ARVINAS

Pioneering Today
with a different kind of medicine

Transforming Tomorrow
for patients who need us

NASDAQ LISTED ARVN

November 2024

Safe harbor and forward-looking statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding ourr expectation of bringing the first PROTAC protein degrader to market in partnership with Pfizer, Inc. and the timing thereof; the future value potential tied to collaborations leveraging our PROTAC protein degradation platform; the timing of release of pivotal data for the VERITAC-2 Phase 3 second-line clinical trial of vepdegestrant as a monotherapy; the timing for release of data for ARV-102; our plans and timing related to multiple commercial launches of vepdegestrant; our capital supporting us through the first years of our planned commercial launch and having a cash runway into 2027; the out-licensing of ARV-766 to Novartis accelerating development of our potential first-in-class option for prostate cancer and Novartis' expertise and scale accelerating and broadening the development of ARV-766 as a potential treatment option for patients with prostate cancer; our potential receipt of additional payments based on achievement of development, regulatory and commercial milestones and future royalties under the license agreement with Novartis; the potential for vepdegestrant to become a first-in-class and an oral, best-in-class targeted therapy and to become a backbone estrogen receptor therapy in the estrogen receptor positive, human epidermal growth factor 2 negative, metastatic breast cancer space; the plans for and anticipated timings related to planned clinical trials, pending regulatory feedback, including second-line Phase 3 clinical trials of vepdegestrant in combination with palbociclib and/or potentially other CDK4/6 inhibitors and a first-line Phase 3 clinical trial of vepdegestrant in combination with Pfizer's CDK4 inhibitor (atirmociclib/PF-07220060) or palbociclib; plans for a potential adjuvant trial, as informed by the TACTIVE-N neoadjuvant trial; the potential therapeutic benefits and market opportunity of our product candidates, including vepdegestrant, ARV-102 and ARV-393; the opportunity for PROTAC degraders to benefit patients with unmet need in neuroscience and ARV-102's potential to address neurodegenerative diseases; whether PROTAC-induced LRRK2 degradation could be a potential treatment for idiopathic Parkinson's disease and Progressive Supranuclear Palsy; whether ARV-393, our B-cell lymphoma 6, or BCl6, PROTAC degrader will be a potential first-in-class therapy for non-Hodgkin Lymphoma and additional the opportunities for a BCL6 degrader; whether a kirsten rat sarcoma, or KRAS,-targeting PROTAC may provide a significant advance in treatment for multiple cancers and our plans related to filing an investigational new drug application for our KRAS G12D targeted PROTAC degrader; our goal to nominate one clinical candidate per year; 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 will be able to successfully conduct and complete development for our other product candidates, including whether we initiate and complete clinical trials for our product candidates and receive results from our clinical trials on our expected timelines, or at all; 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 Novartis will be able to successfully conduct and complete clinical development, obtain marketing approval for and commercialize ARV-766; whether we receive results from our preclinical trials on our expected timelines, or at all; our ability to protect our intellectual property portfolio; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, discussed in the "Risk Factors" section of our quarterly and annual reports on file with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this presentation reflect our current views as of the date of this presentation with respect to future events, and we assume no obligation to update any forward-looking statements, except as required by applicable law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

This presentation may also contain estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. This presentation is intended for the investor community only. It is not intended to promote the products referenced herein or otherwise influence healthcare prescribing decisions. Cross-trial comparisons are not based on head-to-head studies and no direct comparisons can be made.

Arvinas: Advancing a New Therapeutic Modality to Patients

NEW MECHANISM

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

PIONEER IN THE FIELD

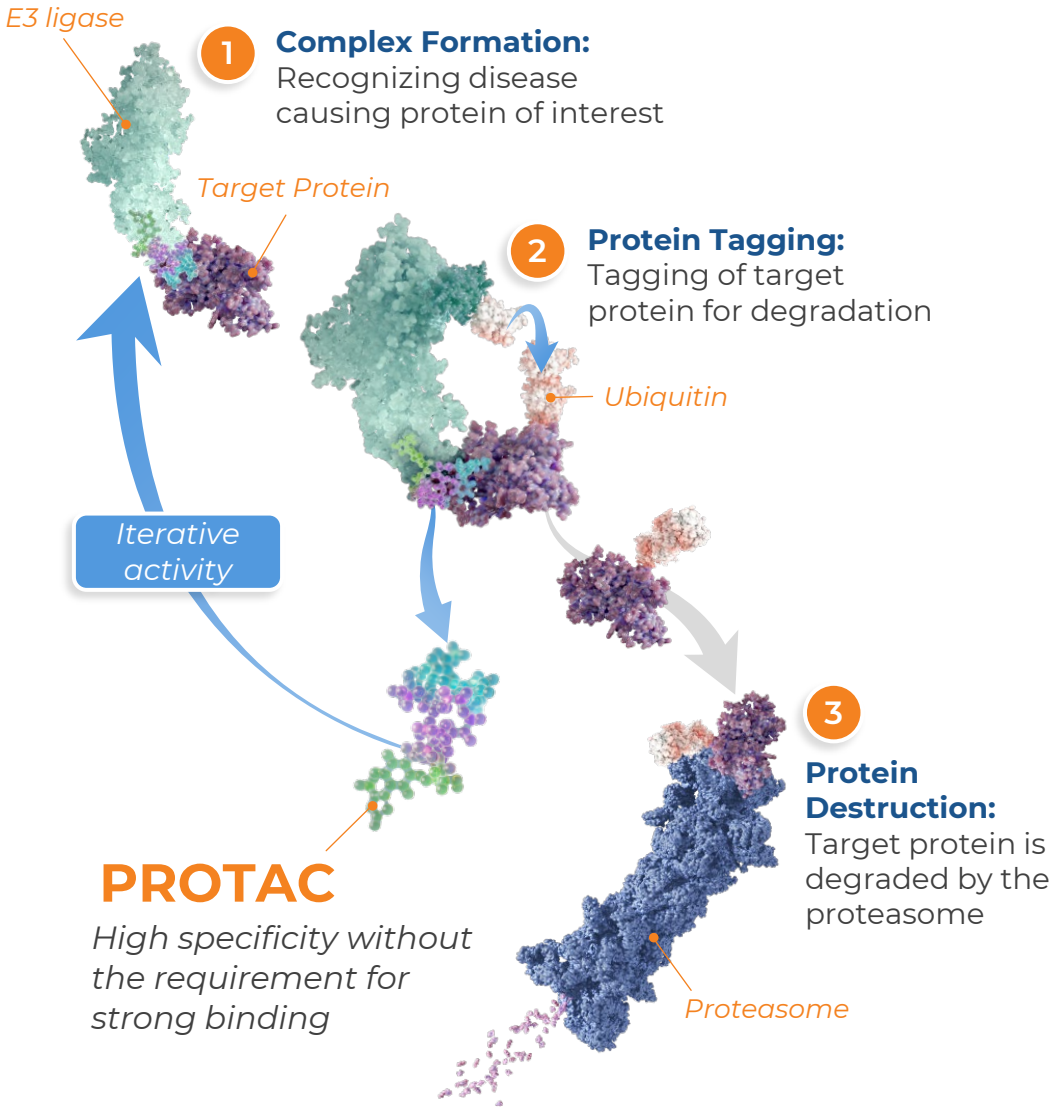
- **On-track to bring the first PROTAC protein degrader to market** (in partnership with Pfizer)
- **Further platform validation** with NOVARTIS deal for ARV-766
- **First neuroscience PROTAC degrader** advanced to the clinic in 2024 (ARV-102)

DEEP PIPELINE

- **Five programs moved into the clinic** since 2019
- **Pipeline of programs** across oncology, neuroscience, hematology, and immuno-oncology
- Strong collaborations leveraging PROTAC protein degradation platform with **future value potential**

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

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



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

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

A History of Pioneering
To transform the treatments of tomorrow

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

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

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

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

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

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

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

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

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

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

2023 IND cleared for BCL6 PROTAC (ARV-393)

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

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

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

Arvinas' clinical programs: Opportunity to benefit patients across a wide range of diseases

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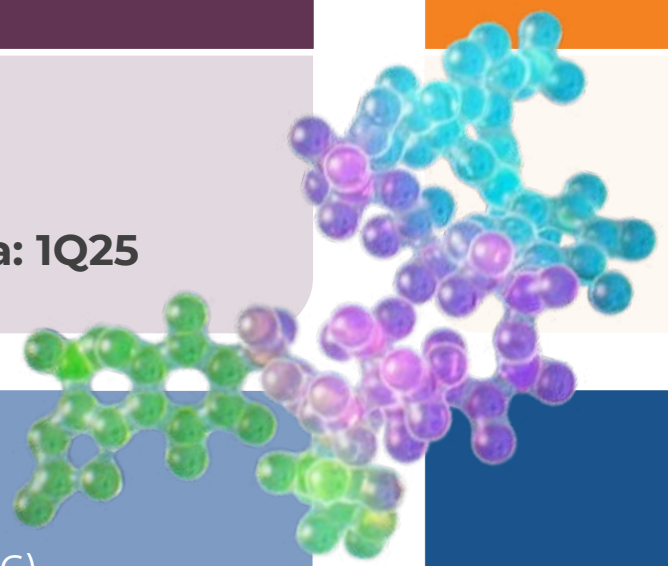
ONCOLOGY
ER+/HER2- Breast Cancer
Vepdegestrant

PROTAC ER degrader
Partnered with Pfizer
Topline VERITAC-2 **pivotal data: 1Q25**

