

UNLOCKING THE POTENTIAL OF AAV GENE THERAPY

Corporate Presentation | October 2022

Forward-Looking Statements

This presentation, posted to Voyager's website on August 18, 2022, contains forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "target," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about Voyager's ability to continue to identify and develop proprietary capsids from its TRACER AAV capsid discovery platform; Voyager's ability to identify and develop proprietary capsids from its TRACER AAV capsid discovery platform with increased transgene expression, increased blood-brain barrier penetration and increased biodistribution compared to conventional AAV5 and AAV9 capsids; Voyager's ability to utilize its novel proprietary capsids in its own product development programs and to progress its own product development programs; Voyager's ability to attract parties to license its novel proprietary capsids or to participate with Voyager in research and development collaborations utilizing its novel proprietary capsids; Voyager's ability to advance its AAV-based gene therapy and anti-tau antibody programs; Voyager's ability to perform its obligations under its license option agreements with Novartis and Pfizer; Voyager's entitlement to receive upfront, milestone and royalty based fees from Novartis and Pfizer under the respective license option agreements; Voyager's ability to maintain its current partnerships and collaborations and to enter into new partnerships or collaborations; and the sufficiency of Voyager's cash resources. These forward-looking statements are only predictions, and Voyager may not actually achieve the plans, intentions, or expectations disclosed in the forward-looking statements. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Voyager expected. Such risks and uncertainties include, among others, the severity and length of the COVID-19 health crisis; the continued development of various technology platforms, including Voyager's TRACER capsid discovery platform; Voyager's scientific approach and program development progress; the ability to attract and retain talented contractors and employees, including key scientists and business leaders; the ability to create and protect intellectual property; the sufficiency of cash resources; the possibility and the timing of the exercise of development, commercialization, license and other options under the Pfizer and Novartis license option agreements and other collaborations; the ability of Voyager to negotiate and complete other licensing or collaboration agreements on terms acceptable to Voyager and third parties; and the availability or commercial potential of Voyager's product candidates. These statements are also subject to a number of material risks and uncertainties that are described in Voyager's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, as updated by its subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which this presentation was posted to Voyager's website. Voyager undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Voyager Highlights

TRACER capsids have potential to address certain fundamental limitations for gene therapy

- Receptor identification further supports human translation potential

Transactions with Novartis and Pfizer provide external validation for TRACER capsids

- Pfizer exercised option to license a TRACER capsid for rare neurologic disease gene therapy; validation of a leading position in this field
- Novartis license option exercise decision expected by March 2023

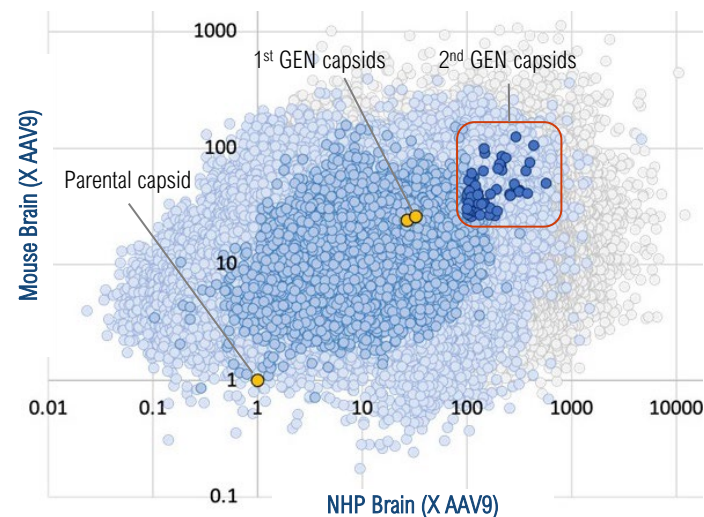
Prioritized pipeline programs designed for robust differentiation and efficient path to potential human proof-of-biology

- Targeting development candidate selection for three lead programs in 2022 and 1H 2023

TRACER: A breakthrough capsid discovery platform powering next-gen AAV

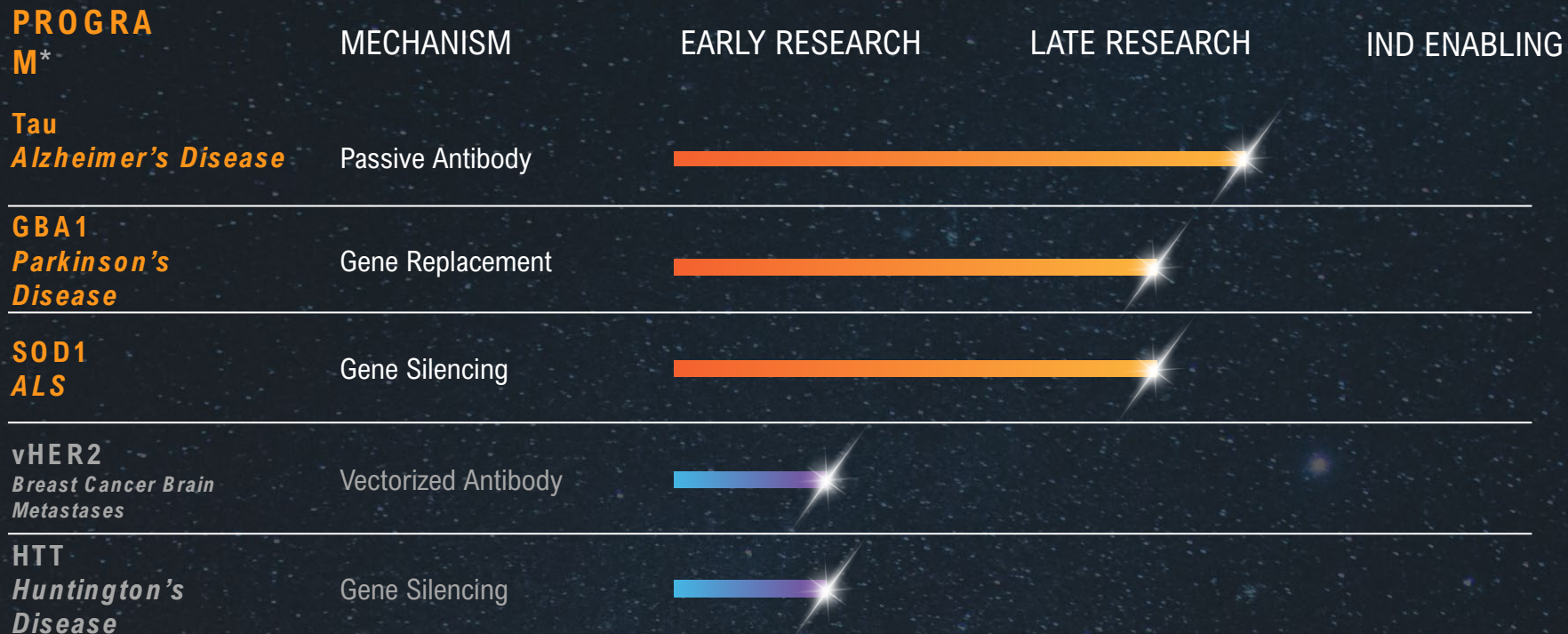
- ✓ Superior BBB penetration*
- ✓ Enhanced neuronal and glial cell tropisms*
- ✓ Broader therapeutic windows and de-targeting of undesired tissues*
- ✓ Cross species transduction and receptor characterization for a leading capsid support human translation potential
- ✓ Selected by Large Pharma partners and enabling other external development opportunities
- ✓ TRACER-derived capsids support internal pipeline programs

