Unlocking the Potential of AAV Gene Therapy

Corporate Presentation
September 2021

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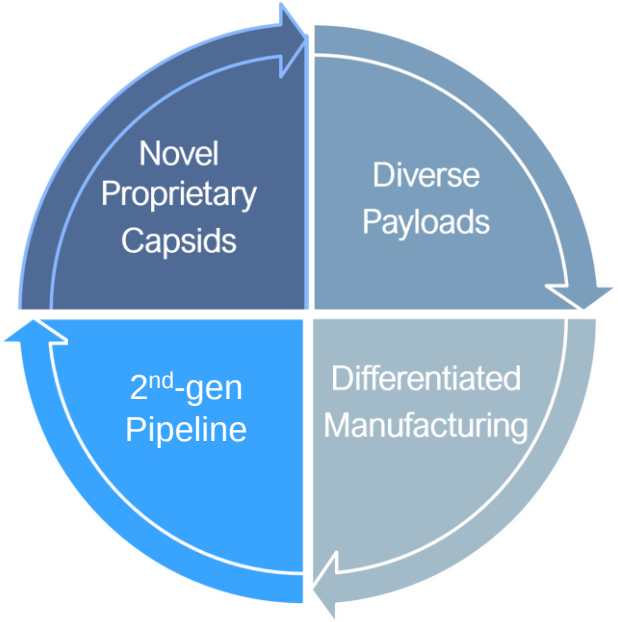
An unparalleled platform for gene therapy development

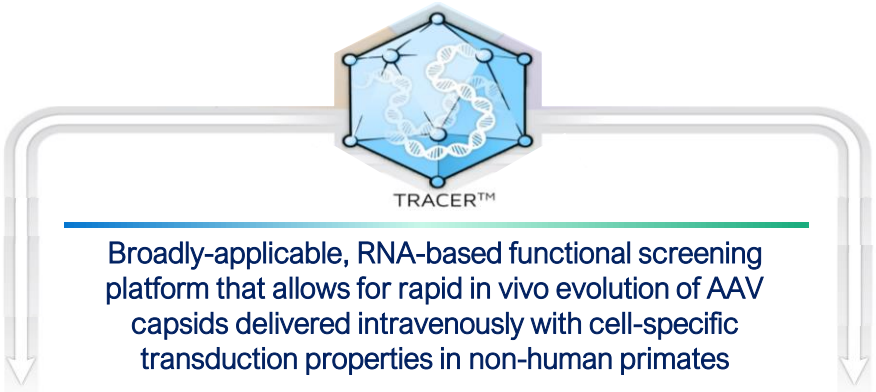


- Novel AAV capsid discovery for selected tissue targets & tropism: demonstrated superior CNS transduction vs. AAV9
- Ability to vectorize diverse payloads for multiple modalities (replacement, knockdown, antibodies, others)
- State of the art process and analytical development for flexible and scalable manufacturing
- Novel capsid and vectorized antibody efforts powering internal pipeline

Breakthroughs in platform technologies support internal product development and expanded partnership opportunities in the CNS and other tissues

A breakthrough approach to power the next-generation of AAV GTx

Proprietary TRACER™ platform technology enables discovery of novel capsids with specified tropism across multiple tissue types