NEUROLOGY
Progressive supranuclear palsy, Parkinson's disease
ARV-102

PROTAC LRRK2 degrader
Wholly-owned
First human data in 1H25



ONCOLOGY
Prostate Cancer
Luxdegalutamide (ARV-766)

PROTAC AR degrader
Luxdegalutamide outlicensed to NOVARTIS
for worldwide clinical development and commercialization in prostate cancer

HEMATOLOGY
Non-Hodgkin Lymphomas
ARV-393

PROTAC BCL6 degrader
Wholly-owned
In phase 1 trial for subsets of NHL

These agents are currently under investigation; their safety and effectiveness for these investigational uses have not yet been established.
ER, estrogen receptor; LRRK2, leucine-rich repeat kinase 2; BCL6, B-cell lymphoma 6; NHL, non-Hodgkin's lymphoma

Our broad pipeline includes the first pivotal trials for PROTAC degraders

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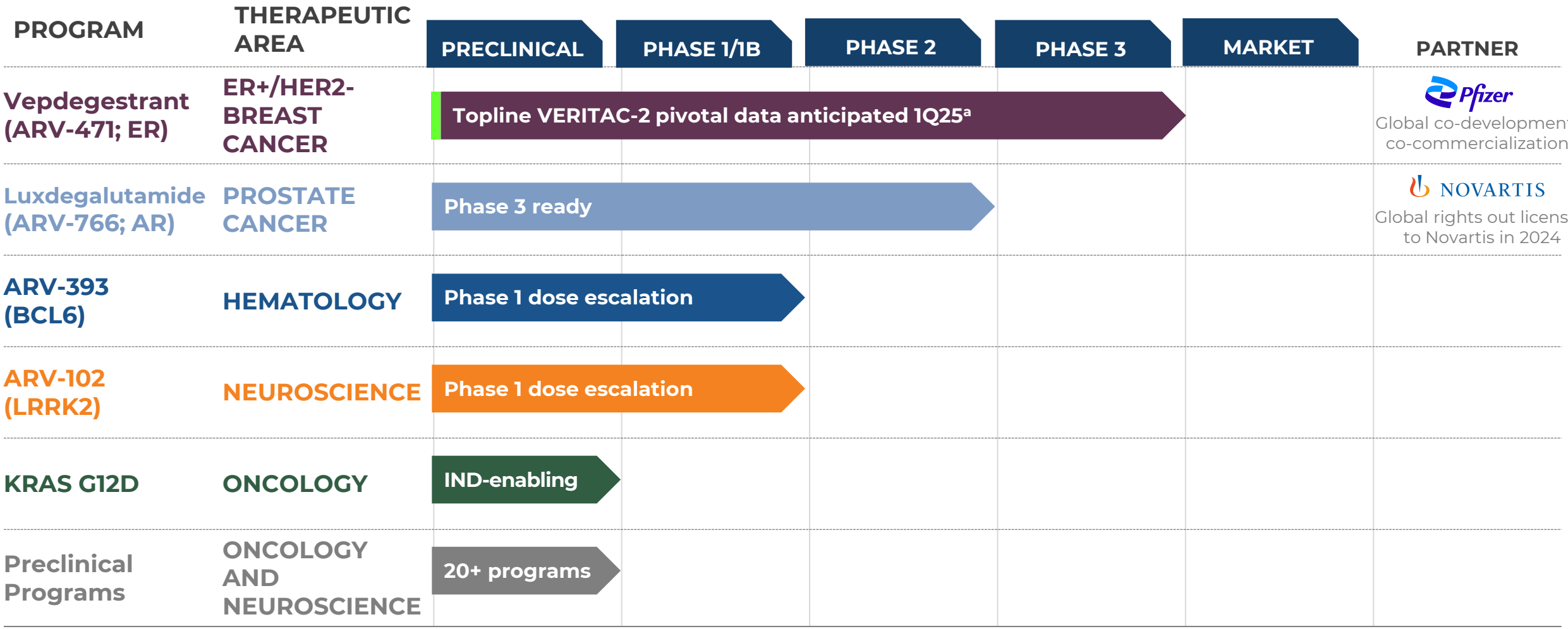


These agents are currently under investigation; their safety and effectiveness for these investigational uses have not yet been established.

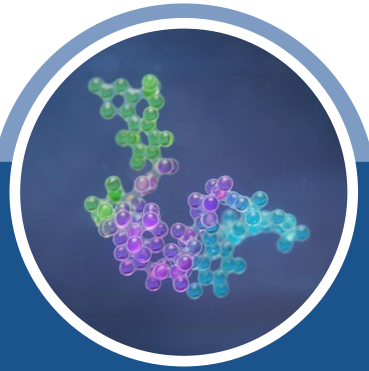
ER, estrogen receptor; HER, human epidermal growth factor receptor; AR, androgen receptor; BCL6, B-cell lymphoma 6; LRRK2, Leucine-rich repeat kinase 2; KRAS, Kirsten rat sarcoma viral oncogene homolog

a. Complete vepdegestrant development program is included ion slide 12 of this presentation or at www.ir.arvinas.com/events-and-presentations

Arvinas' strategy positions us for the next stage of growth

Focused on Near-term Patient Impact

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



Data-driven Approach to Resource Allocation

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

Strong Capitalization

- Cash runway into 2027
- Capital to support us through the first years of our planned commercial launch

Out-licensing of ARV-766 designed to accelerate development of Arvinas' potential first-in-class option for prostate cancer

April 2024 transaction with Novartis:

- $150 million upfront payment for global development and commercialization license agreement for ARV-766 and the sale of Arvinas' preclinical AR-V7 program
- Potential for up to an additional $1.01 billion based on achievement of development, regulatory, and commercial milestones, and future royalties

- Aligned with our strategy of bringing potential first- and best-in-class treatments to patients through innovative R&D, collaborations and partnerships
- Novartis' expertise and scale expected to accelerate and broaden the development of ARV-766 as a potential treatment option for patients with prostate cancer
- Further validates Arvinas' innovative PROTAC protein degrader platform

CLINICAL PROGRAMS

Vepdegestrant

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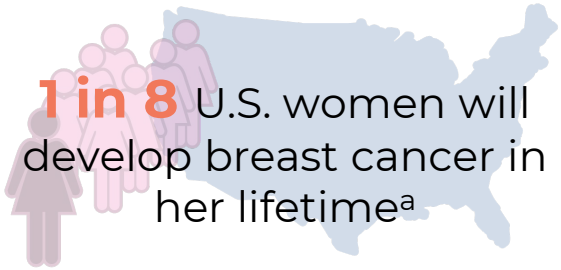
Pfizer

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



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

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

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

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

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

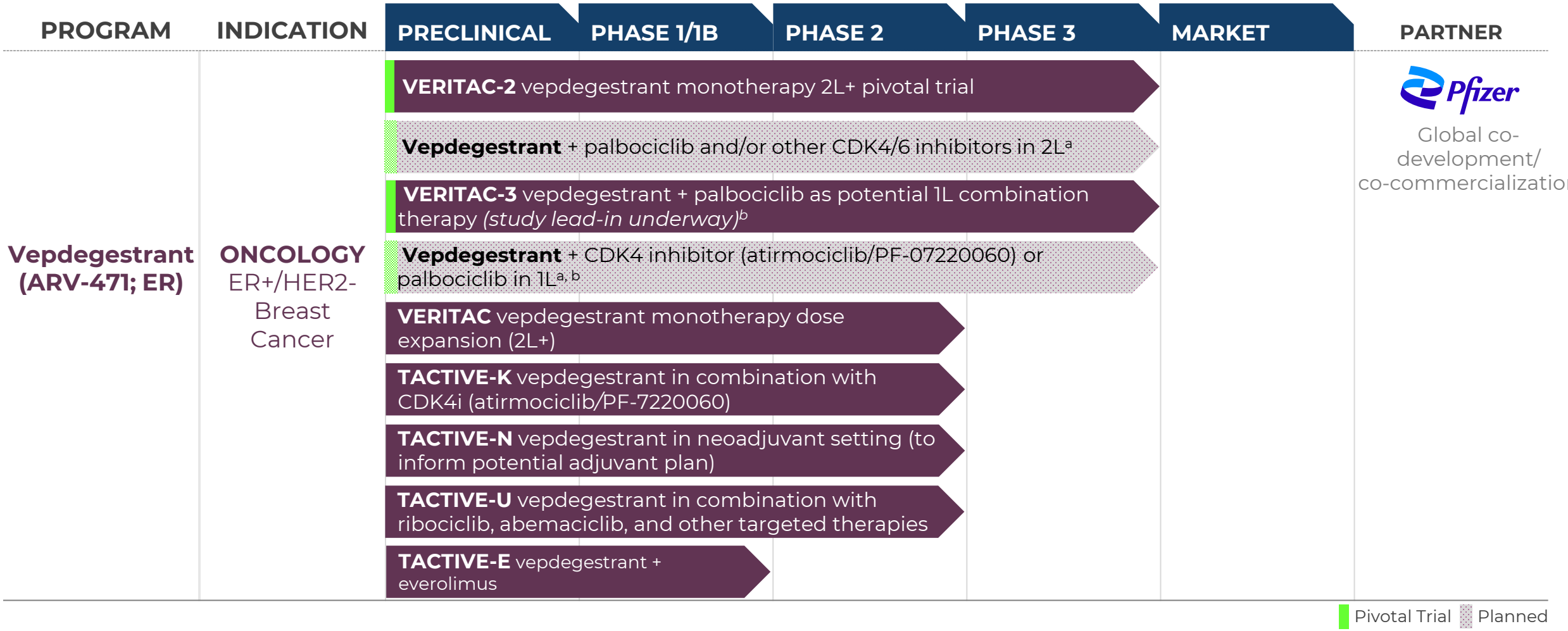
More than **600 patients and healthy volunteers** have been treated with vepdegestrant across 12 clinical trials

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

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

Vepdegestrant is an investigational compound. Its safety and efficacy has not been established
ER, estrogen receptor; HER2, human epidermal growth factor 2; ESR1, estrogen receptor 1 gene
[a] ACS: https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html; accessed 01/06/24; [b] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4549764/, accessed 10/28/2024
[c] Clarivate/Decision Resources Group – Breast Cancer Disease Landscape & Forecast (Nov 2023). 2032 Projection.

