

# UNLOCKING THE POTENTIAL OF AAV GENE THERAPY

Corporate Presentation | April 2022

# Forward-Looking Statements

This presentation, posted to the Company's website on April 8, 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," "undoubtedly," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward-looking statements. For example, all statements Voyager makes regarding Voyager's ability to continue to identify and develop proprietary capsids from its TRACER AAV screening platform; Voyager's ability to identify and develop proprietary capsids from its TRACER AAV screening 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 capsid; Voyager's ability to advance its AAV-based gene therapy programs; Voyager's ability to perform its obligations under its respective 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 are forward looking. All forward-looking statements are based on estimates and assumptions by Voyager's management that, although Voyager believes to be reasonable, are inherently uncertain. 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 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 the presentation was posted to the Company'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.

# A fully-integrated platform for gene therapy development

## A leader in next-generation AAV capsid discovery

- TRACER™ platform has identified highly differentiated AAV9- and AAV5-derived capsids targeting multiple tissue/cell types
- Ongoing discovery campaigns are expanding proprietary capsid library and refining initial capsids to enhance desirable characteristics

## Deep experience vectorizing diverse payload modalities

- Replacement, knockdown/silencing, antibodies, and others
- Differentiated manufacturing

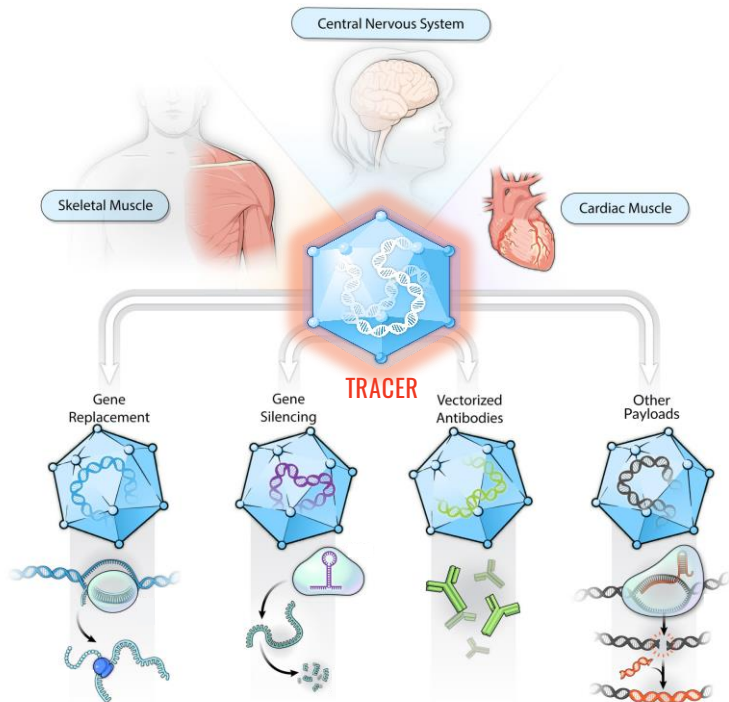
## Expanding breadth of development opportunities

- Collaborations with Novartis, Pfizer, and others create external development opportunities that complement a rich, TRACER-driven internal pipeline



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

TRACER capsids have shown significant potential to overcome limitations of first-gen AAV vectors



## Generating highly differentiated AAV9- and AAV5-derived capsids\*

- ✓ Superior blood-brain barrier (BBB) penetration
- ✓ Enhanced neuronal and glial tropism for more precise CNS targeting
- ✓ Broader therapeutic windows and detargeting of undesired tissues
- ✓ Enhanced cardiac muscle tropism

## Enabling external development opportunities

- ✓ Target-specific license option agreements with Novartis and Pfizer
- ✓ Potential for additional licensing within and beyond CNS targets

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

- ✓ Well-validated targets, pathways to POC, areas of high unmet need
- ✓ Intravenous delivery with CNS-targeted vectors

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

# License option agreements expand opportunities for TRACER capsid deployment

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



Target* (Cells, Tissues, Transgenes)	Upfront Payment	Potential Near-Term Fees**	Potential Milestone Payments	Total Potential Value	Tiered Royalties
3 CNS targets (plus 2 possible undetermined targets)	\$54 million	\$98.5 million	\$1.5 billion	\$1.7 billion	Mid- to high- single-digit
1 CNS target	\$30 million	\$20 million	\$580 million	\$630 million	Mid- to high- single-digit
1 Cardiac target					