Novel Capsids

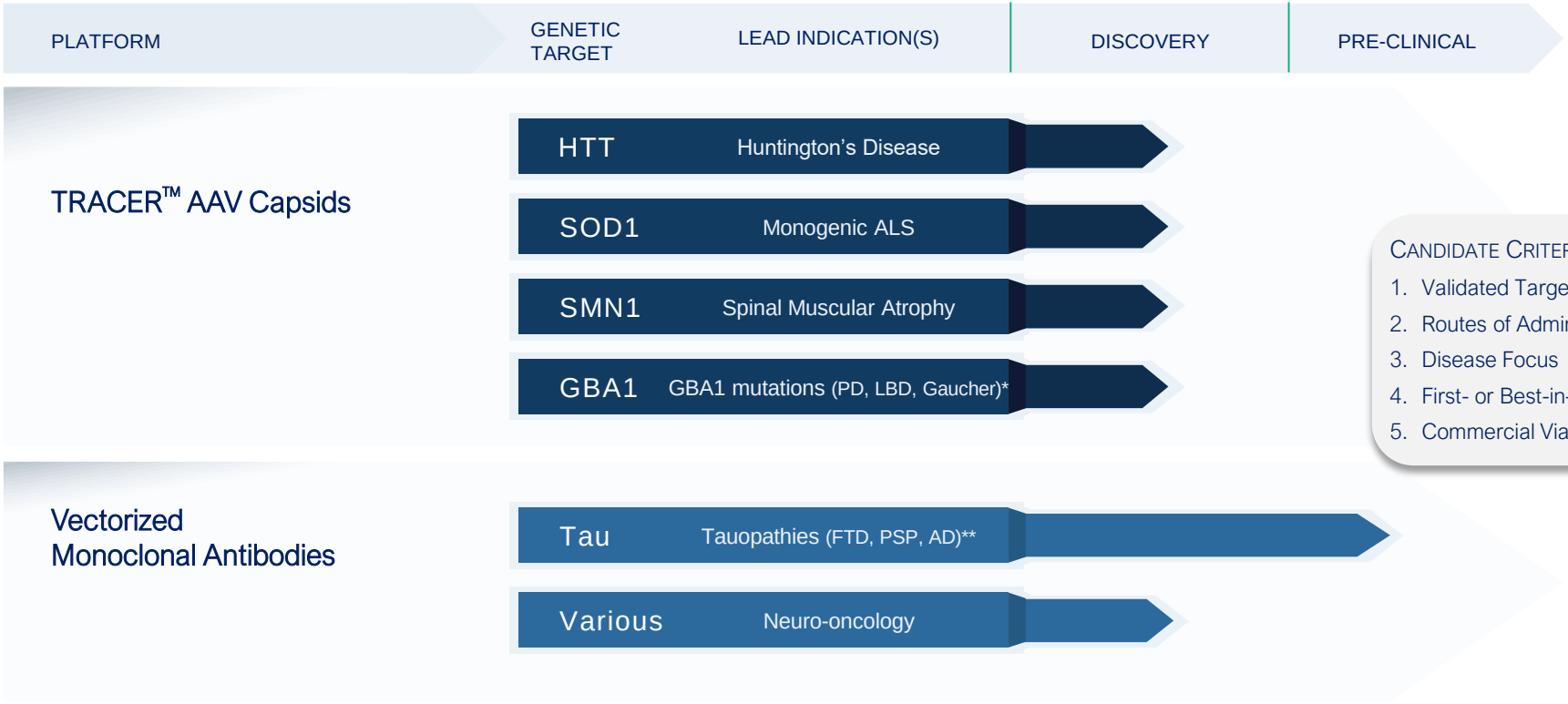
Novel RNA-driven capsids bioengineered to address major field-limiting AAV challenges, support internal product development and external partnerships in several tissue targets

Vectorized Antibodies

Proprietary technology creates potential for single-dose CNS strategy by enabling expression of functional antibodies *in vivo*

TRACER: Tropism Redirection of AAV by Cell-type-specific Expression of RNA

Platform delivery technologies power pipeline designed to achieve best-in-class status



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

*PD: Parkinson's disease; LBD: Lewy body dementia **FTD: Frontotemporal dementia; PSP: Progressive supranuclear palsy; AD: Alzheimer's disease.

TRACER CAPSID DISCOVERY PLATFORM

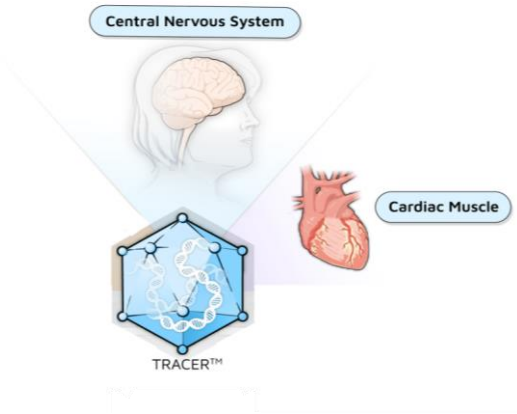
First-generation AAV vectors have limited the gene therapy field for decades

Conventional AAV vectors have a narrow therapeutic window

- Achieving meaningful efficacy with high doses yields safety trade-off, risk/benefit imbalance
- Substantial toxicity risk from off-target effects
- Discoveries with conventional AAV capsids in mice have not translated to primates
- Clear limitations of first-gen AAV to effectively target the CNS and achieve broad transduction
- Direct injection into target tissue can achieve sufficient distribution only for some indications

The enormous promise of the field will not be realized until improved, next-generation AAV vectors emerge

TRACER capsids target tissues with greater specificity and reduced off-target risks



Novel capsids may be more reliably on-target with less risk of dose-limiting toxicities

Capsids may enable:

- Broader distribution of GTx throughout the brain to address many CNS diseases not limited to narrow regions of the brain
- Systemic IV administration, thereby reducing safety issues associated with neurosurgical delivery
- Enhanced gene delivery to the brain at lower, better-tolerated doses, enabling a favorable safety profile
- Direct work in NHPs for better human translation
- Support for many CNS programs, both internally and among peer companies

Notable findings from first TRACER screening library

TRACER capsids demonstrated superior transgene expression in brain compared to AAV9 in NHPs

- Multiple capsids with 10-1000-fold improved BBB penetration vs. AAV9 after IV administration

