Safe harbor and forward-looking statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding: our expectation of bringing the first PROTAC protein degrader to market in breast cancer in partnership with Pfizer, Inc. ("Pfizer"), and the timing thereof; our potential receipt of milestone and royalty payments under our out licensing agreement with Novartis, and our collaboration agreements with Pfizer and Genentech; that the benefits of PROTAC degraders may provide advantages over other modalities in oncology and neurology; our plans related to two Phase 3 clinical trials of vepdegestrant, in the first- and second-line, and the timing related thereto; our plans and timing related to multiple commercial launches of vepdegestrant, as a monotherapy and in combination; our potential best-in-class pipeline and research engine setting us up for long-term impact; the potential to leverage business development to enhance the value of our pipeline; our capitalization, and having cash runway into 2027; the potential for vepdegestrant to become a first in-class and best-in-class targeted therapy and to become a new backbone estrogen receptor therapy in the estrogen receptor positive, human epidermal growth factor 2 negative, metastatic breast cancer space; the timing of release of topline data for the VERITAC-2 Phase 3 second-line clinical trial of vepdegestrant as a monotherapy and plans for presentation of full data at a medical congress; the potential for PROTAC degraders to revolutionize the treatment of neurological diseases and allowing for differentiation versus other existing and experimental modalities; PROTAC-induced leucine-rich repeat kinase 2 ("LRRK2") degradation having the potential to differentiate from kinase inhibition; the opportunity to further explore LRRK2-dependent biomarkers in patients with Parkinson's disease ("PD") and progressive supranuclear palsy; the timing for release of data for the ARV-102 Phase 1 single ascending dose ("SAD") clinical trial in healthy volunteers; the timing for completion of enrollment of the ARV-102 Phase 1 multiple ascending dose ("MAD") clinical trial in healthy volunteers and determination of recommended Phase 2 dose; the timing for completion of enrollment and presentation of initial data from the ARV-102 Phase 1 SAD clinical trial in patients with PD; the timing to initiate the ARV-102 Phase 1 MAD clinical trial in patients with PD; the potential for a PROTAC BCL6 degrader to address substantial unmet need for patients with non-Hodgkin Lymphomas; the potential for our novel Kirsten rat sarcoma ("KRAS")-targeting PROTAC to be a best-in-class therapy for KRAS G12D mutated cancers; our plans related to filing an investigational new drug application for our PROTAC KRAS G12D degrader; whether extended pharmacodynamics of a PROTAC KRAS G12D degrader will allow for intermittent dosing, which may improve tolerability and facilitate combination treatments; and our plans with respect to key program catalysts and timing thereof. 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. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various risks and uncertainties, including but not limited to: whether we and Pfizer will be able to successfully conduct clinical development for vepdegestrant and receive results from our clinical trials of vepdegestrant on expected timelines, or at all; : whether we and Pfizer will successfully perform their respective obligations under the collaboration between us and Pfizer; whether we will be able to successfully conduct and complete development for our other product candidates, including ARV-102 and ARV-393, including whether we initiate and complete clinical trials for our product candidates and receive results from our clinical trials on our expected timelines, or at all; whether we and Pfizer, as appropriate, will be able to obtain marketing approval for and commercialize vepdegestrant and other product candidates on current timelines or at all; whether we receive results from our preclinical trials on our expected timelines, or at all; our ability to protect our intellectual property portfolio; our reliance on third parties; whether we will be able to raise capital when needed; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, discussed in the "Risk Factors" section of our quarterly and annual reports on file with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this presentation reflect our current views as of the date of this presentation with respect to future events, and we assume no obligation to update any forward-looking statements, except as required by applicable law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

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ARVINAS

IGNITING A

TRANSFORMATIVE CHANGE

in the fight for patients with cancer and neurodegenerative diseases

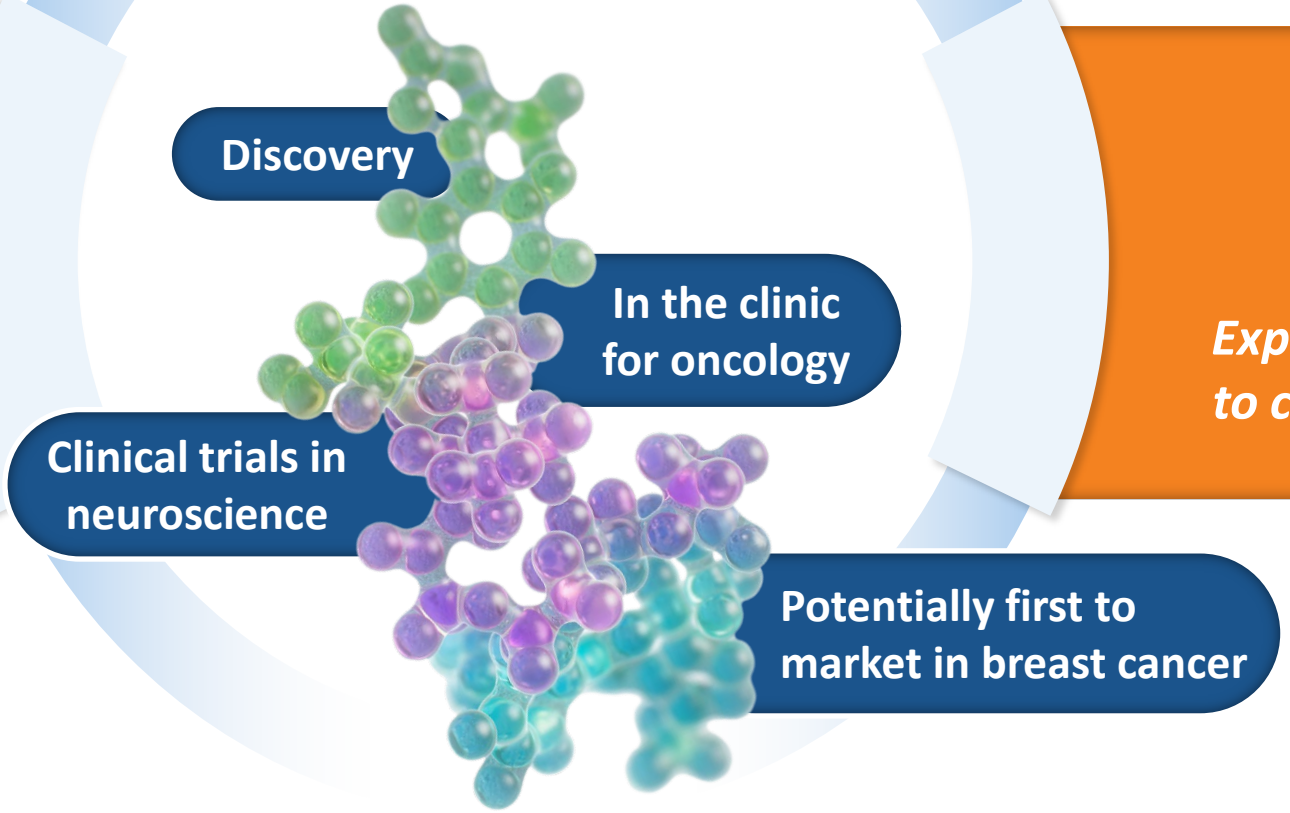
Our experienced and talented team is advancing a new therapeutic modality for patients

ARVINAS

Promising preclinical results are translating into the clinic

5 programs entered the clinic in 5 years, targeting significant unmet needs for patients

History of FIRSTS with our novel PROTAC therapeutic modality:



Strong, experienced leadership team

Expertise from bench to commercialization

Multiple partnerships reinforce Arvinas' leadership position in PROTAC protein degradation

ARVINAS

Pfizer

- Global co-development and co-commercialization agreement for vepdegestrant, our PROTAC estrogen receptor degrader
- Arvinas and Pfizer to split profits 50/50 worldwide
- Arvinas to book sales in the US

NOVARTIS

- Global out-licensing agreement for luxdegalutamide, our PROTAC androgen receptor degrader
- Arvinas received an upfront payment and is eligible for development milestones, commercial milestones, and tiered royalties

Genentech **Pfizer**

- Multi-target discovery collaborations to identify novel PROTAC medicines for Pfizer and Genentech
- Arvinas eligible for milestones and royalties

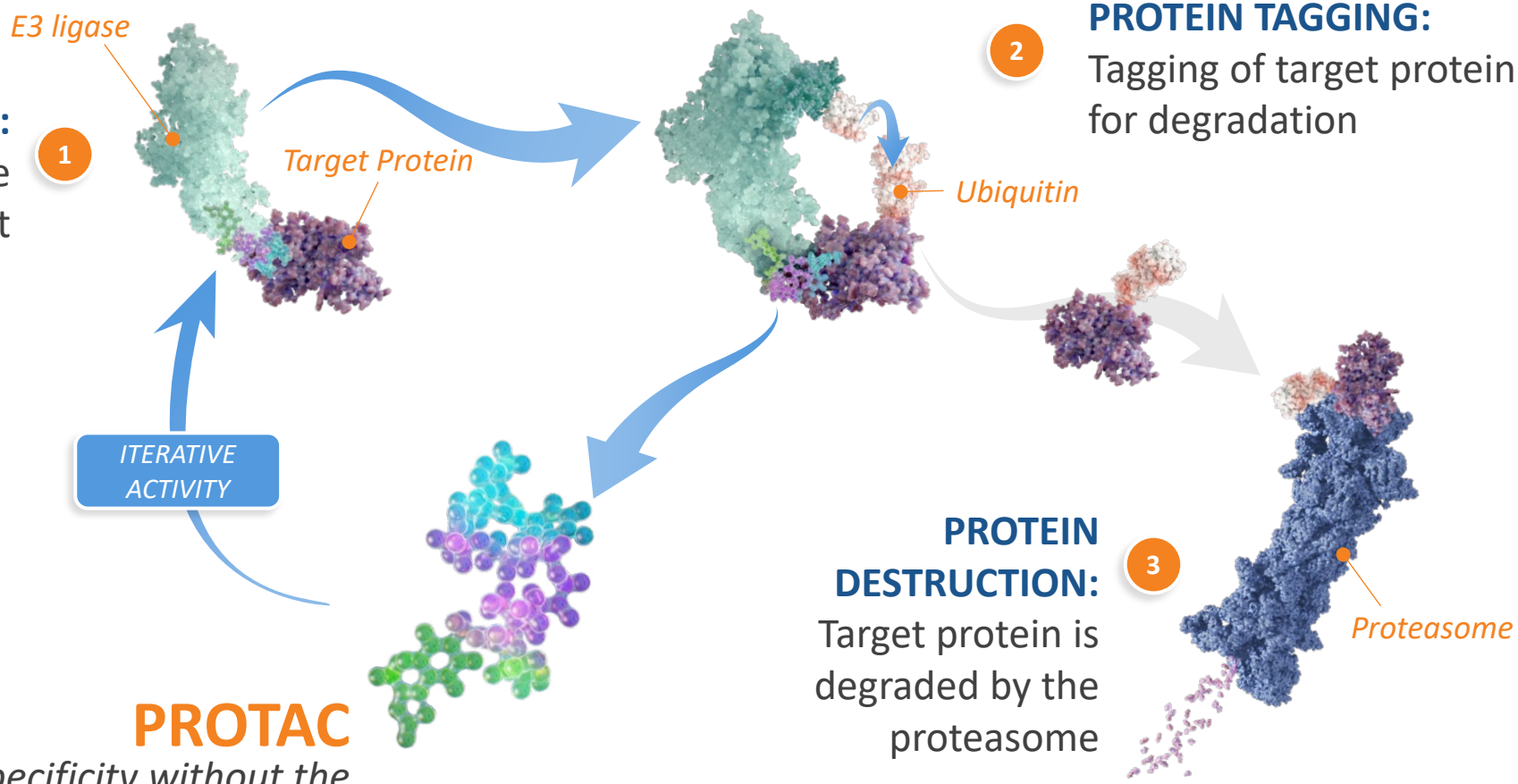
BAYER **Oerthbio**

- Arvinas and Bayer created Oerth Bio, an agricultural biotechnology joint venture focused on creating PROTACs for agricultural applications
- Arvinas and Bayer own Oerth 50/50

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

COMPLEX FORMATION:
Recognizing disease causing protein of interest

1



2

PROTEIN TAGGING:
Tagging of target protein for degradation

3

PROTEIN DESTRUCTION:
Target protein is degraded by the proteasome

PROTAC
High specificity without the requirement for strong binding

PROTAC degraders have clear 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
- ✓ Oral therapies that improve upon biologics

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 vs. wildtype specificity
- ✓ Efficient manufacturing and routes of synthesis (versus biologics and cell therapies)

BENEFITS IN
NEURODEGENERATION

- ✓ Blood-brain barrier penetration
- ✓ Potential avoidance of 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

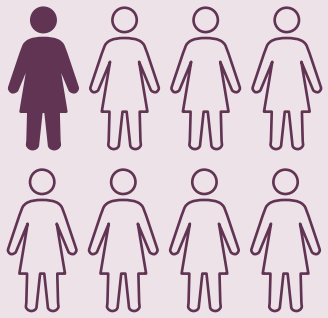
ONCOLOGY

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 and new treatments are needed[6]**

NEURODEGENERATION

By 2040

neurodegenerative diseases will be the

#2 LEADING CAUSE OF DEATH

in developed countries[4]

10M+ people with Parkinson's disease worldwide[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 01/03/25. 2. ACS: https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer; accessed 01/03/25. 3. World Health Organization: https://www.who.int/news-room/fact-sheets/detail/cancer; accessed 01/03/25. 4.. *Nature:* https://doi.org/10.1038/nj7526-299a; accessed 01/06/25.5. Parkinson's Foundation: https://www.parkinson.org/understanding-parkinsons/statistics; accessed 01/03/25.6. Our World in Data: https://ourworldindata.org/cancer.

Broad pipeline including the first pivotal trials for PROTAC degraders

ARVINAS

PROGRAM	INDICATION	PRECLINICAL	PHASE 1/1B	PHASE 2	PHASE 3	MARKET
Vepdegestrant (ARV-471; ER)	BREAST CANCER multiple indications as mono & combo	2L VERITAC-2 monotherapy Phase 3 data anticipated in 1Q2025				Global co/co with Pfizer
		2L combination Phase 3 with a CDK4/6 inhibitor[a]				
		1L combination Phase 3 with Pfizer's CDK4 inhibitor atirmociclib[a]				
ARV-393 (BCL6)	HEMATOLOGY	Phase 1				
ARV-102 (LRRK2)	NEUROSCIENCE	Phase 1 in healthy volunteers				
		Phase 1 in Parkinson's disease				
KRAS G12D	ONCOLOGY	IND-enabling				
Preclinical Programs	ONCOLOGY AND NEUROSCIENCE					
Luxdegalutamide (ARV-766; AR)	PROSTATE CANCER	*Global rights out-licensed to Novartis in 2024*				NOVARTIS

These agents are currently under investigation; their safety and effectiveness for these investigational uses have not been established.

1L, first-line; 2L, second-line; AR, androgen receptor; BCL6, B-cell lymphoma 6; CDK, cyclin-dependent kinase; ER, estrogen receptor; IND, investigational new drug; KRAS, Kirsten rat sarcoma viral oncogene homolog; LRRK2, leucine-rich repeat kinase 2.

a. Pending emerging data and health authority feedback.

Planned Pivotal Trial

Strategically positioned for the next stage of growth

ARVINAS

Vepdegestrant Launch Potential Focuses Arvinas on Near-Term Patient Impact

- Pursuing 2L monotherapy as a beginning; we are striving for multiple launches with Pfizer for vepdegestrant as monotherapy and in combination
- Potential best-in-class pipeline and research engine sets up Arvinas for long-term impact

Prudent, Data-Driven Approach to Capital Allocation

- Investing effectively for commercial success
- Choose and invest in highest value drivers across the pipeline
- Continued potential to leverage BD to enhance the value of our pipeline

Strong Capitalization

- Cash runway into 2027
- Multiple value-inflecting milestones ahead, with potential to receive milestone payments from existing partners, including NOVARTIS

CLINICAL PROGRAMS

Vepdegestrant (ARV-471)

PROTAC estrogen receptor degrader

ARVINAS

Pfizer

Vepdegestrant is an investigational compound. Its safety and effectiveness have not been established.

