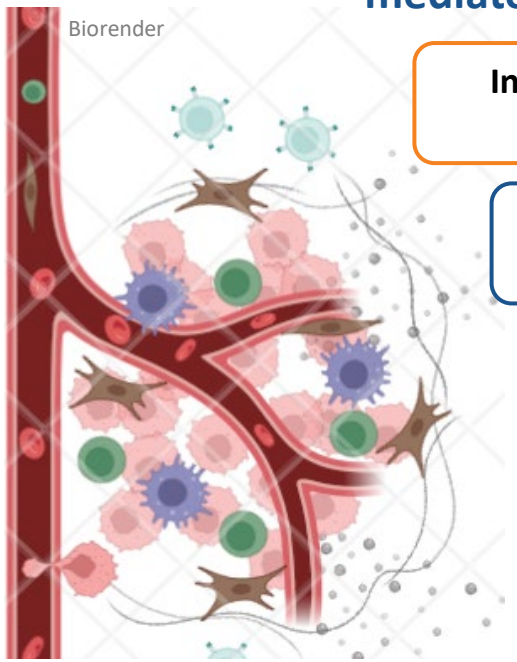
ARV-6723 is a potent PROTAC degrader of hematopoietic progenitor kinase 1 (HPK1), a central regulator of immune suppression



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)

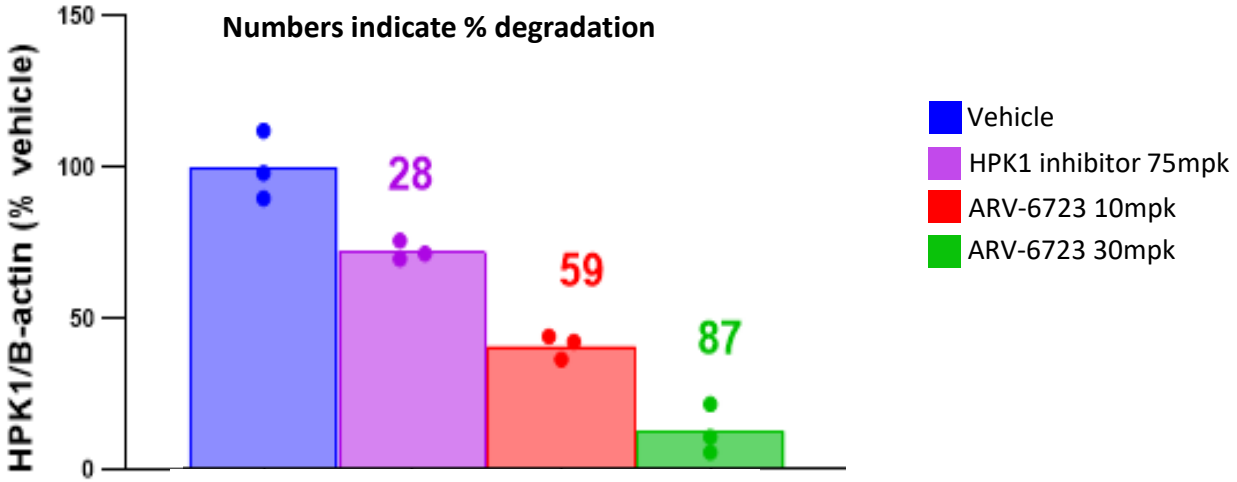
- **Increase** immune function (T/dendritic cells) and immune attack (T/NK cells)
- **Counter** activation of T cell exhaustion
- **Block** suppressive TME (PGE_2, Adenosine)
- **Reprogram** the TME to unleash immune Response

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

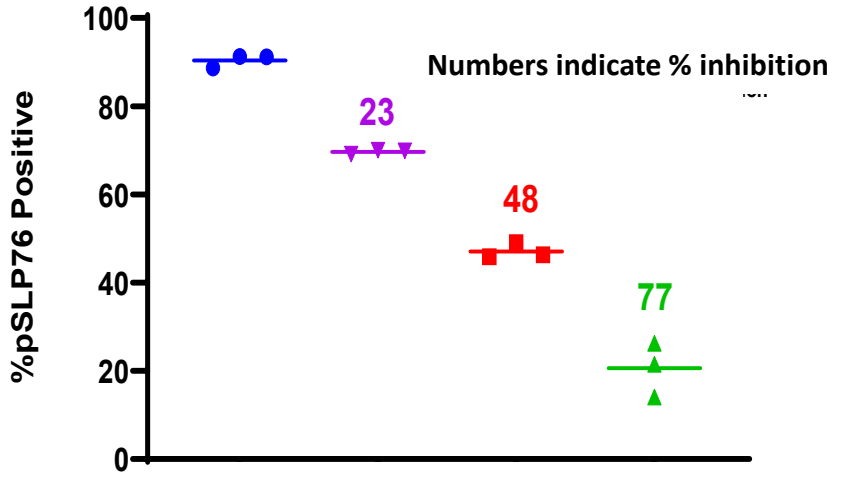
NK, natural killer; PGE_2, prostaglandin E2; SoC, standard of care;