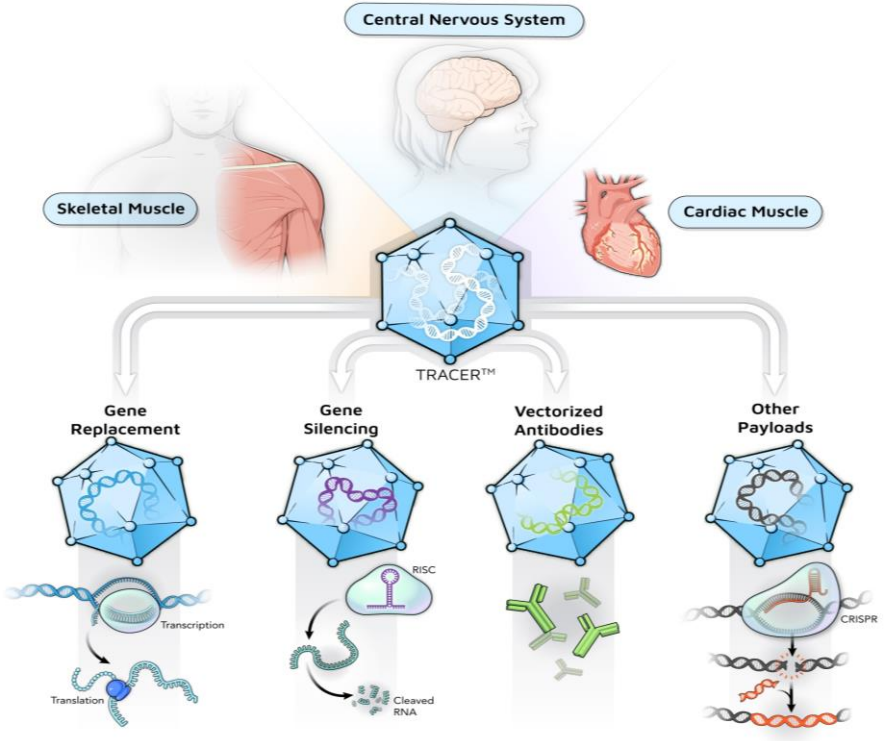
Capsid 9P804 demonstrated strong cardiac transduction and significant DRG detargeting following IV administration

- May avoid delivery toxicities associated with AAV9

NHPs: non-human primates

TRACER can be targeted to identify capsids for several tissue types

Novel capsids may have enhanced tropism for target tissues



Continuing 9 additional capsid campaigns

- Expand library and identify capsids optimized for specific applications

Additional tissue targets being evaluated: cardiac and skeletal muscle, eye, kidney, lungs, pancreas

- Flexible library-generating method; further cell specific fine-tuning possible
- Designed to target one cell type in a complex tissue
- Identify capsids w/ multiple attributes, cell type affinity, evade antibodies

Platform generates proprietary knowledge, IP around capsids with most promising and meaningfully differentiated tissue affinities

- Novel IP generated with new capsids and platform
- Capsids covered by patent filings for new compositions of matter

Exploring alternate ROAs to deliver novel capsids and improve transduction efficiency/immune response