>100-fold improved CNS delivery across species



*Compared to conventional AAV9 dosed intravenously in non-human primates (NHPs)

Voyager Pipeline





*Programs named according to target and lead indication.

Voyager is partnering with Neurocrine Biosciences on a preclinical Friedreich's Ataxia (FA) program and two undisclosed discovery programs. Voyager has an option to co-develop/co-commercialize the FA program in the U.S. or to grant Neurocrine global commercial rights.








License option agreements for TRACER capsids

Potential for similar transactions across various target cells, tissues and transgenes

	Target* (Cells, Tissues, Transgenes)	Upfront Payment	Potential Option + Option Exercise Fees**	Potential Development + Commercial Milestone Payments	Total Potential Value	Tiered Royalties
 NOVARTIS	3 CNS targets (plus 2 possible undetermined targets)	\$54 million	\$98.5 million	\$1.5 billion	\$1.7 billion	Mid- to high-single-digit
 Pfizer	1 rare neurologic disease target	\$30 million	\$10 million – <i>completed</i>	\$290 million	\$340 million	Mid- to high-single-digit

\$94 million in total upfront payments and option exercise payments extended cash runway into 2024
Initial Novartis option exercise decision by March 2023

Partnerships expand number of programs that may leverage TRACER capsids

TARGET	PARTNER	DEVELOPMENT STAGE
CNS	 NOVARTIS	Undisclosed
CNS	 NOVARTIS	Undisclosed
CNS	 NOVARTIS	Undisclosed
Rare neurologic disease	 Pfizer	Undisclosed
Friedreich's Ataxia	 NEUROCRINE BIOSCIENCES	Undisclosed
CNS	 NEUROCRINE BIOSCIENCES	Undisclosed
CNS	 NEUROCRINE BIOSCIENCES	Undisclosed

Voyager retains global rights to all licensed TRACER capsids for use with other targets across various cells, tissues, and transgenes and to all other applications of the technology

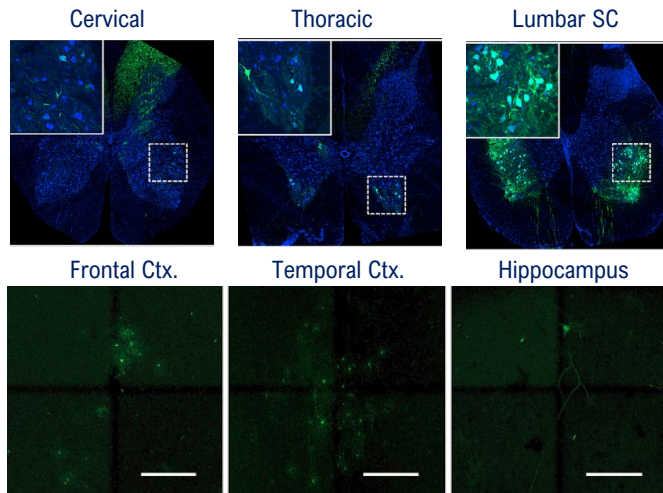
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TRACER CAPSID DISCOVERY PLATFORM

Limitations of AAV gene therapy with currently used capsids

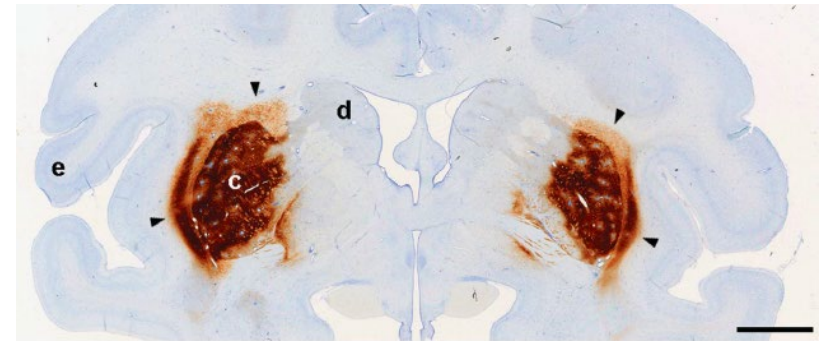
- **IV dosing:** Low BBB penetration and CNS cell transduction → inefficient delivery has necessitated high doses with weak pharmacology, and safety/tolerability risks
- **Direct CNS delivery** (into CSF or brain parenchyma) → localized delivery characterized by steep gradients and restricted spread, leading to safety/tolerability risks and/or inadequate efficacy

Heterogeneous CNS expression after intrathecal AAV9.GFP injection in NHP



Bey, *Mol Ther Meth Clin Dev*, 2020

Highly restricted localization of expression after intraputaminial AAV5.GFP injection in NHP



Samaranch, *Gene Ther*, 2017

TRACER platform enables discoveries of capsids with enhanced tropisms across cell types, tissues

