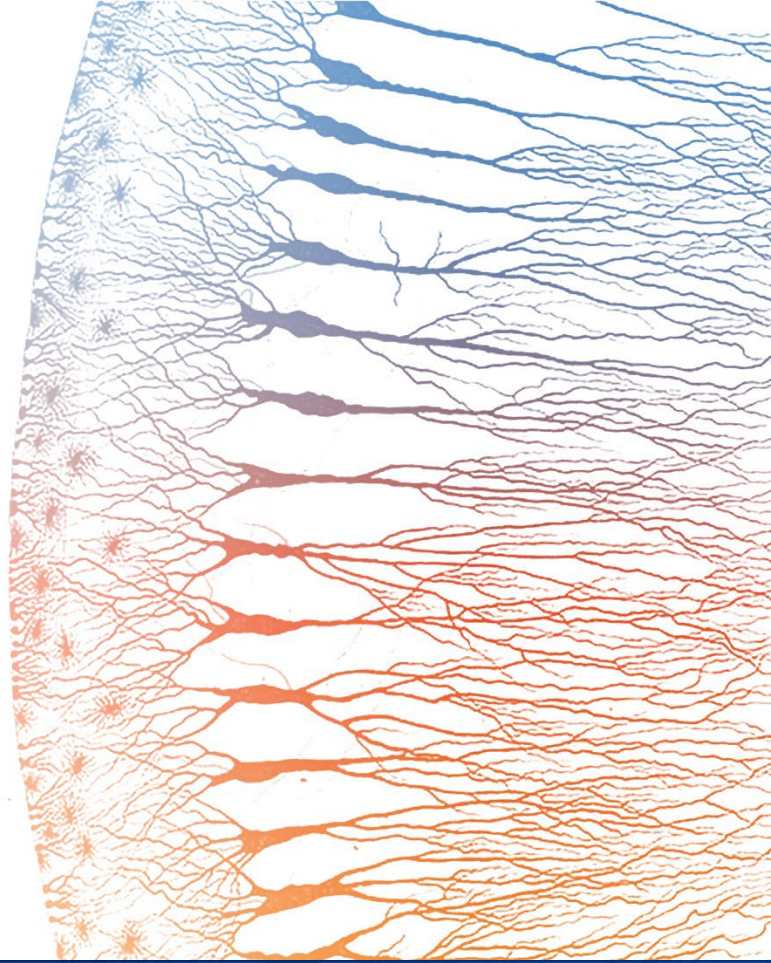
voyager therapeutics

Leveraging Genetics to Treat Neurological Diseases

SOD1 Update / February 2025



Forward-Looking Statements

This presentation 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 “expect,” “anticipate,” “believe,” “future,” “plan,” “estimate,” or “potential,” 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 plans for the future of its SOD1 ALS gene therapy program, including its plan to assess alternate payloads for the program and expectations with respect to providing further updates on the program; Voyager’s beliefs regarding the potential cause of development candidate VY9323’s failure to achieve the desired product profile, including Voyager’s belief that such failure is not related to the capsid; Voyager’s cash runway; expectations for Voyager’s achievement of preclinical and clinical development milestones for its potential development candidates such as the identification of lead development candidates, IND and CTA filings, the initiation of clinical trials, and the generation of clinical data and proof-of-concept; the potential for third-party clinical data to inform Voyager’s product development programs; Voyager’s ability to expand from gene therapy and antibodies into other modalities of neurogenetic medicine; Voyager’s plans to present scientific data at future conferences and other scientific forums; Voyager’s ability to generate near-term and long-term funding through reimbursement, upfront, milestone and royalty-based fees (as applicable) under its existing licensing and collaboration agreements, and to obtain data regarding the performance of its TRACER-derived capsid families licensed to its collaborators and partners under such agreements; Voyager’s ability to maintain and advance product development programs under its current partnerships and 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 based on estimates and assumptions by Voyager’s management that, although Voyager believes such forward-looking statements to be reasonable, are inherently uncertain and 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 expectations and decisions of regulatory authorities; the timing, initiation, conduct, and outcomes of Voyager’s preclinical studies and clinical trials; the availability of data from clinical trials; the success of Voyager’s product candidates; the availability or commercial potential of