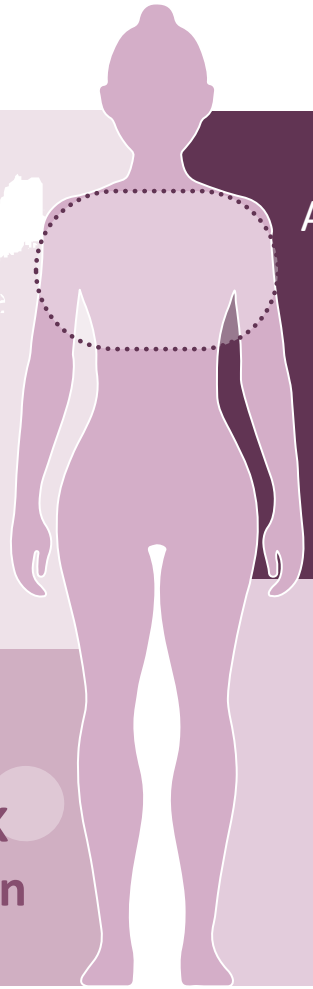
Breast cancer is the most common cancer in women

IN THE U.S.

~317K
Estimated new cases in 2025[1]

1 in 8
Will develop breast cancer in her lifetime[3]

Second leading cause of cancer deaths, with **~42K deaths projected in 2025**[1]



WORLDWIDE

Among women, breast cancer was the most commonly diagnosed cancer in 2022 with an estimated

2.3M new cases,
comprising **11.6%** of all cancer cases[2]

Breast Cancer is the fourth leading cause of cancer mortality, with nearly **670,000** deaths estimated in 2022[2]

1. Siegel et al. Cancer Statistics, 2025. CA Cancer J Clin. 2025; Jan-Feb;75(1):10-45. 2. Bray et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024; May-Jun;74(3):229-263. 3. American Cancer Society: https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html; accessed 01/06/24.

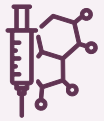
Unmet need in ER+/HER2- metastatic breast cancer

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]



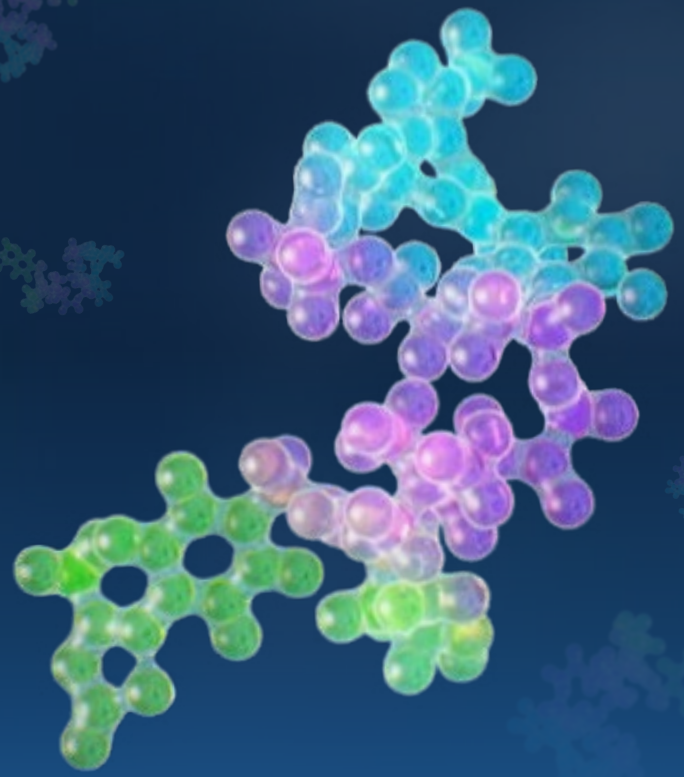
First-line treatments for ER+/HER2- advanced or metastatic breast cancer are typically endocrine therapies combined with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor;[3] opportunity to improve care with novel agents

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 develop treatment resistance and experience 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.

VEPDEGESTRANT: Investigational first-in-class PROTAC estrogen receptor degrader

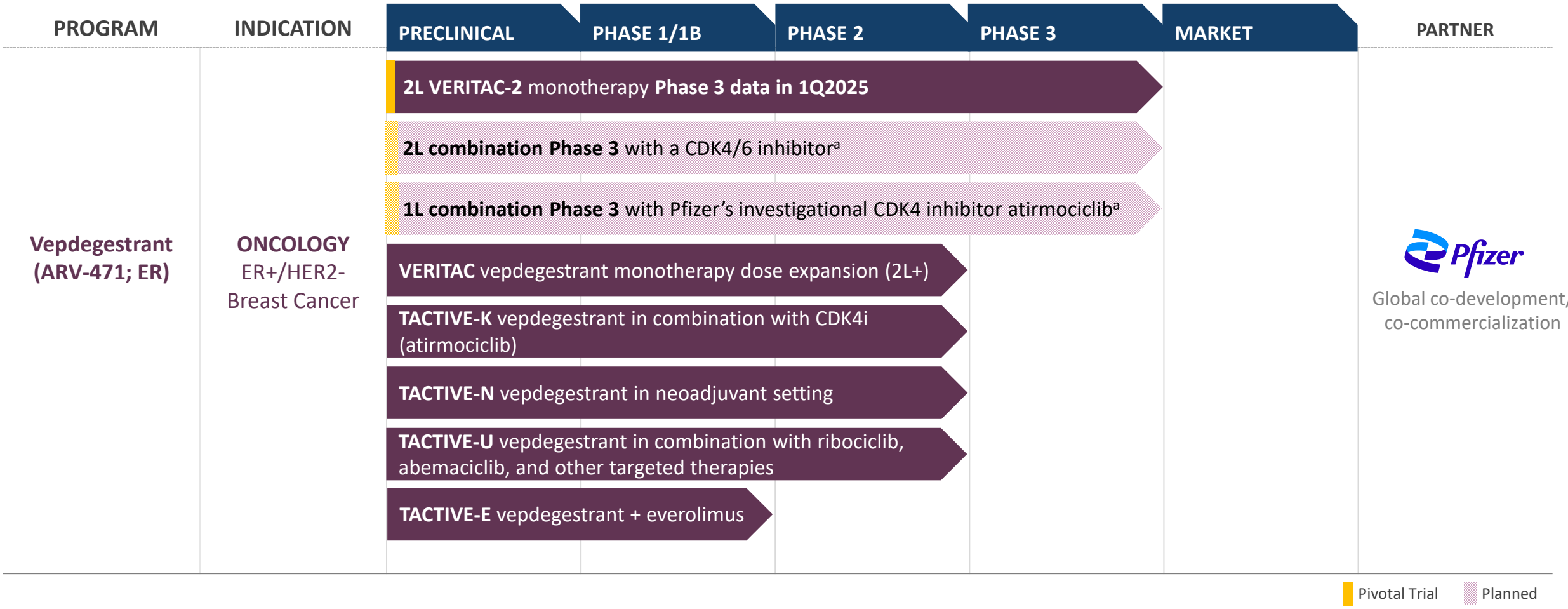


- **Degrades both ESR1 wild type and ESR1 mutant ER**
- **Potential to be a best-in-class targeted therapy**
- **Preclinically, vepdegestrant yielded substantially greater ER degradation and tumor growth inhibition** than fulvestrant in xenograft models[1]
- **In Phase 1/2 monotherapy trials 2L, vepdegestrant has shown strong signs of activity in heavily pre-treated patients**
- **As a monotherapy, once daily, oral dosing has been well-tolerated with low rates of discontinuation in Phase 1/2 trials**
- **Compelling opportunity as a combination with CDK inhibitors** in patients with 1L and 2L+ disease
- **More than 1,000 patients and healthy volunteers have been treated** with vepdegestrant across the clinical program

Vepdegestrant has the potential to be a new ER backbone in the ER+/HER2- metastatic breast cancer space (total market: ~$17B)[2]

1. American Association for Cancer Research, https://aacrjournals.org/clincancerres/article/30/16/3549/746781/Oral-Estrogen-Receptor-PROTAC-Vepdegestrant-ARV.
2. Clarivate/Decision Resources Group – Breast Cancer Disease Landscape & Forecast (Nov 2023). 2032 Projection.

Vepdegestrant is the first PROTAC protein degrader to enter Phase 3 pivotal trials



Vepdegestrant is currently under investigation; its safety and effectiveness for these investigational uses have not been established.

1L, first-line; 2L second-line; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ER, estrogen receptor; HER, human epidermal growth factor receptor.

a. Pending emerging data and health authority feedback.

In Phase 2, vepdegestrant showed favorable tolerability and signs of efficacy in a heavily pre-treated patient population

Vepdegestrant Phase 2 Patients *Prior Treatment:*	Prior CDK4/6i **100%**	Prior Fulvestrant **74%**	Prior Metastatic Chemo **46%**
Vepdegestrant (200 mg) demonstrated strong signs of efficacy in the VERITAC Phase 2 trial	**Clinical Benefit Rate**[1] (Phase 2):	**37%** (All patients) **47%** (Patients with ESR1 mutant tumors)	
	Median Progression-Free Survival (Phase 2):	**3.5 Months** (All patients) **5.7 Months** (Patients with ESR1 mutant tumors)	
Vepdegestrant (200 mg) has been well tolerated	Grade 3/4 TRAE reported in 6% (2/35) of patients at RP3D 200 mg		
	In 35 patients treated at the **RP3D** (200 mg), **no dose reduction and 2 discontinuations due to TEAEs**		

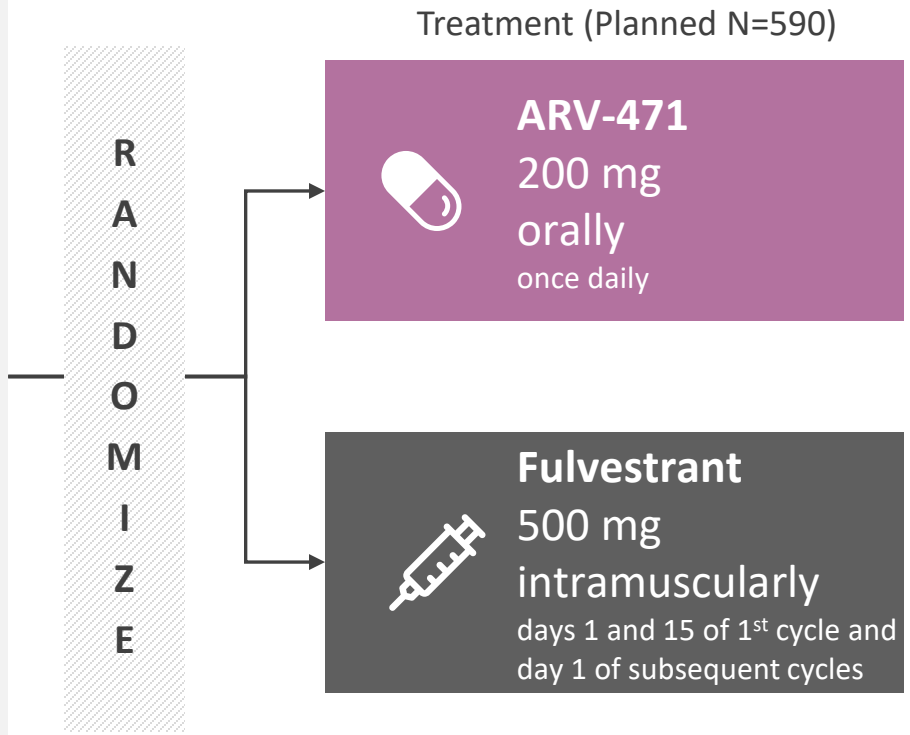
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; *ESR1,* estrogen receptor 1 gene; RP3D, recommended phase 3 dose; TEAE, treatment emergent adverse events.
a. Hurvitz SA, et al. Presented at SABCS; December 5-9, 2023; San Antonio, TX, USA. Poster PO3-05-08.
1. Clinical benefit rate defined as rate of confirmed complete response or partial response or stable disease ≥24 weeks.

The VERITAC-2 Phase 3 monotherapy study is fully enrolled, with topline data expected 1Q25

Phase 3

Key eligibility criteria

- Women or men aged ≥18 years
- Confirmed ER+/HER2- advanced breast cancer
- 1 line of CDK4/6 inhibitor therapy in combination with endocrine therapy
- ≤1 additional endocrine therapy
- Most recent endocrine treatment given for ≥6 months prior to disease progression
- No prior fulvestrant
- No prior chemotherapy for locally advanced/metastatic disease
- Radiological progression during or after the last line of therapy



Stratification factors

- *ESR1* mutant (yes vs no)
- Visceral disease (yes vs no)

Primary endpoint:

- PFS by BICR in
  - ITT population
  - *ESR1* mutant population

Secondary endpoints:

- Overall survival
- ORR, DOR, and CBR
- Safety
- QoL measurements

Topline results expected in 1Q25[a]

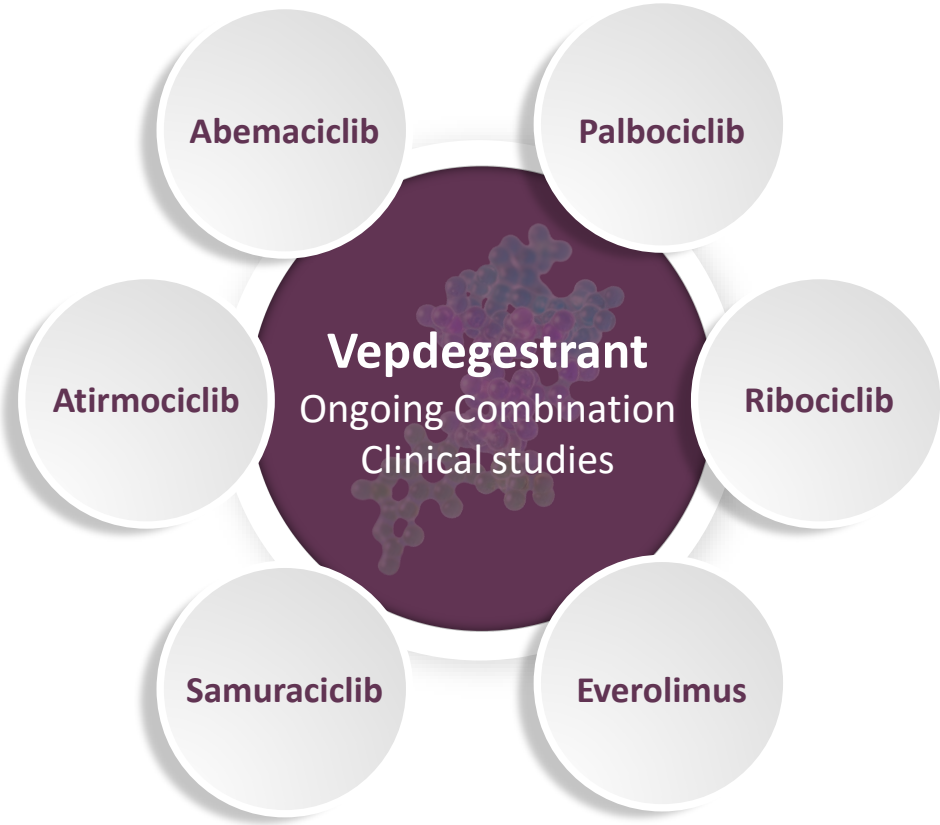
AE, adverse event; BICR, blinded independent central review; CBR, clinical benefit rate; CDK, cyclin-dependent kinase; DOR, duration of response; ER, estrogen receptor; *ESR1,* estrogen receptor 1 gene; HER2, human epidermal growth factor receptor 2; ORR, overall response rate; PFS, progression-free survival; QoL, quality of life
a. Full data to be provided at a medical congress in 2025.

