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ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE®
July 26-30, 2021 > DENVER, USA AND ONLINE

Heterobifunctional Degrader Molecules that lead to the clearance of Pathologic Proteins in Neurodegeneration

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Safe harbor and forward-looking statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the development and regulatory status of our product candidates, such as statements with respect to our lead product candidates, ARV-110, ARV-471 and ARV-766 and other candidates in our pipeline, and the timing of clinical trials and data from those trials and plans for registration for our product candidates, and our discovery programs that may lead to our development of additional product candidates, the potential utility of our technology and therapeutic potential of our product candidates, the potential commercialization of any of our product candidates, the potential benefits of our collaborative partnerships, and the Bayer joint venture, and the sufficiency of our cash resources. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various risks and uncertainties, including but not limited to: whether we will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-471, initiate and complete other clinical trials for our product candidates, and receive results from our clinical trials on our expected timelines, or at all, whether our cash resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements, each party's ability to perform its obligations under our collaborations and/or the Bayer joint venture, our expected timeline 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 the Company's quarterly and annual reports on file with the 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.

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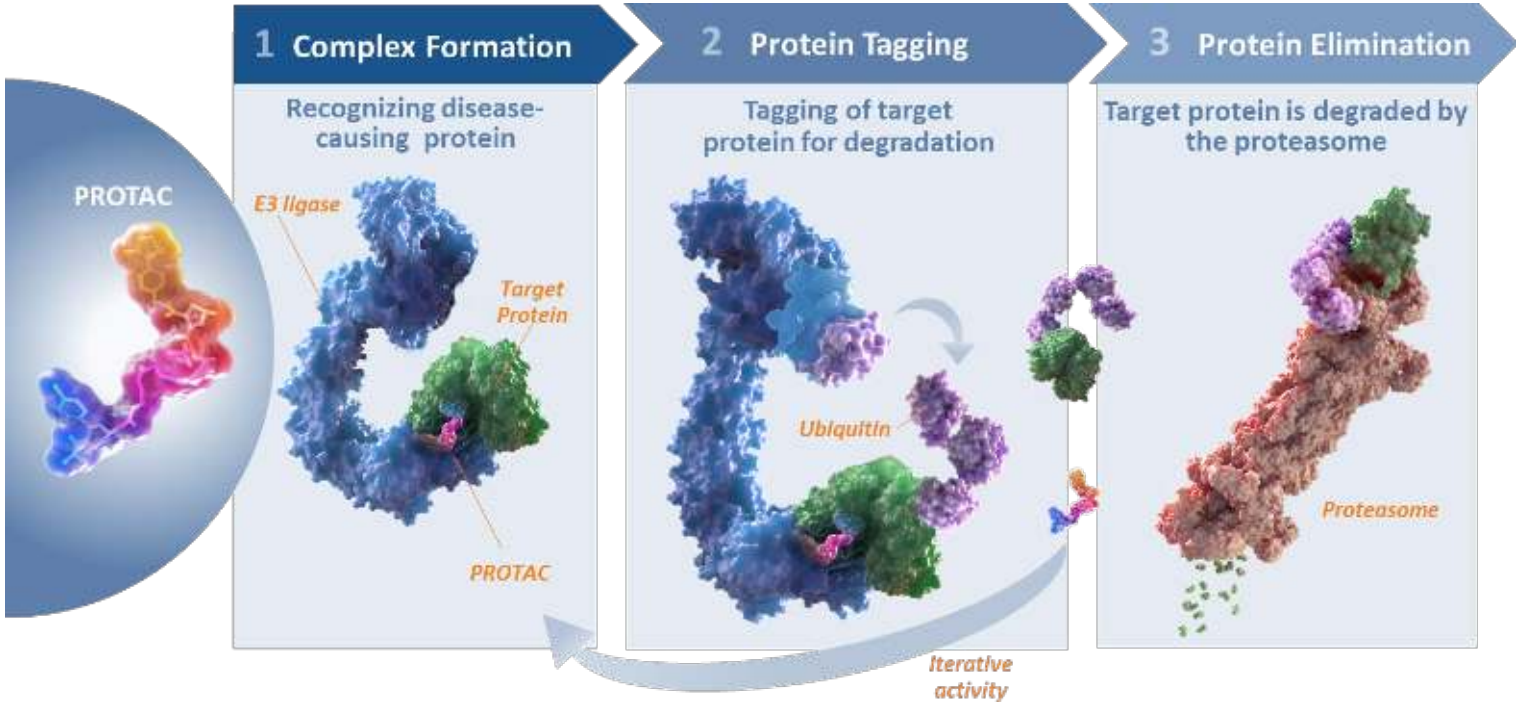
PROTAC® protein degraders harness the ubiquitin-proteasome system to induce the degradation of disease-causing proteins