\$84 million in total upfront payments extend cash runway into 2024

\*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  
 \*\*exercisable within 12 months of signing (or 30 months with respect to two additional targets for Novartis)

# TRACER™ CAPSID DISCOVERY PLATFORM

---

# First-gen 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
- Insufficient BBB penetration and target cell transduction with intravenous dosing
- Intraparenchymal and ICM, intrathecal delivery provide insufficient distribution for many indications

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

ICM: Intracisterna magna



# TRACER platform identifies capsids with enhanced tropisms across tissue, cell types

## Additional capsid campaigns are in process

- Ability to produce capsids with enhanced tropisms beyond CNS, including cardiac and skeletal muscle, eye, and liver, and for use in different routes of administration



TRACER

## Top capsid candidates are being further refined to enhance desirable characteristics

- Flexible library-generating method enables iteration and cross-species investigation
- Approach is tropism- and species-agnostic, and can be applied accordingly

## Platform generates proprietary knowledge and IP covering promising capsids

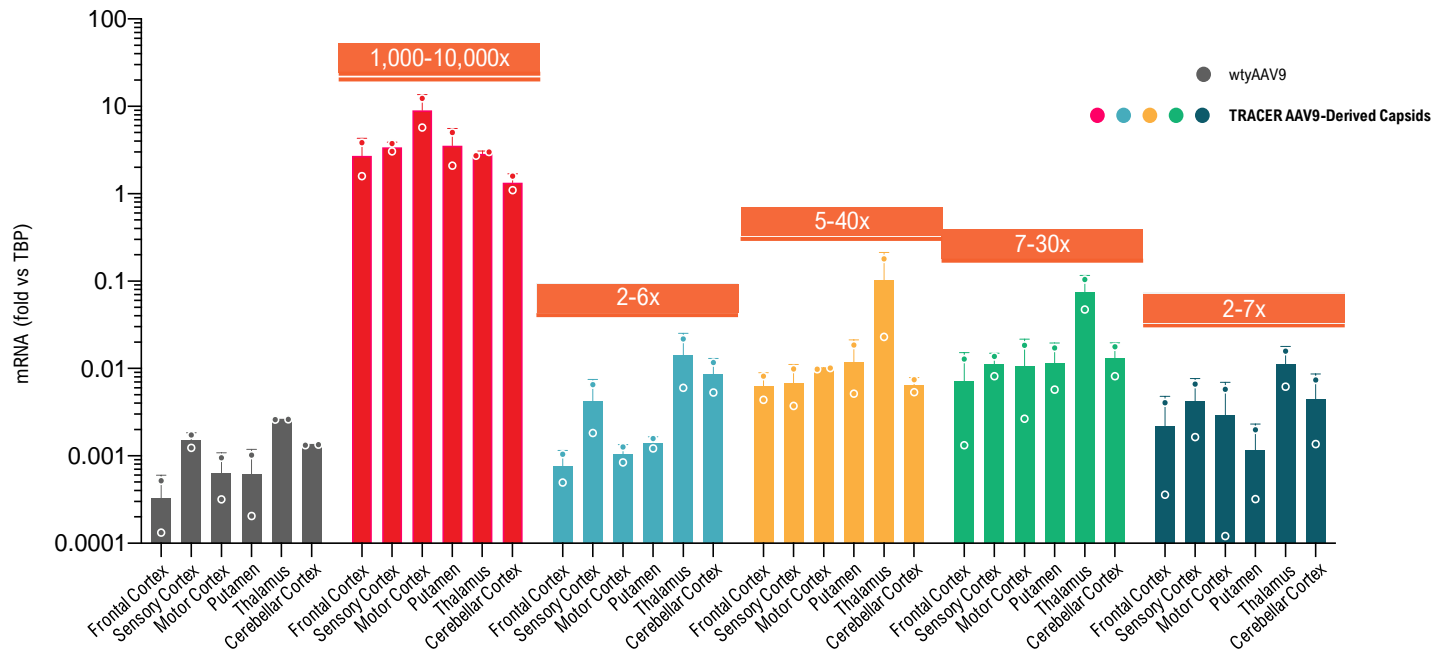
- Capsids generated are patent-eligible, novel compositions of matter
- Proprietary learnings from novel capsids inform a roadmap for patent-eligible improvements

