

# UNLOCKING THE POTENTIAL OF AAV GENE THERAPY

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## A fully-integrated platform for gene therapy development

### A leader in next-gen AAV capsid discovery

- TRACER<sup>TM</sup> platform has identified highly differentiated AAV9- and AAV5-derived capsids
- Further discovery campaigns growing array of capsids targeting multiple tissue/cell types and refining initial sets of capsids to enhance desirable characteristics

### Deep experience vectorizing diverse payload modalities

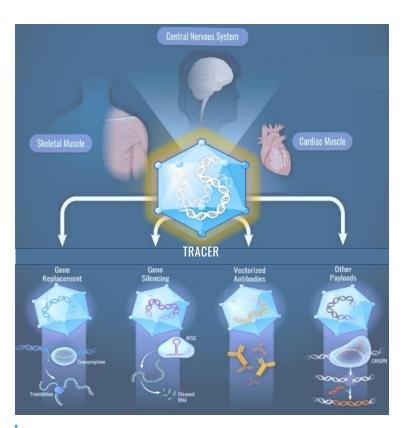
- Replacement, silencing, antibodies, other
- Differentiated vectorization and manufacturing

### **Expanding breadth of development opportunities**

Partnerships create 'external pipeline' and complement rich internal portfolio



## TRACER AAV capsid discovery platform: powering next-gen gene therapy



#### **Generating highly differentiated AAV9 capsids to overcome** critical gene therapy limitations\*

- Superior blood-brain-barrier penetration
- Enhanced cardiac muscle tropism
- Increased transgene expression in target tissues
- New class selective for glial cells more precise CNS targeting
- AAV5 capsids with enhanced brain, spinal cord tropism\*\*

#### **Enabling external development opportunities**

Transgene-specific license options for CNS/cardiac programs

#### Powering internal pipeline with best-in-class potential

✓ Well-validated targets, pathways to POC, areas of high unmet need



## **Recent Highlights**



# First transgene-specific licensing agreement reserves potential to execute similar transactions across various target cells, tissues, transgenes

- \$30 million upfront with \$20 million in near-term options
- Potential for \$580 million in milestones, plus royalties
- Option to access capsids for two CNS/cardiac transgenes
- Retain global rights to use licensed capsids in other transgenes, TRACER applications
- Potential for similar transactions across various target cells, tissues, transgenes







# Al Sandrock joins Board/Executive Committee to help shape future strategies for TRACER, therapeutic programs, external collaborations



 Scientific visionary who led the development of multiple transformational therapies for serious neurological diseases

Cash runway into second half of 2023 supported by \$130+ million position as of Dec. 31, 2021



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

### Conventional AAV vectors have a narrow therapeutic window

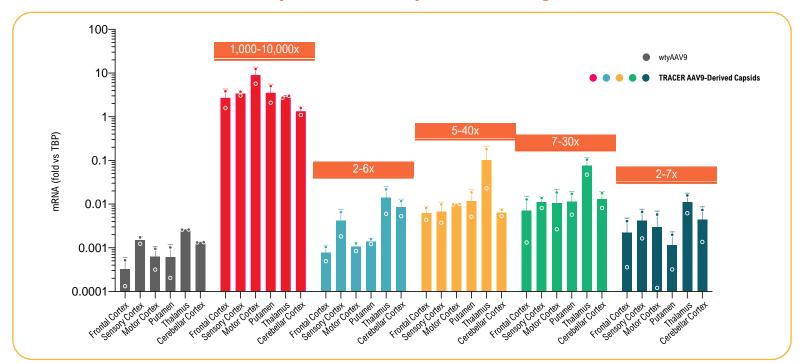
- Achieving meaningful efficacy with high doses yields a safety trade-off and risk-benefit imbalance
- Substantial toxicity risk from off-target effects
- Discoveries with conventional AAV capsids in mice have not translated to primates
- Clear limitations to effectively target the CNS and achieve broad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

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



## First TRACER campaign generated exceptionally improved capsids in NHPs\*

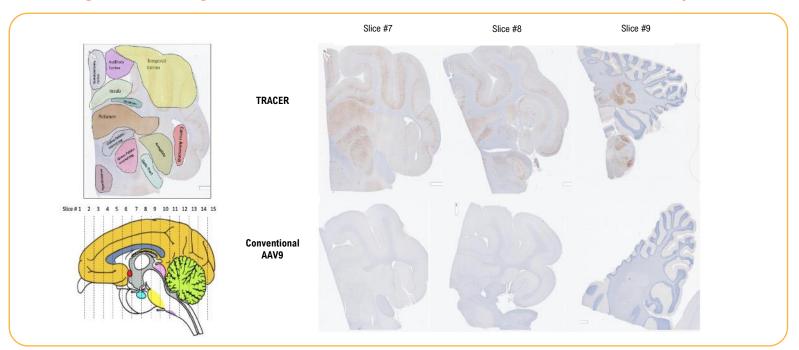
#### Initial studies demonstrate unprecedented expression throughout CNS with no toxicities