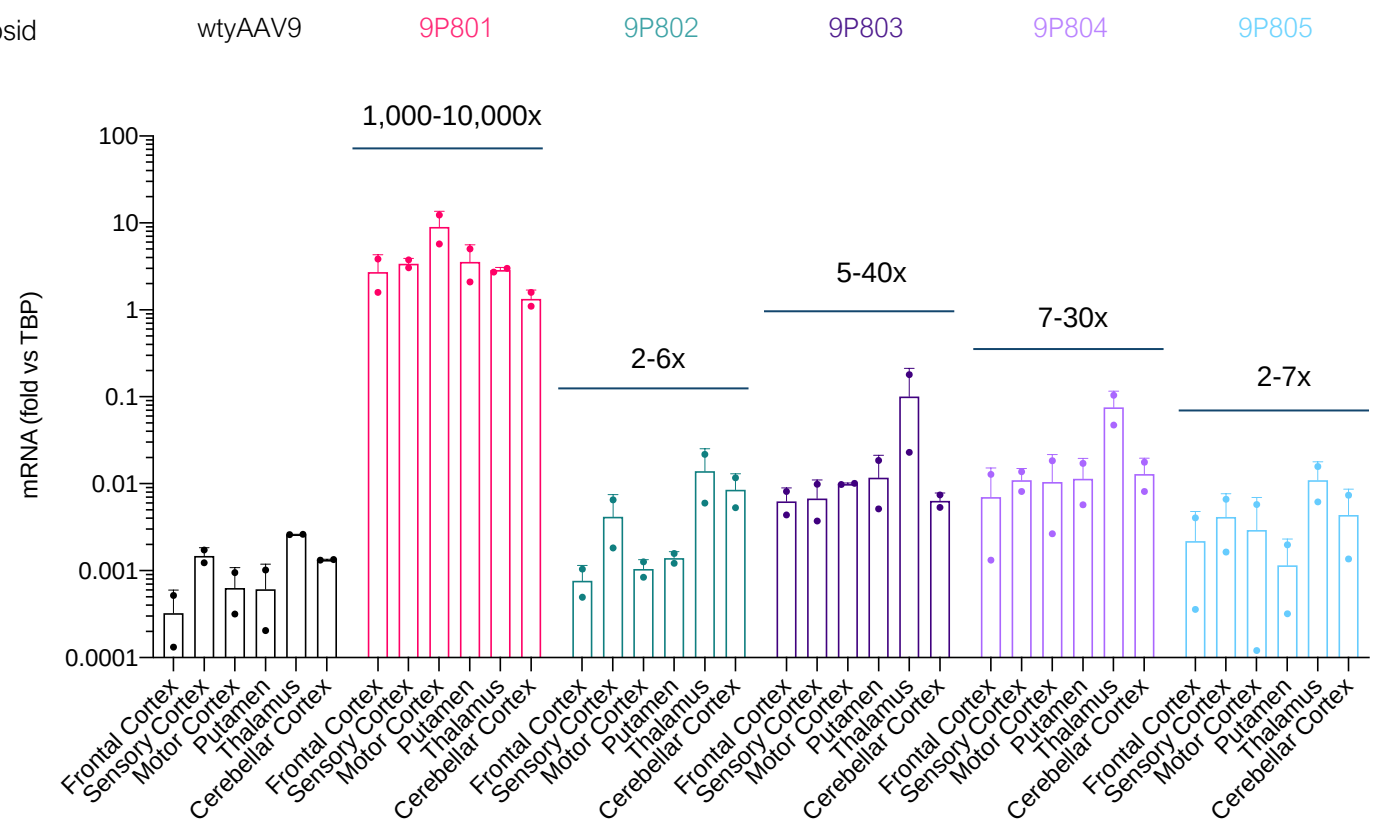
Cutting edge vector genome optimization: Cell-specific promoters, de-targeting technology

TRACER capsids achieve unprecedented CNS transduction, strong cardiac transduction in NHPs

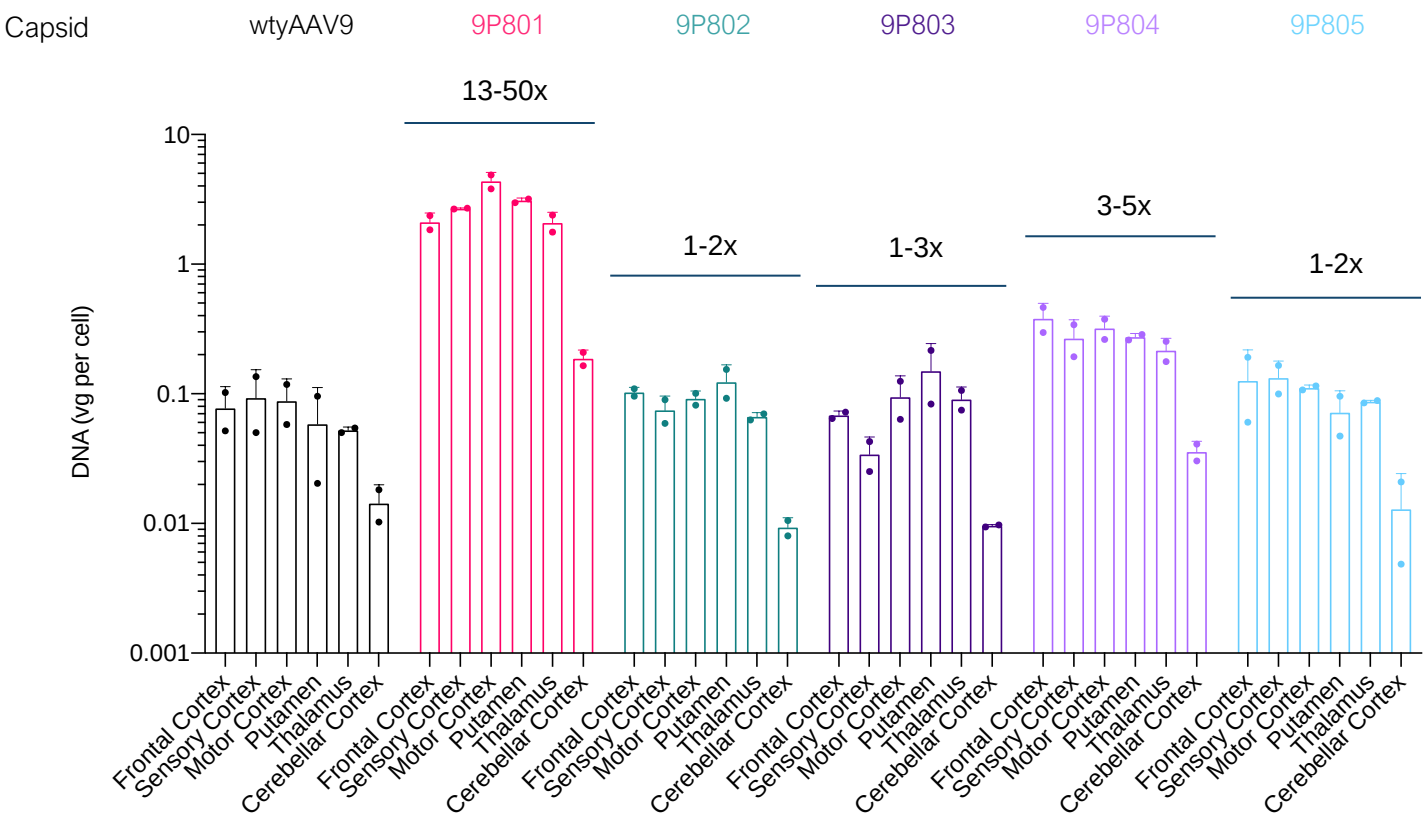
- First screening of capsid library using TRACER platform in NHPs identified several BBB-penetrating capsids
- Capsid 9P801 allows unprecedented levels of primate CNS transduction by IV dosing, no toxicity was observed in the liver, spinal cord or DRG
- Capsid 9P804 displaying strong heart transduction and partial DRG detargeting
- Nine additional NHP libraries are in late screening or characterization phase