product candidates under collaborations; the willingness and ability of Voyager's collaboration partners to meet obligations under collaboration agreements with Voyager; the continued development of Voyager’s technology platforms, including Voyager’s TRACER capsid discovery platform and its antibody screening technology; Voyager’s scientific approach and program development progress, and the restricted supply of critical research components; the development by third parties of capsid identification platforms that may be competitive to Voyager’s TRACER capsid discovery platform; Voyager’s ability to create and protect intellectual property rights associated with the TRACER capsid discovery platform, the capsids identified by the platform, and development candidates for Voyager’s pipeline programs; the possibility and the timing of Voyager’s receipt of program reimbursement, development or commercialization milestones, option exercise, and other payments under Voyager’s existing licensing or collaboration agreements; the ability of Voyager to negotiate and complete licensing or collaboration agreements with other parties on terms acceptable to Voyager and the third parties; the success of programs controlled by third-party collaborators in which Voyager retains a financial interest; the ability to attract and retain talented directors, employees, and contractors; and the sufficiency of Voyager’s cash resources. 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 presented. 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.

VY9323 NHP Study Did Not Achieve Desired Therapeutic Window

- **Asset:** VY9323 = SOD1 miRNA payload + IV-delivered, second gen TRACER capsid (VCAP-Gen2)
- **Study:** Four doses explored in 6-month NHP GLP tox study; data from 3-month interim analysis
- Outcome:
  - All doses: No liver or systemic toxicity typical of AAV studies; no immunogenicity concerns
  - Higher doses: significantly reduced SOD1 mRNA (~60%) across multiple CNS regions; also resulted in late onset neurotoxicity (primarily tremors, delayed NfL increase, and nerve fiber degeneration)
  - Lower doses: did not result in adverse events; also did not result in sufficient SOD1 mRNA reduction

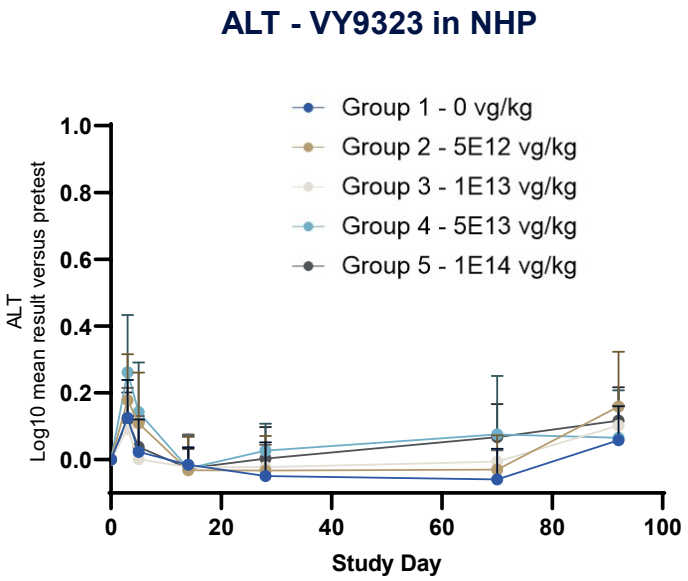
Key Data from Additional Studies: The VY1706 (tau silencing; same capsid) gene therapy program achieved desired activity levels and was well-tolerated in three-month NHP studies.