Vepdegestrant is the first PROTAC degrader to enter phase 3 pivotal trials



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

ER, estrogen receptor; HER, human epidermal growth factor receptor; mBC, metastatic breast cancer; 1L, first-line; 2L second-line

a. Pending emerging data and health authority feedback; b. First-line phase 3 trial in mBC will be either vepdegestrant + atirmociclib **or** vepdegestrant + palbociclib

Phase 3 VERITAC-2 trial in the 2L+ setting is fully enrolled and on track for topline data in 1Q25

Two ongoing monotherapy trials:

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

VERITAC Phase 2 subset analysis:

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

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

Treatment (N = 560)

Randomize 1:1

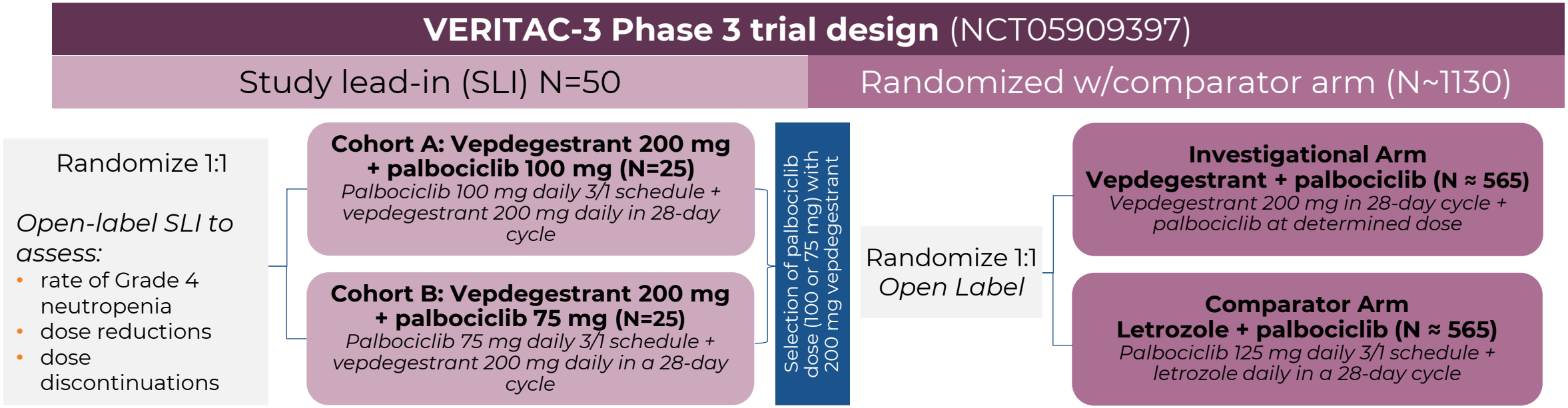
Vepdegestrant
200 mg orally once daily

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

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

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

The study lead-in for our 1L Phase 3 VERITAC-3 trial in combination with palbociclib is fully enrolled



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

CDK, cyclin-dependent kinase

Results from Phase 1b trial with vepdegestrant + palbociclib presented at the 2024 ESMO Breast Cancer Annual Congress

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

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

	PACE[1] Palbo/fulvestrant after CDK4/6i	BioPER[2] Palbo/PC after CDK4/6i	MAINTAIN[3] Ribo/ET after CDK4/6i	PALMIRA[4] Palbo/ET after CDK4/6i	Vepdeg + palbo P1b
Prior CDK4/6i	100%	100%	100%	100%	87.0%
Prior chemo for mBC	14.4%	12.5%	6.7%	0%	45.7%
Prior fulvestrant	0%	43.8%	16.8%	11.8%	80.0%
Overall Response Rate (Evaluable)[a]	13.7% (n=73)	6.3% (n=32)	20.0% (n=35)	6.4% (n=94)	41.9% (n=31)
Clinical Benefit Rate (Evaluable)	32.4% (n=111)	34.4% (n=32)	42.9% (n=49)	41.9% (n=136)	63.0% (n=46)
Progression-Free Survival Median (95% CI), months	4.6 (3.6–5.9) (n=111)	2.6 (1.8–6.7) (n=32)	5.3 (3.0–8.1) (n=60)	4.9 (3.6–6.0) (n=136)	11.2 (8.2-16.5) (n=46)

Data presented at ESMO BC 2024

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

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

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

Safety/tolerability in Phase 1b trial

- The safety profile of vepdegestrant + palbociclib 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

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

Adjuvant (Post-Surgical) Breast Cancer in US (~190K[a])	Metastatic Breast Cancer in US (~60K[1])	
	First Line	**Second/Third Line**
TACTIVE-N neoadjuvant trial *to inform potential adjuvant trial*	VERITAC-3 vepdeg + palbo combination ***pivotal trial*** • Assessing SLI data to determine the RP3D of palbociclib to be administered in combination with vepdegestrant	VERITAC-2 monotherapy ***pivotal trial***
		TACTIVE-E: in combination with everolimus
		TACTIVE-K: in combination with CDK4i (PF-07220060)
		TACTIVE-U: in combination with ribo/abema/CDK7i

Active Trials

Planned trials[b]

Pending further data and regulatory agreement:

Planned: *Pivotal* Vepdeg + Pfizer's novel CDK4 inhibitor atirmociclib or palbociclib	**Planned: *Pivotal*** Vepdeg combo with palbo and/or other CDK4/6i

CDK, cyclin-dependent kinase; SLI, study lead-in; RP3D, recommended phase 3 dose

[a.] Kantar Cancer MPact Patient Metrics (accessed Nov. 2023); [b.] Pending health authority feedback on potential pivotal trials

CLINICAL PROGRAMS

ARV-102 (LRRK2-targeting PROTAC)
ARV-393 (BCL6-targeting PROTAC)

ARVINAS

Advancing an industry leading pipeline of PROTAC degraders

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

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

Arvinas' pipeline is differentiated and sustainable

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

- ***LRRK2*-targeting PROTAC *ARV-102* shown to reach and degrades in deep brain regions**
- ***BCL6*-targeting PROTAC *ARV-393* addresses a historically undruggable target**

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

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

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

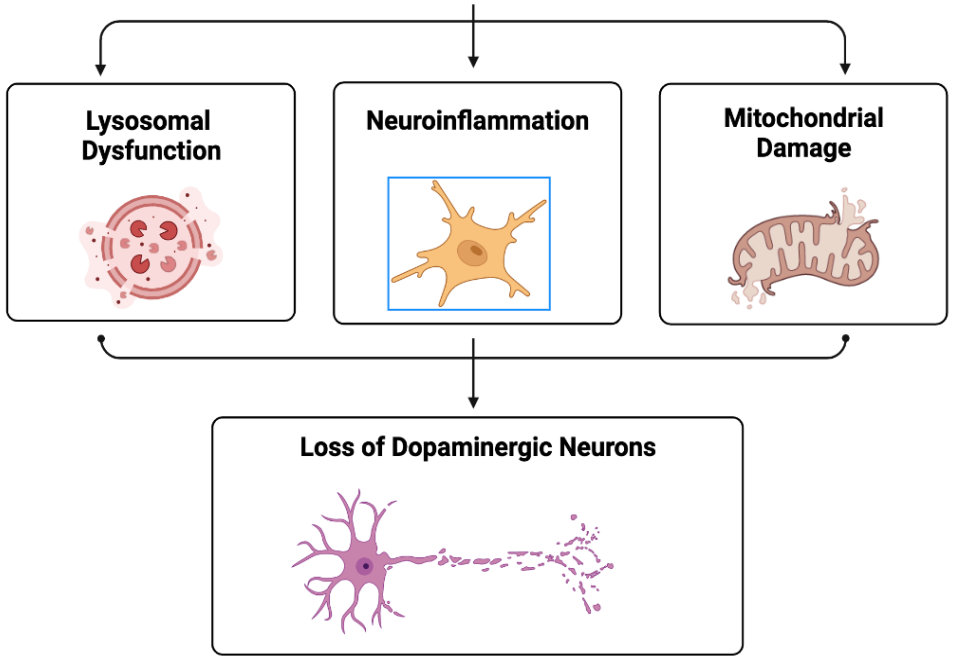
- **LRRK2 is a large multidomain scaffolding kinase**