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

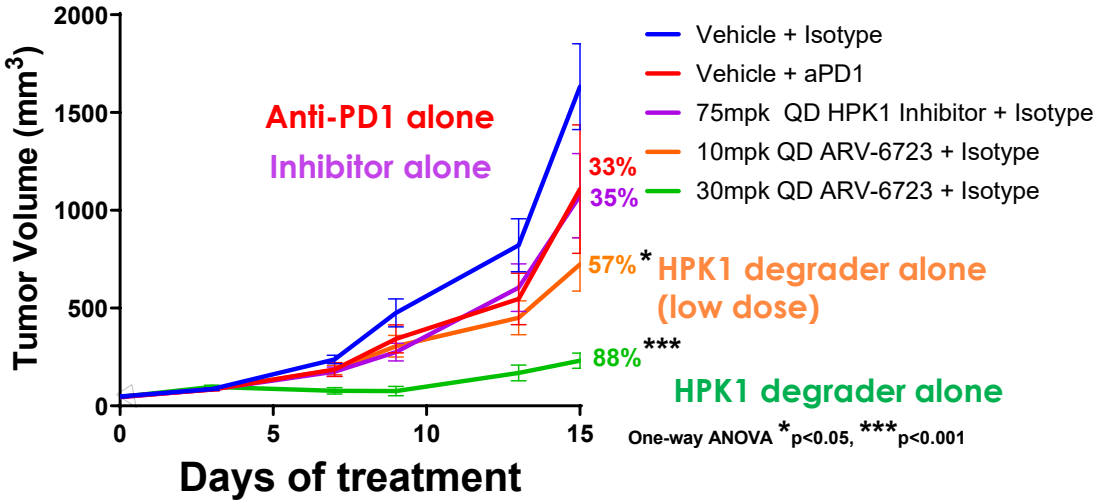
- ARV-6723 is a potent single-digit nanomolar degrader of HPK1, leading to sustained downstream pathway inhibition (via pSLP76) and induction of IL-2 release (data on file)
- This enhanced PK/PD profile results in more complete *in vivo* pathway suppression that recapitulates a genetic KO phenotype upon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

As presented at

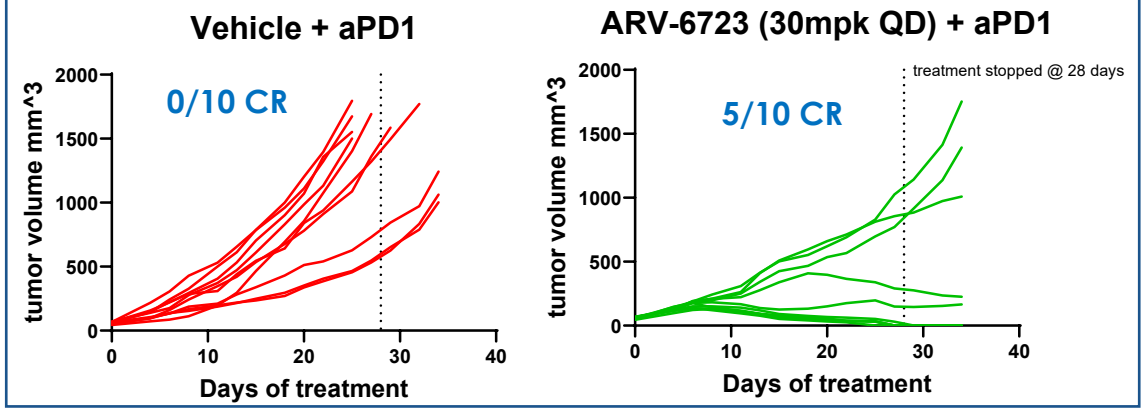
HPK1 , hematopoietic progenitor kinase 1; KO, knock out; mpk, milligrams per kilogram; PK/PD, pharmacokinetic/pharmacodynamic; pSLP76, SH2 domain-containing leukocyte protein of 76 kDa, phosphorylated.