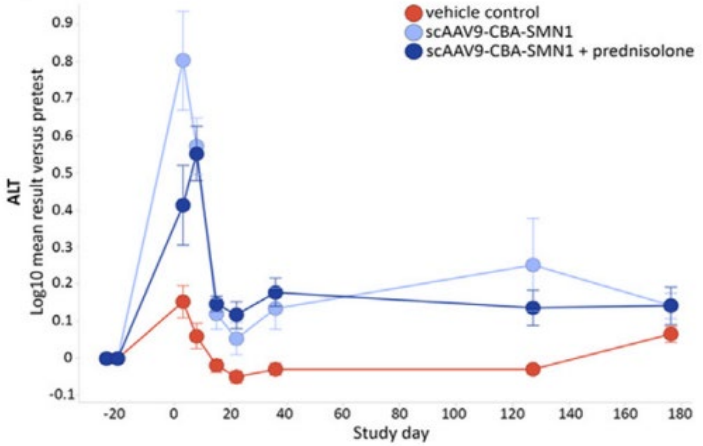
Conclusions:

- Cause believed to be off-target payload activity; not capsid or SOD1 target related
- VY9323 will not advance; assessing alternate payloads for potential path forward
- Cash runway extended into mid-2027

No AAV-Related Liver Toxicities Observed

VY9323 shows robust liver de-targeting even at 1E14 vg/kg



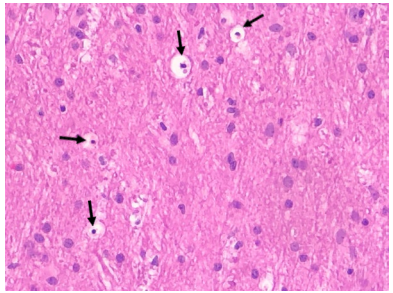


Hudry E et al (2023) Molecular Therapy; scAAV9-CBA-SMN1 administered IV at a dose of $1.1E10^{14}$ vg/kg

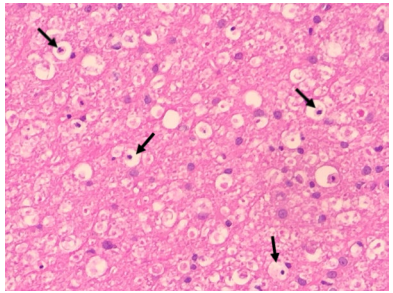
Histopathologic Findings Limited to Neurologic Tissues

- **Cortex:** Moderate nerve fiber degeneration in the cerebral hemisphere white matter
- **Spinal Cord:** Nerve fiber degeneration primarily in the dorsal and ventral white matter tracts
- **Dorsal Root Ganglia and Nerve:** Nerve fiber degeneration, increased cellularity, neuronophagia, and mononuclear cell infiltration

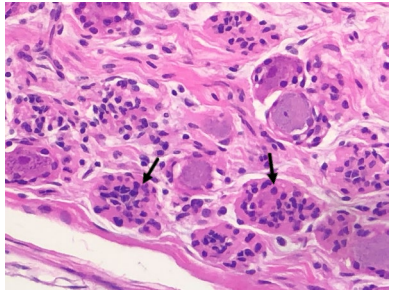
Cerebral hemisphere, White Matter:, Nerve Fiber Degeneration (arrows)



Cervical Spinal Cord, White Matter: Nerve Fiber Degeneration (arrows)