## TRACER AAV9-derived capsid mediates widespread transgene expression in NHP brain\*

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

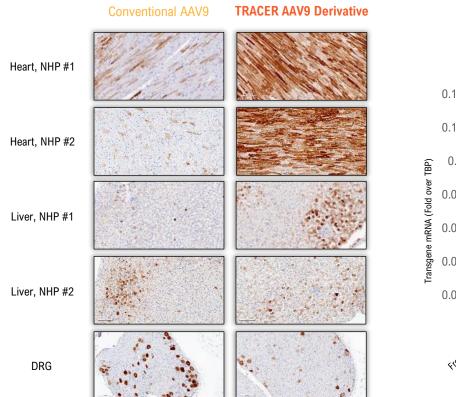




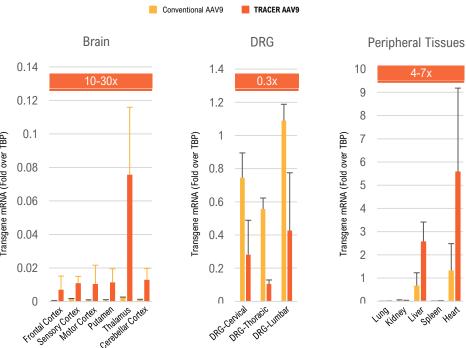
\*compared to conventional AAV9 dosed intravenously

8

## TRACER AAV9-derived capsid displays strong heart transduction and DRG detargeting\*



#### **TRACER-Derived AAV9 Transgene Expression Pattern in NHPs**



\*compared to conventional AAV9 dosed intravenously in NHPs



9

## New class of TRACER AAV9-derived capsids selective for glial cells in NHPs and rodents

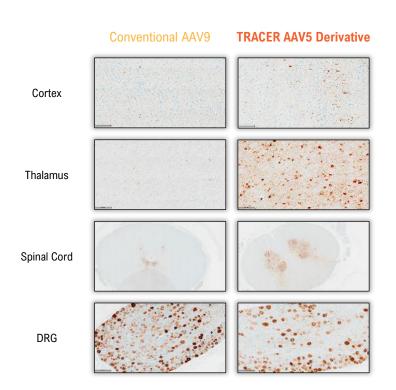
#### **CNS Tropism in Mouse**



- Strong tropism for glial cells may enable more precise targeting of certain CNS diseases affecting non-neuronal cells
- 40-70-fold increase in CNS transduction relative to conventional AAV9, when dosed intravenously
- Robust CNS targeting in both non-human primates and rodents, facilitating preclinical development



## TRACER AAV5-derived capsid displays enhanced CNS tropism in NHPs\*



- Low prevalence of neutralizing antibodies to AAV5 in general population
- Manufacturing advantages
- Cross-species translatability among primates and rodents
- Approximately 20-fold improvements in brain transduction compared with AAV9 (and greater versus AAV5) in NHPs
- Partial DRG detargeting (~2-fold)\*

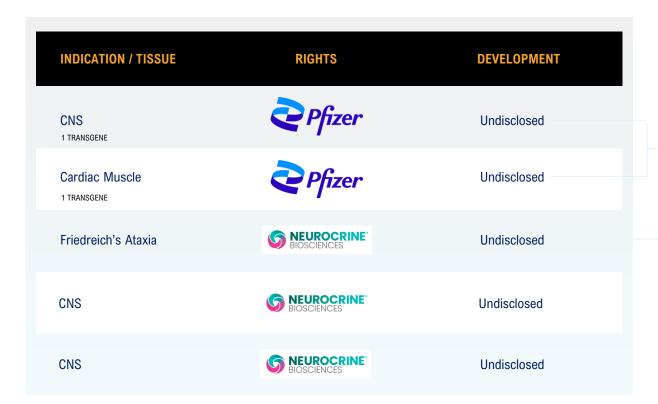


## TRACER-powered pipeline designed to achieve best-in-class status





## Partnerships expand growing number of development opportunities



Voyager retains global rights to all licensed TRACER capsids for use with other transgenes and to all other applications of the technology

Voyager has the option to co-develop or co-commercialize the program in the U.S. or grant Neurocrine global commercial rights



## **Powering the Next Generation of AAV Gene Therapy**

- Growing franchise of novel TRACER capsids with potential to overcome limitations and toxicities of first-generation AAV vectors\*
- First capsid licensing deal signed with Pfizer, significant BD interest for further applications
- Highly differentiated, integrated AAV gene therapy product engine
  - Industry-leading capabilities across delivery, vector engineering, and process/analytical development
- Expanding internal and external pipeline with best-in-class potential





**Unlocking the Potential** of AAV Gene Therapy

investors@vygr.com voyagertherapeutics.com