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

Single agent ARV-6723 treatment showed superior single agent activity to HPK1 inhibitor and anti-PD1 antibody*

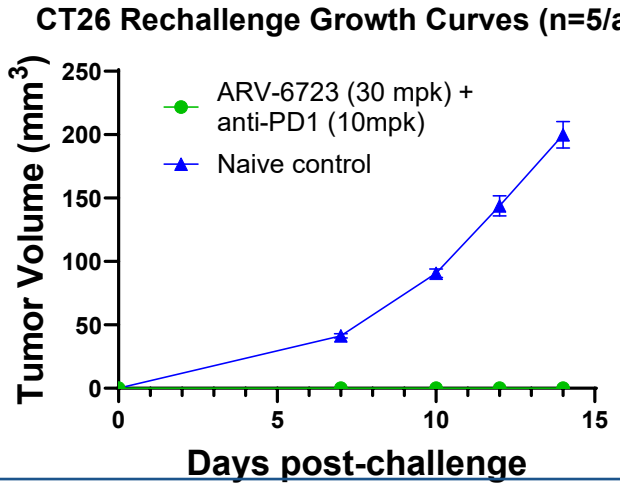


Combines with anti-PD1 to achieve complete regressions (CRs)*



- HPK1 PROTACs have yielded strong single agent efficacy in other highly immunogenic syngeneic tumor models (EMT6, MC38; data on file)

CRs reject tumor rechallenge*



As presented at

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

* In a syngeneic CT26 model (highly immunogenic)

Single-agent ARV-6723 demonstrates superior anti-tumor activity in pre-clinical models compared to anti-PD-1 + anti-CTLA-4