TRACER holds strong potential to develop enhanced capsids that target a broad range of tissues with high specificity to deliver GTx for several diseases

TRACER capsids show increased transgene mRNA expression in NHP brain

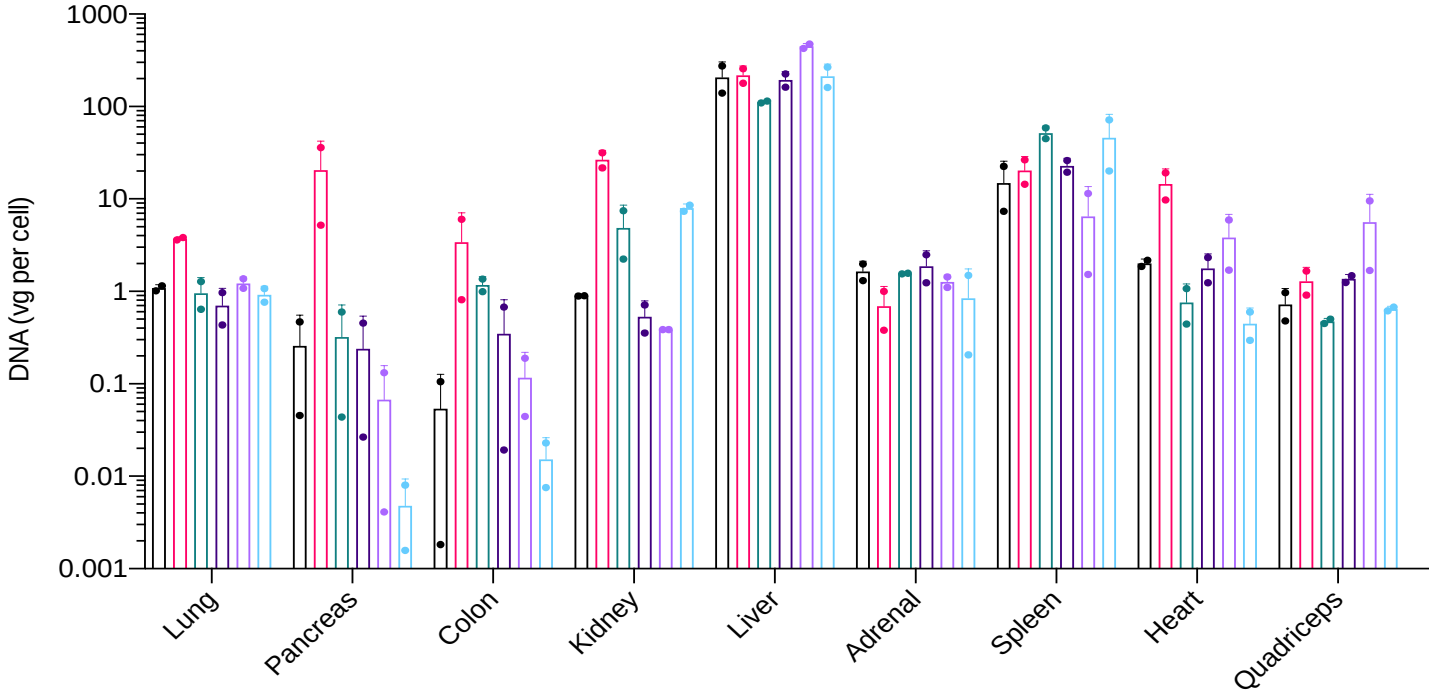