Vepdegestrant combination strategy in metastatic breast cancer (mBC)

Preclinical and pharmacokinetic (PK) data support our combination strategy:

Preclinical and clinical pharmacokinetic studies have explored vepdegestrant's effect on key metabolic pathways used by common treatments for mBC

Drug-drug interaction modeling suggest that the predicted effects of vepdegestrant on palbociclib, abemaciclib, ribociclib, and everolimus (related to CYP3A4 metabolism) are unlikely to have a major impact in clinical combinations[1]



Current preclinical data, PK data, and clinical data all support the strategy to combine vepdegestrant with other targeted therapies in metastatic breast cancer

1. Tan W et al. Presented at SABCS; December 10–13, 2024; San Antonio, TX, USA. Poster P4-08-13.

Vepdegestrant + palbociclib safety and tolerability overview

Efficacy Benchmarks in CDK4/6i After CDK4/6i Trials

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

	PACE[1] Palbo/fulvestrant after CDK4/6i	BioPER[2] Palbo/PC after CDK4/6i	MAINTAIN[3] Ribo/ET after CDK4/6i	PALMIRA[4] Palbo/ET after CDK4/6i	Vepdeg + palbo P1b
Prior CDK4/6i	100%	100%	100%	100%	87.0%
Prior chemo for mBC	14.4%	12.5%	6.7%	0%	45.7%
Prior fulvestrant	0%	43.8%	16.8%	11.8%	80%
Overall Response Rate (Evaluable)[a]	13.7% (n=73)	6.3% (n=32)	20.0% (n=35)	6.4% (n=94)	41.9% (n=31)
Clinical Benefit Rate (Evaluable)	32.4% (n=111)	34.4% (n=32)	42.9% (n=49)	41.9% (n=136)	63.0% (n=46)
Progression-Free Survival Median (95% CI), months	4.6 (3.6–5.9) (n=111)	2.6 (1.8–6.7) (n=32)	5.3 (3.0–8.1) (n=60)	4.9 (3.6–6.0) (n=136)	11.2 (8.2-16.5) (n=46)

Data presented at ESMO BC 2024[5]

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

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

1. Mayer E et al SABCS 2022. 2. Albanell J et al. Clin Cancer Res 2023. 3. Kalinsky K et al. J Clin Oncol 2023. 4. Llombart-Cussac A et al. ASCO 2023. 5. Hamilton et al. ESMO BC 2024.

Safety/tolerability in Phase 1b trial[5]

- The safety profile of vepdegestrant 200 mb + palbociclib 125 mg remained consistent with the known safety profiles of the two agents, except for increased grade 4 neutropenia, which was managed with laboratory monitoring and dose modifications per palbociclib label
- **No febrile neutropenia** and few palbociclib discontinuations

Preliminary vepdegestrant + abemaciclib Phase 1b data support combination strategy in metastatic breast cancer

Key Eligibility Criteria for Phase 1b/2 TACTIVE-U (NCT05548127)

- ER+/HER2- advanced/metastatic breast cancer
- ≥1 measurable lesion as defined by RECIST v1.1
- 1 or 2 prior therapies for advanced/metastatic breast cancer
- 1 line of a prior CDK4/6 based regimen in any setting (dose reductions of prior CDK4/6i due to AEs were not allowed)
- Eastern Cooperative Oncology Group performance status ≤1

Dosing	Vepdegestrant 200 mg QD + abemaciclib 150 mg BID

Ph 1b Efficacy Results

	Total (N=16)	Mutant ESR1 (n=8)	Wild-type ESR1[a] (n=8)
CBR[b], % (95% CI)	62.5 (38.6–81.5)	62.5 (30.6–86.3)	62.5 (30.6–86.3)

	Total (N=15)	Mutant ESR1 (n=8)	Wild-type ESR1[a] (n=7)
ORR[c], % (95% CI)	26.7 (10.9–52.0)	37.5 (13.7–69.4)	14.3 (2.6–51.3)

4 patients had confirmed PR and 6 had SD for ≥24 weeks per RECIST v1.1

Tolerability

- The safety profile of vepdegestrant in combination with abemaciclib was manageable and generally consistent with the known profiles of each agent
- Preliminary PK data showed no significant drug-drug interaction
- The Phase 2 portion of the study is evaluating the combination at the full standard doses of vepdegestrant (200 mg once daily) and abemaciclib (150 mg twice daily)
- Phase 2 portion is fully enrolled

AE, adverse event; BID, twice daily; CBR, clinical benefit rate; ESR1, estrogen receptor 1 gene; ORR, objective response rate; PR, partial response; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease

Hilton J, et al. Presented at SABCS; December 10–13, 2024; San Antonio, TX, USA. Poster P4-12-03.

a. Wild-type ESR1 indicates a valid ctDNA sequencing result was generated but no ESR1 mutation was detected. b. Rate of confirmed complete response, PR, or SD for ≥24 weeks. c. In patients with measurable disease at baseline.

Clinical program designed to position vepdegestrant as a potential backbone ER-targeting therapy in ER+/HER2- mBC

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

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

TACTIVE-N: Phase 2 neoadjuvant trial

First Line

Phase 3 planned initiation in 2025: in combination with Pfizer's investigational CDK4i atirmociclib[a]

Second/Third Line

Phase 3 VERITAC-2 monotherapy trial

Phase 3 planned initiation in 2025: in combination with a CDK4/6i[a]

TACTIVE-K: Phase 1b/2 in combination with atirmociclib

TACTIVE-E: Phase 1b in combination with everolimus

TACTIVE-U: Phase 1b/2 in combination with ribociclib/ abemaciclib/ samuraciclib

Active Trials | Pivotal Trial | Planned Trial

Vepdegestrant is an investigational compound. Its safety and effectiveness for these investigational uses have not been established.

CDK, cyclin-dependent kinase; CDK4i, cyclin-dependent kinase 4 inhibitor; mBC, metastatic breast cancer; SLI, study lead-in; RP3D, recommended phase 3 dose

a. Pending emerging data and health authority feedback.

1. US incidence, Kantar Cancer MPact Patient Metrics (accessed Nov. 2023).

CLINICAL PROGRAMS

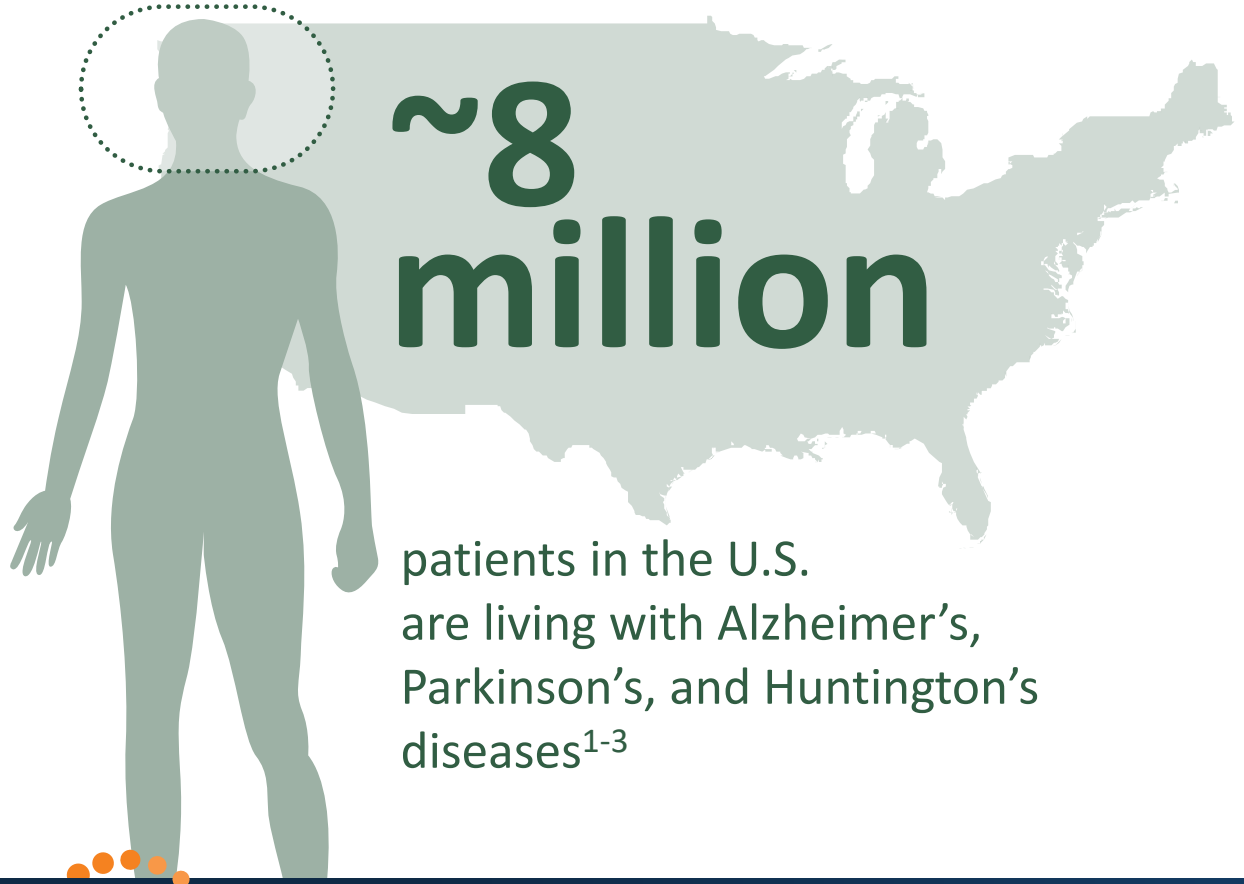
ARV-102

PROTAC LRRK2 degrader

ARVINAS

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

Neurodegeneration: An area of tremendous unmet need



patients in the U.S.
are living with Alzheimer's, Parkinson's, and Huntington's diseases[1-3]

Unmet need is high:

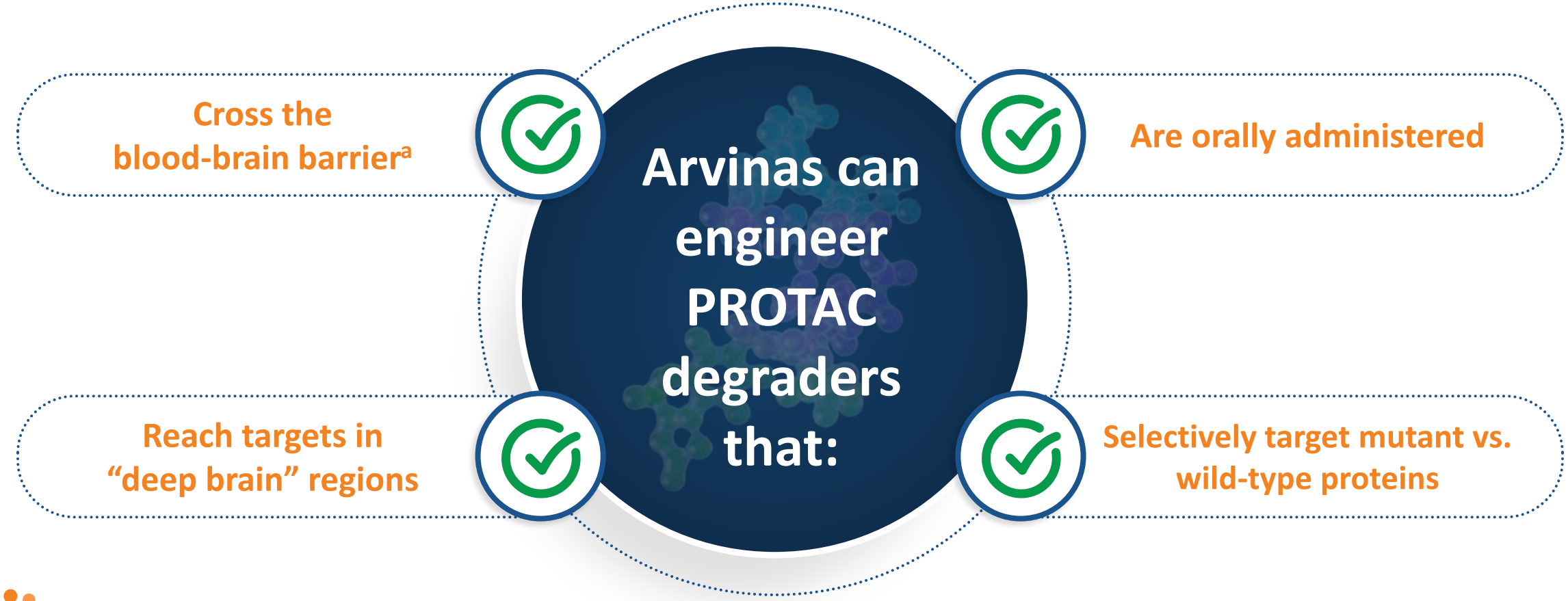
- No approved therapies for multiple important target proteins (e.g., tau, α-synuclein)
- Very few disease-modifying therapies exist
- Blood-brain barrier penetration is a challenge for other modalities (e.g., antibodies and antisense oligonucleotides)
- Other existing and potential therapies have difficult routes of administration, e.g., intrathecal

Arvinas ARV-102 PROTAC LRRK2 degrader is currently enrolling a Phase 1 trial in healthy volunteers and in patients with PD

1. Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures. Alzheimer's Dement 2024;20(5). 2. Willis et al. npj Parkinson's Dis. 2022. 3. Yohrling, et al. Neurology 2020.

PROTAC degraders could potentially revolutionize the treatment of neurological diseases

ARVINAS



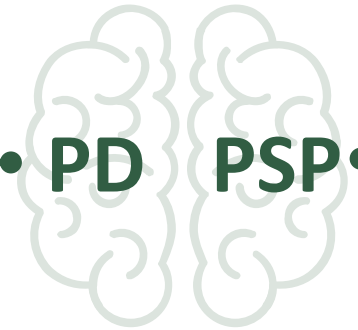
Potentially allowing for differentiation versus other existing and experimental modalities

a. In preclinical studies

LRRK2 is linked to both Parkinson's disease (PD) and progressive supranuclear palsy (PSP)

Human genetics and biology create a strong rationale for the involvement of LRRK2 in PD and PSP

- **PD** is a neurodegenerative disorder that affects movement, balance, and coordination
- PD has a diagnosed prevalence of ~1M in the US and more than 10M worldwide[1]
  - No approved disease-modifying therapies exist for patients with PD[a]
- Mutations in the LRRK2 gene are one of the most common genetic causes of PD, and variants have also been observed in sporadic cases[4]
- Animal models have shown that a reduction of LRRK2 protein may impact the pathology and dysfunction in PD, making it an attractive therapeutic target



- **PSP** is a rare progressive neurological disorder that affects movement, balance, and cognitive function
- Between 30,000 and 40,000 people are diagnosed with PSP in the US each year[2]
  - No approved disease-modifying therapies exist for patients with PSP, which often leads to death within 5-7 years[3]
- Emerging research suggests that LRRK2 plays a role in PSP by contributing to disease mechanisms such as neuroinflammation and cellular dysfunction[5,6]
  - Neuroinflammation & Tau Pathology – LRRK2 is involved in immune system regulation and may influence tau protein accumulation, a hallmark of PSP
  - Disrupted Cellular Processes – LRRK2 plays a role in autophagy and inflammation, which could contribute to the neurodegeneration seen in PSP
  - Genetic Association – Variants in the LRRK2 gene have been associated with PSP progression and survival

Given its role in neurodegeneration, therapies that target LRRK2 are being explored as possible treatments for PD, PSP, and related disorders

LRRK2, Leucine-rich repeat kinase

a. LRRK2 kinase inhibitors and an ASO in clinical trials.

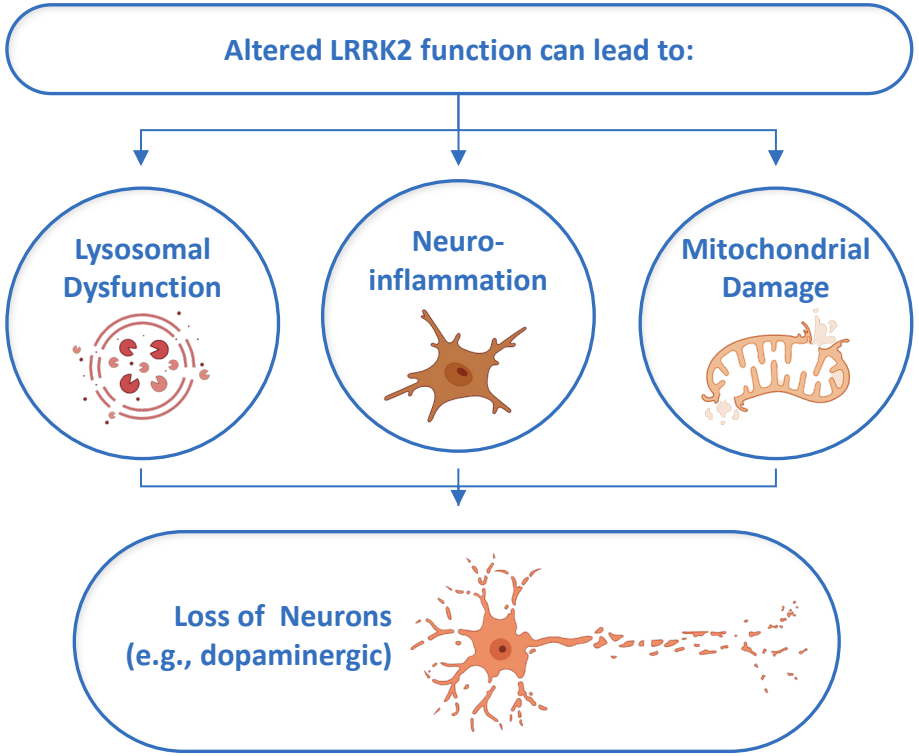
1.Parkinson's Foundation. Who has Parkinson's?. https://www.parkinson.org/understanding-parkinsons/statistics. 2. CurePSP, https://www.psp.org/assets/resources/items/65d60040c6d15PSP-Some-Answers-2023(1).pdf. 3. Armstrong, Movement Disorder Clinical Practice 2014 https://pmc.ncbi.nlm.nih.gov/articles/PMC6182982. 4. Kluss Biochem Soc Trans 2019, https://pmc.ncbi.nlm.nih.gov/articles/PMC6563926/. 5. Iannotta. Essays in Biochemistry 2021, https://portlandpress.com/essaysbiochem/article-abstract/65/7/859/230434/LRRK2-signaling-in-neurodegeneration-two-decades/. 6. Sanchez-Contreras. Mov Disord 2016, https://pmc.ncbi.nlm.nih.gov/articles/PMC5269612/.