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

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

- LRRK2 kinase inhibitors and an ASO in clinical trials

Mutations in and increased expression of LRRK2



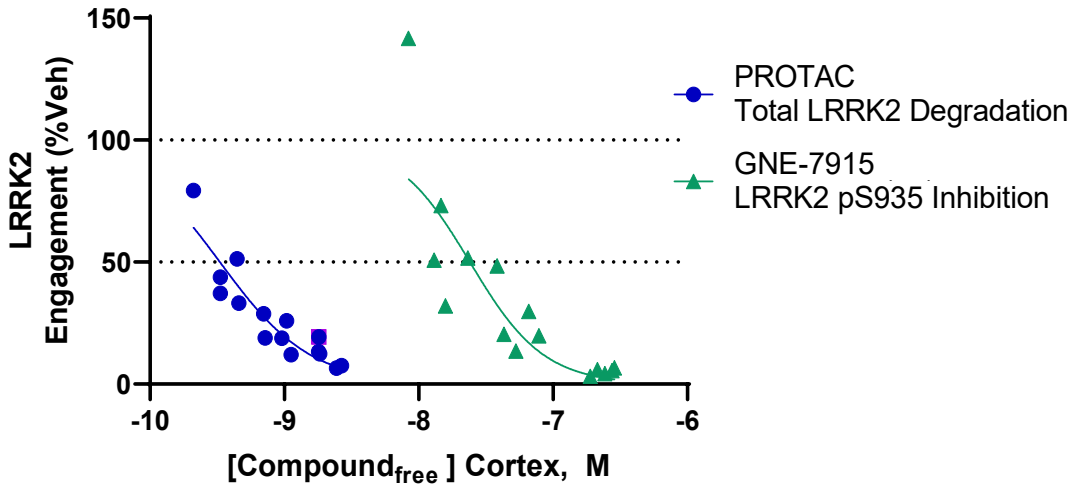
LRRK2, Leucine-rich repeat kinase, ASO, antisense oligonucleotide

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

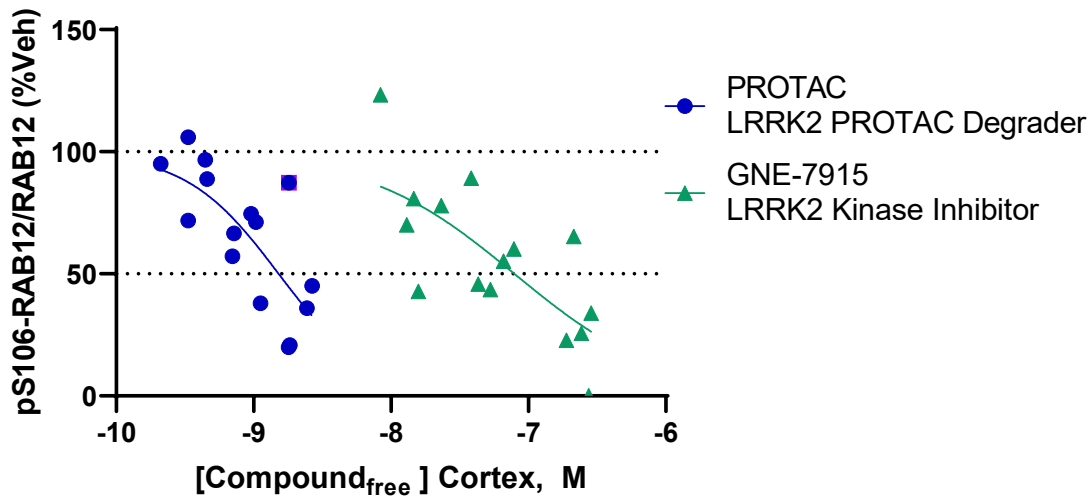
In preclinical models, a PROTAC LRRK2 degrader shows better target and pathway engagement versus a LRRK2 inhibitor

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

Protein Target Engagement at T_{max} (LRRK2 PROTAC vs. Kinase Inhibitor)



Lysosomal Pathway Engagement (LRRK2 PROTAC vs. Kinase Inhibitor)



LRRK2, Leucine-rich repeat kinase 2; T_{max} for PROTAC is 24h ; T_{max} for GNE-7915 is 1h

[a] G2019S familial Parkinson's Disease mouse model

PROTAC LRRK2 degraders induce only modest, reversible pneumocyte enlargement & no pro-fibrotic changes vs. inhibitors

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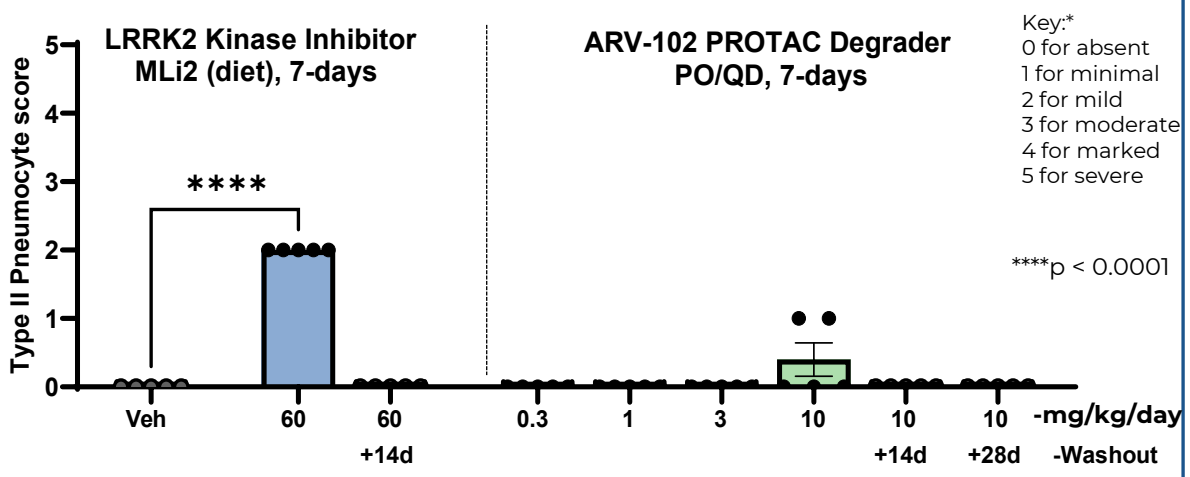
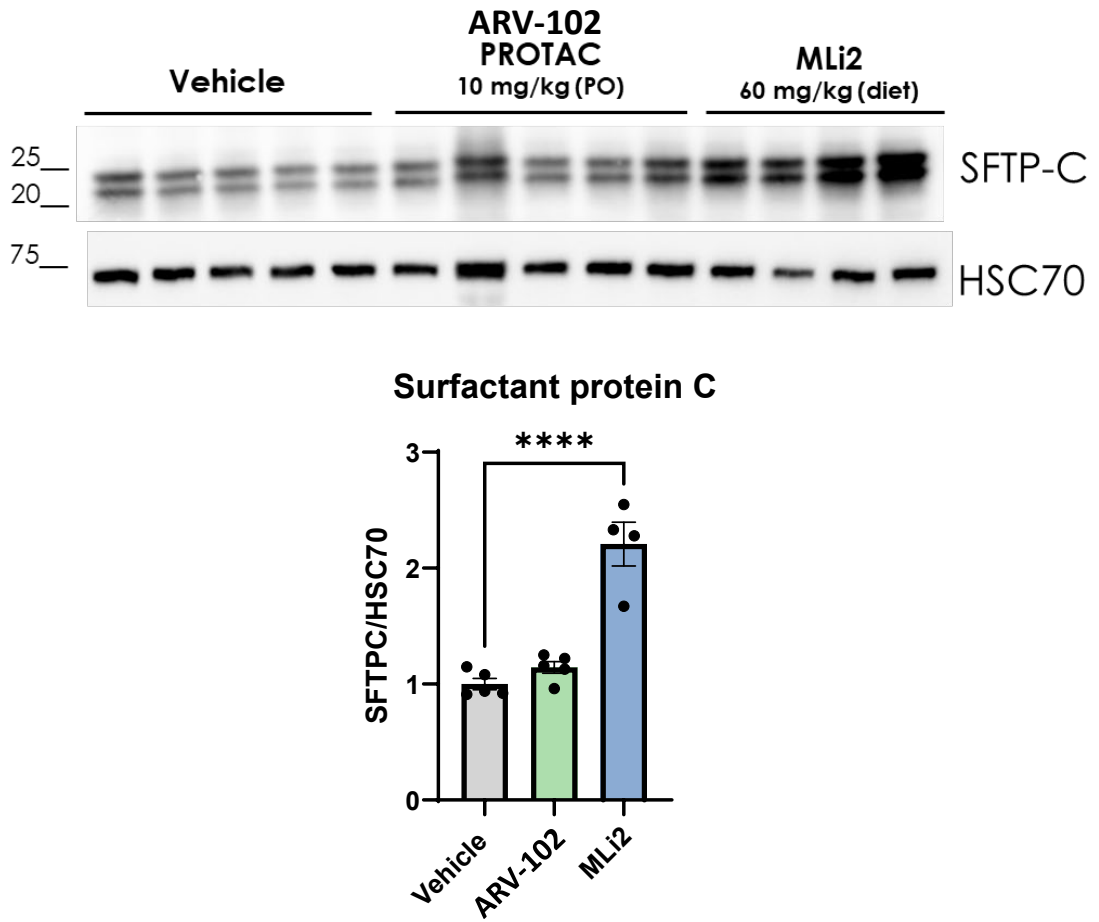
Lung Type II Pneumocyte Enlargement/ Hypertrophy (Histopathologic Score)