Improved transduction efficiency

- Ability to produce capsids with enhanced tropisms for CNS and beyond, including cardiac and skeletal muscle, eye, and liver
- Enables both targeting and de-targeting of select tissues
- Additional capsid discovery campaigns in process

Top capsid candidates are being further refined

- Flexible library-generating method enables iteration and cross-species investigation
- Approach is tropism agnostic and species agnostic

Platform generates proprietary knowledge and IP covering promising capsids

- We believe capsids generated are patent-eligible, novel compositions of matter

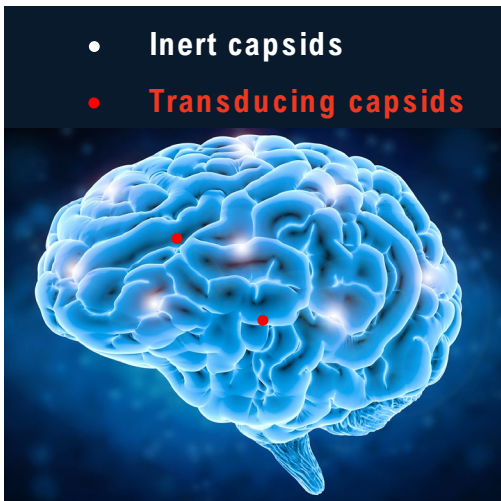


TRACER

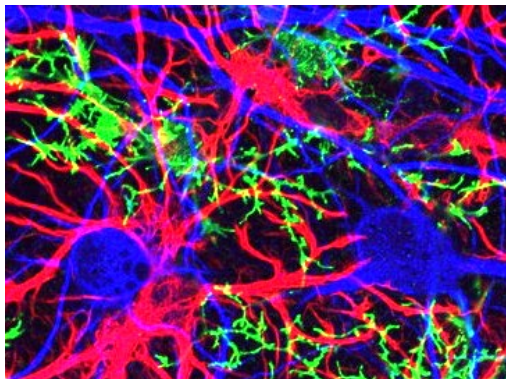
The TRACER Platform: Differentiating Features

TRANSDUCTION-DRIVEN *IN VIVO* SELECTION

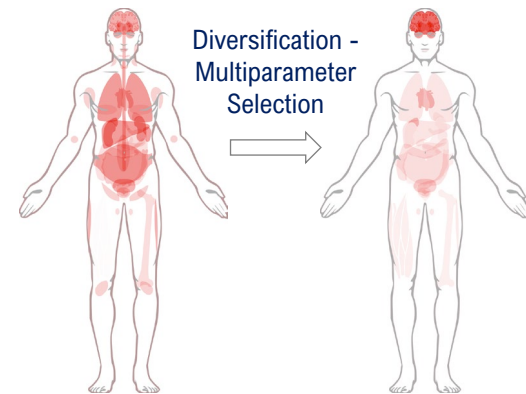
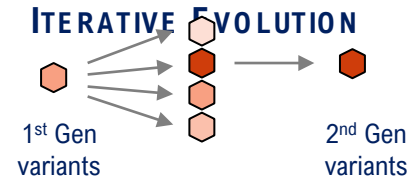
- Inert capsids
- **Transducing capsids**



CELL-SPECIFIC BIOPANNING



ORGAN-SPECIFIC TARGETING BY ITERATIVE EVOLUTION



Rapid and focused screening method yields fit-for-function capsids with minimal false

TRACER multi-species iterative evolution maximizes capsid potential, translatability

AAV SEROTYPES 5, 9

PEPTIDE DISPLAY
DIVERSIFICATION

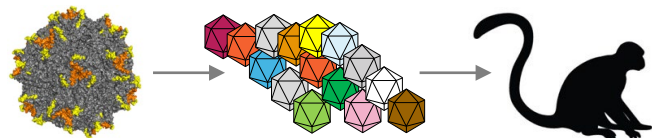
RNA-DRIVEN
BIOPANNING (2X)

SYNTHETIC
MULTIPLEX ANALYSIS

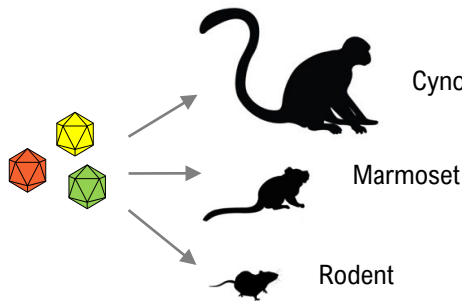
CROSS-SPECIES
CHARACTERIZATION

MATURATION

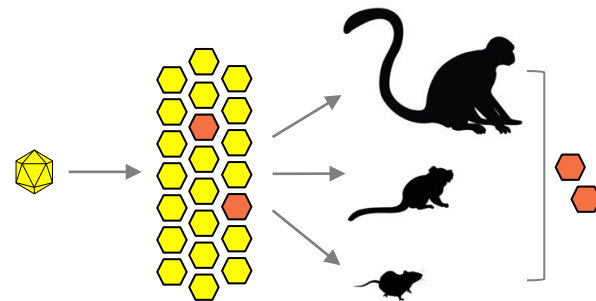
MULTI-PARAMETER OPTIMIZATION
(POTENCY, TROPISM, MANUFACTURING)



~2e7 Variants



100-1,000
Top candidates



1-10 Stem
candidates

~300,000
Variants

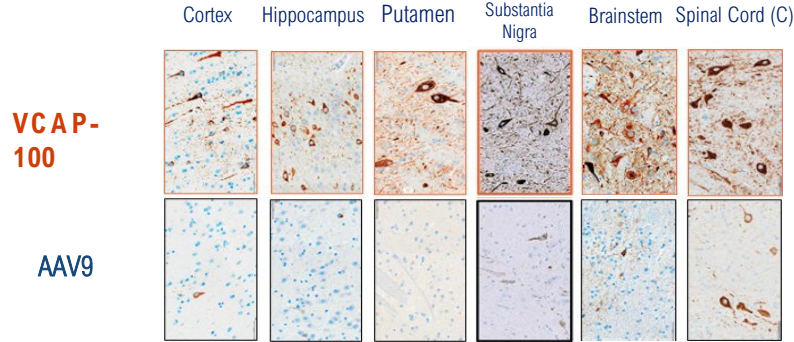
>10 Gen2
candidates

Maturation of top 1-10 stem candidates enables further improvements for potency, tropism, detargeting of select tissues, and manufacturability