TRACER capsids show increased viral DNA biodistribution in the NHP brain

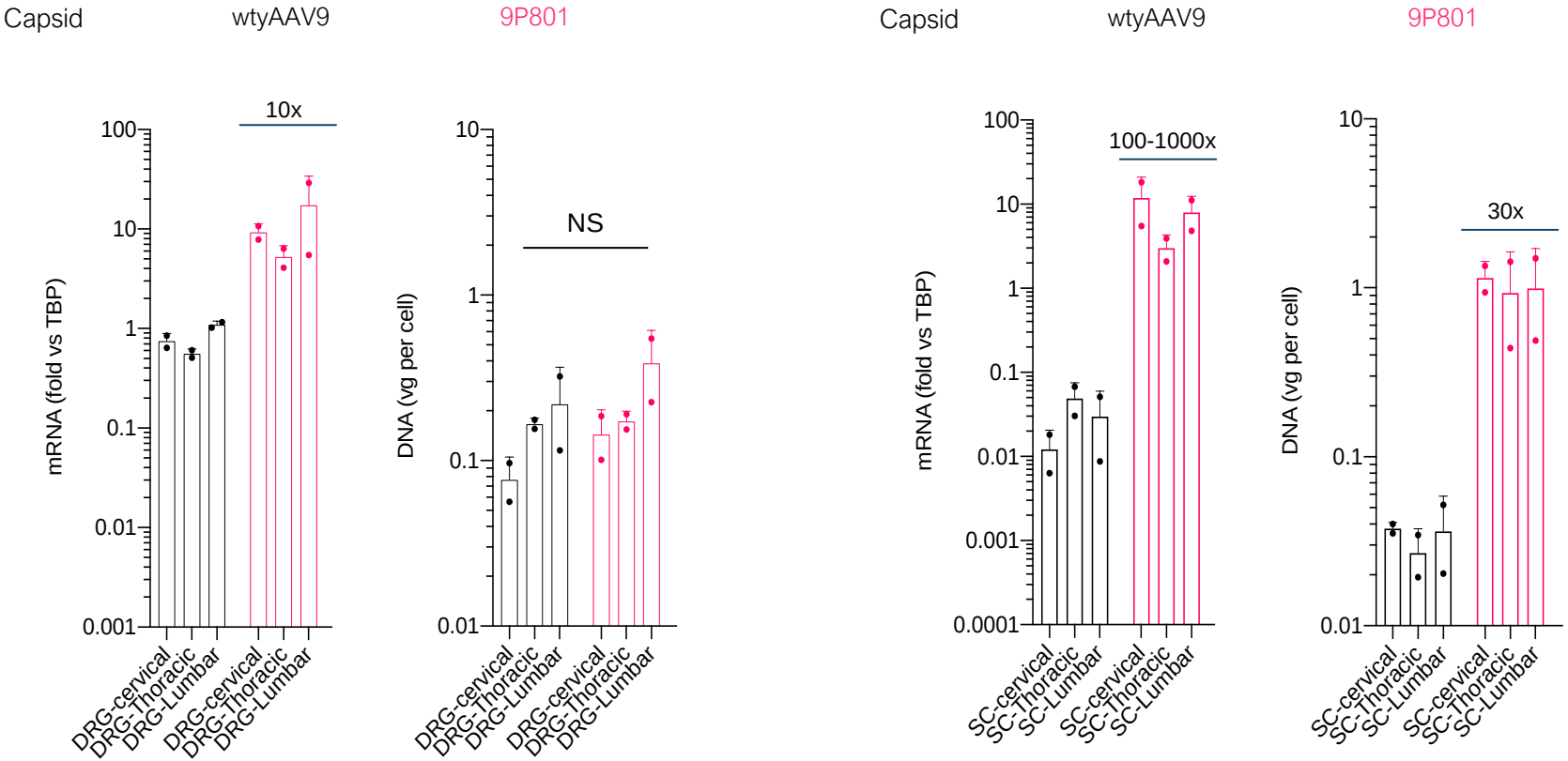


Viral DNA biodistribution and transduction in peripheral tissues

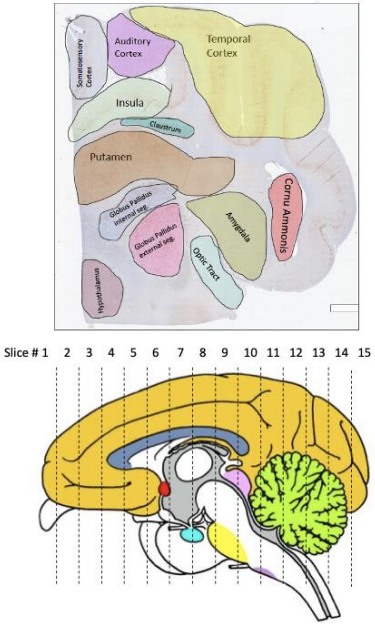
Capsid wtyAAV9 9P801 9P802 9P803 9P804 9P805