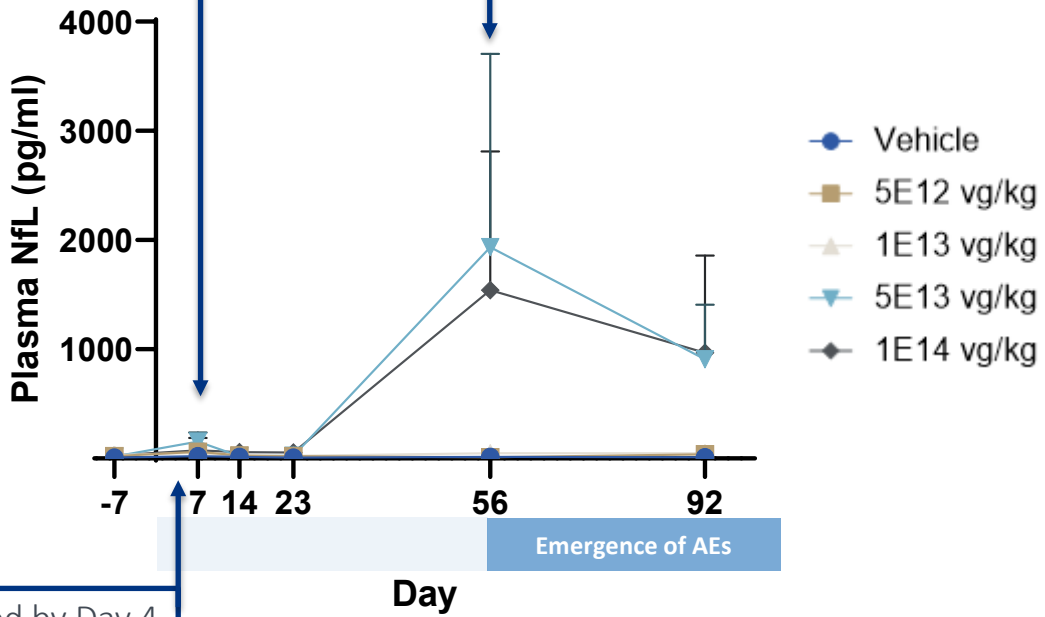
Dorsal Root Ganglion: Increased Glial Cellularity with aggregate (arrows), Decreased Neuronal Cellularity



Capsid Not a Driver of the Late-Onset Neurotoxicity

Mild, transient increase in NfL, consistent with but lower magnitude vs reported in AAV literature, resolved in 2-3 weeks

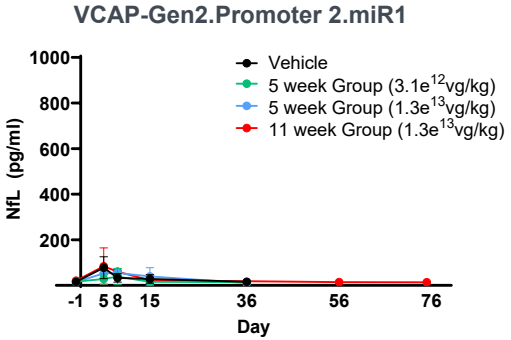
Significant increase in NfL concurrent with AE onset in NHPs, implicating payload activity

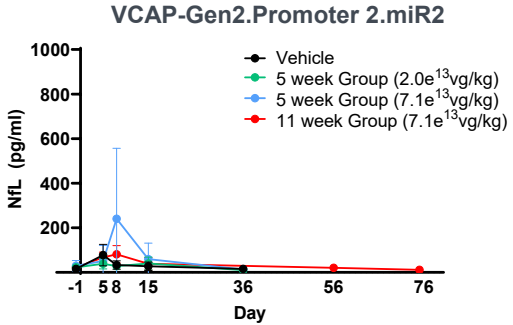


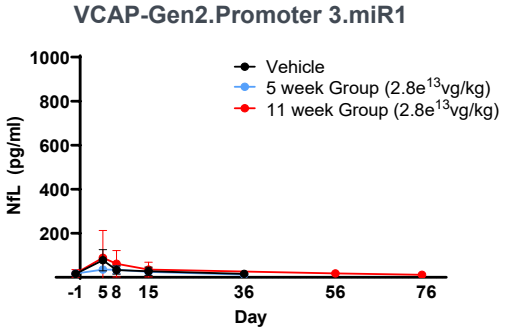
>99% capsid shed from blood by Day 4

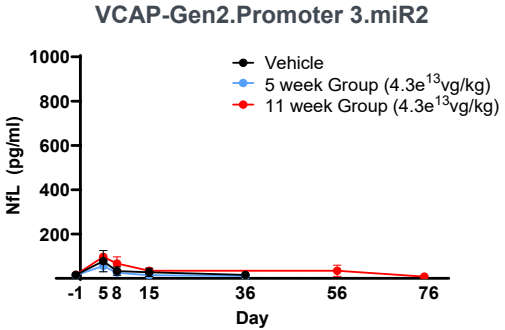
Same Capsid Shows No Delayed NfL Increase with Four Different Payloads at IV Doses Up To 7E13 in NHPs

VY1706
(tau silencing)









- No dose-limiting toxicology signals were observed at 3 months, including doses where toxicity was observed in ALS-SOD1
- All constructs, including VY1706, showed substantial target knockdown in relevant brain regions

Different studies of different constructs tested different doses; all doses tested in each study are shown.