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Arvinas' pipeline encompasses a range of validated and undruggable targets in oncology, I-O, and neuroscience

	ARVN Program	Indication	Exploratory	Research	IND Enabling	Phase 1	Phase 2	Phase 3
Oncology / Immuno-oncology	ARV-110	mCRPC						
	ARV-766	mCRPC						
	AR-V7	mCRPC						
	ARV-471	ER+/HER2- Breast Cancer						
	BCL6	B-cell Malignancies						
	KRAS	NSCLC, CRC, Pancreatic						
	Undisclosed	Solid Malignancies						
	Myc	Solid Malignancies						
	HPK1	Solid Malignancies						
Neuroscience	Tau	FTLD-TAU, PSP, AD						
	Alpha Synuclein	MSA, Parkinson's						
	mHTT	Huntington's						
	Undisclosed	Neurodegeneration						

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ARV-471 and ARV-110: Proof-of-concept and opportunities to benefit patients in large areas of unmet need

ARV-471

Estrogen receptor-degrading PROTAC®

Breast Cancer

Potential best profile of any ER-targeting therapy:

- Tolerability
- **ER degradation**
- Clinical benefit

Potential future endocrine therapy of choice in both adjuvant and metastatic settings

Initiated Phase 2 VERITAC trial; while Phase 1 dose escalation continues

>200k patients† per year with high unmet need

ARV-110

Androgen receptor-degrading PROTAC®

Prostate Cancer

AR degradation and clear signals of efficacy observed in late-line mCRPC

Initiated Phase 2 ARDENT trial; two potential paths to registration: 3L molecularly defined, and broader 1L/2L

Extensive molecular profiling of tumors to understand drivers of resistance

>250k patients† per year with high unmet need

† US incidence data from SEER database
AR, androgen receptor; ER, estrogen receptor

Data as presented 12/14/2020

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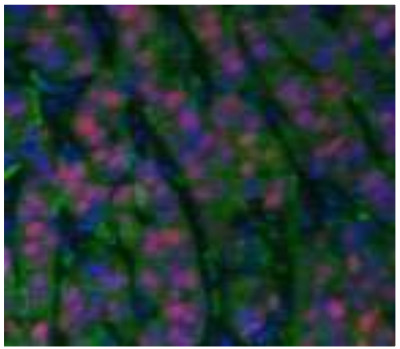
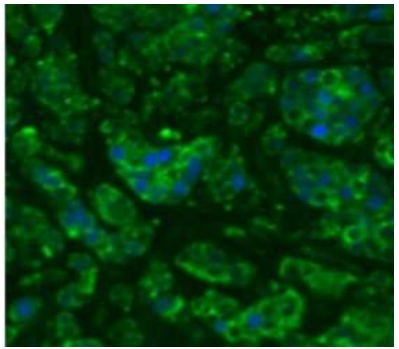
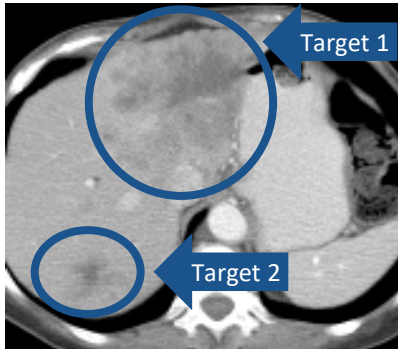
The Ultimate Platform Validation: PROTAC®s can be Drugs

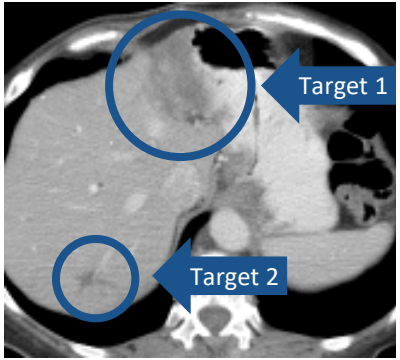
***ARV-471**: ER Degradation & Confirmed RECIST Partial Response (cPR) in late-stage patients with extensive prior therapy*