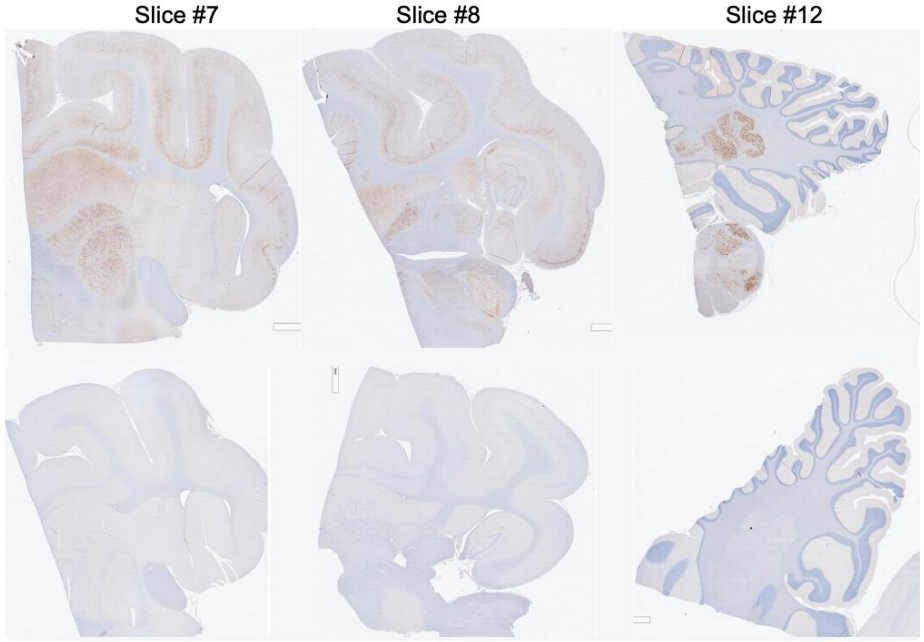


Transduction in the DRG and spinal cord: AAV9 vs. Capsid 9P801



TRACER capsid 9P801 mediates widespread transgene expression in NHP brain





Capsid variants crossed BBB and achieved widespread transduction of multiple brain regions including the cortex, thalamus, striatum, cerebellum, brainstem and spinal cord

VECTORIZED ANTIBODY DELIVERY

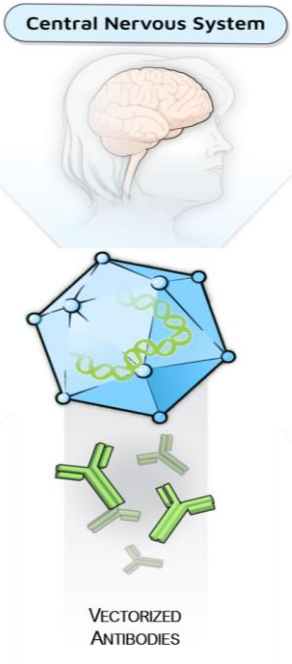
There are significant opportunities for innovation in CNS-targeted antibodies

Targeted antibody therapies in neurological indications have been met with major challenges

- Delivery to CNS with passive immunotherapy is very limited
  - 0.1% of antibodies pass through the BBB
- Inability to target the intracellular proteome
- Delivery of antibody fragments remains a challenge due to PK liabilities
- Potential for unspecific or toxic off-target effects
- Prohibitive manufacturing volumes & costs

Better approaches are needed for antibody therapies for serious neurologic and neuro-oncology diseases

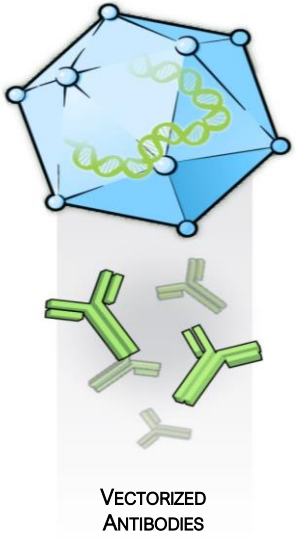
vAb platform delivers antibodies directly to brain regions associated with disease progression