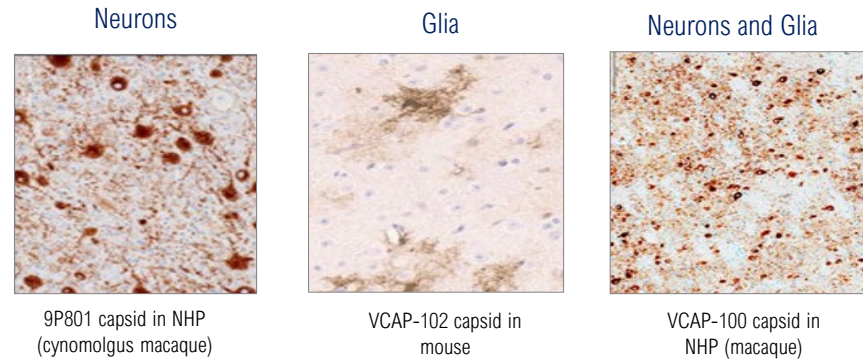
Cross-species characterization improves potential for human translatability

Novel capsids with potential to transform treatment of CNS diseases

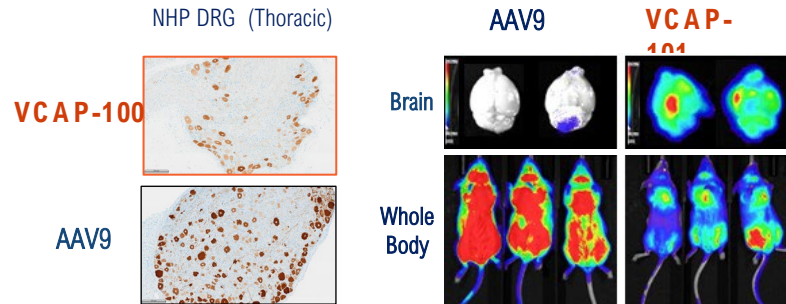
Widespread CNS distribution



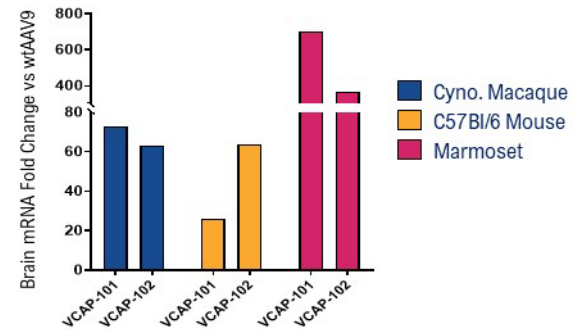
CNS neurons and glia transduced



Detargeting of peripheral tissues



Cross species transduction



Receptor identified for TRACER capsid

- Receptor identified for one of our most promising TRACER AAV capsids
- Expression confirmed in human endothelial cells and multiple CNS cell types
 - Data to be shared at ESGCT Annual Meeting



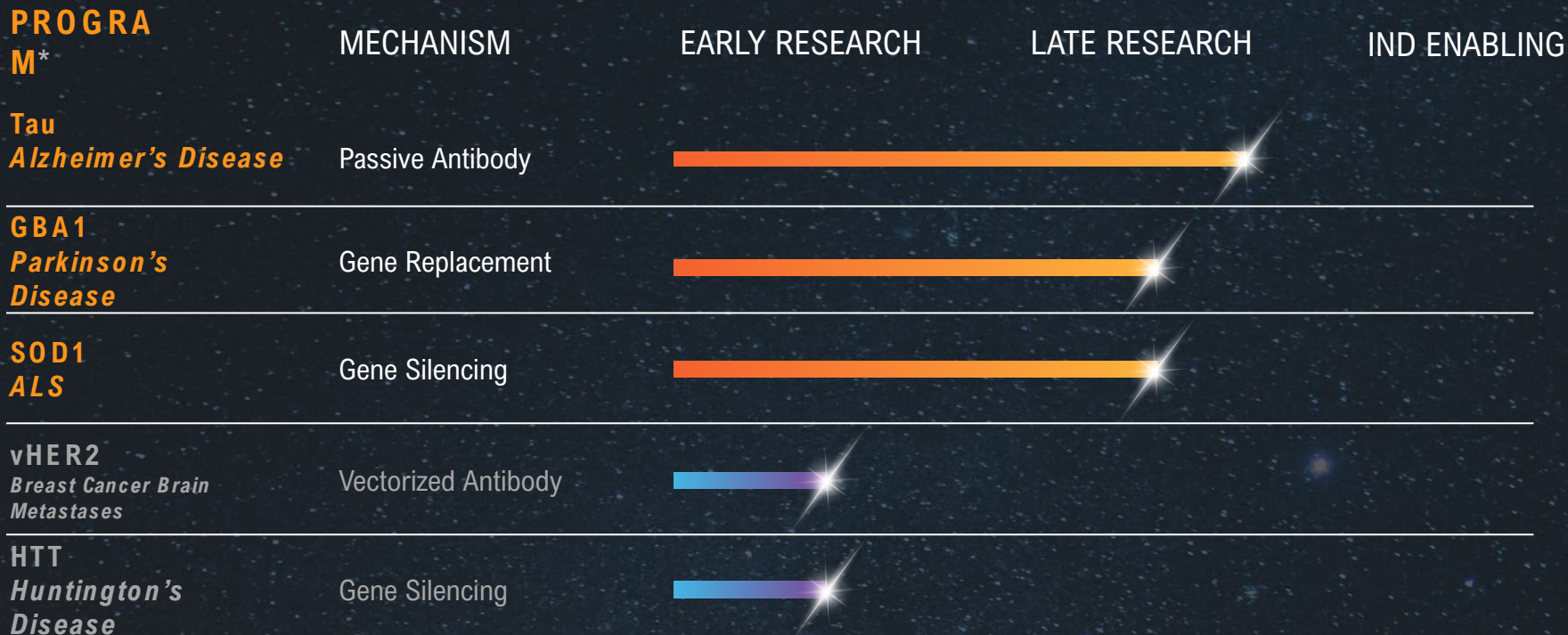
- *Characterizing the applicable receptor increases probability that the related capsid will cross the BBB in humans*
- Should facilitate rational design of AAV capsids for targeted IV delivery
- May enable IV delivery to CNS for diverse therapeutic modalities
 - Preclinical experiments underway

