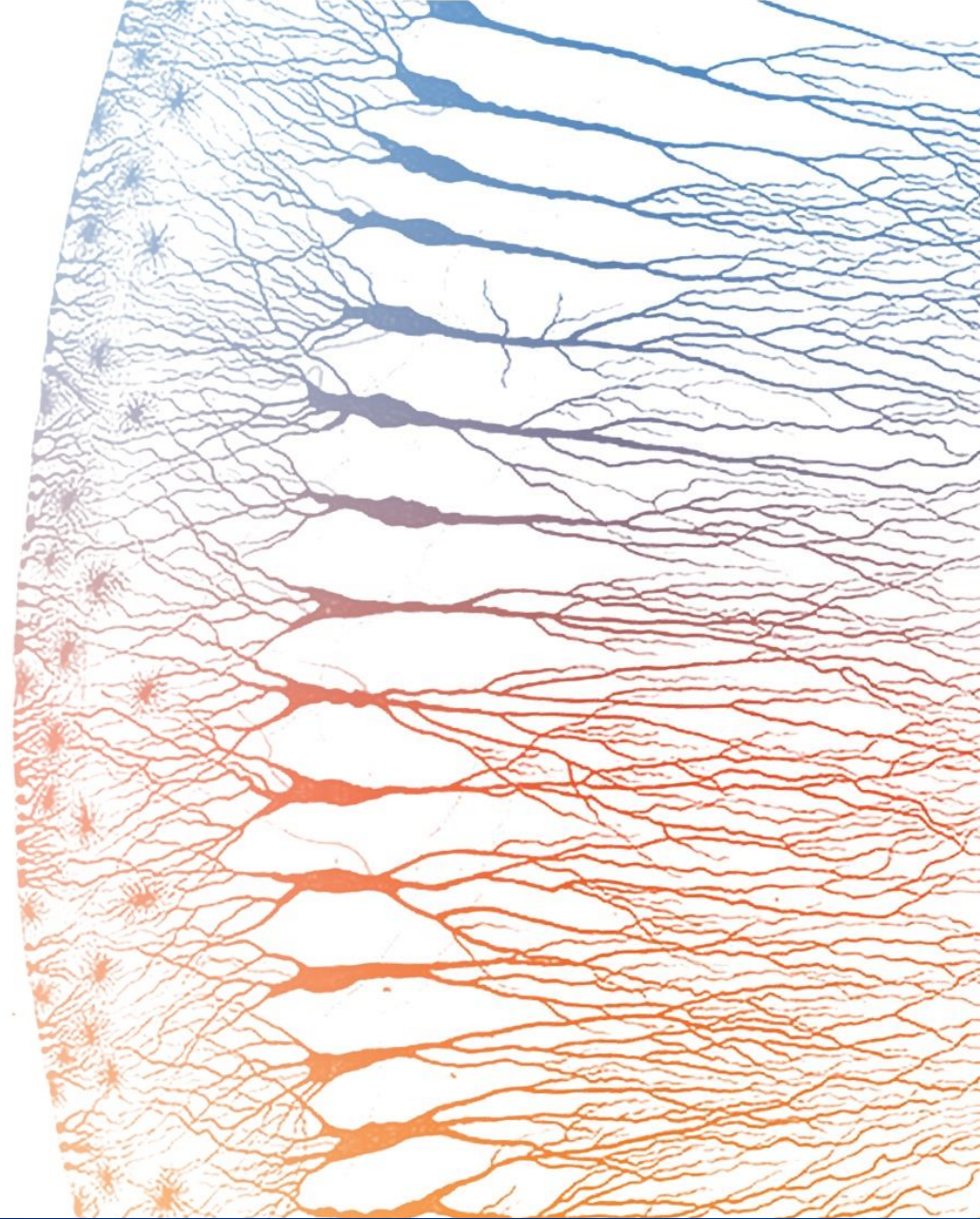




Defining Neurogenetic Medicines

Wells Fargo 2024 Healthcare Conference

Sept. 5, 2024



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PIPELINE

Pipeline of wholly-owned and partnered neurogenetic medicines; VY7523 anti-tau antibody in Phase 1a clinical trial; three gene therapies with IND filings expected in 2025¹; potential for **clinical data** in 2025/2026.