Leucine-rich repeat kinase-2 (LRRK2) is important for lysosome function, and altered LRRK2 leads to multiple pathologies

LRRK2 is required for healthy form and function of intracellular lysosomes[1,2]

- LRRK2 is a multi-domain scaffolding kinase and a critical regulator of lysosomal activity
- LRRK2 is required for healthy form and function of lysosomes, impacting the processes of endocytosis, autophagy, and phagocytosis
- Dysregulation of LRRK2 can impair the cell's ability to clear damaged proteins, contributing to disease pathology
- Mutations and dysregulation of LRRK2 may contribute to the progressive loss of dopamine-producing neurons

Mutated or over-expressed LRRK2 leads to multiple pathologies



1. Madureira, Front Neurosci 2020. 2. Nguyen, PNSAS 2020.

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

A PROTAC LRRK2 degrader has multiple opportunities to differentiate from other therapeutic modalities

		Inhibitor	PROTAC
LRRK2	Kinase activity	✓	✓
	GTPase activity	✗	✓
	Signaling scaffold	✗	✓
	Increased protein level	✗	✓

LRRK2 single nucleotide polymorphisms are associated with elevated LRRK2 levels in patients with PD[1]

Degrading the complete LRRK2 protein (rather than inhibiting kinase activity) may impact **multiple pathways** linking LRRK2 to PD and PSP:

- Lysosome formation and activity
- Neuroinflammation
- Cellular metabolism
- Synaptic Integrity

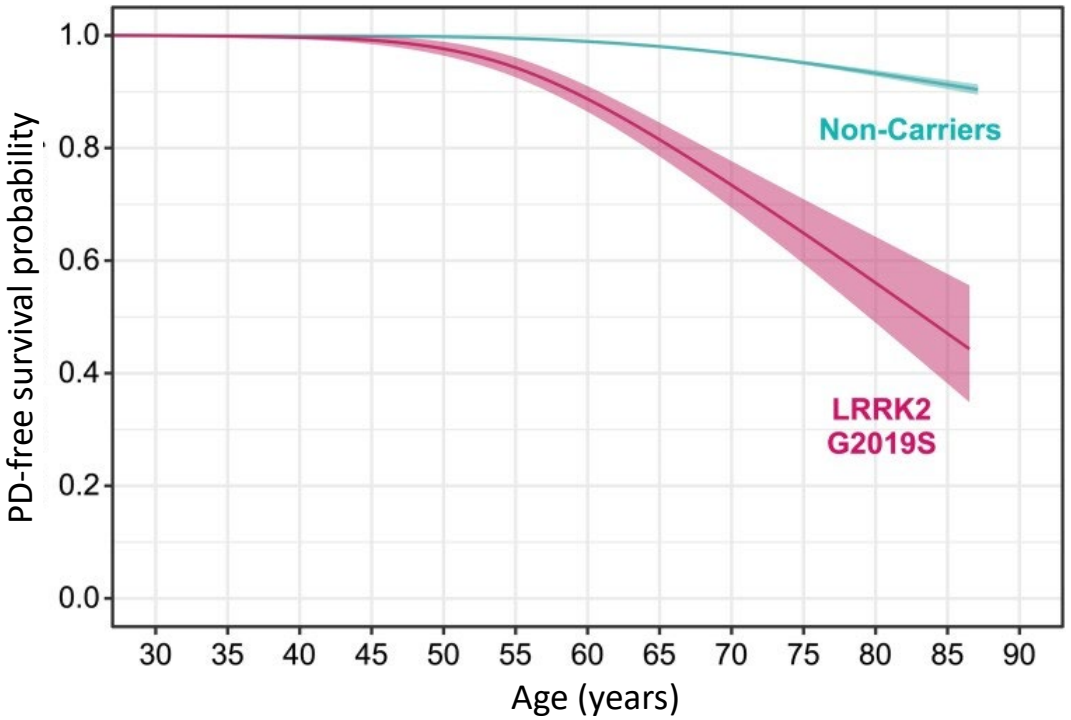
We can measure the potential impact of a PROTAC LRRK2 degrader:

- **Kinase inhibitor engagement** by level of phosphorylation
- **PROTAC engagement** by reductions in LRRK2 protein levels
- **Pathway engagement** by phosphorylation of downstream proteins

ASO, antisense oligonucleotide; LRRK2, Leucine-rich repeat kinase 2.

1. Kluss JH et. al, Biochem Soc Trans 2019, https://pmc.ncbi.nlm.nih.gov/articles/PMC6563926/.

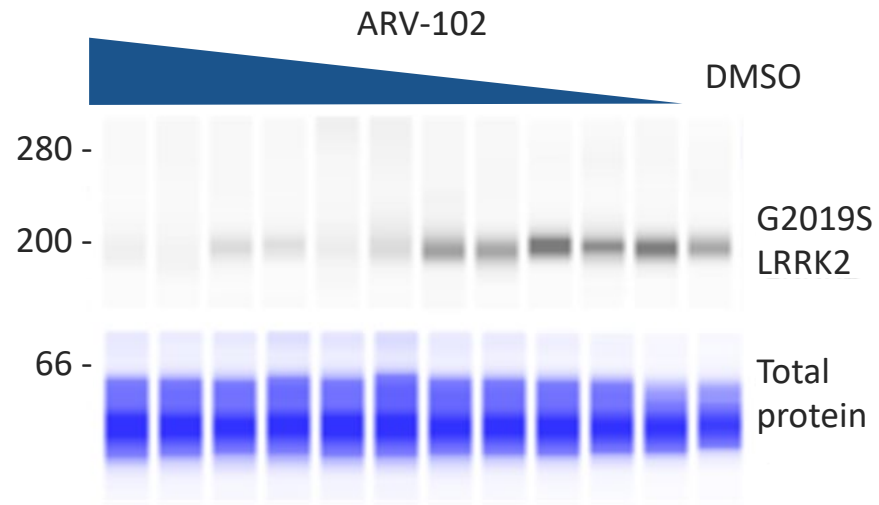
In human microglia, ARV-102 degrades LRRK2 G2019S, a kinase activating mutation linked to increased PD risk



Versus non-carriers of the mutation, the LRRK2 G2019S kinase activating mutation substantially reduces PD-free survival[1]

ARV-102 Potently Degrades LRRK2 in a Human Patient Model of Parkinson's Disease

LRRK2 Degradation in G2019S iPSC-Microglia



DC_{50}= 0.6 nM
D_{max}= 94% degradation

Data as presented at the Michael J. Fox Foundation Conference in November 2024

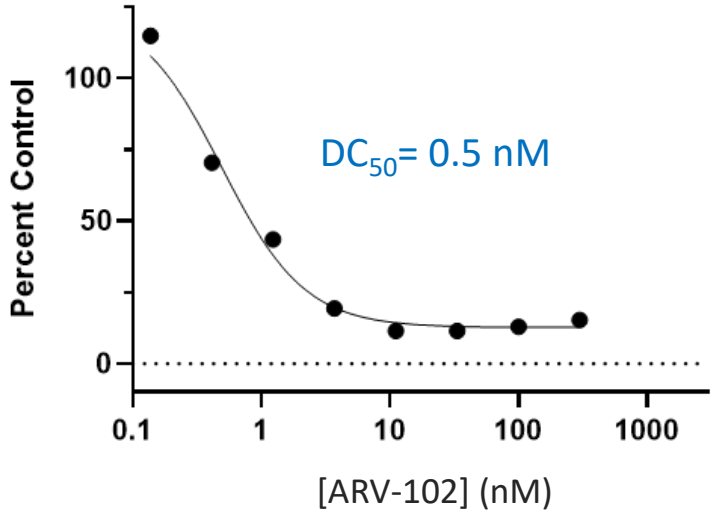
DC50, half-maximal degradation concentration that makes a protein for 50% degradation; D_{max}, maximal % reduction of a protein; E3i- PROTAC with Chemically inactivated E3 binder; iPSC, induced pluripotent stem cells; LRRK2, Leucine-rich repeat kinase 2.

1. Kmiecik et al, Brain , 2024.

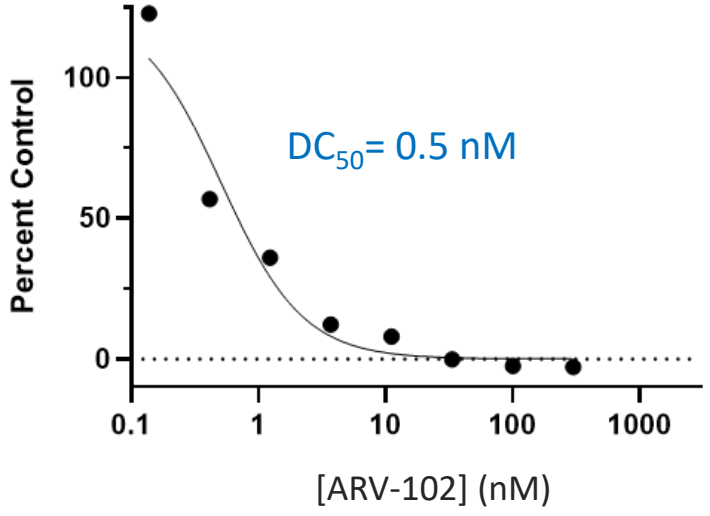
PROTAC LRRK2 degrader ARV-102 reduces LRRK2 and engages the lysosomal pathway in PBMCs

PROTAC-induced LRRK2 degradation aligns with effects on target and pathway engagement in human PBMCs

PROTAC Target Engagement (shown by LRRK2 Degradation)



Lysosome Pathway Engagement (shown by reduction in phospho-Rab10 pT73)

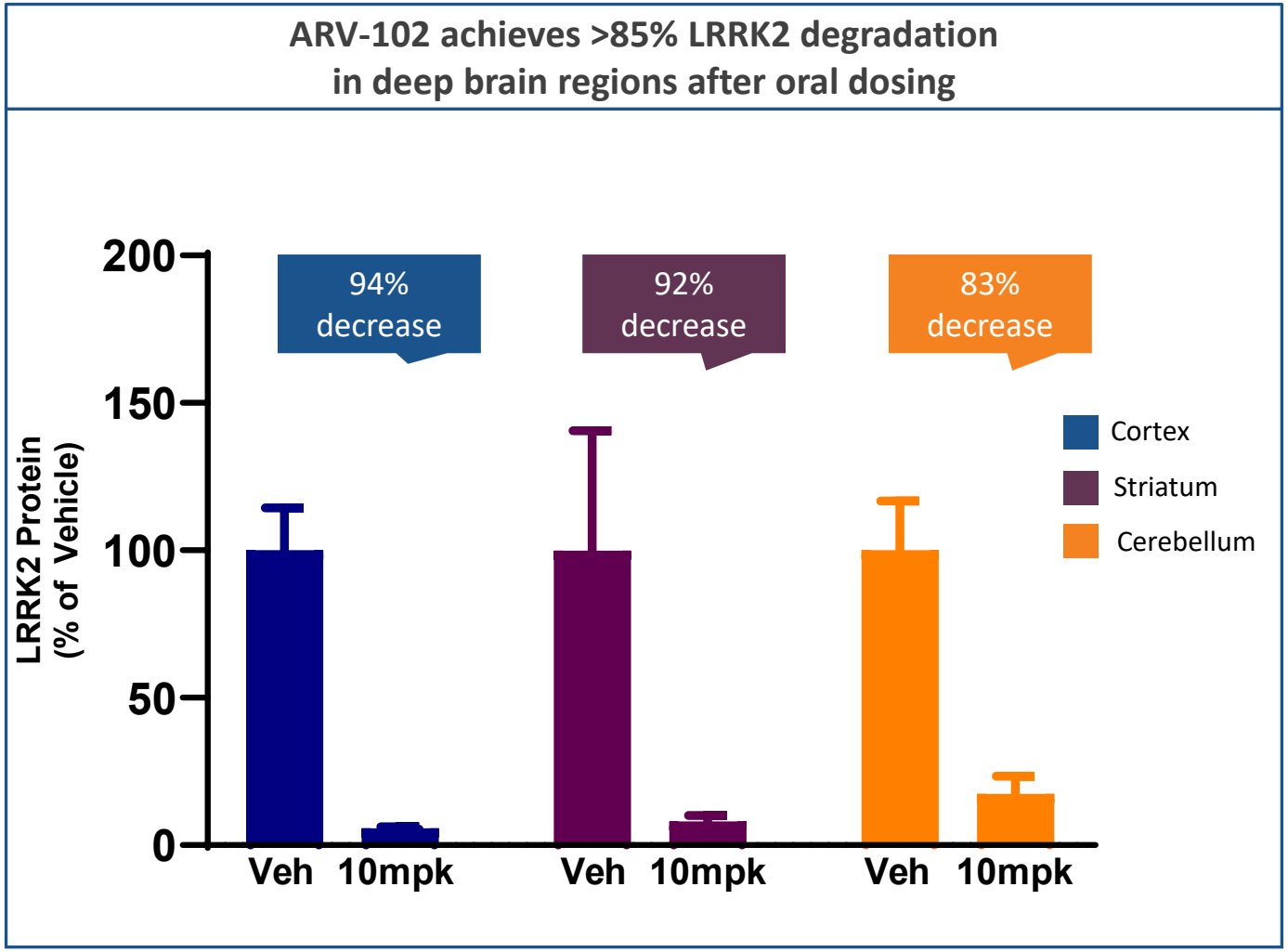


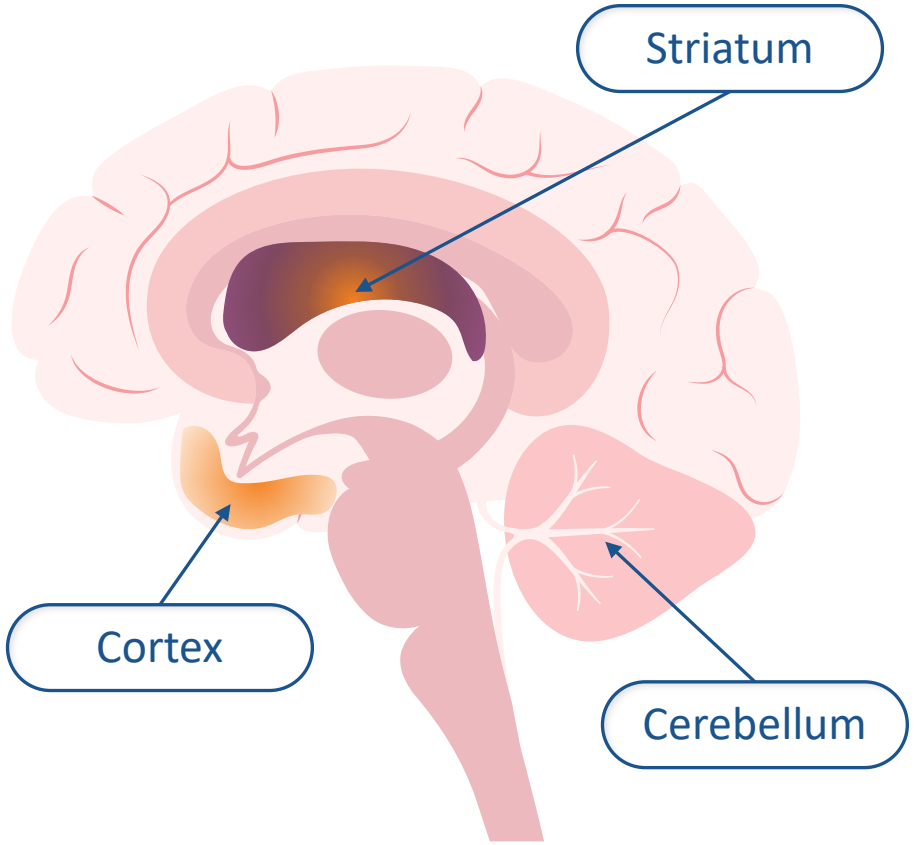
LRRK2 degradation is E3-dependent and on mechanism (data not shown)

Data presented at 2024 Keystone Summit: Targeted Protein Degradation.