Baseline	After treatment 60 mg ARV-471	Baseline CT Scan	After 4 Cycles









Estrogen receptor Nuclei Cytokeratin

Data as presented 12/14/2020

ER degradation tumor biopsies

51% reduction in target lesions (RECIST partial response)

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Integrated PROTAC® drug discovery for Neurology

Genetic Disease:
Protein is the cause of the disease

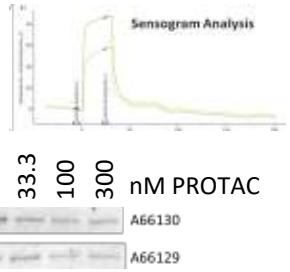
Translational Medicine:
Biomarkers support efficient path to assessing efficacy in humans

PK/PD Models:
Protein target engagement in vivo

Neurodegeneration
Precision Medicine
Genetic/
Proteinopathy
Target root cause
PROTAC
differentiator
Biomarker PoC

Discovery Engine:
Ligand ID-DEL, HTS, HT-chem/SAR
E3KnowlegeBASE, structure, AI

Discovery Engine:
Biophysics, Ternary, Mechanistic
Degradation, Proteomics



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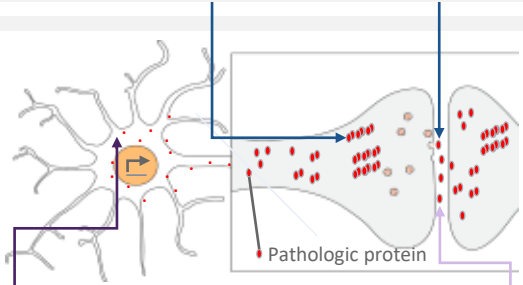
PROTAC® heterobifunctional degrader molecules create a strong opportunity in neuroscience compared to other modalities

PROTAC® degrader small molecules may overcome the limitations of other platforms

PROTAC *Potential*

- Reduce intra- and extracellular pathologic protein
- Discriminate between wild type and pathologic protein
- Oral administration with BBB biodistribution



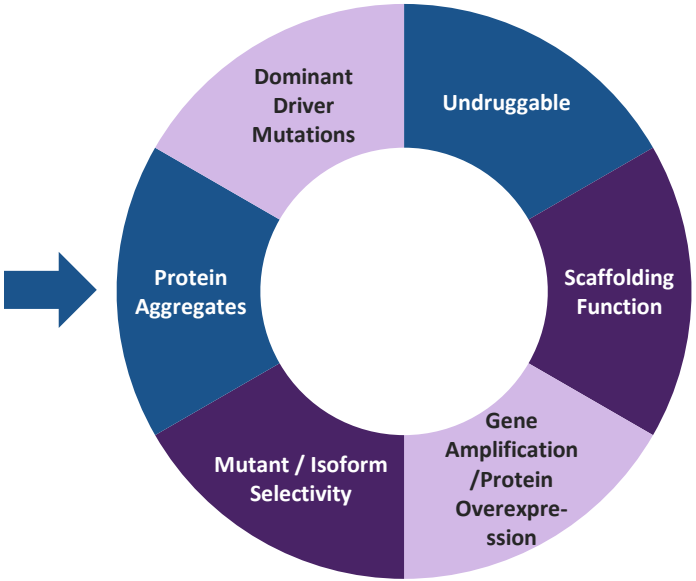
ASO

- Requires intrathecal dosing
- Does not discriminate wt from pathologic protein

Ab

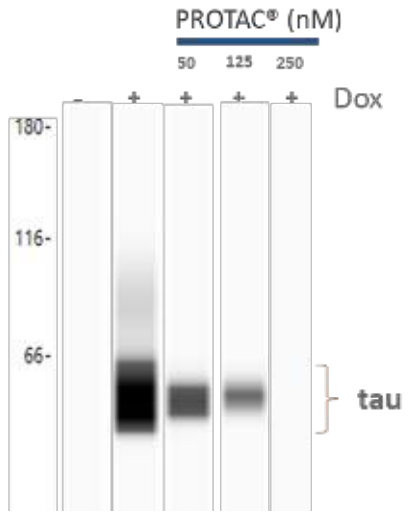
- Blocks only extracellular pathologic protein
- IV dosing results in only 0.5% in CSF