PLATFORM

Leading platform for CNS gene therapy delivery; cross-species preclinical data show widespread payload expression across CNS following IV delivery; enabling multiple development candidates in CNS gene therapy programs¹.



PARTNERSHIPS

Blue-chip partnerships support strong cash position: **runway into 2027²**, not including \$8.2B in potential longer-term milestone payments.



POTENTIAL

Potential to expand into additional **neurogenetic medicine** modalities. Evaluating potential for identified receptor to enable non-viral delivery of payloads across BBB.

¹Two of these IND filings/programs are pursuant to Neurocrine-partnered programs. ²Based on our current operating plans, cash and cash equivalents and marketable securities as of June 30, 2024, along with amounts expected to be received as reimbursement for development costs under the Neurocrine and Novartis collaborations and interest income.

CNS Pipeline Focuses on Validated Targets with High Potential Value



	Mechanism / Indication		Research	IND-Enabling	Phase I	Phase II	Phase III
WHOLLY-OWNED PIPELINE	Anti-tau Antibody (VY7523) / Alzheimer's Disease		▶				
	SOD1 Silencing Gene Therapy (VY9323) (siRNA) / ALS		▶				
	Tau Silencing Gene Therapy (siRNA) / Alzheimer's Disease		▶				
	Anti-Aβ Gene Therapy (Vectorized Antibody) / Alzheimer's Disease		▶				
COLLABORATIONS (REIMBURSED)	FXN Gene Therapy / Friedreich's Ataxia	Neurocrine (VYGR has 40% co/co option)	▶				
	GBA1 Gene Therapy / Parkinson's /Other	Neurocrine (VYGR has 50% co/co option)	▶				
	Five Gene Therapy Programs / Undisclosed	Neurocrine	Undisclosed				
	Huntington's Gene Therapy / Huntington's	Novartis	Undisclosed				
CAPSID LICENSES	Gene Therapy / Rare Neurological Disease	Alexion, AstraZeneca Rare Disease License					
	Four Gene Therapy Programs / SMA + 3 CNS Diseases	Novartis Licenses					
	Gene Therapy / Prion Disease	Sangamo License					

~7M Alzheimer's disease patients in the U.S.¹

- Tau pathology closely correlates with disease progression and cognitive decline¹
- Tau PET tracers enable imaging of tau pathology and use as clinical trial biomarkers
- Third-party clinical data showed reducing tau led to reduced tau pathology (per tau PET imaging) and produced favorable trends in cognition²



VY7523 ANTI-TAU ANTIBODY (formerly VY-TAU01):

- **Modality:** monoclonal antibody, IV-delivered.
- **Approach:** inhibit cell-to-cell spread of pathological tau.
- **Differentiation:** targets C-terminal domain of pathological tau. Multiple failed approaches had targeted N-terminal.
- **Data:** inhibited spread of human pathological tau by >70% in mouse seeding model (AAIC 2022).