- Proprietary technology to enable expression of functional antibodies *in vivo*, incorporating multiple peptide chains with assembly, folding and transport within the cell
- Potential for single dosing targeting CNS tissue
- Capsid and promoter design enables highly refined targeting to specific CNS cell types
- Active research in drugging intracellular proteome through vectorized nanobodies, degraders, and other innovative platforms

vTau program validates single-dose vAb approach

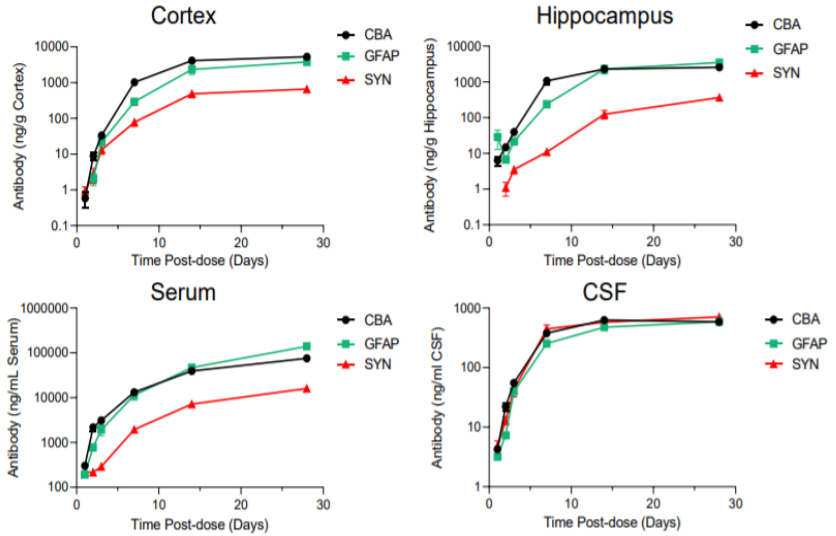
Strategy directs CNS-targeted AAV vectors to encode a novel anti-tau monoclonal antibody



- Modular antibody vectorization cassettes consisting of AAV vector + transgene encoding anti-tau monoclonal full-length antibodies
- Cassettes designed to deliver more therapeutically relevant antibodies directly to critical brain regions associated with disease progression
- vAbs demonstrate efficacy in multiple animal tauopathy models
- vAb platform delivers high levels of antibody to the CNS; shows reduction of pathological tau + durable CNS expression

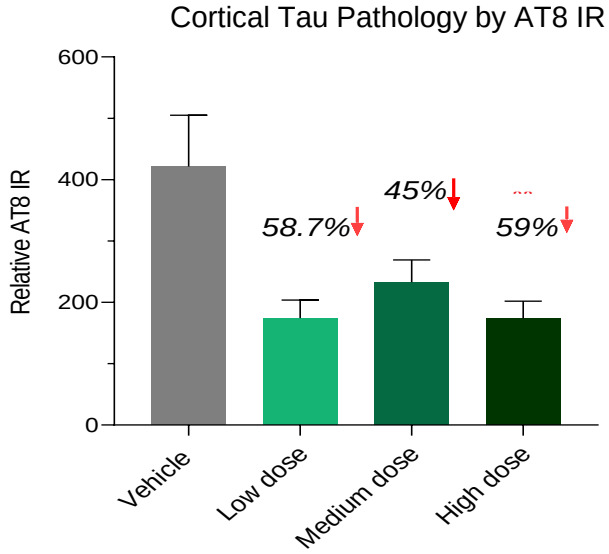
vAb platform delivers high levels of antibody to the CNS; shows reduction of pathological tau and durable CNS expression

Kinetics of Antibody Expression



Anti-tau antibody expression was detected as early as 2 days post-dose, reaching maximum levels at day 7, with **durable expression extending to 28 days following IV administration** of vectorized anti-tau antibody to rodents.

Efficacy Measured by AT8 ELISA



Decreases in the levels of pathological tau and neurofibrillary tangles were observed following IV administration of a vectorized anti-tau antibody to a rodent tauopathy model, resulting in up to **59% reduction in tau pathology**.

NEXT STEPS

Symbiotic platform/program approach poised to unlock significant value

TRACER Platform

- First of nine screening libraries generates capsids with unprecedented CNS transduction in NHPs, strong cardiac transduction, both via IV dosing
- Nine additional NHP libraries with strong potential to generate enhanced capsids beyond CNS/heart (skeletal muscle, eye, kidney, lungs, pancreas)
- Additional data anticipated by year-end 2021

vAb Platform

- Preclinical data suggest vAb may be a new single-dose IV strategy for various tauopathies
- On track for lead candidate selection 1H 2022

Pipeline

- Re-focused on validated targets with best-in-class potential; primed for early-stage execution

Cash runway into early 2023