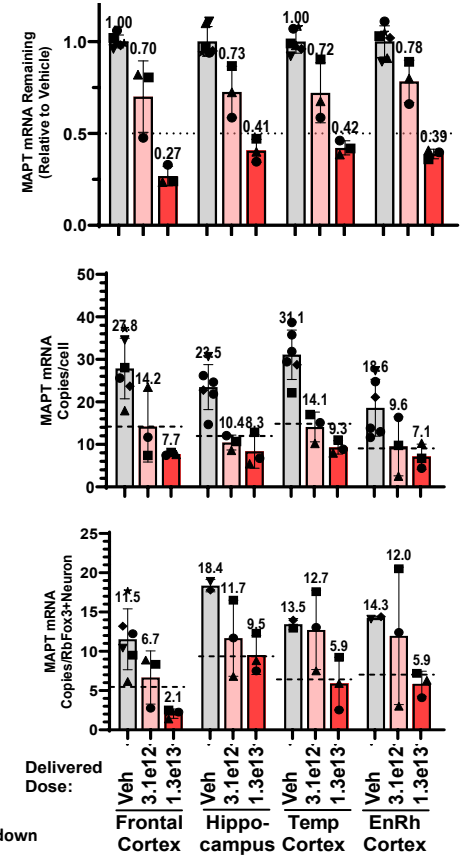
VY1706 Shows Robust and Widespread Tau Knockdown IV in NHPs

voyager therapeutics

Tissue punch PCR
Strong and broad tau mRNA knockdown

In situ hybridization
Strong and broad tau mRNA knockdown observed in cells

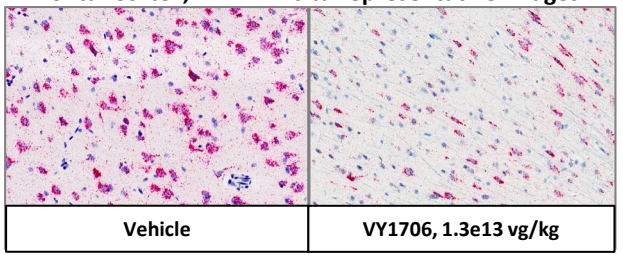
Fluorescent in situ hybridization
Strong and broad *neuronal* tau mRNA knockdown



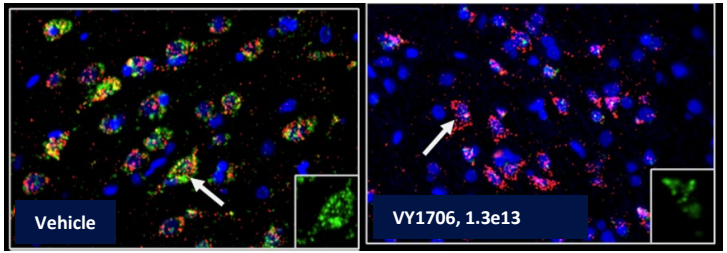
Single IV dose of VY1706 resulted in **50% to 73%** reductions in tau mRNA levels across cerebral cortex.

Additional NHP data to be presented at ADPD.