STATUS: Single ascending dose trial ongoing

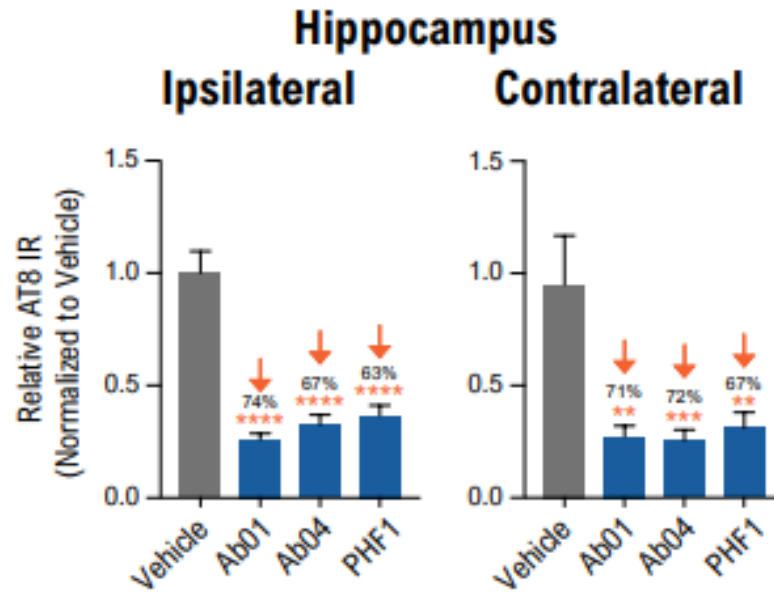
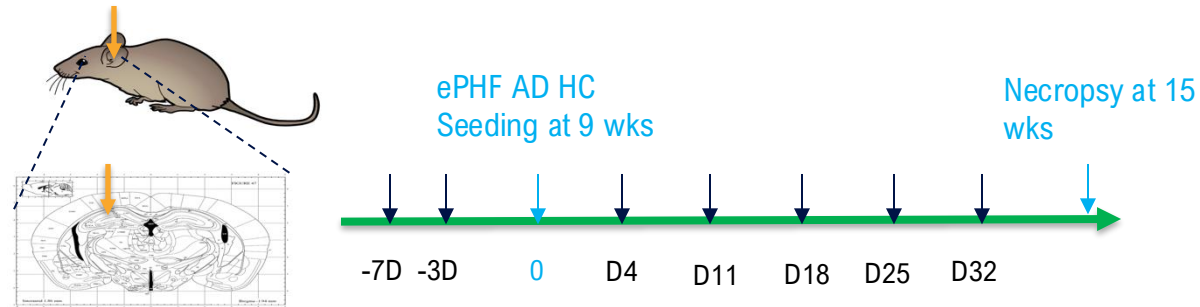


TAU SILENCING GENE THERAPY

- **Modality:** gene therapy, IV-delivered single dose.
- **Approach:** inhibit expression level of tau mRNA and protein.
- **Differentiation:** gene therapy approach could offer potential for single dose treatment.
- **Data:** single IV administration robustly reduced tau mRNA and protein in brain of mice expressing human tau (ASGCT 2024).

STATUS: IND filing anticipated in 2026

Why we chose to move forward with VY7523, our anti-tau antibody currently in a Phase 1 SAD trial

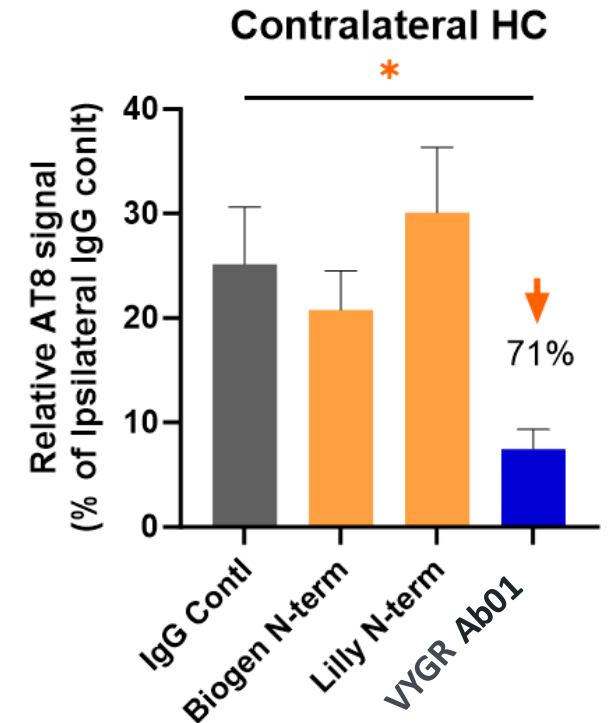
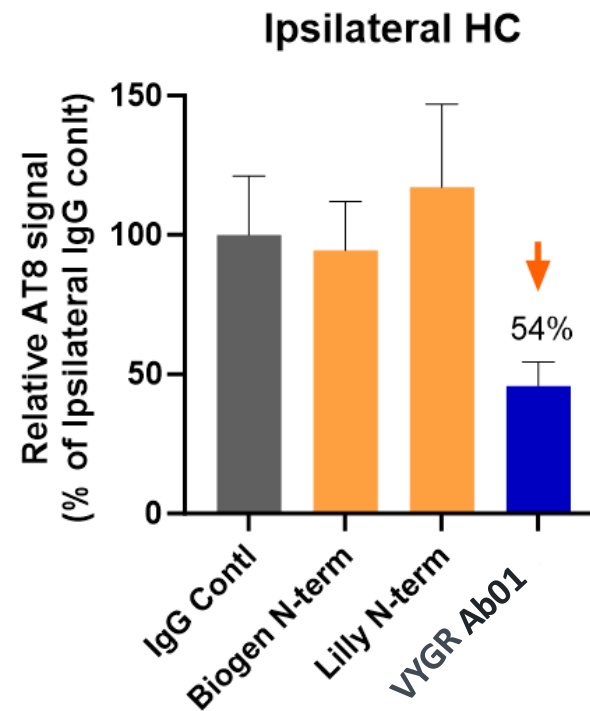