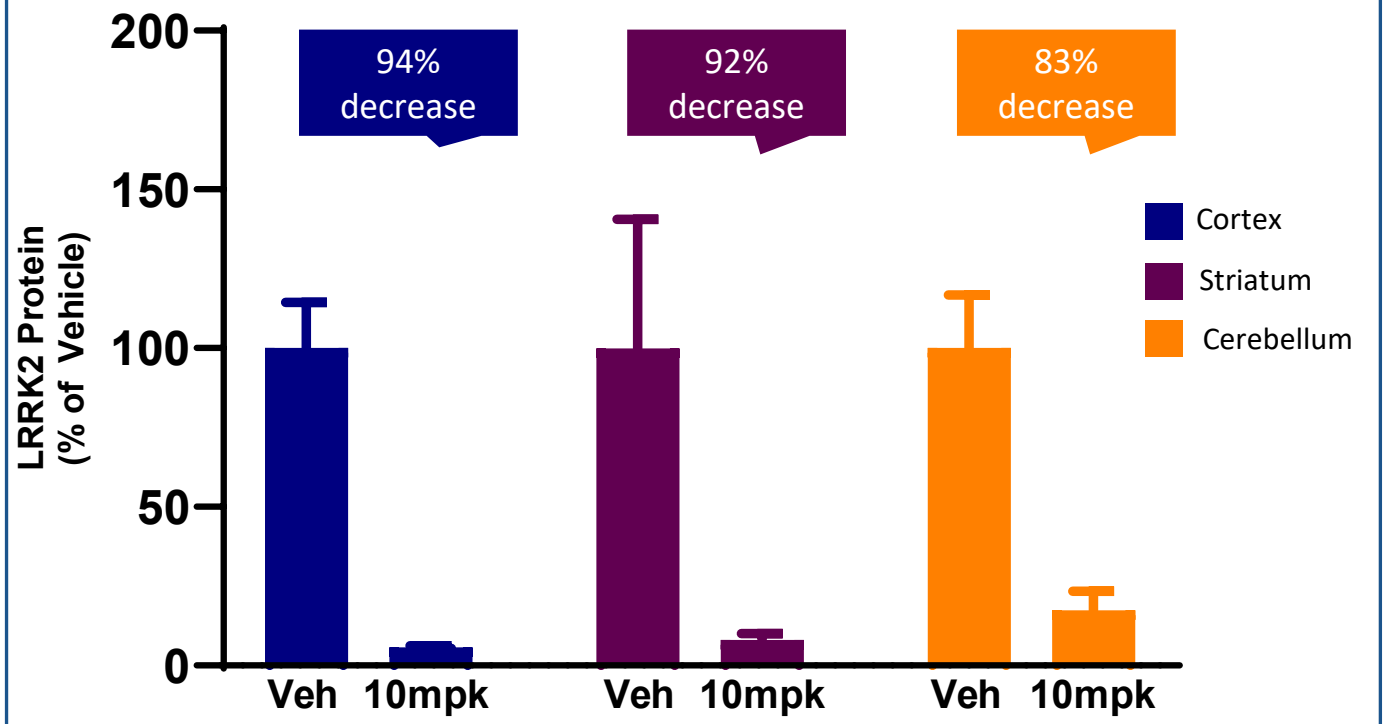
- Full kinase inhibition for MLi2 LRRK2 kinase inhibitor and near complete degradation of LRRK2 in mice lung (data not shown)
- Less pneumocyte hypertrophy observed with LRRK2 PROTAC compared to kinase inhibitor MLi2 (positive control for type II pneumocyte enlargement)
- Effect is reversible after 14-day wash-out
- No evidence of collagen deposition in lung with LRRK2 PROTAC degraders in NHP (tox studies to date; data not shown)

Surfactant protein C increased by Mli2 LRRK2 kinase inhibitor not by ARV-102 in Lung



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

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



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

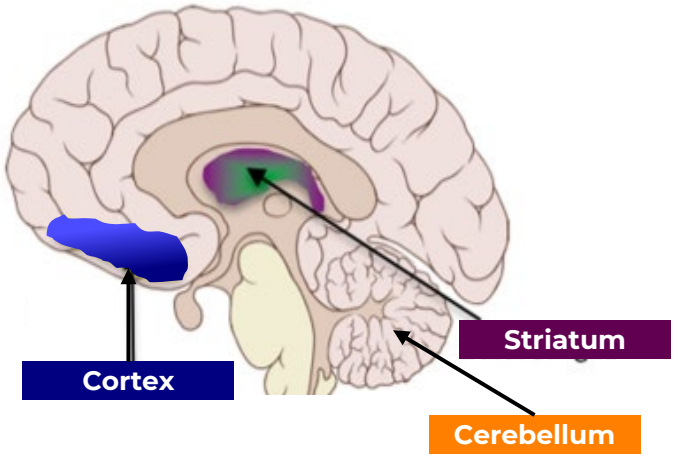


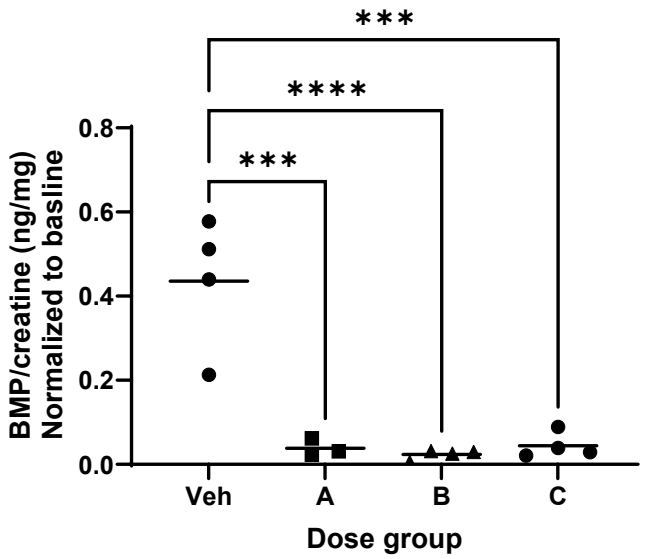
Figure modified from Beuriat et al. 2022

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

Our PROTAC LRRK2 degrader induces biomarker changes that reinforce confidence in the PROTAC MoA in the periphery and brain of non-human primates

PROTAC-induced reductions observed in key urine lysosomal marker in NHPs

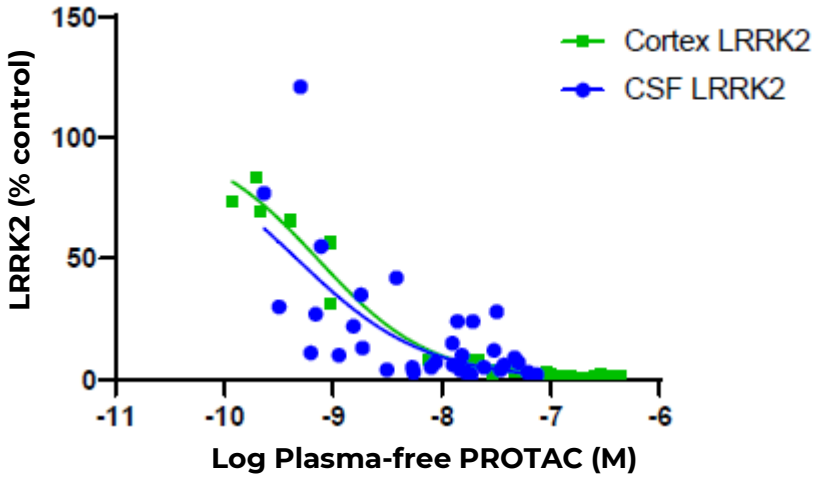
BMP reductions in cynomolgus monkeys



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

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

CSF LRRK2 reductions in cynomolgus monkeys; surrogate compartment for brain

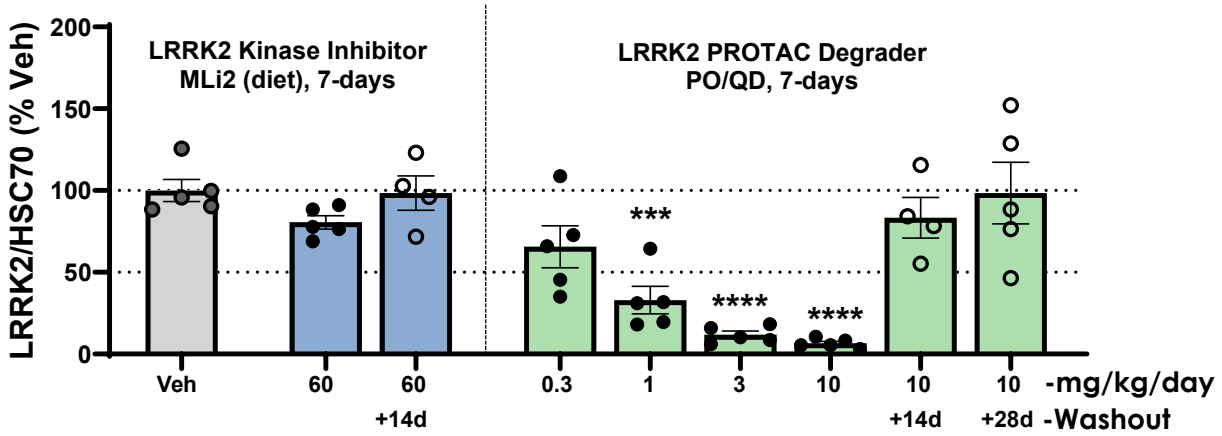


Equivalent PK/PD supports the utility of measuring CSF LRRK2 as a surrogate for monitoring LRRK2 reductions in the brain.