Dmax= maximal % reduction of a protein; PBMC, peripheral blood mononuclear cells; E3i- PROTAC with Chemically inactivated E3 binder; iPSC, induced pluripotent stem cells; LRRK2, Leucine-rich repeat kinase 2.

ARV-102, an oral PROTAC LRRK2 degrader, degrades LRKK2 in multiple “deep brain” regions in non-human primates



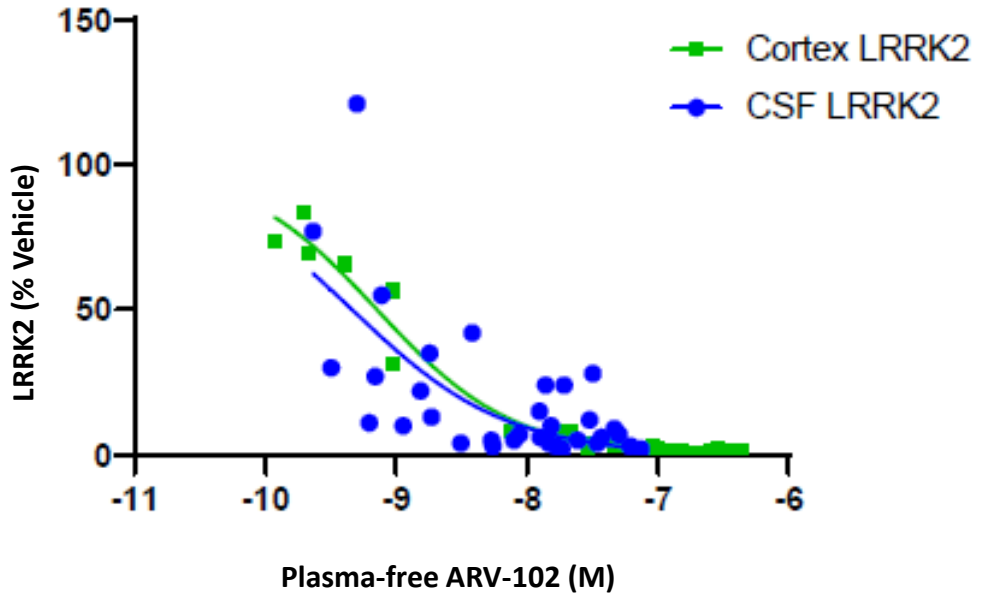


LRRK2, leucine-rich repeat kinase 2; mpk, milligrams per kilogram.

Figure adapted from Beuriat et al. 2022.

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

PK/PD of LRRK2 are reduced in both cortex and CSF following oral dosing in NHP



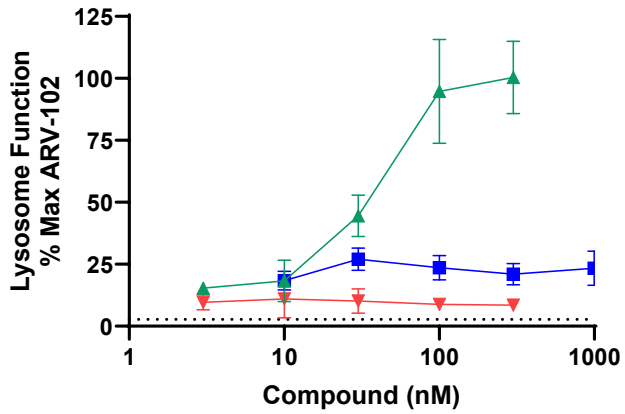
Data as presented at the Michael J. Fox Foundation Conference in November 2024.

CSF, Cerebrospinal fluid

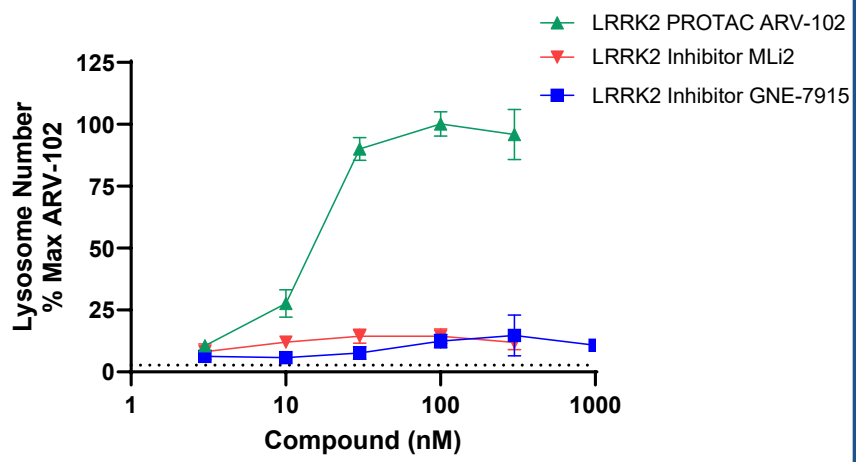
*Human CSF LRRK2 levels in healthy volunteers range from 5 – 104 pg/mL, averaging 32 pg/mL. The average in LRRK2+PD+ is 68 pg/mL ~2 fold elevated LRRK2 levels.

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

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



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



- ARV-102 dose-dependently increased degradation efficiency and lysosome number compared to kinase inhibitors
- LRRK2 PROTAC activity is consistent with literature showing an increase in lysosome number and carrying capacity observed in LRRK2 KO astrocytes[3]

Data presented at 2023 Keystone Summit: Autophagy and Neurodegeneration; Figure: Marwaha and Sharma, Bio-protocol, 2017.
DQ-BSA, Dye Quenched-Bovine Serum Albumin; KO, genetic knock out; LRRK2, Leucine-rich repeat kinase 2; PD, Parkinson's disease;
1. Dehey et al., 2013. Lysosomal impairment in Parkinson's disease. 2. R. Wallings et al., 2019. 3. Henry et al., 2015.

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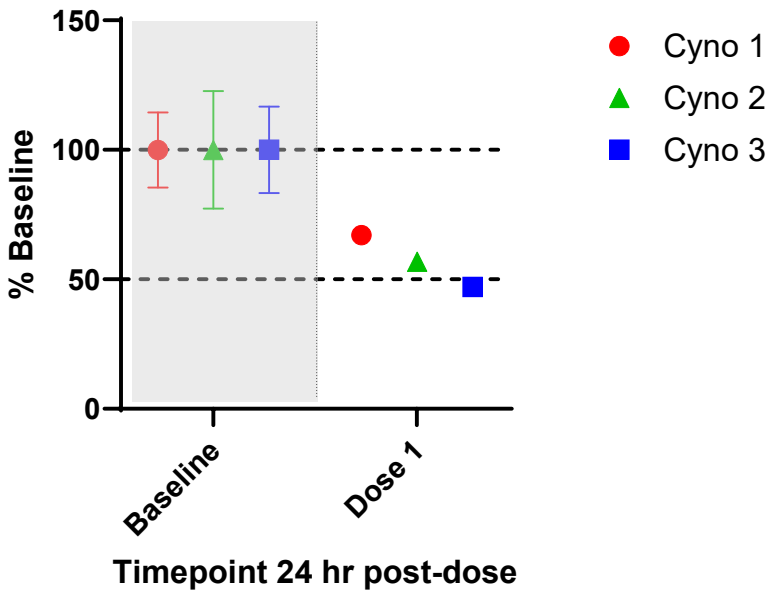
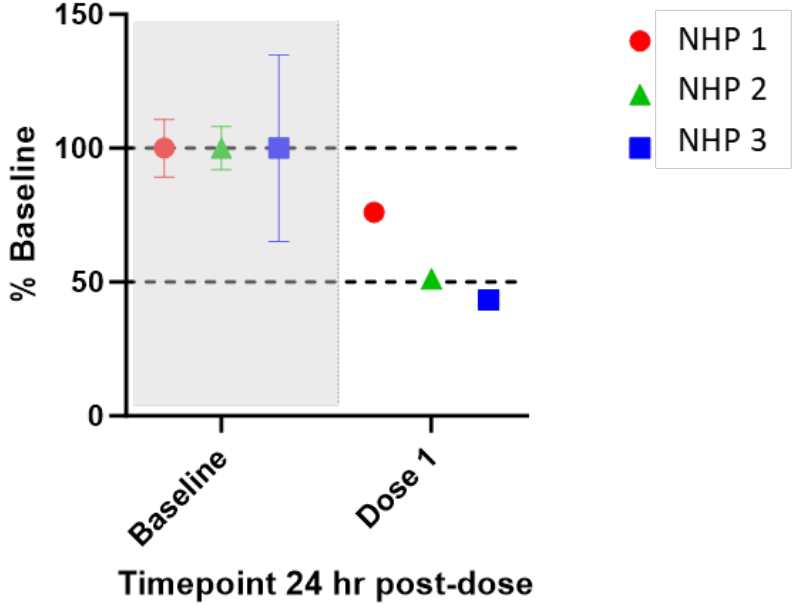
- **Mutant familial PD and increased LRRK2 expression "puts the brakes" on lysosomal clearance system**
- **Lysosome function and number are reduced in PD patients[1] and models**
- **Autophagy (clearance dependent on lysosome) is reduced with increased LRRK2 expression, LRRK2 familial mutation (G2019S), and LRRK2 activity/levels in rodent neurons[2]**

A single dose of ARV-102 induced unprecedented reductions in CSF pathway biomarkers in NHPs

IBA1: A marker of pathologic neuroinflammation



Cathepsin B: A lysosomal hydrolase implicated in PD



- ARV-102 is dosed orally, crosses the blood-brain barrier, and degrades LRRK2 in deep brain regions
- IBA1 and Cathepsin B both reduced only 24 hours after a single dose of ARV-102
- Other modalities have failed to show similar biomarker impact in NHPs

Opportunity to further explore LRRK2-dependent biomarkers in patients with Parkinson's Disease and PSP

Now enrolling Phase 1 trials in both healthy volunteers and in patients with PD

Data as presented at the Michael J. Fox Foundation Conference in November 2024.

CSF, cerebrospinal fluid; IBA1, Ionized Calcium-Binding Adapter Molecule 1; LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate; PD, Parkinson's disease; PSP, progressive supranuclear palsy

PROTAC LRRK2 degraders induce reduction of pathologic tau *in vitro* and *in vivo*

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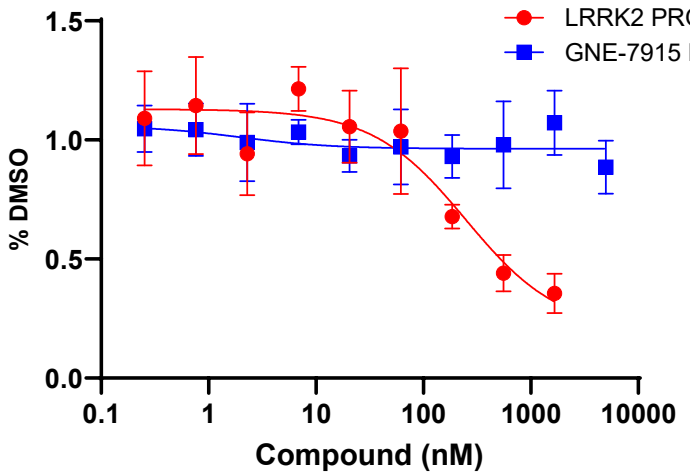
LRRK2 PROTAC, but not a LRRK2 inhibitor, induces reduction of pathologic AT8-tau *in vitro*

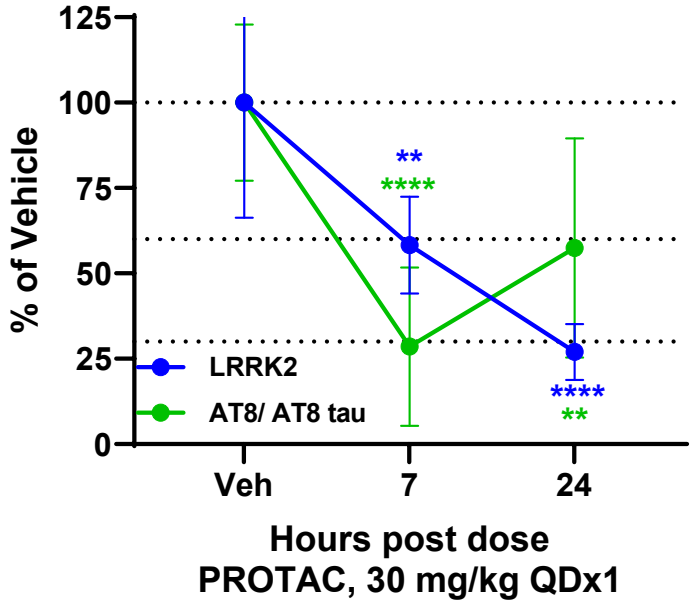
Reduction of pathologic (AT8) Tau induced by LRRK2 PROTAC



AT8 tau is significantly elevated in the brains of patients with PSP and a key marker for diagnosing PSP

PROTAC LRRK2 degraders induce pathologic tau protein reduction *in vivo*

PS19 (~12 weeks old)



Reductions of soluble AT8+ tau aggregates occur as early as 7 hours post-dosing

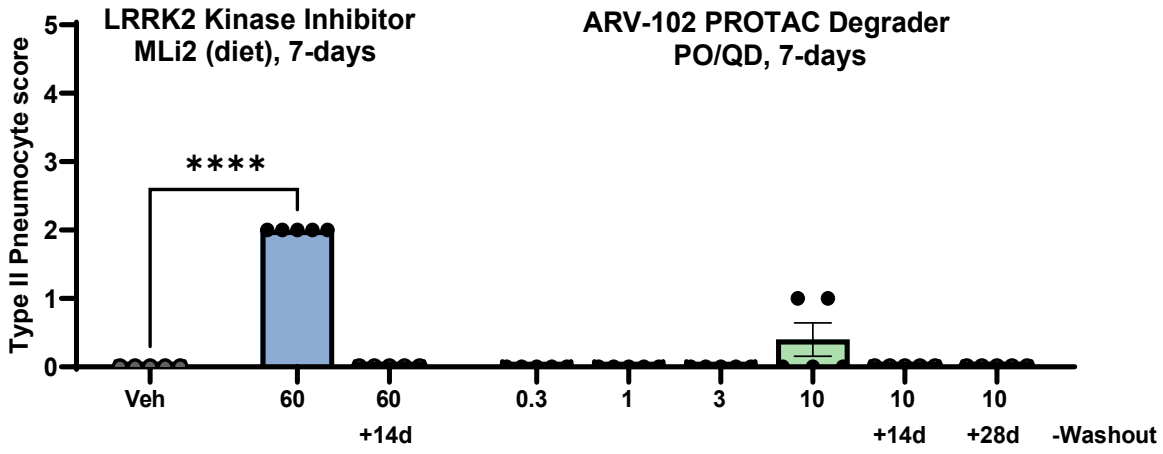
One-way ANOVA with Dunnett's multiple comparison test (**p < 0.01, ****p < 0.0001).

Data as presented at the Michael J. Fox Foundation Conference in November 2024.

PS19 is a murine tau model that harbors the T34 isoform of microtubule-associated protein tau with one N-terminal insert and four microtubule binding repeats (1N4R) encoding the human P301S mutation.