TRACER capsids designed to enable differentiated therapeutic opportunities



PRODUCT DEVELOPMENT

Prioritized Voyager Pipeline



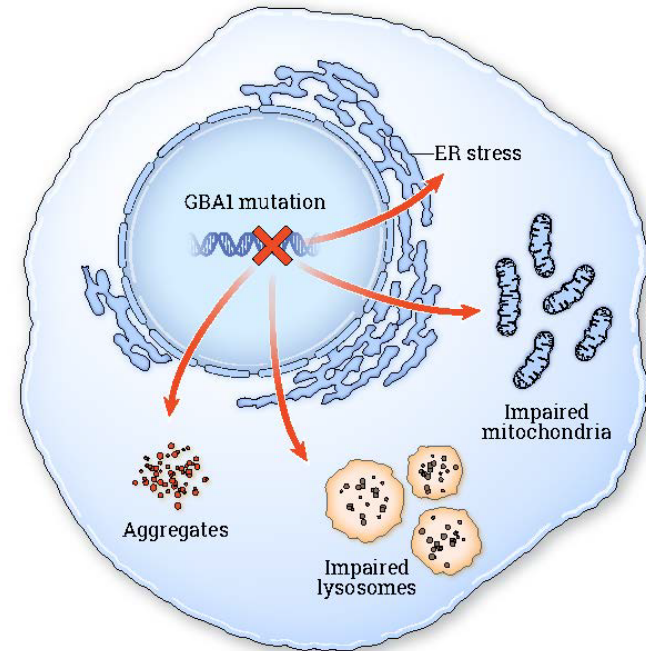
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GBA1 Parkinson's Disease

Parkinson's disease (PD) with GBA1 mutations

- ~1M PD patients in the U.S., >10M worldwide
- Up to 10% of PD patients have a GBA1 mutation, and these mutations increase the risk of PD ~20-fold*
- GBA1 encodes lysosomal enzyme, GCCase, which degrades glycosphingolipid substrates
- GBA1 mutations decrease expression of GCCase protein, leading to
 - Substrate elevation
 - Accumulation of α -synuclein aggregates
 - Neuronal toxicity
- Potential for treating idiopathic PD

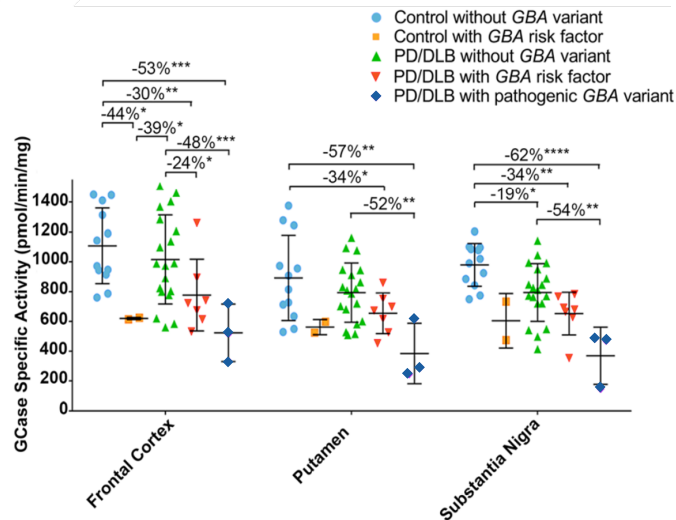


GCCase: glucocerebrosidase

Adapted from Mazulli et al., Cell, 2011

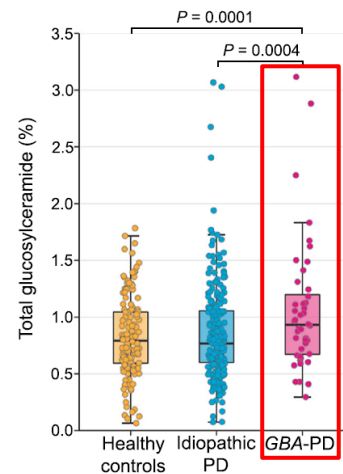
GBA1 biomarkers offer potential for rapid proof-of-biology in PD-GBA

Reduced GCase activity in key brain regions due to GBA mutations



Moors, *Mol Neurobio*, 2019

Elevated CSF GluCer levels in GBA-PD patients

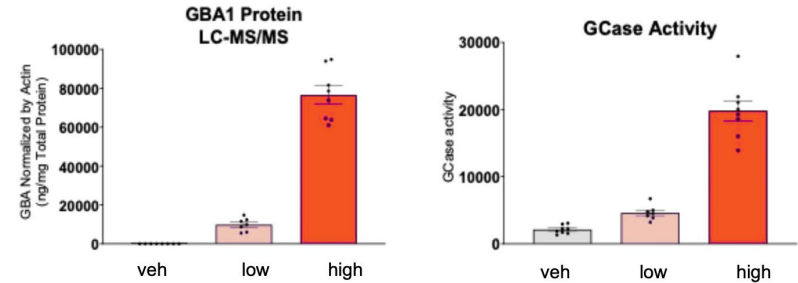


Huh, *npj Parkinson's Disease*, 2021

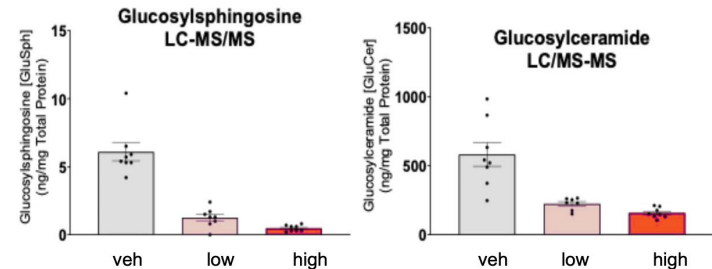
Restoration of GCase with IV-administered, BBB-penetrant AAV capsids