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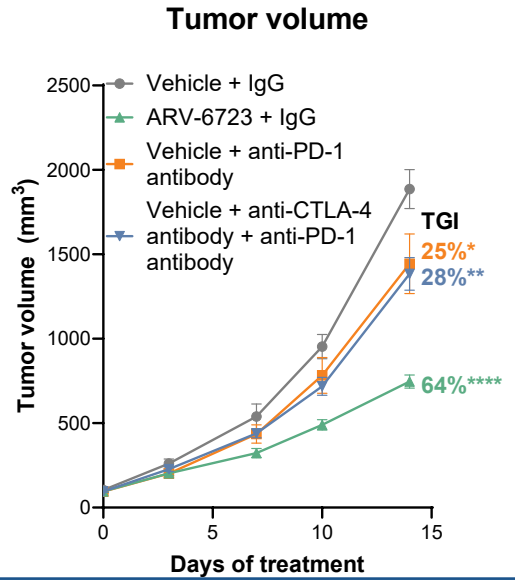
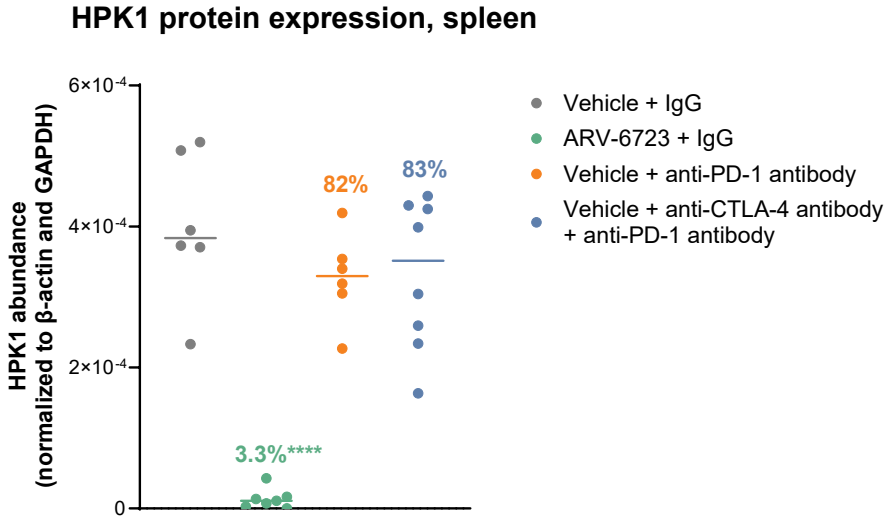
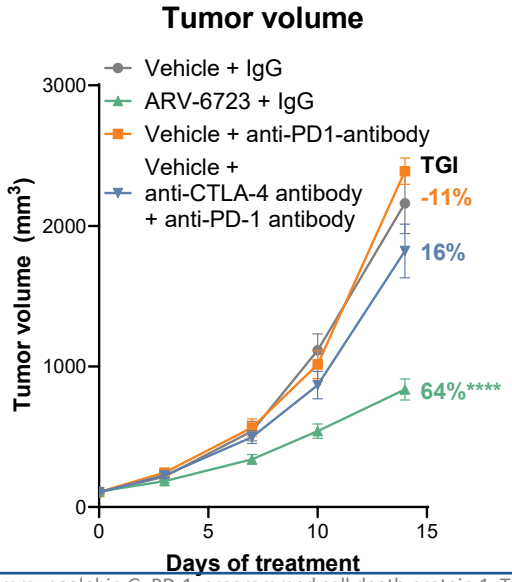
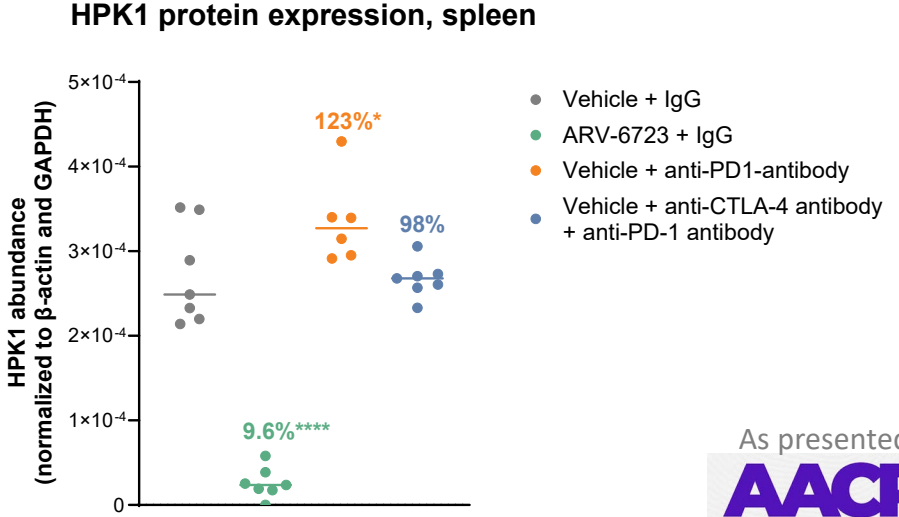
ARV-6723 single agent outperforms anti-PD-1 and anti-CTLA-4 in LLC1 parental model





ARV-6723 single agent outperforms anti-PD-1 and anti-CTLA-4 in LLC1-IFNγ parental model