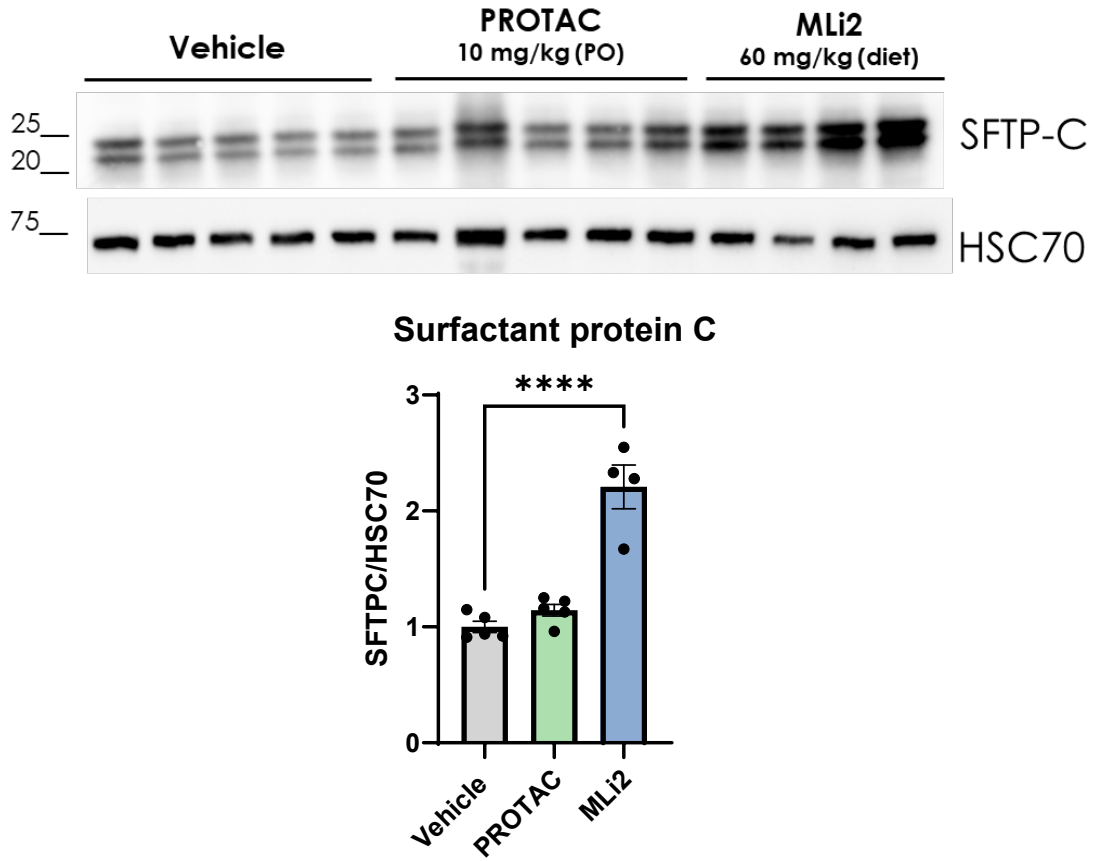
Preclinically, PROTAC LRRK2 degraders induced modest, reversible pneumocyte enlargement, and no pro-fibrotic changes

Lung Type II Pneumocyte Enlargement/Hypertrophy
(Histopathologic Score)



- Less pneumocyte hypertrophy observed with PROTAC LRRK2 degrader versus kinase inhibitor MLi2 (positive control for type II pneumocyte enlargement)
- Effect is reversible after 14-day wash-out
- No evidence of collagen deposition in lung with PROTAC LRRK2 degraders in NHPs (tox studies to date; data not shown)

Surfactant protein C increased by MLi2 LRRK2 kinase inhibitor, but not by ARV-102, in murine lung



Kelly K, Presented at Biennial International LRRK2 Meeting, June 2024

LRRK2, leucine-rich repeat kinase 2; NHP, non-human primate; PO, peri-oral; QD, once daily

Phase 1 clinical trials of ARV-102 are ongoing in both healthy volunteers and in patients with Parkinson's disease

Study ARV-102-101 **HEALTHY VOLUNTEERS**		Study ARV-102-103 **PATIENTS WITH PD**
OBJECTIVES: Safety, tolerability, PK, and PD of ARV-102		
SINGLE ASCENDING DOSE Part A; Enrollment complete	**MULTIPLE ASCENDING DOSE** Part B; Ongoing	**SINGLE ASCENDING DOSE** Ongoing
Anticipated 2025 Milestones		
• First-in-human data accepted for oral presentation at Alzheimer's disease/Parkinson's disease conference (April 2025)	• Complete enrollment • Determine RP2D	• Complete enrollment and present initial single ascending dose data • Initiate multiple ascending dose trial

PK; Pharmacokinetics; PD, pharmacodynamics; RP2D, Recommended phase 2 dose.

CLINICAL PROGRAMS

ARV-393

PROTAC BCL6 degrader

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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 lymphomas (NHL)

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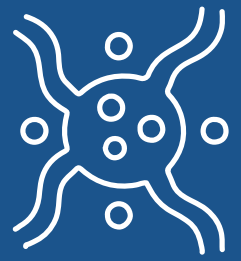


Key Unmet Needs for Patients with Non-Hodgkin Lymphomas

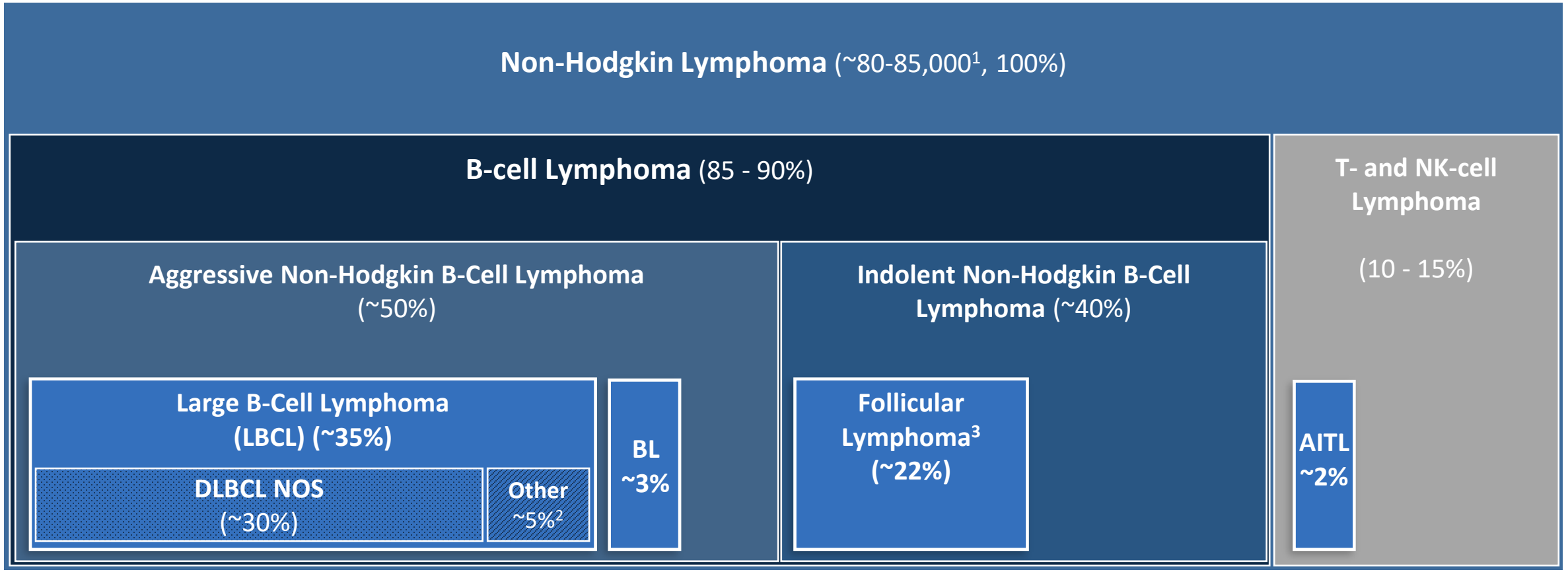
Safe and effective **oral alternatives** to chemo or immuno-chemotherapy standard of care regimens **for patients with relapsed disease,** high risk disease, and particularly older adults.

Heterogeneous nature of disease leads to variable patient outcomes. **Therapies based on actionable biomarkers are needed.**

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	• Angioimmunoblastic T-cell lymphoma (AITL) is a rare disease with no dedicated approved therapies • AITL tumors show high levels of BCL6 expression[4]

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. Nishizawa et al, Int J Hematol, 2017, 105(4):465.

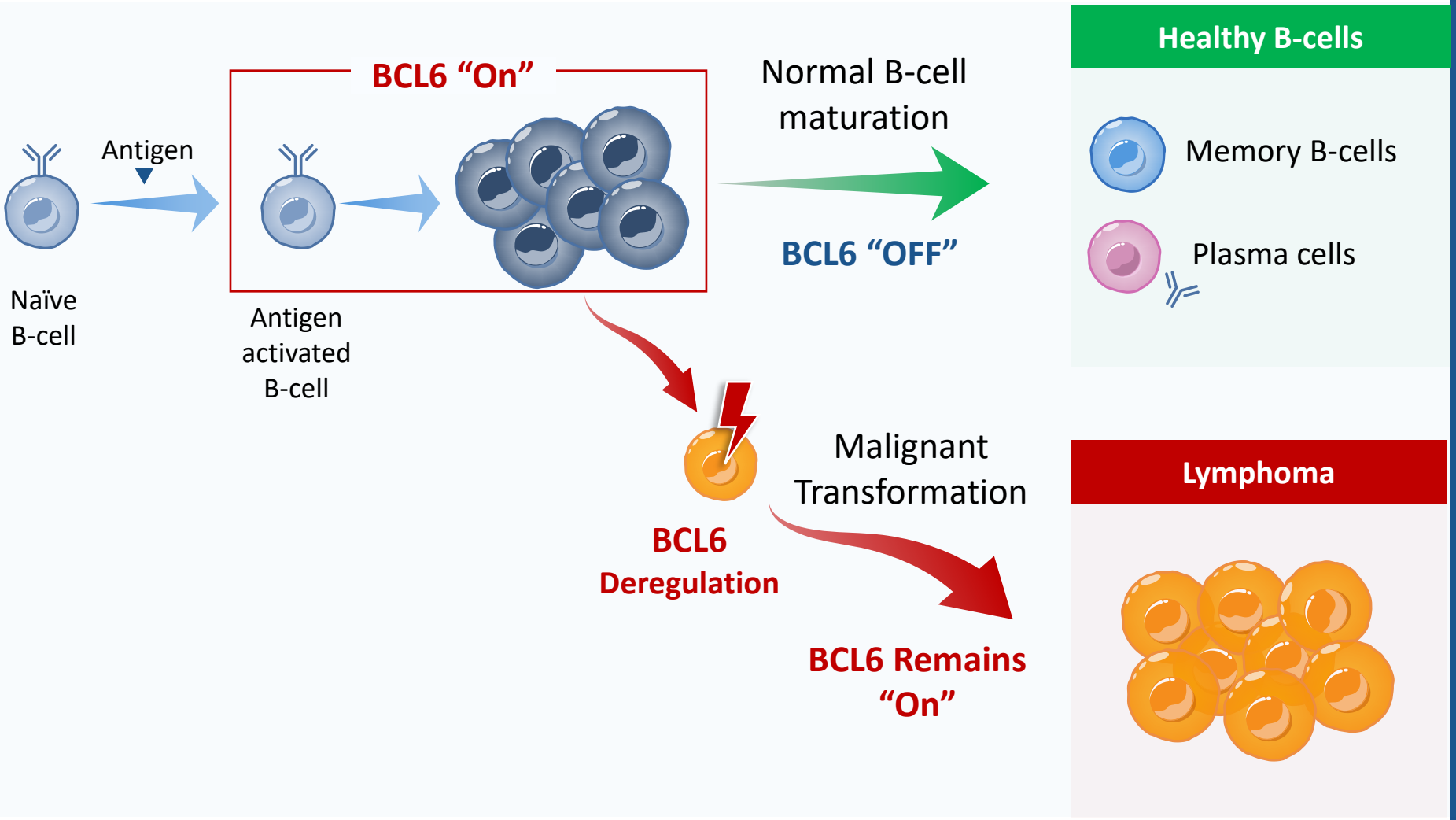
Multiple subsets of NHL include potentially BCL6-dependent disease



AITL, Angioimmunoblastic T-cell lymphoma; BL, Burkitt's Lymphoma; DLBCL NOS, Diffuse Large B-cell Lymphoma Not Otherwise Specified;

1. US new cases a year, SEER 2024. 2. LBCL other: 17 subtypes, including Diffuse large B-cell lymphoma/high-grade B-cell lymphoma with MYC and BCL2 rearrangements, T-cell/histiocyte-rich large B-cell lymphoma among others (Kurz et al, Cancers 2023, 15, 2285). 3. BCL6 mutation is associated with transformation of indolent FL into more aggressive transformed FL (Akasaka et al, Blood, 2003, 102(4):1443-8).

The 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

ARV-393 is a potent, **orally bioavailable** PROTAC small molecule degrader of BCL6[1]

ARV-393 degrades BCL6, a target that has long been considered “undruggable”

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

ARV-393 has demonstrated significant anti-tumor activity in numerous preclinical *in vivo* models of NHL

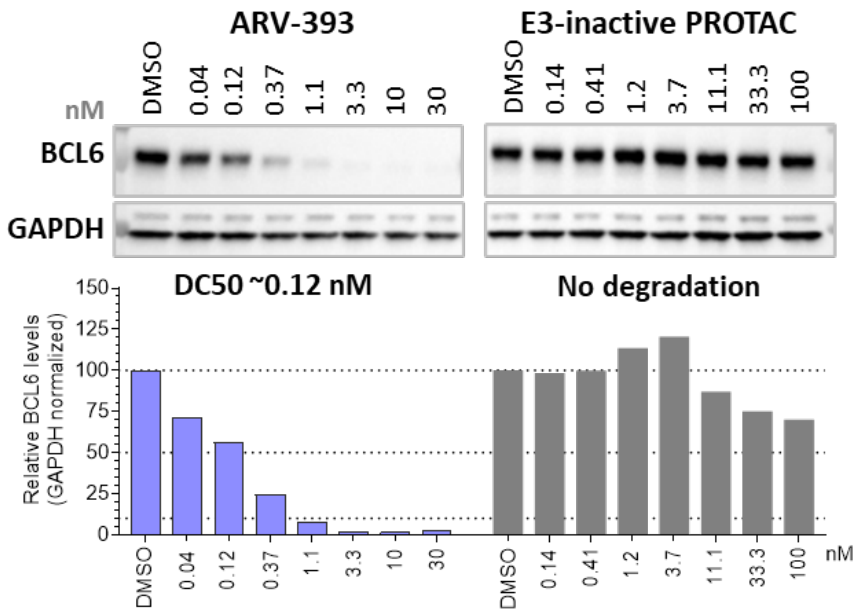
A Phase 1 monotherapy dose escalation study (NCT06393738) of ARV-393 is currently recruiting patients with relapsed/refractory NHL

BCL6, B cell lymphoma 6; NHL, non-Hodgkin lymphoma

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

ARV-393 potently degrades BCL6 in human lymphoma cell lines

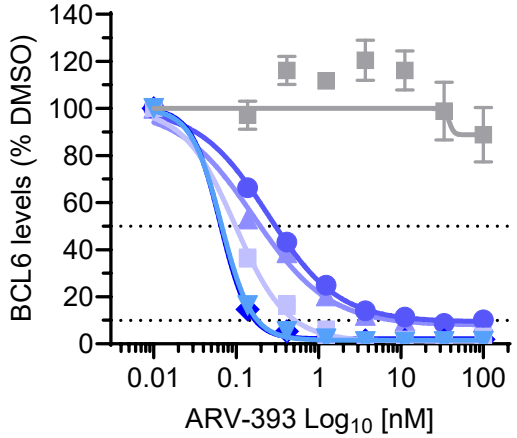
ARV-393, but not its E3-inactive analogue, robustly degrades BCL6 in the OCI-Ly1 model of DLBCL