Ab01 = murine surrogate of VY7523

Vehicle = negative control. PHF1 = positive control. Ab01 and Ab04 = Voyager murine antibodies; **Ab01 is murine surrogate of VY7523**. *, **, *** and **** indicate $p < 0.05$, 0.005, 0.0005 and 0.0001, respectively, compared to the vehicle control group. Ab01 data presented at AAIC 2022 and ADPD 2023 by Liu, et al. Data supporting points #2 and #3 above from data on file at Voyager.

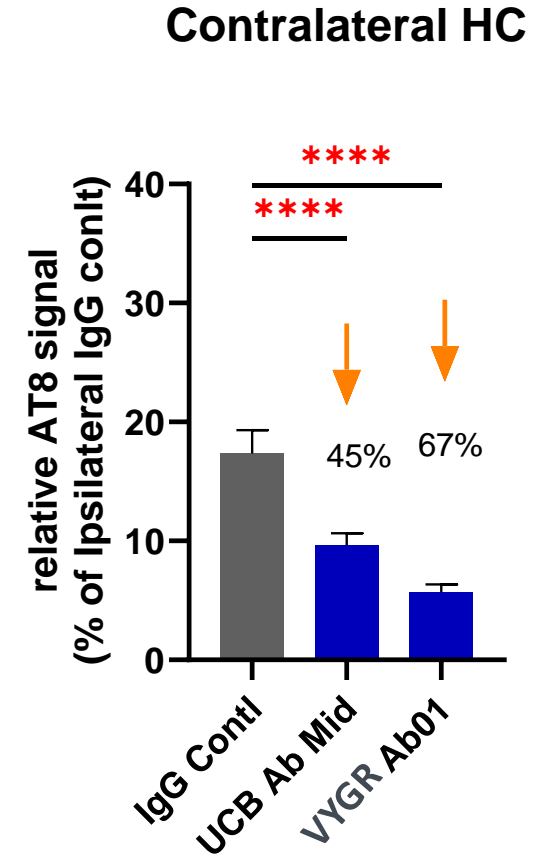
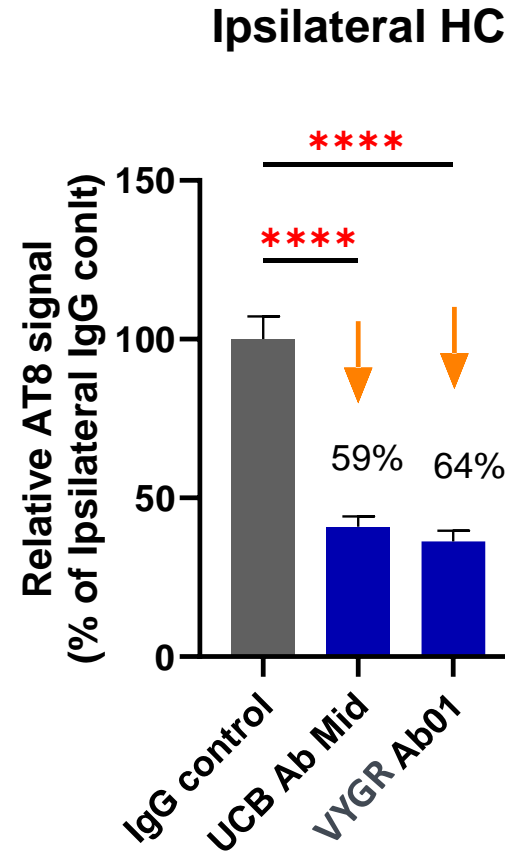
Negative Predictive Value: Head-to-Head Study Comparing VY7523 to N-Terminal Targeted Antibodies (Murine Forms)