PROTAC *Tenets -- Differentiation from small molecule inhibitors*



PROTAC® small molecules can degrade tau P301L insoluble aggregates

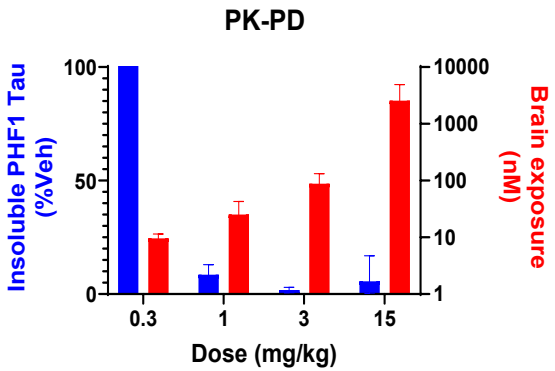
In vitro insoluble tau PROTAC degradation



*on mechanism

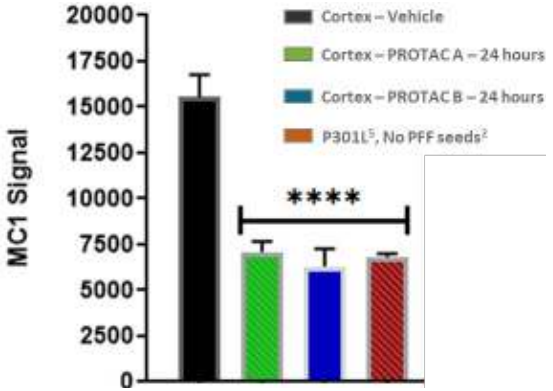
In vivo insoluble tau PROTAC degradation

Tg2508 24h post single PROTAC IV dose



Reduced Seed Potential Ex vivo brain extracts

Tg2508 brain extracts 24h post single IV dose



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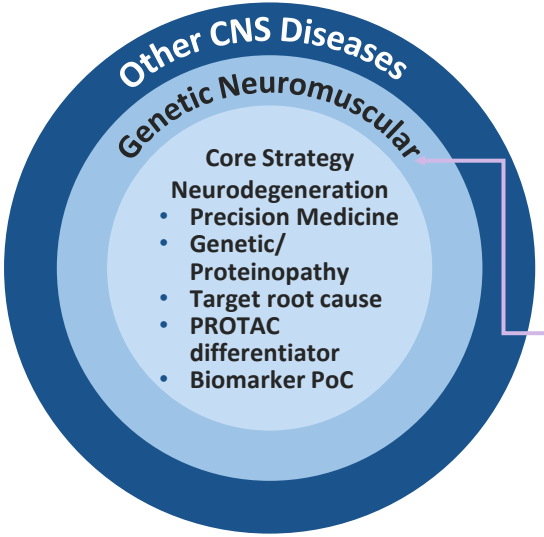
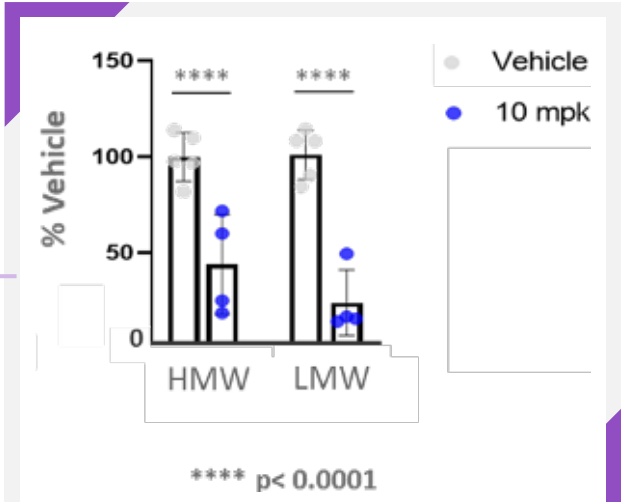
Neuromuscular Diseases: PROTAC®s degrade toxic aggregating protein within muscle cells