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

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

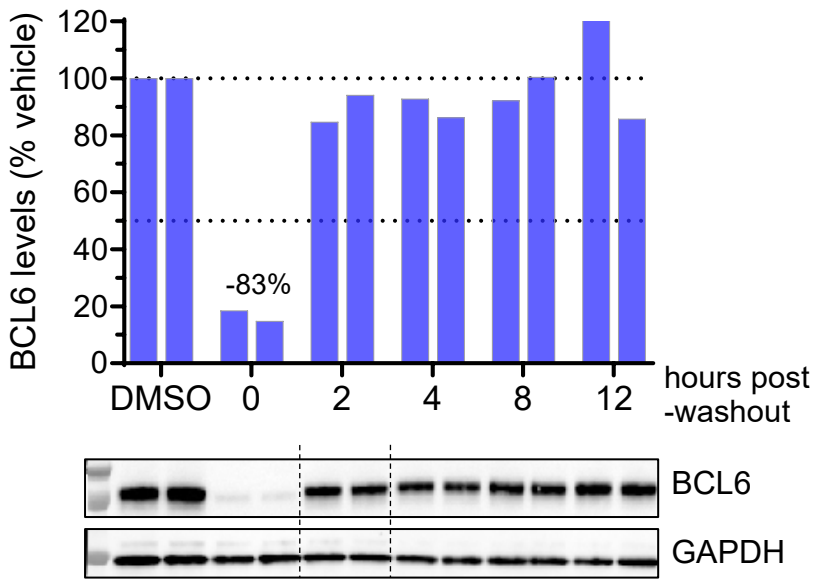


	DC_{50} [nM]	D_{max}
OCI-Ly1	0.07	99%
Farage	0.06	98%
SU-DHL-4	0.33	91%
SU-DHL-6	0.21	92%
OCI-Ly7	0.10	99%
OCI-Ly1 (E3-inactive ARV-393 analogue)	-	-

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

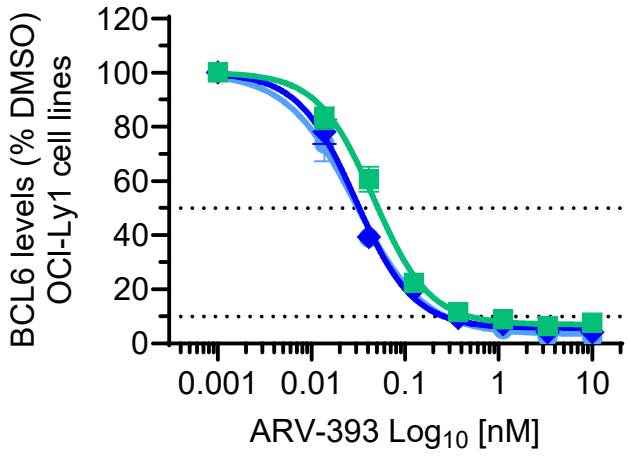
ARV-393 rapidly degrades BCL6 and overcomes its high resynthesis rate

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

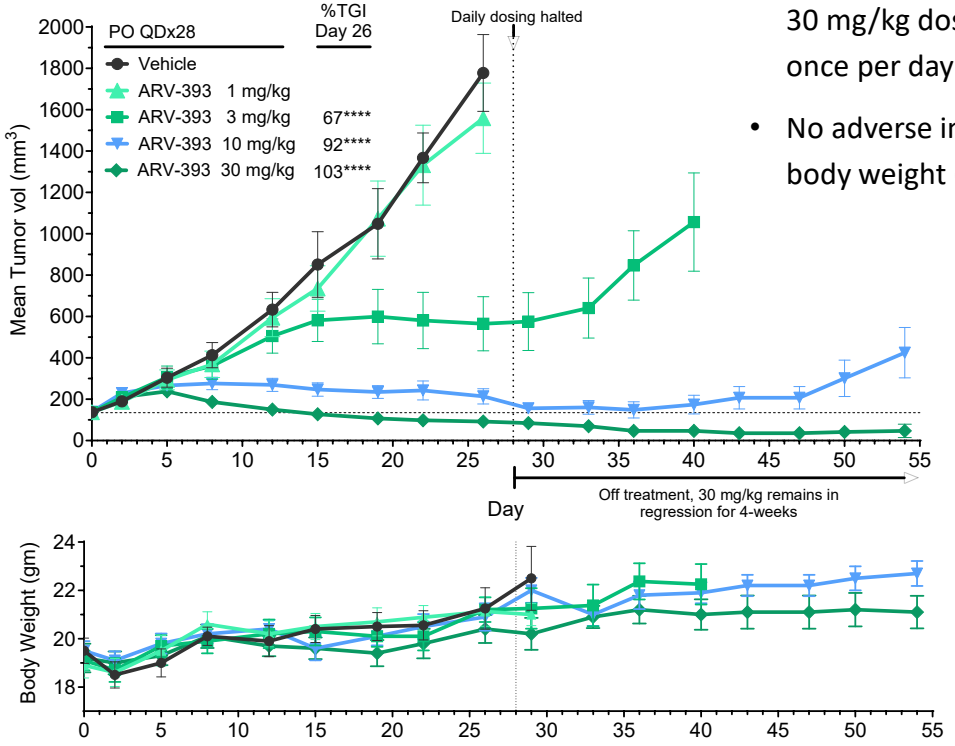


	DC_{50} [nM]	D_{max}
2 hours	0.05	93%
4 hours	0.03	94%
24 hours	0.03	97%

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

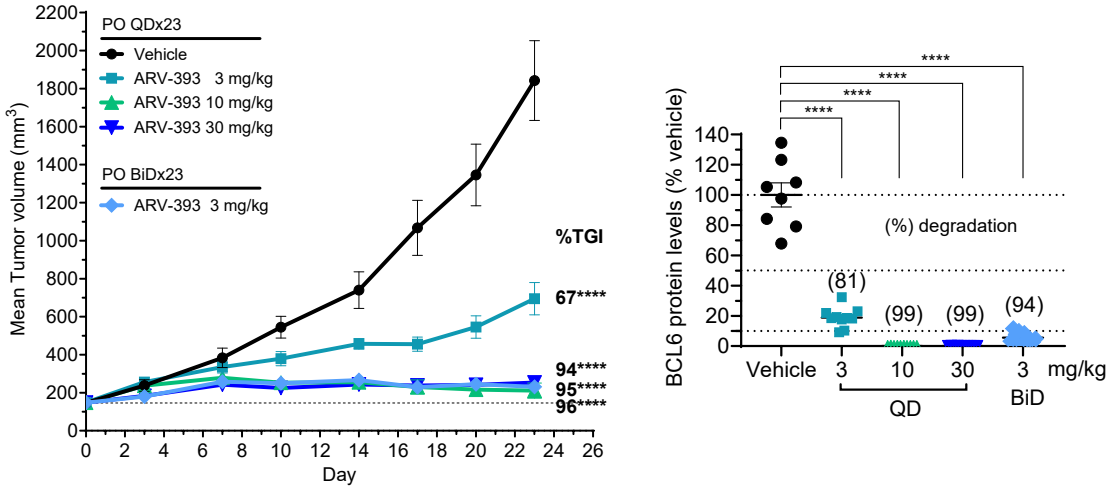
Oral ARV-393 induces dose-dependent tumor growth inhibition (TGI) *in vivo*

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



- Tumor regression at 30 mg/kg dosed once per day (QD)
- No adverse impact on body weight (bottom)

BCL6 degradation >90% is required for optimal TGI (>100%)

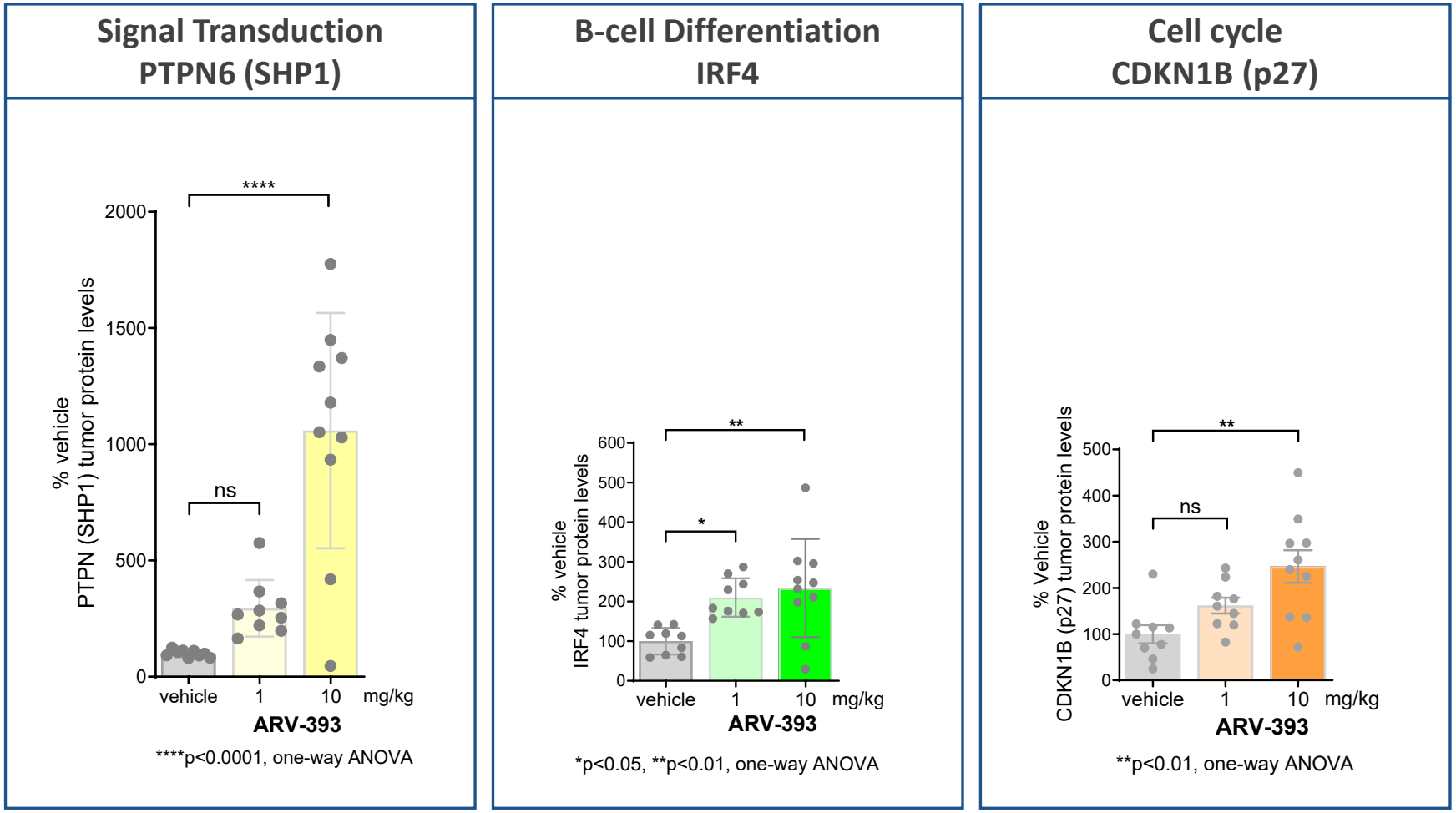


- TGI assessment of different dosing regimens of ARV-393 in the OCI-Ly1 CDX model demonstrate that after 22 days, BCL6 degradation >90% in tumor lysates (right panel) is required for tumor stasis or regression (left panel)

CDX, cell line derived xenograft model; TGI, Tumor Growth Inhibition; DLBCL, Diffuse Large B-Cell Lymphoma.

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.

BCL6 degradation by ARV-393 leads to increased expression of genes normally repressed by BCL6



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

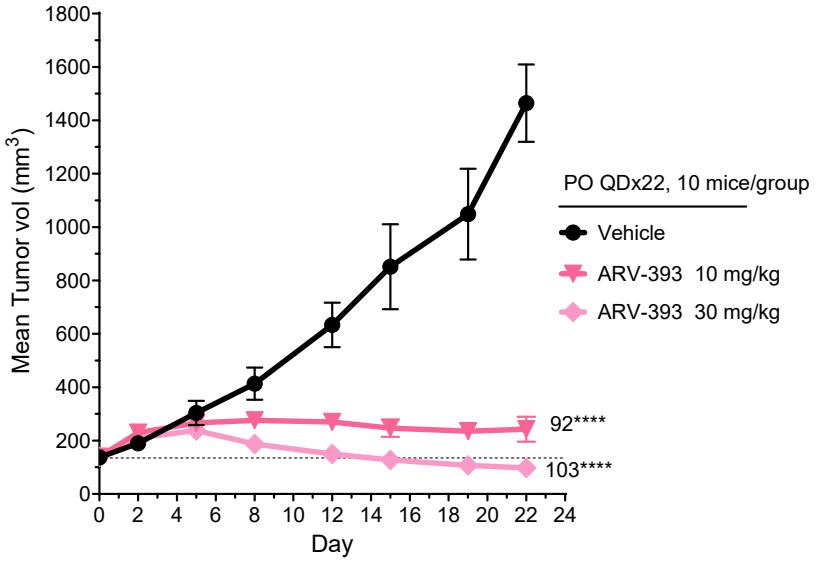
- **BCL6 Repression** – BCL6 is a transcriptional repressor and expression of PTPN6, IRF4, and CDKN1B are repressed by it
- **Pathway Activation** – Treatment with ARV-393 increased the expression of PTPN6, IRF4, and CDKN1B, indicating BCL6 pathway engagement

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

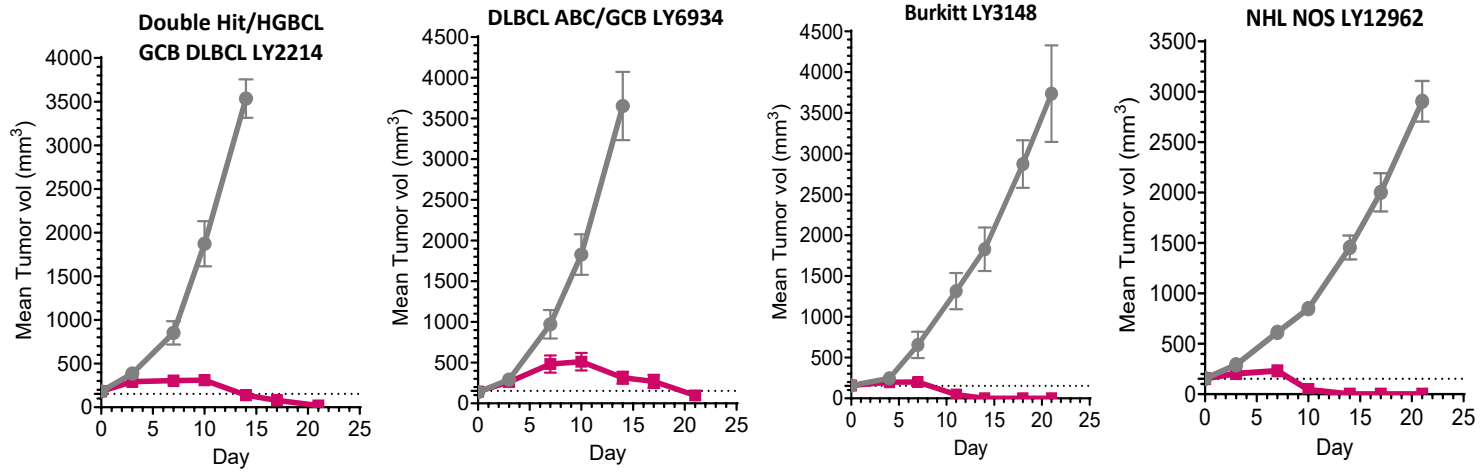
Gough et.al, European Hematology Association (EHA) Poster P1256. June 2024, Madrid Spain. Statistics performed using one-way ANOVA with Dunnett's multiple comparison test.