Antibody	Terminal	Outcome in Clinic	Outcome in Model
Ab01: murine Ab of VY7523 (Voyager)	C	SAD ongoing	Ipsilateral: 54 ± 8.7% Contralateral: 71 ± 1.9%*
Murine Ab of gosuranemab (Biogen)	N	Failed primary endpoint	No significant reduction
Murine Ab of zagotenemab (Lilly)	N	Failed primary endpoint	No significant reduction



Potential for Positive Predictive Value: Head-to-Head Study Comparing VY7523 to UCB/Roche's Bepranemab (Murine Forms)

Antibody	Terminal	Outcome in Clinic	Outcome in Model
Ab01: murine Ab of VY7523 (Voyager)	C	SAD ongoing	Ipsilateral: $64 \pm 3.4\%$ **** Contralateral: $67 \pm 0.7\%$ ****
Murine Ab of bepranemab (UCB/Roche)	Mid	Ph 2 data expected Q4 '24	Ipsilateral: $59 \pm 3.3\%$ **** Contralateral: $45 \pm 1.0\%$ ****



Summary: 3 key findings on the effects of anti-tau antibodies in the mouse seeding model:

1. Murine surrogate of VY7523 (Ab01) consistently and robustly inhibits spread of human pathological tau in the mouse seeding model
2. N-terminal targeted anti-tau antibodies that failed in the clinic also FAILED in model
3. UCB/Roche mid-domain anti-tau antibody REDUCED SPREAD in model; clinical success could derisk VY7523

- **First-in-human, dose-escalation trial to assess safety**
- **Single Ascending Dose (SAD) trial underway in healthy volunteers**
 - *Design:* Randomized, placebo-controlled, single dose trial in multiple cohorts with approximately 48 participants
 - *Timing:* top-line safety and pharmacokinetic data expected H1 2025
- **Multiple Ascending Dose (MAD) trial expected to be conducted in patients with early Alzheimer’s disease**
 - *Timing:* expected to initiate in 2025; potential to generate initial tau PET imaging data to determine if treatment can slow the spread of pathological tau in H2 2026