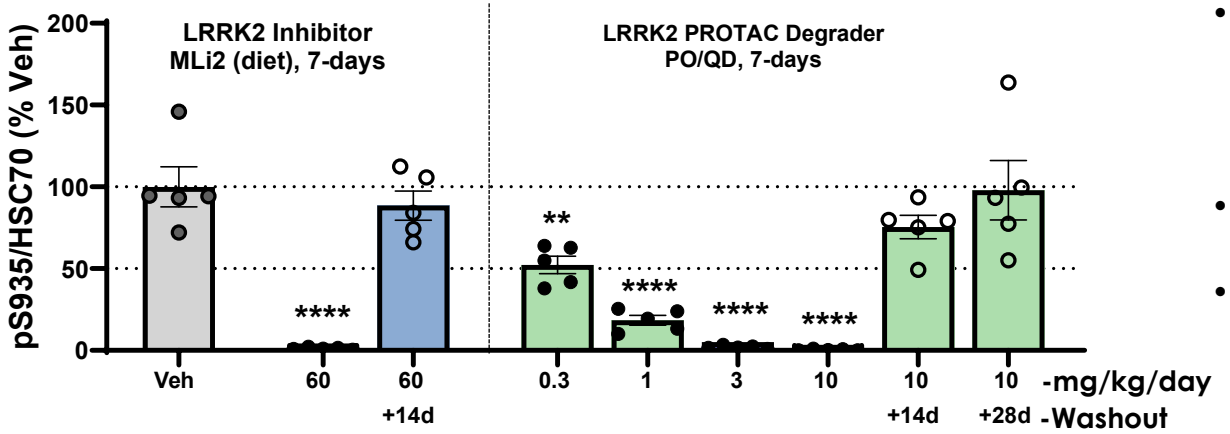
MoA, mechanism of action; LRRK2, Leucine-rich repeat kinase 2; Non-human primate (NHP), PK/PD, pharmacokinetic-pharmacodynamic; CSF, cerebrospinal fluid; BMP, basic metabolic panel; ULPC, ultra high-performance liquid-chromatography; MS, mass spectrometry

PROTAC LRRK2 degrader induced less severe Type II pneumocyte enlargement in mice compared to a kinase inhibitor

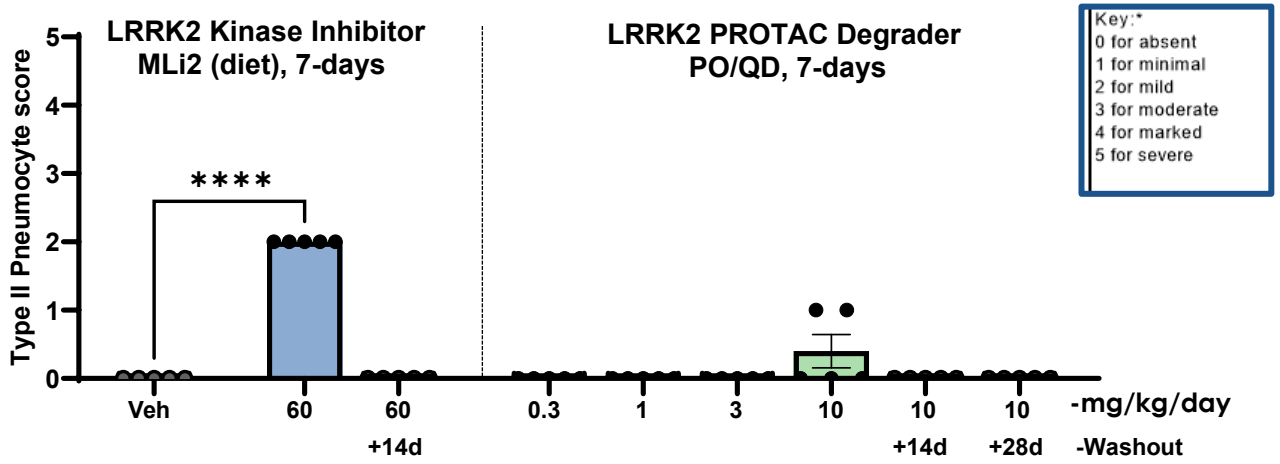
LRRK2 Degradation/ Target Engagement



LRRK2 Kinase Inhibition/ Target Engagement



Lung Type II Pneumocyte Enlargement/ Hypertrophy (Histopathologic Score)



- After 7 days of oral daily dosing, a PROTAC LRRK2 degrader induced less severe Type II pneumocyte enlargement compared to kinase inhibitor
- Effect is reversible after 14-day wash-out
- In tox studies to date, there has been no evidence of collagen deposition in lung with PROTAC LRRK2 degraders in nonhuman primates (data not shown)

PO, oral dosing; QD, once daily dosing

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

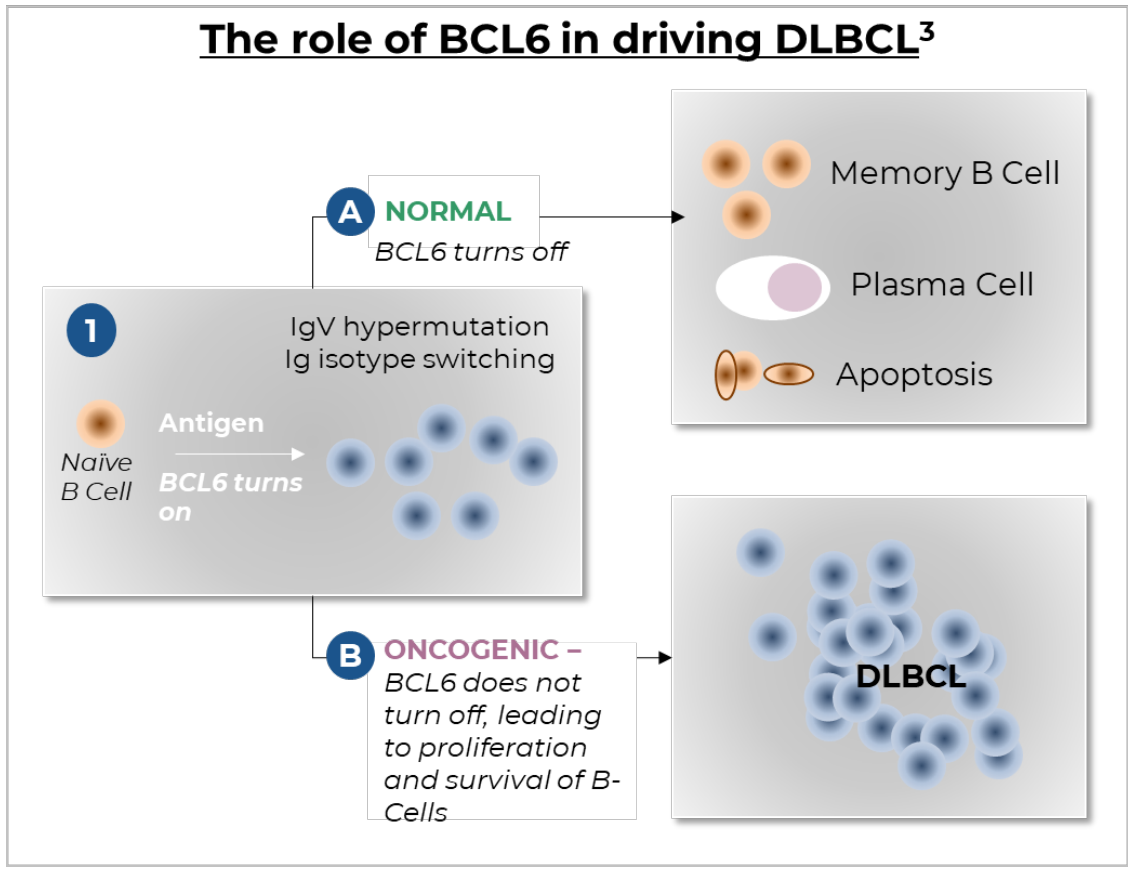
ARVINAS

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

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

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

BCL6 also play a role in the biology of Burkitt's Lymphoma, Follicular Lymphoma, T-cell lymphomas, and solid tumors



ARV-393: Phase 1 trial currently enrolling patients with B-cell lymphomas

BCL6, B-cell lymphoma 6; DLBCL, diffuse large B cell lymphoma; Ig, immunoglobulin; IND, investigational new drug application

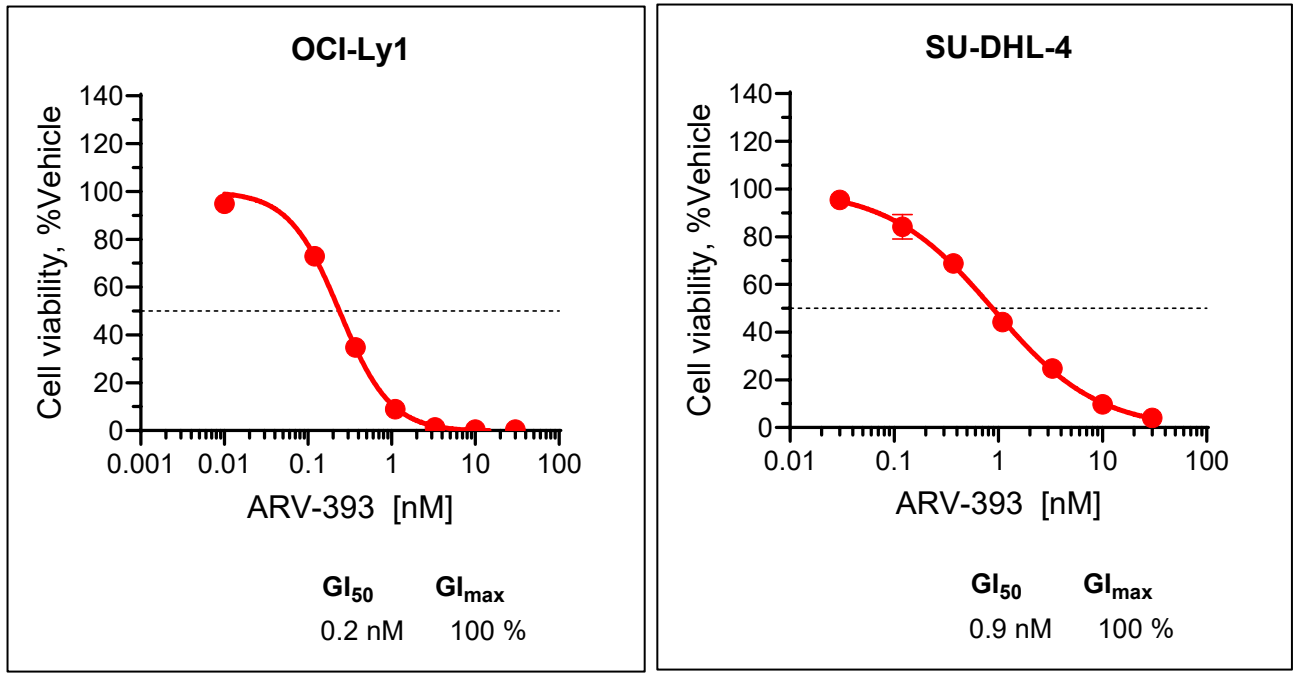
[1]. J Iqba et. al., 2007; [2].2023 Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia Disease Landscape & Forecast Report from Decision Resources; includes US, EU4, UK, and Japan