- BBB-penetrant AAV capsid provides *in vivo* proof-of-concept (POC) for increase in GCase with concomitant reduction of substrates
- Delivery of therapeutically relevant levels of GCase may attenuate disease process, and potentially slow neurodegeneration
- IV delivery with CNS-tropic capsid may enable widespread distribution to multiple affected brain regions and avoid need for more invasive approaches

GCCase increased in GBA1 LOF mouse model

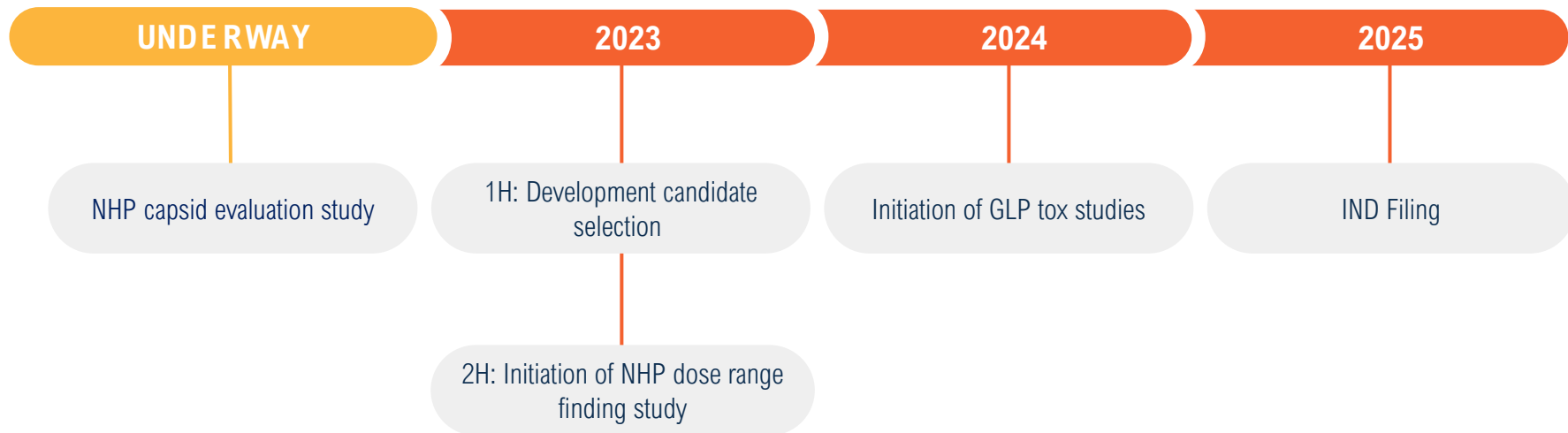


Substrate decreased in GBA1 LOF mouse model



Data shown reflects Day 0 IV dosing in GBA1 loss-of-function(LOF) mouse of 2E12, 2E13 vg/kg dosing of Voyager-optimized PHP.eB.GBA1, Day 28 necropsy with measures of GCCase protein, activity, and substrate levels

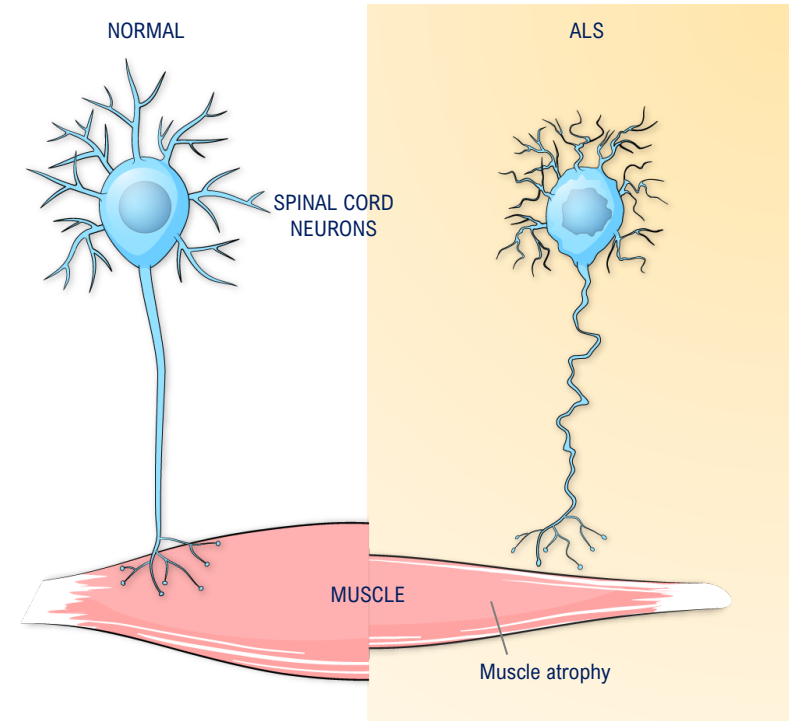
GBA1 Parkinson's Disease: Key Anticipated Milestones



SOD1-ALS

SOD1-ALS: Devastating disease with minimally effective therapies

- SOD1 mutations cause toxic gain of function in forms of familial ALS
 - Typically fatal within 3 years of diagnosis
 - >180 mutations in SOD1 gene linked to human disease
- Approximately 800 patients U.S., 1,000 patients EU, and 500 patients Japan
- Approved treatments minimally effective