Fit with Neuroscience Strategy

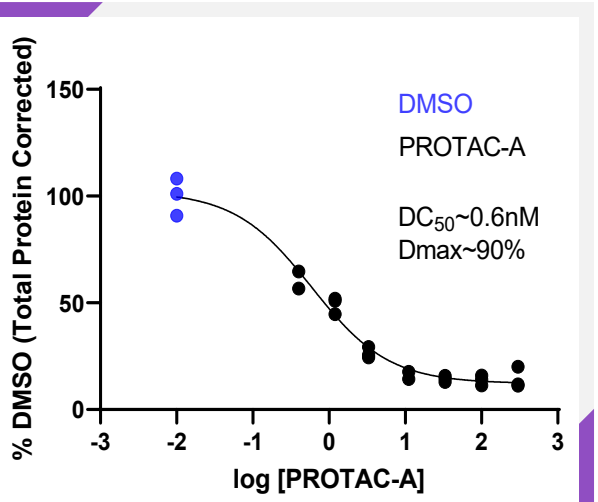


PROTAC degrades toxic aggregating protein in muscle following oral administration in a disease mouse model and in iPSC- myotubes from patients

Neuromuscular degeneration Mouse Model (3xQD PO)



hiPSC-patient derived myotubes Potent Degradation of aggregate



*Functional studies are ongoing in mouse model

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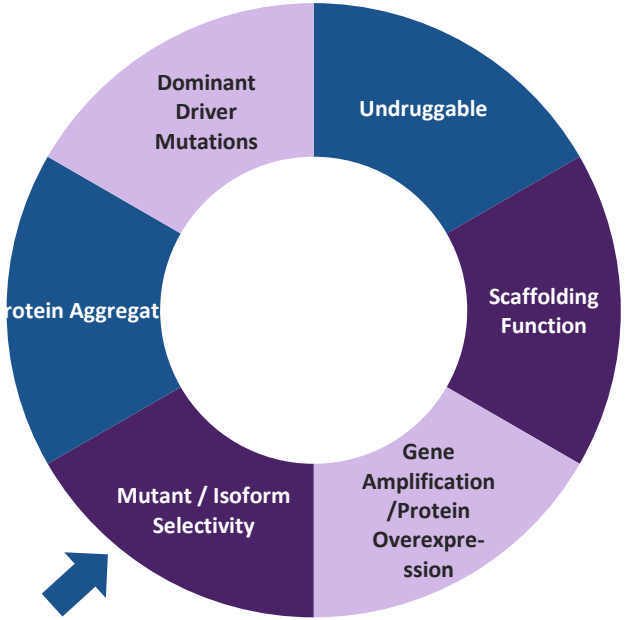
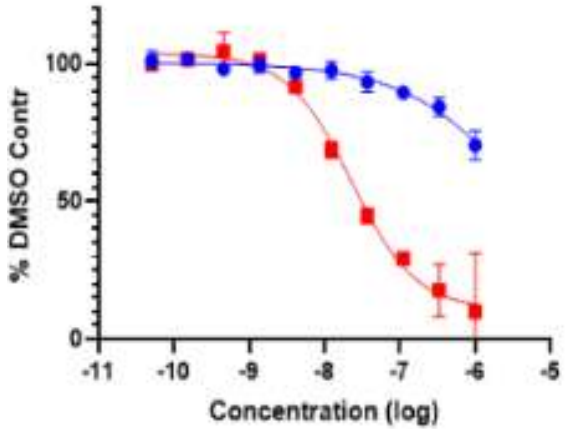
PROTAC® targets mutant and spares WT to tackle genetically defined disease target in CNS