[3]. Figure adapted from Pasqualucci et. al., 2003 (figure at bit.ly/3Q8IGHH)

ARV-393 has broad antiproliferative activity in-vitro against numerous NHL cell lines

Potent BCL6 degradation leads to robust in vitro antiproliferative activity in GCB, ABC and BL cell lines

Antiproliferative activity in GCB cell lines at increasing drug concentrations



BCL6 degradation in all tested GCB, ABC and BL subtypes

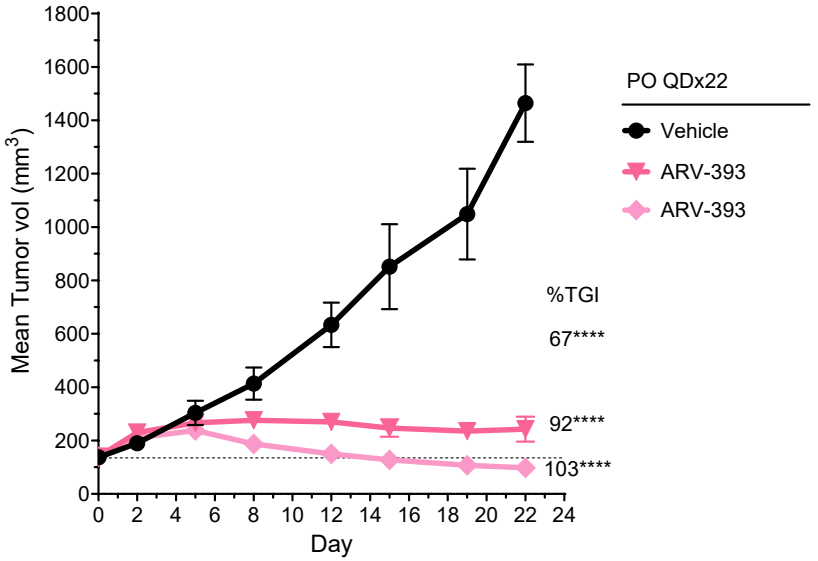
Cell line	Subtype	DC_{50} (nM)	D_{Max}	9-Day GI_{50} (nM)
OCI-Ly-1	GCB	0.06	97%	0.2
OCI-LY-7	GCB	0.10	97%	1.2
OCI-LY-10	ABC	0.11	95%	0.4
SUDHL2	ABC	0.07	95%	0.2
SUDHL4[a]	GCB	0.16	95%	0.9
SUDHL6	GCB	0.14	96%	0.9
Daudi	BL	0.15	99%	2.9
Ramos	BL	0.09	100%	0.4

Data presented at American Association for Cancer Research, April 2024

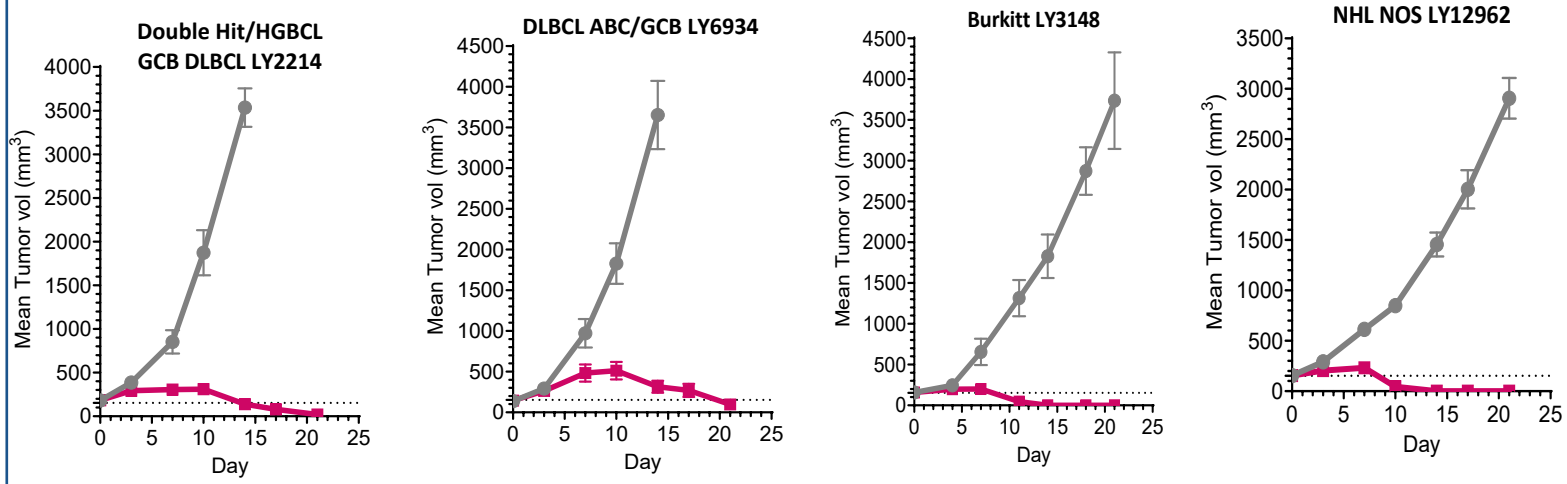
GCB: Germinal Center B-Cell; ABC: Activated B-Cell; BL, Burkitt lymphoma; DC_{50}, 50% degradation of target protein; GI_{50}, 50% growth inhibition, GI_{max}, maximum growth inhibition
[a]SU-DHL-4 is a triple hit, high grade BCL and GCB R-CHOP resistant cell line

ARV-393 shows robust tumor inhibition in murine models of DLBCL and other subtypes of Non-Hodgkin's Lymphoma

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



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



4 mice/group, PO QDx21
Vehicle
ARV-393

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

SELECT PRECLINICAL PROGRAM

KRAS G12D-targeted PROTAC degrader

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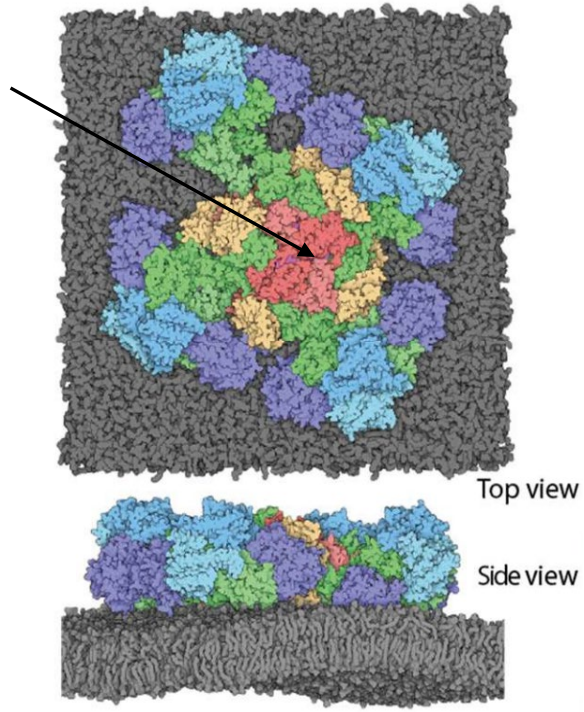
KRAS-targeting PROTAC may provide a significant advance in treatment for multiple cancers

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

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

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



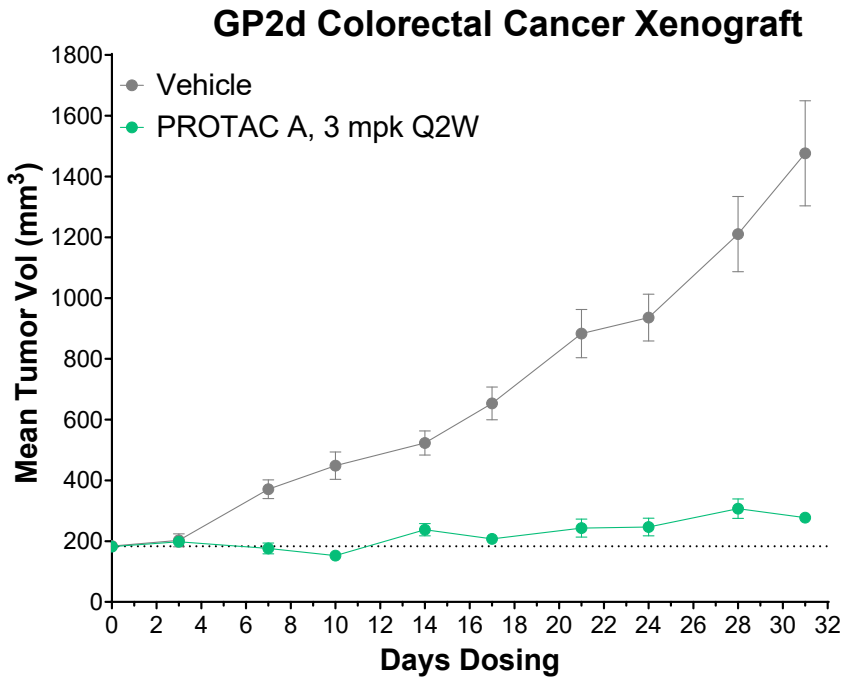
Mysore et al., BioRxiv, 2020

KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); G12D, mutations in codon 12 on KRAS oncogene
[1]Lee, *et al*. npj Precis. Onc. 2022. [2]Cook *et al.* Nat Comm 2021. [3]Prior *et al.* Cancer Research 2020. [4]NIH TCGA: https://www.cbioportal.org