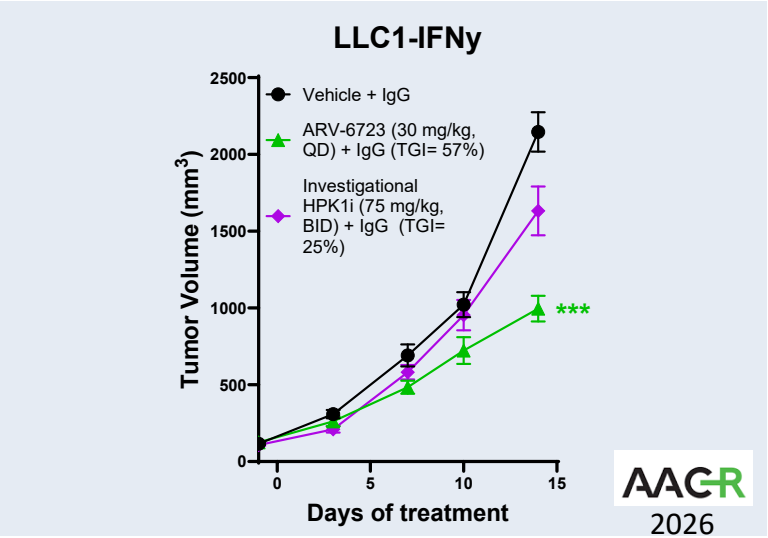


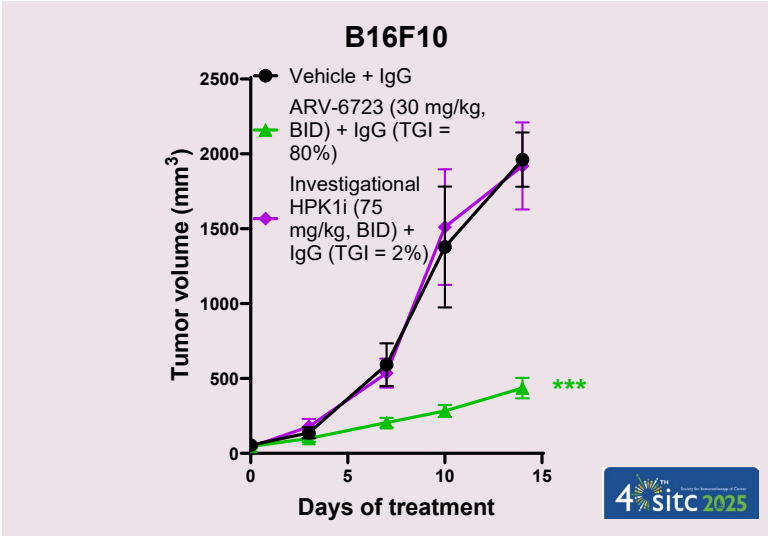
HPK1, hematopoietic progenitor kinase 1; CTLA-4, protein found on T cells; IgG, immunoglobin G; PD-1, programmed cell death protein 1; TGI, tumor growth inhibition