Fit with Tenets of PROTACs



PROTAC selectively degrades mutant and spares WT protein



WT DC_{50} >5µM
Mutant protein DC_{50} = 23nM

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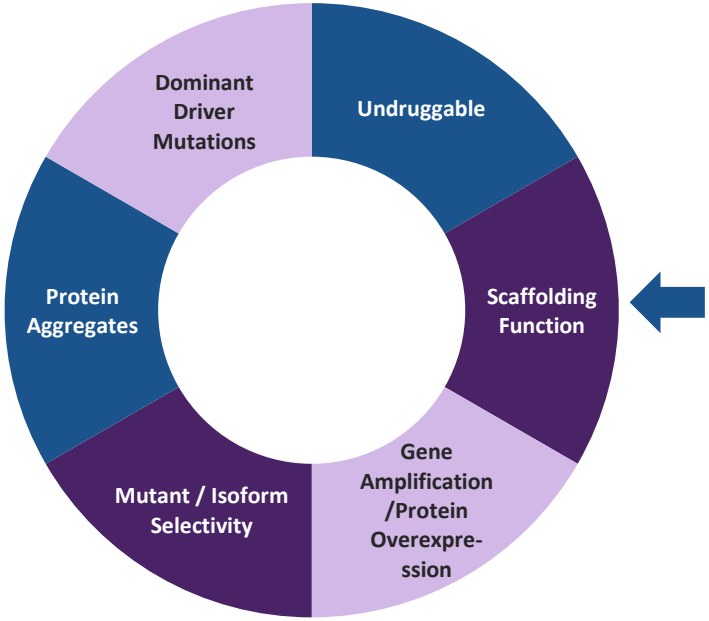
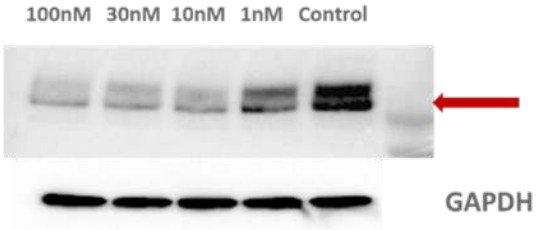
PROTAC®-B is on mechanism and degrades endogenous target in iPSC-derived microglia

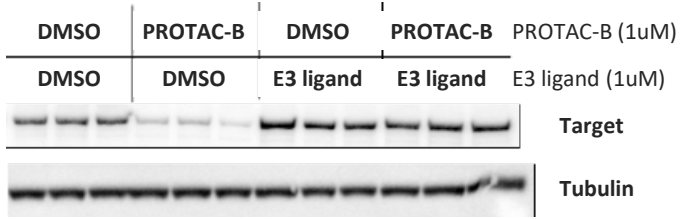
Fit with Tenets of PROTACs



PROTAC-B degrades endogenous target in iPSC-derived microglia



PROTAC-B degrades endogenous target and is on Mechanism



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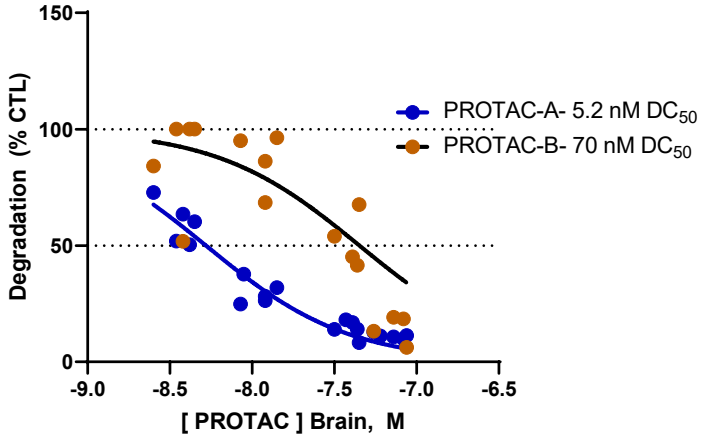
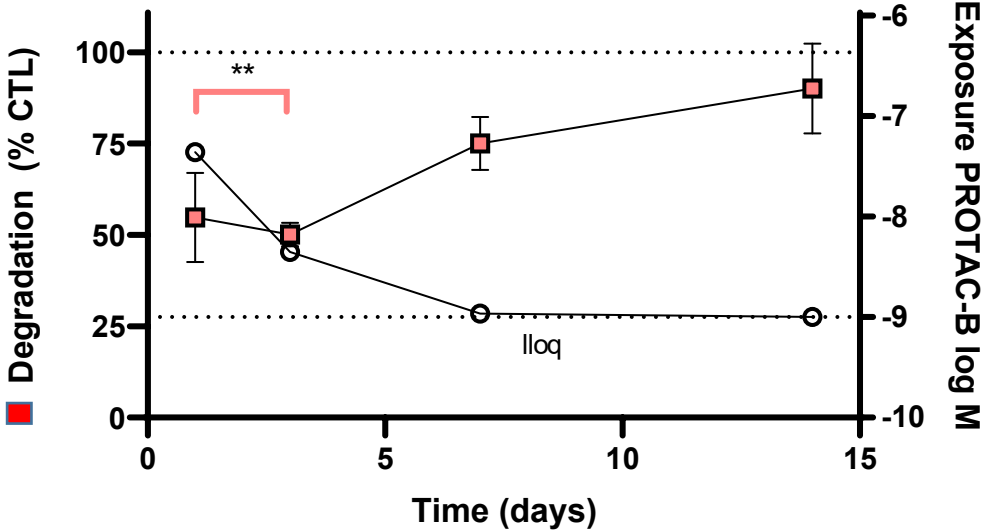
PROTAC®-B dose-dependently and durably degrades target in brain 24h following single oral administration