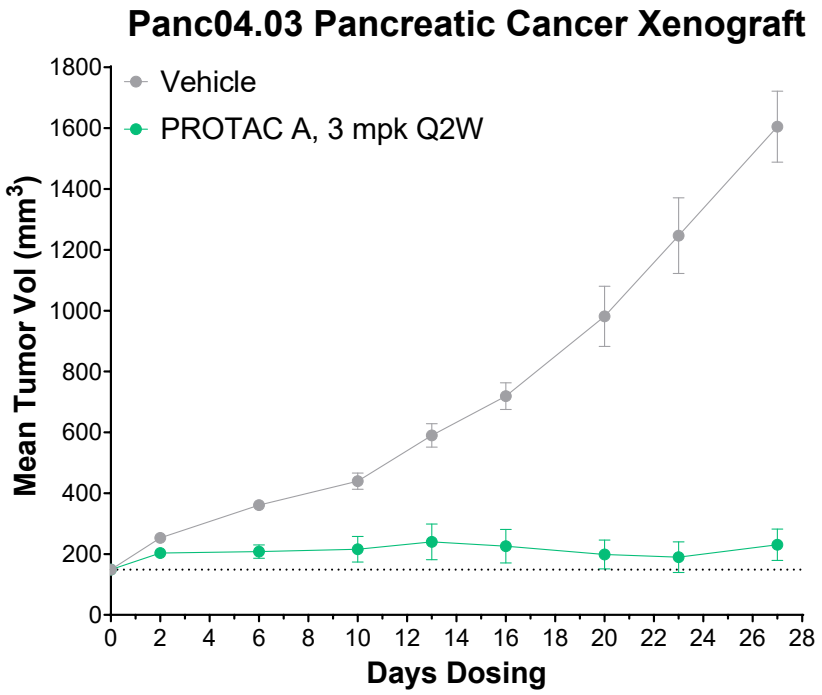
KRAS G12D-targeting PROTAC degrader demonstrates robust tumor growth inhibition with every other week dosing

ARVINAS

Colorectal cancer xenograft preclinical model



Pancreatic cancer xenograft preclinical model

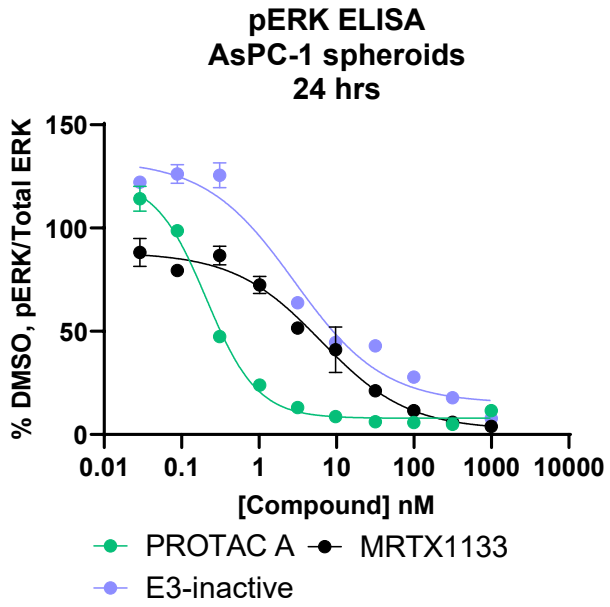


KRAS, Kirsten rat sarcoma (a frequently mutated oncogene in cancers); G12D, mutations in codon 12 on KRAS oncogene; mpk, milligrams per kilogram; Q2W, once every 2 weeks

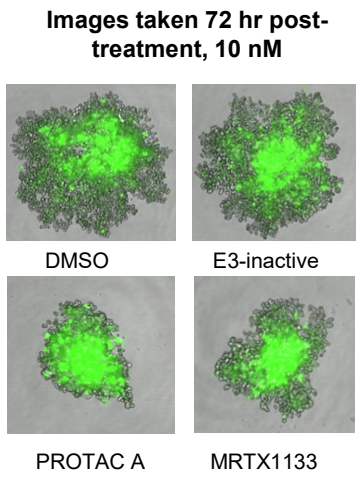
KRAS G12D-targeting PROTAC degrader potently suppresses signaling and proliferation versus an inhibitor

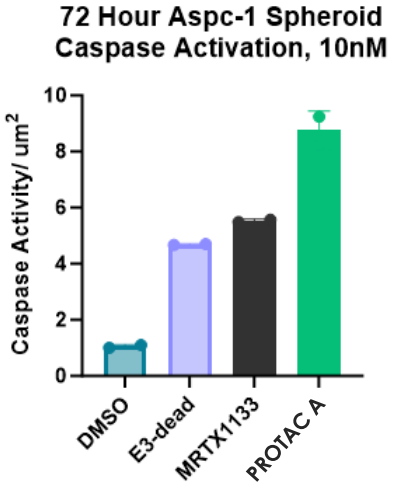
In preclinical models, a KRAS G12D-targeting PROTAC degrader demonstrated potent outcomes in multiple measures of cancer cell inhibition

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

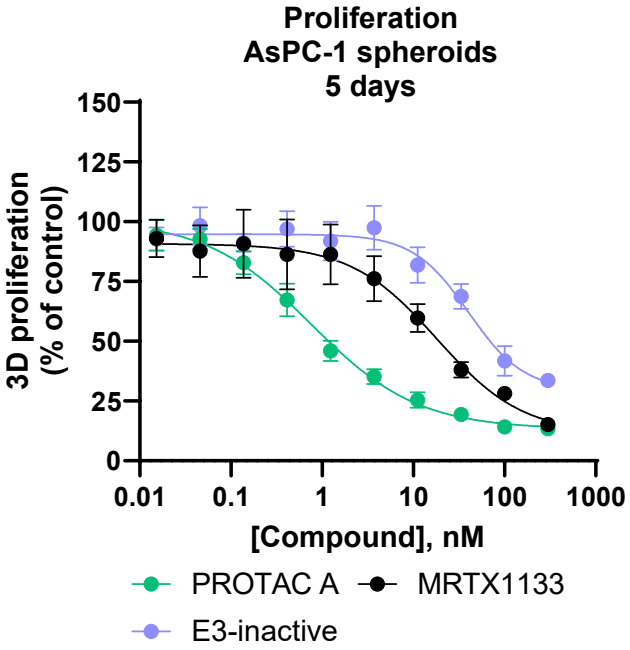


Spheroid size reduction and apoptosis induction





Proliferation
PROTAC **30-fold** more potent



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

Significant milestones anticipated in 2025

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Vepdegestrant with Pfizer

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

Expected near-term **monotherapy milestones**:

- **1Q25:** Phase 3 VERITAC-2 **topline data**
- **2025:** 2L monotherapy New Drug Application submission

Expected near-term **combination milestones**:

- **4Q24:** Vepdegestrant + abemaciclib data at SABCS (December)
- **2025:** Initiate 1L and 2L phase 3 combination trials[b]
  - 1L: vepdegestrant + atirmociclib or palbociclib
  - 2L: vepdegestrant + palbociclib and/or another CDK4/6i

Wholly-owned pipeline

Potential first-in-class, next-generation therapies

Expected near term milestones:

- **2Q25:** Initial ARV-102 (LRRK2 degrader) Phase 1 data at AD/PD (April 2025)
- **1H25:** Initiate Phase 1 trial with ARV-102 in patients with PD
- **2025:** ARV-393 (BCL6 degrader) Phase 1 data
- **2025:** Submit IND for PROTAC KRAS G12D degrader

Strong capital position with $1.1B cash on hand and runway into 2027[c]

ER, estrogen receptor; HER2, human epidermal growth factor 2; PCD, primary completion date; SABCS, San Antonio Breast Cancer Symposium; CDK4/6i, cyclin-dependent kinase inhibitor; LRRK2, leucine-rich repeat kinase 2; AD/PD, Alzheimer's disease and Parkinson's disease Conference; KRAS, Kirsten rat sarcoma viral oncogene homolog; G12D, mutations in codon 12 on KRAS oncogene; PD, Parkinson's disease; PSP, progressive supranuclear palsy; BCL6, B-cell lymphoma 6

[a] Clarivate/Decision Resources Group – Breast Cancer Disease Landscape & Forecast (Nov 2023). 2032 Projection.; [b] Final designs and combinations based on internal evaluation of data from TACTIVE-U (ClinicalTrials.gov Identifiers: NCT05548127, NCT05573555, and NCT06125522), VERITAC-3 study lead-in (NCT05909397), and TACTIVE-K (NCT0620683); [c] Cash, cash equivalents, and marketable securities position as of September 30, 2024

Thank You

For More Information

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