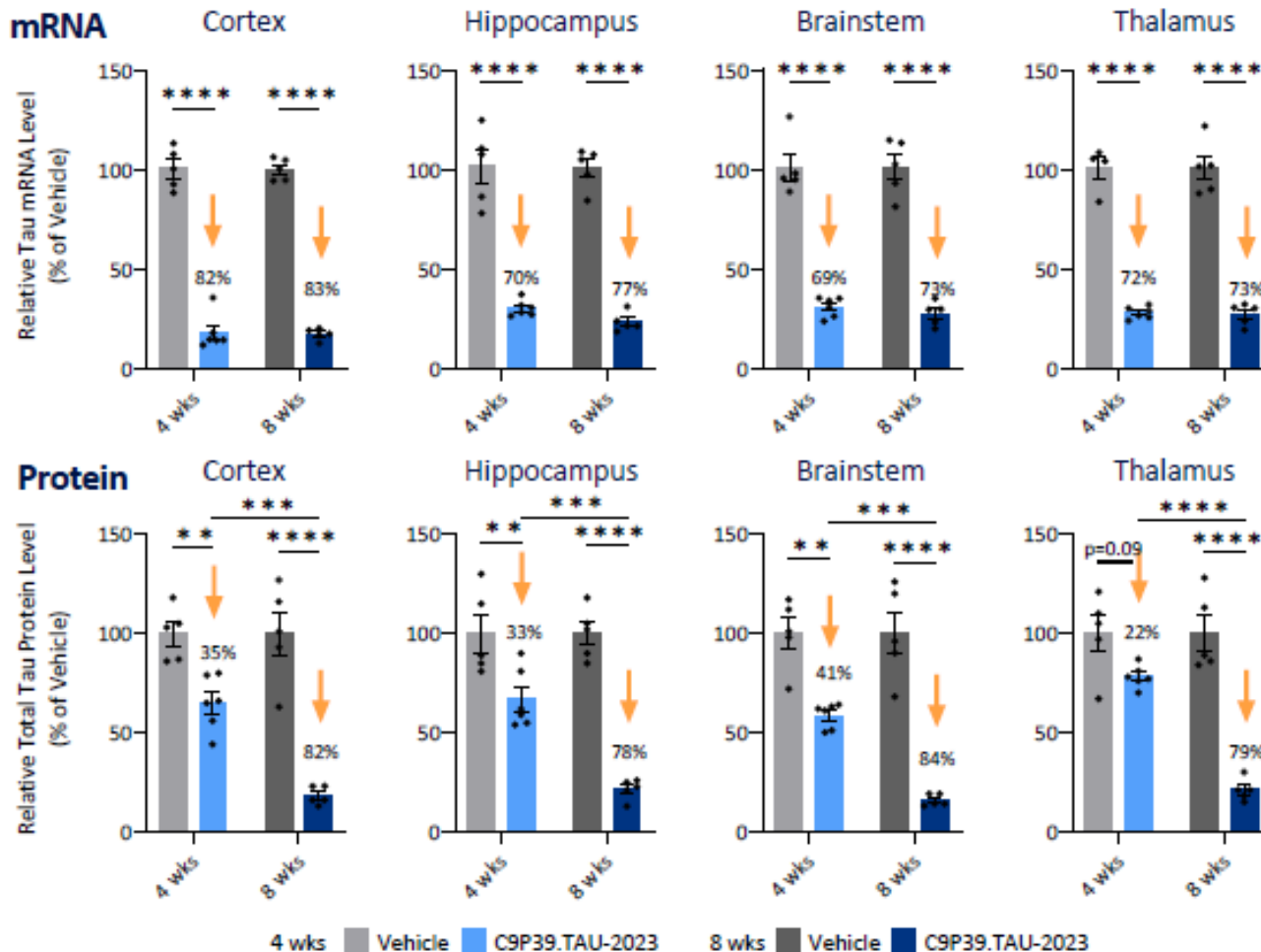
Key Milestones:

- ✓ Q2 2023: Received pre-IND feedback from the FDA
- ✓ Q1 2024: Completed GLP toxicology studies
- ✓ H1 2024: Filed IND with FDA
- ✓ 2024: Initiated Phase 1a single ascending dose (SAD) trial in healthy volunteers
- Q4 2024: Phase 2 data expected on bepranemab (mid-domain anti-tau antibody from UCB/Roche); potential read-through to VY7523
- H1 2025: Topline safety/PK data expected from SAD trial
- 2025: Initiate Phase 1b multiple ascending dose study in early AD patients
- H2 2026: Initial clinical data expected (Tau PET imaging)

Intravenous Administration of Tau Silencing Gene Therapy Robustly Reduced Tau mRNA and Protein in Brain of Mice Expressing Human Tau



Tau Silencing Gene Therapy offers knock-down approach and potential for single dose treatment



Robust reductions in human Tau mRNA and protein across multiple brain regions of hTau mice following a single intravenous administration; presented at ASGCT 2024

Anticipate IND filing in 2026

Vectorized primary artificial microRNA targeting human tau mRNA delivered by BBB-penetrant capsid administered by intravenous injection to hTau transgenic mice at 12-13 weeks of age; tissue harvested for analysis 4 weeks following administration; mRNA measured by RT-qPCR; protein measured in soluble fraction of brain regions by AlphaLISA. Asterisks correspond to statistical significance, with * indicating $p < 0.05$ and **** indicating $p < 0.0001$



Thank You

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