PROTAC-A and B Dose-Response PK/PD In Cortex 24h post dose



PROTAC-B PK/PD In Cortex following time-course



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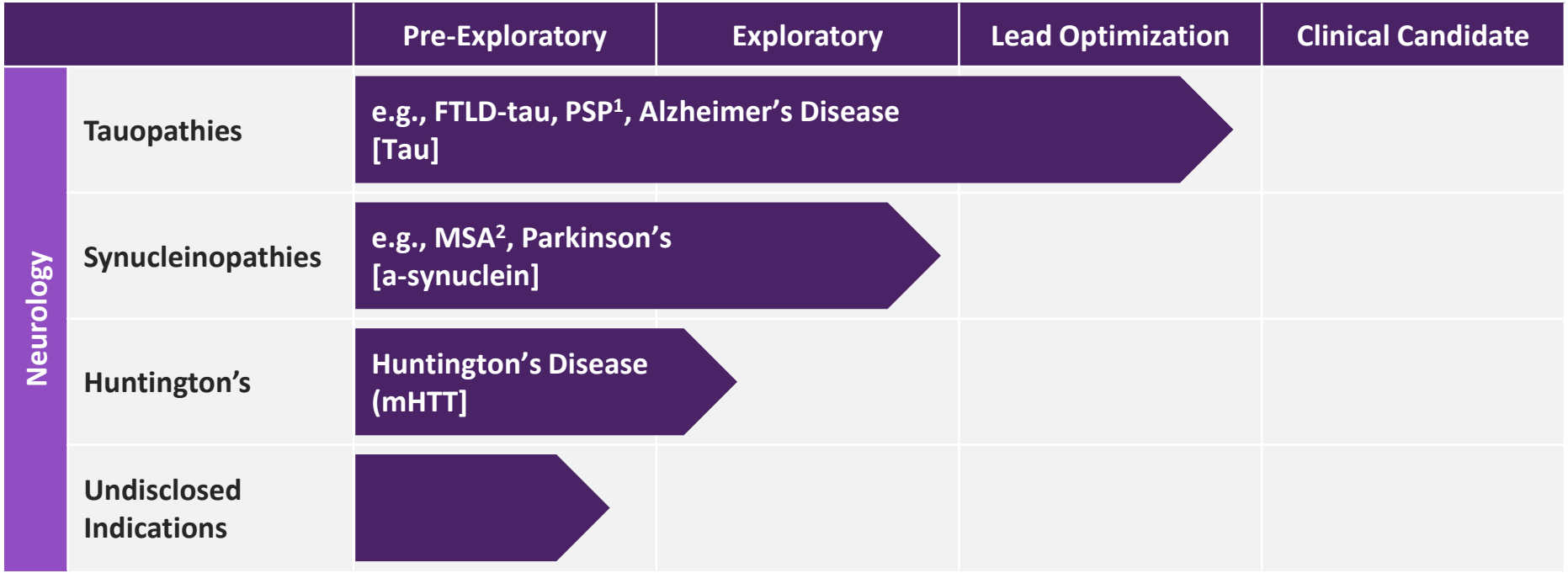
Building and accelerating exciting high potential neurology bifunctional degrader small molecule pipeline

Opportunity: No Approved Disease Modifying Therapies in Neurodegenerative Diseases



1- Progressive Supranuclear Palsy
2- Multiple Systems Atrophy

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Thank you to the fantastic team at Arvinas!!!