Frontal Cortex, MAPT in situ representative images

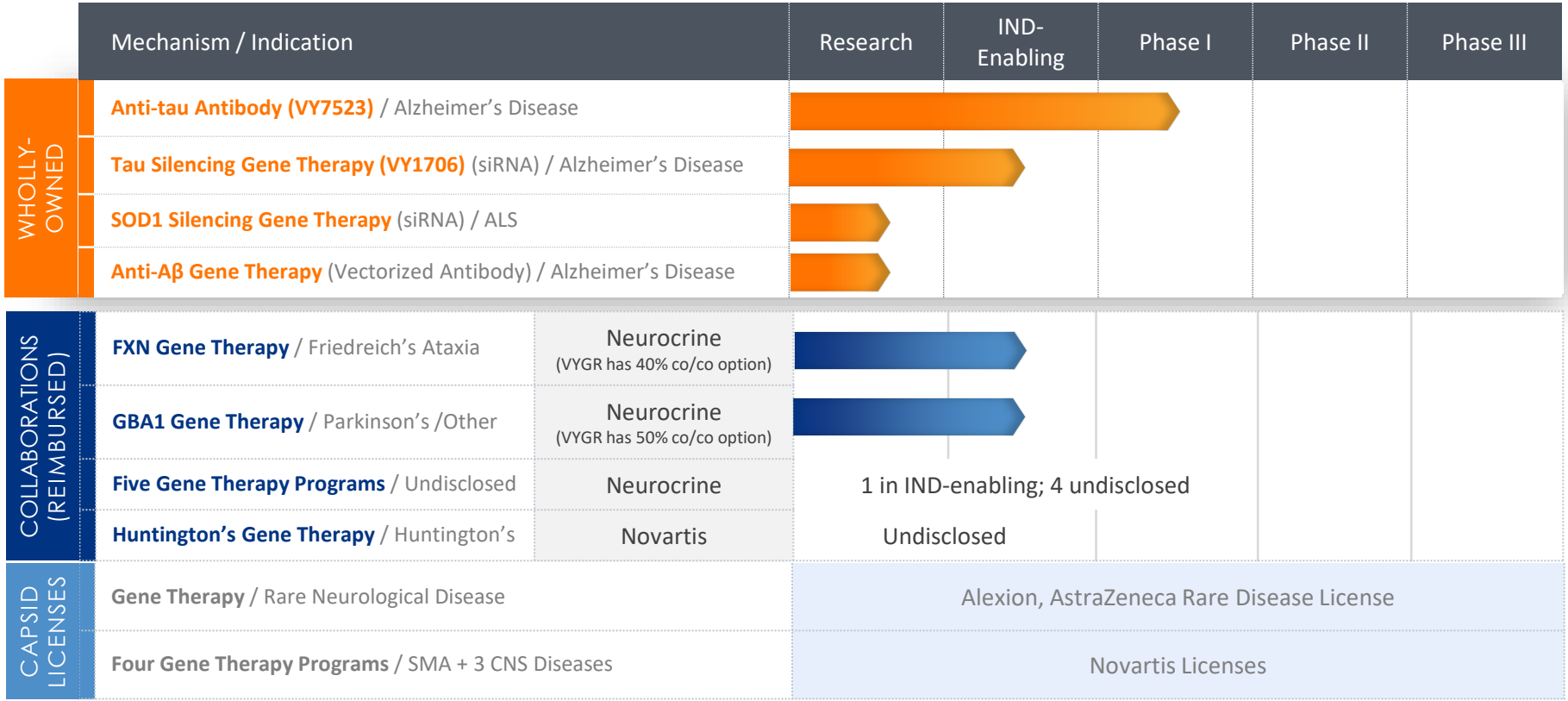


Frontal Cortex, NeuN/MAPT in situ representative images



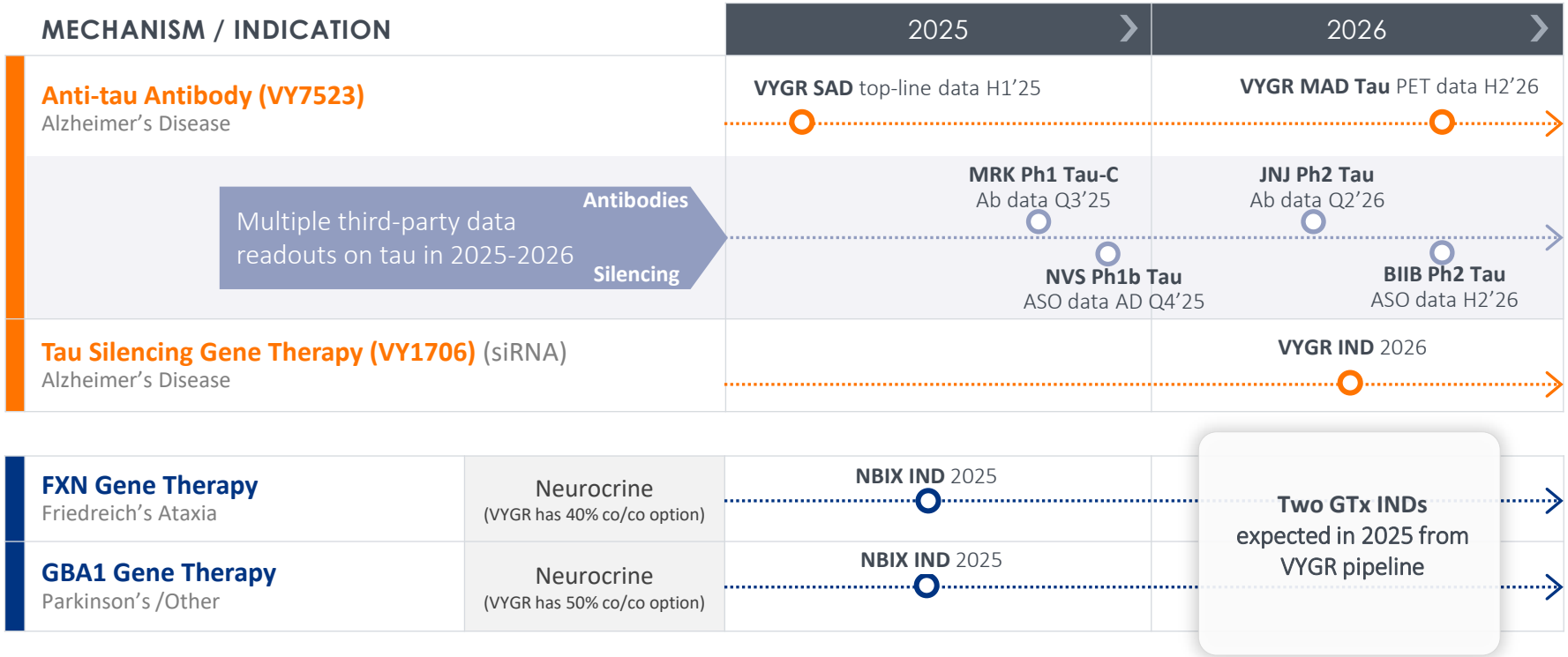
CNS Pipeline Focuses on Validated Targets with High Potential Value

voyager therapeutics



Runway Extended into Mid-27; Beyond Multiple Potential Catalysts

voyager therapeutics



Voyager (NASDAQ: VYGR) Investment Rationale

PIPELINE	Multiple clinical data readouts expected 2025/26; cash into mid-2027[1]	Two approaches to tau (mAb and GTx) – and all-star team
PLATFORMS	Intravenous CNS GTx platform; robust preclinical data + partnerships	Emerging ALPL shuttle may enable multi-modality CNS delivery
PARTNERSHIPS	Blue-chip partners include Novartis, Neurocrine, Alexion	$8.2B in potential milestone payments, incl. $2.9B development

[1] Based on our current operating plans, cash and cash equivalents and marketable securities as of September 30, 2024, along with amounts expected to be received as reimbursement for development costs under the Neurocrine and Novartis collaborations and interest income.

voyager therapeutics

Thank You

www.voyagertherapeutics.com