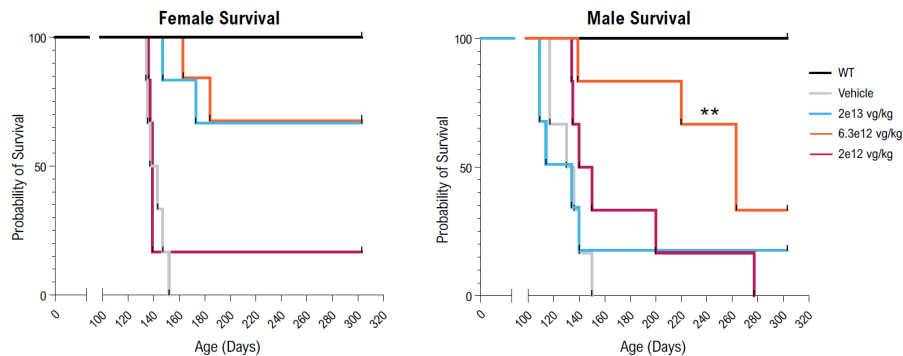


CSF SOD1 and plasma neurofilament light chain biomarkers will facilitate early

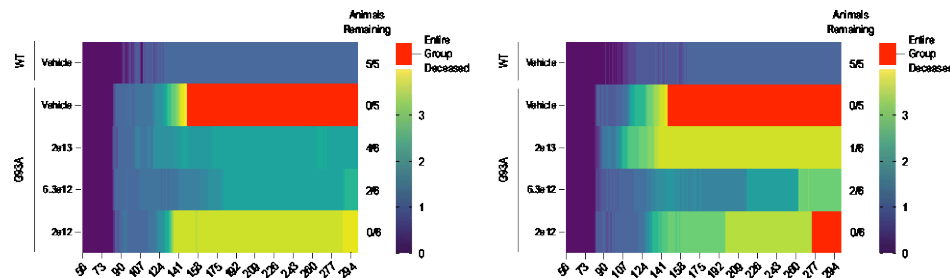
IV-delivered SOD1 knockdown approach shows preclinical survival and motor performance benefit in mouse models

- Strategy to combine highly potent siRNA construct with CNS-tropic, BBB penetrant TRACER capsid
 - May enable broad CNS knockdown of SOD1, potentially addressing disease manifestations beyond the spinal cord
- Promising preclinical results in mouse model
 - Robust SOD1 knockdown in all levels of the spinal cord with IV dosing using a mouse BBB penetrant capsid
 - Significant improvements in motor performance, body weight and survival

Increase in Survival

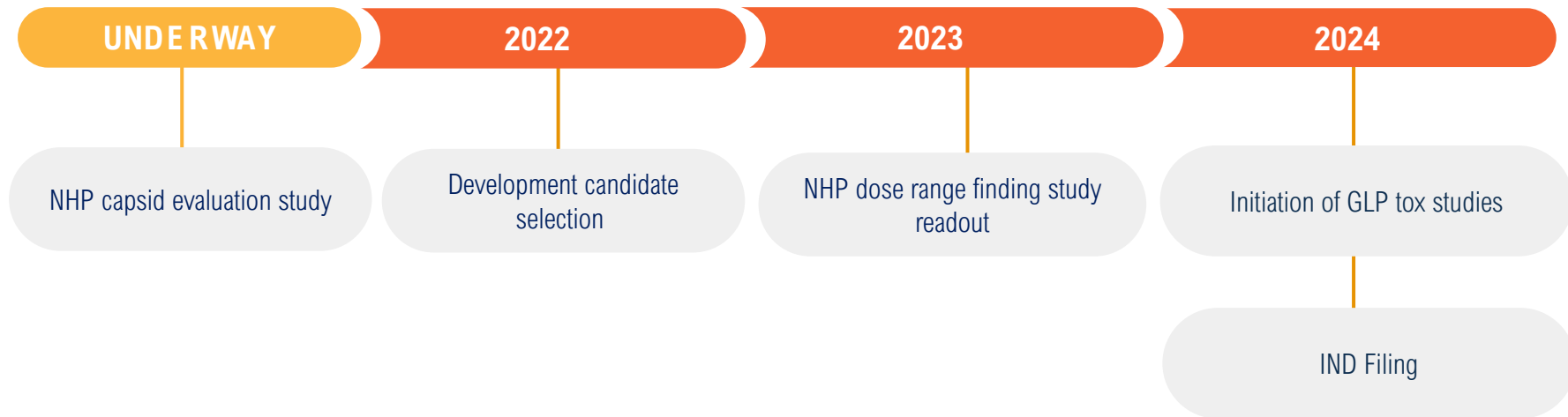


Improvements in Motor Performance*



* Neuroscore composite rating assessment in G93A mice. Mice were assessed for motor performance using the Neuroscore rating scale 3-7x/week for the duration of the study. The scale ranges from 0-4, with 0 = no deficit, 1 = first symptoms, 2 = onset of paresis, 3 = paralysis, 4 = humane endpoint. Animals currently remaining are shown for each treatment group.
Source: Grannan, et al. 2022

SOD1-ALS: Key Anticipated Milestones



Tau Alzheimer's Disease

Anti-tau antibody immunotherapy program

Novel antibodies selectively targeting pathological tau with:

- High affinity and differentiated biophysical characteristics
- Robust efficacy in animal models
- Differentiated in preclinical studies from clinically ineffective anti-tau antibodies

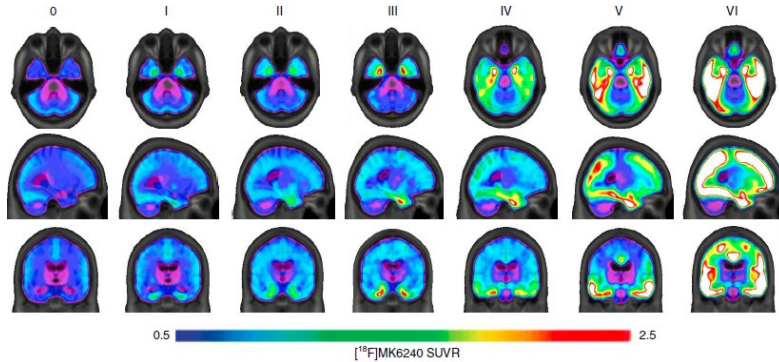


Novel tau antibodies as immunotherapy:

- Tau PET imaging may allow for rapid demonstration of human proof-of-biology
- Potential high value clinical candidates for the treatment of Alzheimer's and other tauopathies

Pathological tau: A compelling target for Alzheimer's Disease

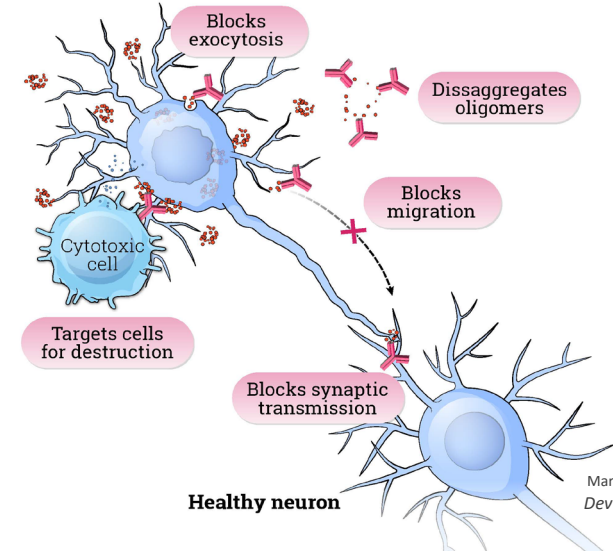
Tau PET imaging-based staging aligns with neuropathological staging