ARV-393 demonstrated tumor regressions in several subtypes of CDX and PDX non-Hodgkin lymphoma models

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



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



Similar results seen in nine PDX models of various NHL subtypes

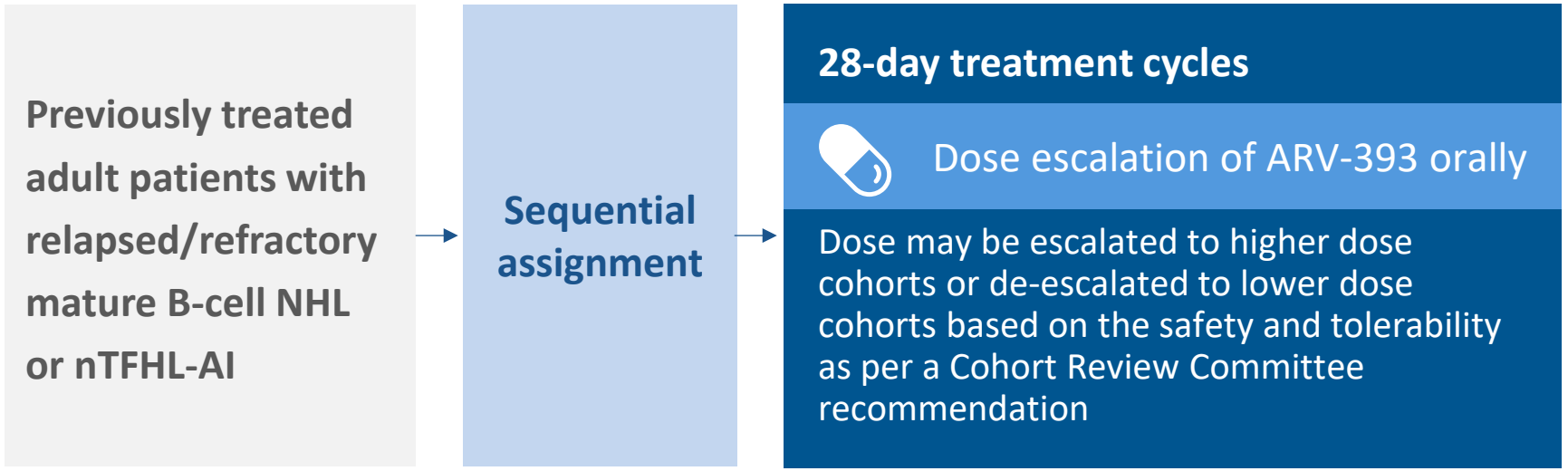
4 mice/group, PO QDx21

- Vehicle
- ARV-393 30 mg/kg

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

a. Body weights not shown.

A Phase 1 clinical trial of ARV-393 in relapsed/refractory non-Hodgkin lymphoma is enrolling patients



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)

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

CLINICAL PROGRAMS

PROTAC KRAS G12D degrader

ARVINAS

Arvinas' PROTAC KRAS G12D degrader is an investigational compound. Its safety and effectiveness have not been established.

Arvinas' novel PROTAC KRAS G12D degrader has the potential to be a best-in-class therapy

ARVINAS

KRAS G12D

KRAS is one of the most frequently mutated human oncogenes and is **commonly altered in pancreatic, colorectal, and lung cancers**, among others; **G12D is the most common** mutation of the KRAS protein

Arvinas' PROTAC KRAS G12D degrader is a potent small molecule degrader of KRAS G12D protein

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

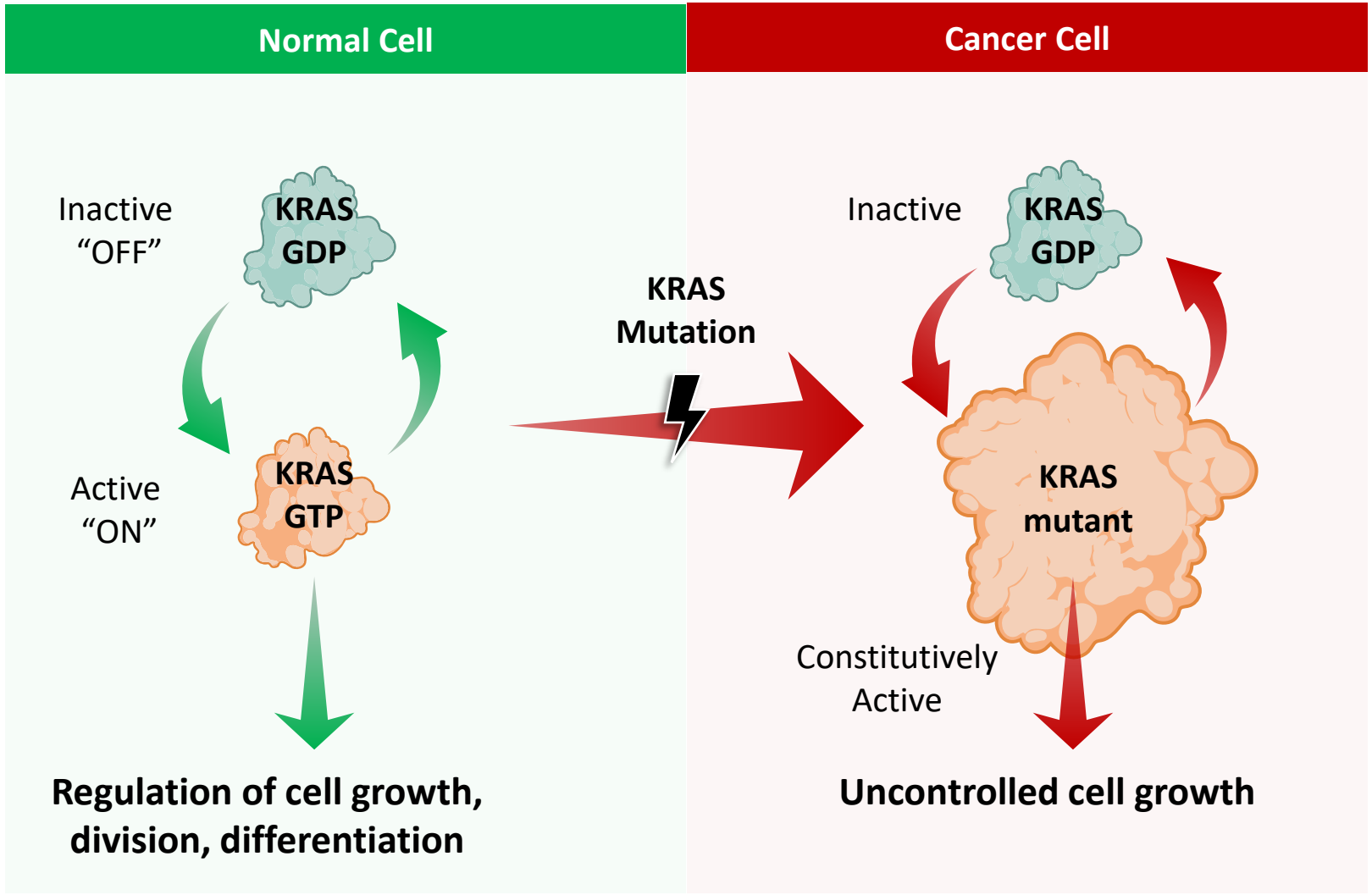
Arvinas' PROTAC KRAS G12D degrader is differentiated from other G12D targeting agents in development and has potential to be a best-in-class therapy for KRAS G12D mutated cancers

Investigational New Drug (IND) application expected in 2025

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

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



*Lee et al., NPJ Precis. Oncol., 2022; Cox et al., Nat Rev Drug Dis, 2014. Vasan et al. 2014, Clin Cancer Res.

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.

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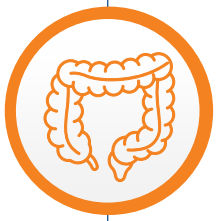
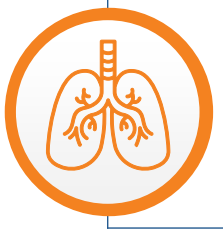
Role of KRAS G12D in Cancer[1]

- 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

Metastatic pancreatic, colorectal, and non-small cell lung cancers patients have poor survival outcomes with no approved KRAS G12D-targeted therapy

ARVINAS

Key Tumors Harboring KRAS G12D Mutations	5-year Survival Rate for Metastatic Setting	Prevalence of KRAS G12D Mutations	US 2024 Newly Diagnosed Patient Population Year
 Pancreatic ductal adenocarcinoma	3%	~35 - 40%[1,2]	~66,000
 Colorectal carcinoma	16%	~12 - 15%[1,2]	~153,000
 Non-small cell lung cancer	6%	~3 - 4%[1,2,3]	~200,000

SEER Database, 1 Lee et al., NPJ Precis. Oncol., 2022, 2 AACR Genie, 3 Acker et al., Frontiers in Oncol., 2021.

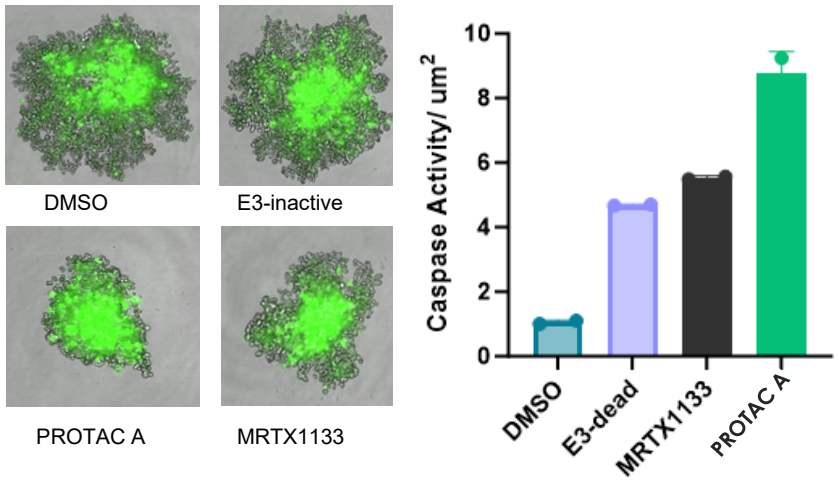
Versus an inhibitor, a PROTAC KRAS G12D degrader demonstrated more potency at inducing cell death and blocking cell proliferation *in vitro*

ARVINAS

Induction of cell death

Arvinas' PROTAC KRAS G12D degrader demonstrated more potency in inducing cell death than an inhibitor or an E3-dead analogue

AsPC-1 Pancreatic Cancer Cells
72 hr treatment, 10 nM

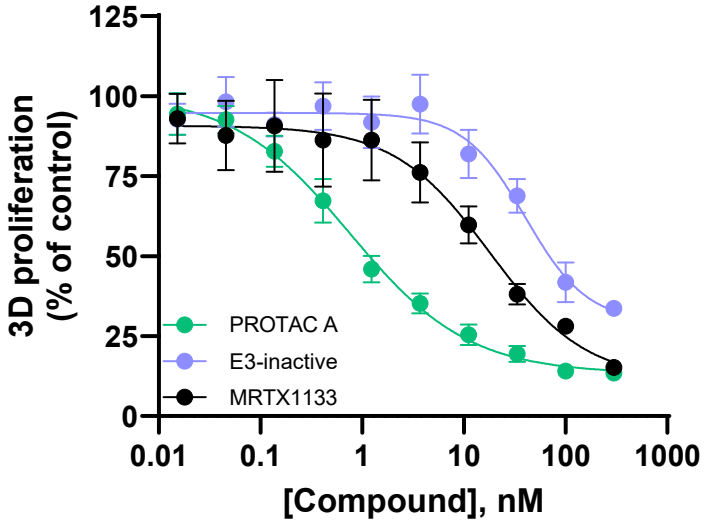


- AsPC-1 is a human pancreatic cell line
- Caspase activity (in green dye at left) is a measure of cell death (apoptosis)

Cell proliferation block

Arvinas' PROTAC KRAS G12D degrader demonstrated 30-fold more potency than an inhibitor *in vitro*

Proliferation of AsPC-1 Pancreatic Cancer Cells

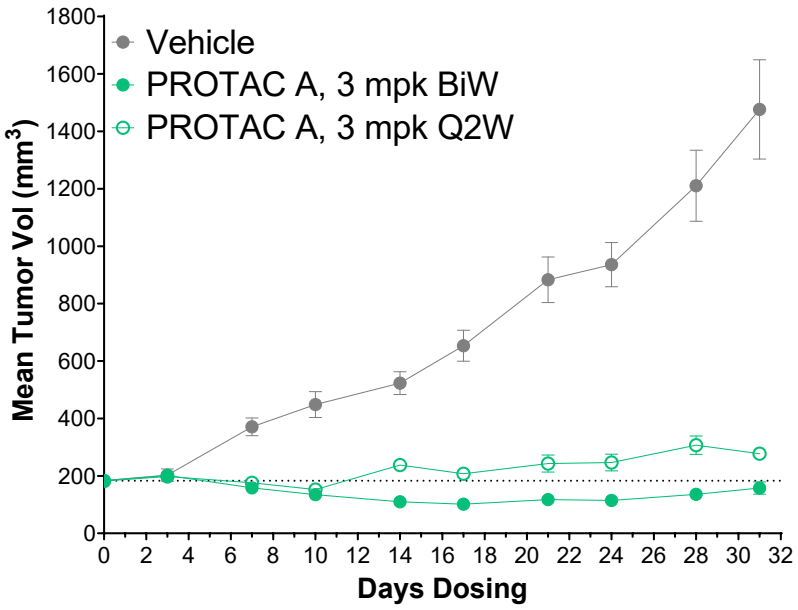


Arvinas' KRAS G12D "PROTAC A" demonstrated more potency at blocking proliferation than either an inhibitor (MRTX1133) or an E3-inactive PROTAC analogue

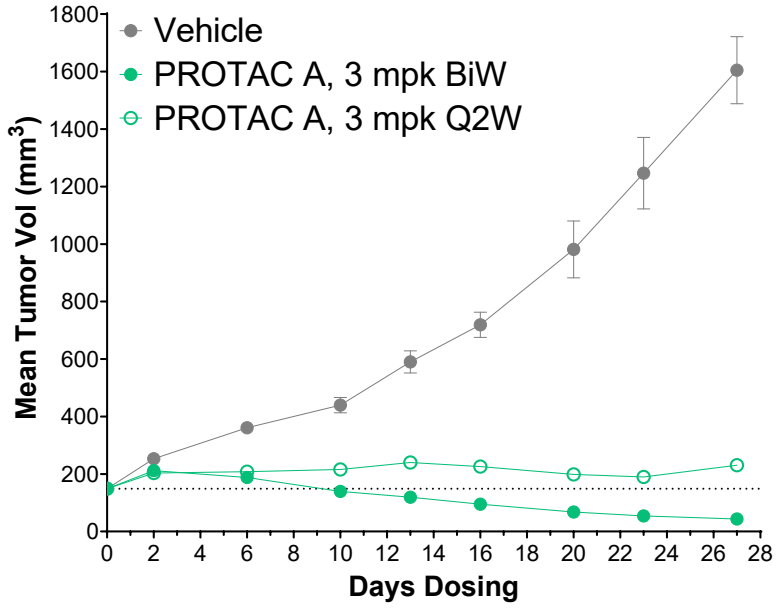
G12D, mutations in codon 12 on KRAS oncogene; KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); MAPK, Mitogen-activated protein kinase.

Extended PD of a PROTAC KRAS G12D degrader may allow for intermittent dosing, which may improve tolerability and facilitate combination treatments

GP2d Xenograft Model of Colorectal Cancer



Panc04.03 Xenograft Model of Pancreatic Cancer



- Arvinas' PROTAC KRAS G12D degrader demonstrates tumor regression in preclinical models of colorectal and pancreatic cancer
- Robust tumor growth inhibition is maintained even with every other week dosing

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

TRANSFORMING TOMORROW WITH MAJOR MILESTONES

Vepdegestrant Could be a Backbone ER Therapy in the ER+/HER2- mBC Space (Total Market, ~$17B[1])

***Vepdegestrant** with Pfizer*

Expected near-term **monotherapy milestones**

- **1Q25** Phase 3 VERITAC-2 **topline results**[a]
- **2025** 2L monotherapy New Drug Application submission[a]

Expected near-term **combination milestones**

- **2025** Initiate 1L and 2L phase 3 combination trials[b]
  - 1L: vepdegestrant + atirmociclib
  - 2L: vepdegestrant + a CDK4/6i

Strengthened by a Potential Best-In-Class Pipeline and Research Engine

Wholly-Owned

Expected 2025 **pipeline milestones**

- **ARV-102 (LRRK2) Degrader:** Phase 1 data in both healthy volunteers (April 2025) and patients with Parkinson's disease (2H25)
- **ARV-393 (BCL6 Degrader):** Preclinical and Phase 1 data
- **KRAS G12D Degrader:** Submit IND application

Strong capital position with $1B cash on hand and runway into 2027[c]

The agents listed on this slide are investigational. Their safety and effectiveness for these investigational uses have not been established.

1IL, first-line; 2L, second-line; BCL6, B-cell lymphoma 6; CDK4/6i, cyclin-dependent kinase inhibitor; ER, estrogen receptor; G12D, mutations in codon 12 on KRAS oncogene; HER2, human epidermal growth factor 2; IND, investigational new drug; KRAS, Kirsten rat sarcoma viral oncogene homolog; LRRK2, leucine-rich repeat kinase 2.

a. Full data to be provided at a medical congress in 2025. b. Pending emerging data and health authority feedback. c. Cash, cash equivalents, and marketable securities position as of December 31, 2024.

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