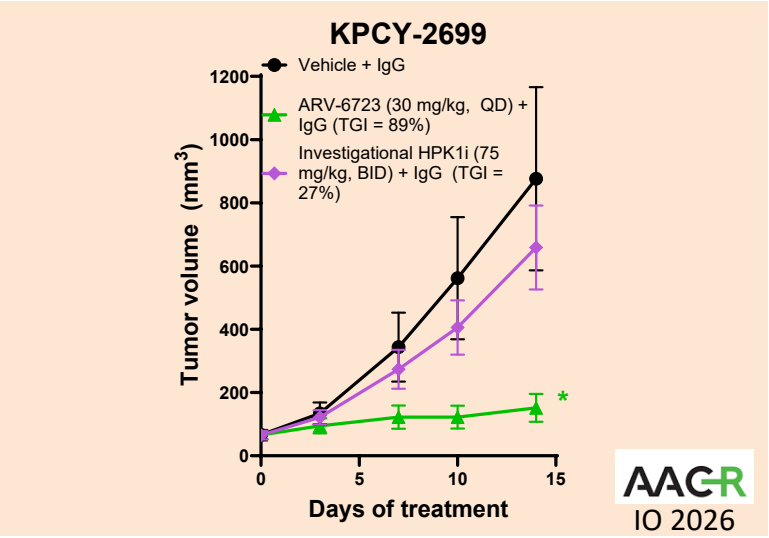
As presented at AACR 2026

ARV-6723 outperforms an investigational HPK1 inhibitor in ICI-resistant models

Tumor Growth Efficacy Studies





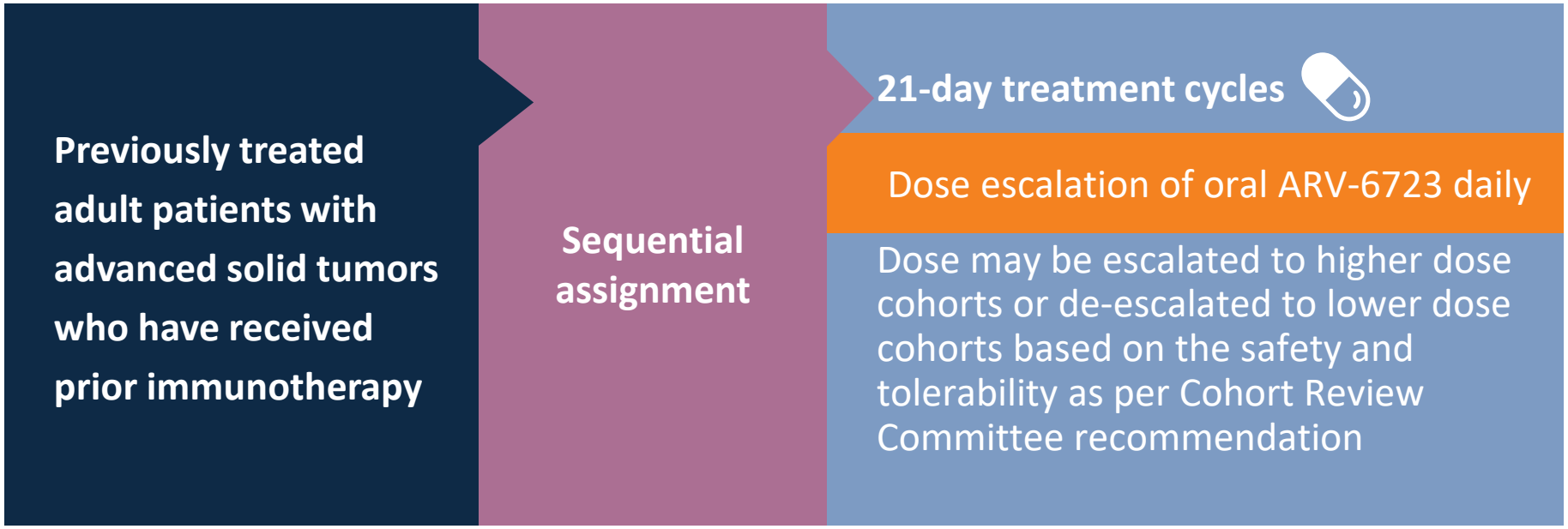


Biological context	Mouse model	ARV-6723 anti-tumor activity (TGI%) as a single agent	Head-to-head comparison to investigational HPK1 inhibitor (TGI%)
T cell exhaustion	LLC1-IFNγ	**57% TGI;** (30 mg/kg, QD)	25% (non- significant); (75 mg/kg, BID)
Low tumor antigens	B16-F10	**65-80% TGI;** (30 mg/kg, BID)	2% TGI (non- significant); (75 mg/kg, BID)
T cell exclusion	KPCY	**89% TGI;** (30 mg/kg, QD)	27% (non- significant); (75 mg/kg, BID)

ARV-6723 has significant single agent anti-tumor activity in 7 ICI-resistant models (3 models shown)

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

Planned Phase 1/2 clinical trial of ARV-6723 as monotherapy and in combination with pembrolizumab in advanced solid tumors



- Phase 1 monotherapy dose escalation cohort is on-track to initiate enrollment in Q3 2026
  - Trial design includes plan for dose escalation and expansion combination cohort with immune checkpoint inhibitor (pembrolizumab) once sufficient monotherapy data are available

ARV-6723 will be evaluated in a Phase 1/2 open-label study to evaluate safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity administered as monotherapy and in combination with pembrolizumab in participants with advanced solid tumors

Cohort Review Committee is comprised of study investigators, sponsor/CRO medical lead, select sponsor/CRO clinical team members

Multiple value-driving milestones anticipated ahead

Upcoming milestones: *Neurology*

ARV-102
Oral LRRK2 degrader

- Share additional biomarker data from Phase 1 trial in patients with PD (October 2026)
- Initiate clinical trials in in patients with PSP (2027*)

ARV-027
Oral polyQ-AR degrader

- Complete enrollment in the multiple dose cohorts in the Phase 1 trial healthy volunteers (2H 2026)
- Share Phase 1 healthy volunteer data (1H 2027)

Upcoming milestones: *Oncology*

ARV-393
Oral BCL6 degrader

- Present Phase 1 monotherapy dose escalation data from early cohorts (2H 2026)
- Share additional Phase 1 monotherapy dose escalation data and data from the combination cohort with glofitamab (mid-2027)

ARV-6723
Oral HPK1 degrader

- Initiate Phase 1 clinical trial in patients with advanced solid tumors (Q3 2026)

Strong capital position with ~$568M cash on hand[a] and runway into second half 2028

The agents listed on this slide are investigational. Their safety and effectiveness for these investigational uses have not been established.
BCL6, B-cell lymphoma 6; DLBCL, diffuse large b-cell lymphoma; HPK1, hematopoietic progenitor kinase 1; LRRK2, leucine-rich repeat kinase 2; PD, Parkinson's disease; polyQ-AR, polyglutamine-expanded (polyQ) androgen receptor (AR); PSP, progressive supranuclear palsy.
a. Cash, cash equivalents, and marketable securities position as of June 30, 2026. *Upon health authority clearance to proceed with clinical trials..

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