Therriault, *Nature Aging*, 2022

Anti-tau antibodies target neuron-to-neuron spread of tau

Diseased neuron

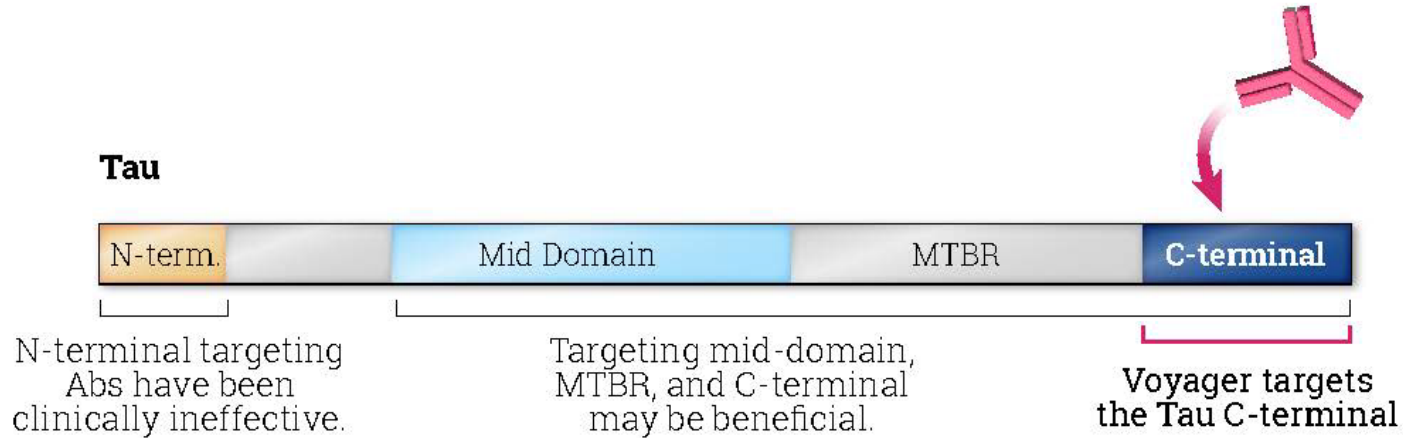


Neurofibrillary tangles and tau track with neuronal loss and clinical signs

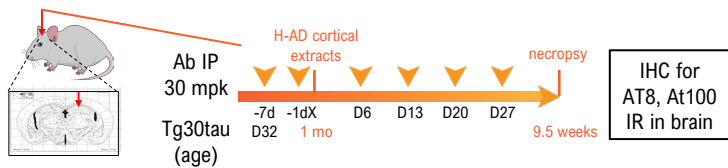
- Neuronal loss and neurofibrillary tangles increase with illness duration and severity*
- Tau pathology based on PET imaging closely correlates with disease progression (MRI) and cognitive decline in AD

Tau PET imaging biomarkers will be used to test human proof-of-biology

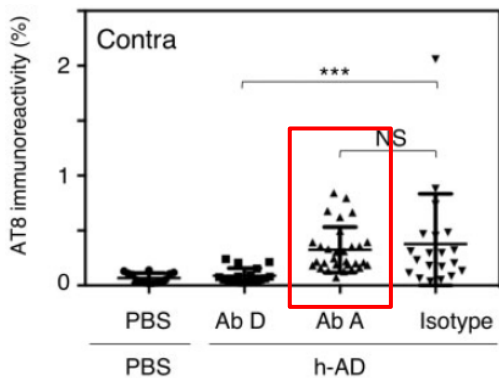
Voyager's anti-tau antibody targets the C-terminal domain



Voyager's anti-tau antibody is differentiated from other anti-tau antibodies

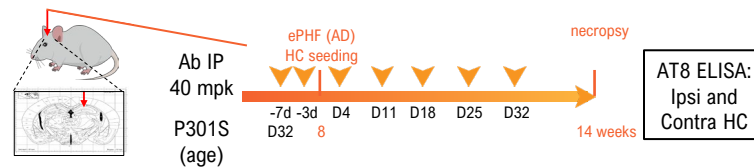


N-terminal Ab IPN002 is **ineffective** in both mouse seeding model and clinic

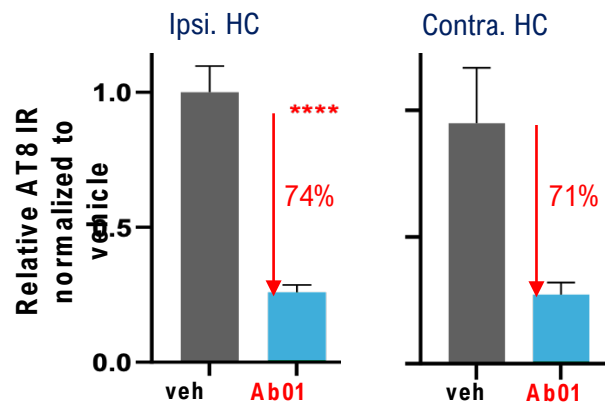


Note: Ab A targets N-terminus (aa15-24, IPN002)

Albert, *Brain*, 2019



Ab01 inhibits spread of pathological tau in mouse seeding model



Liu, *AAIC* 2022

Tau Alzheimer's Disease: Key Anticipated Milestones

UNDERWAY

Humanization of murine Ab

2023

Development candidate selection

Initiation of GLP tox studies

2024

IND Filing

SUMMARY

Unlocking the Potential of AAV Gene Therapy

TRACER capsids have potential to address certain fundamental limitations for gene therapy

- Receptor identification further supports human translation potential

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Prioritized pipeline programs designed for robust differentiation and efficient path to potential human proof-of-biology

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THERAPEUTICS

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