IP: Intellectual property



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

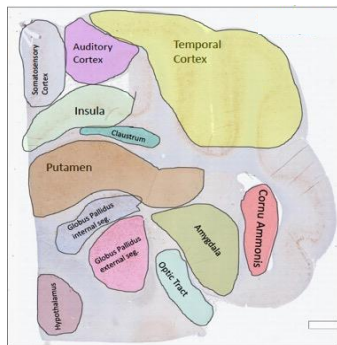
Initial studies demonstrate unprecedented expression throughout CNS with no observed toxicities



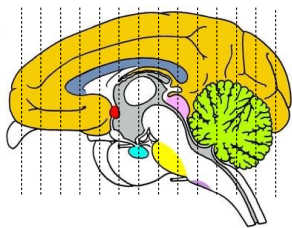
\*compared to conventional AAV9 dosed intravenously

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

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



Slice # 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

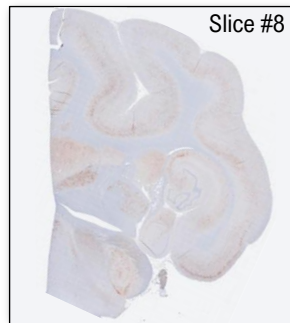


TRACER

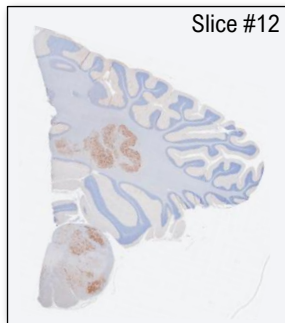
Slice #7



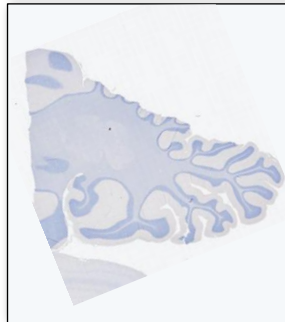
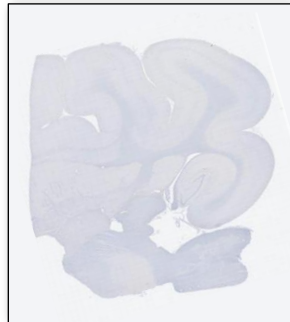
Slice #8



Slice #12

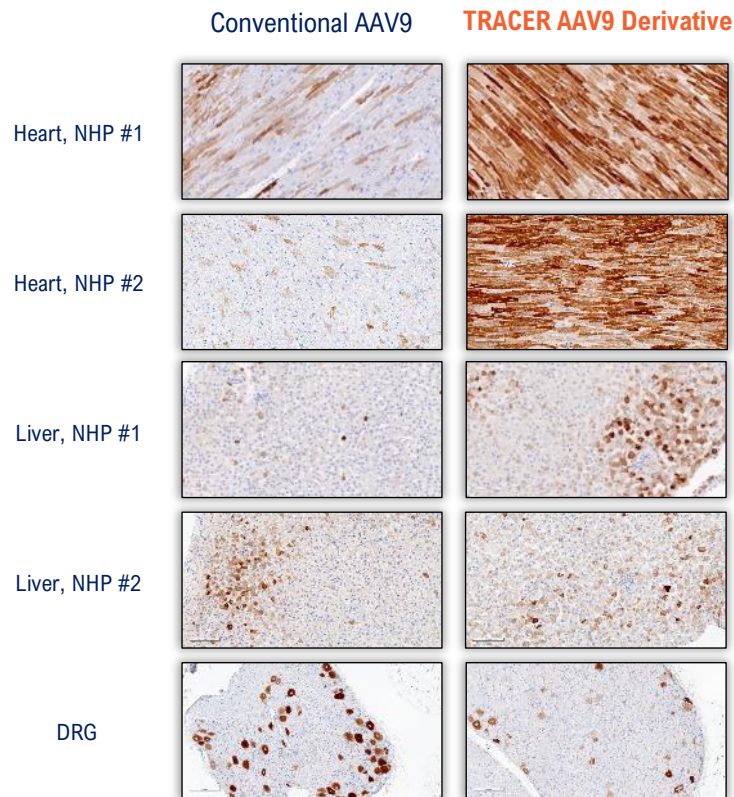


Conventional  
AAV9

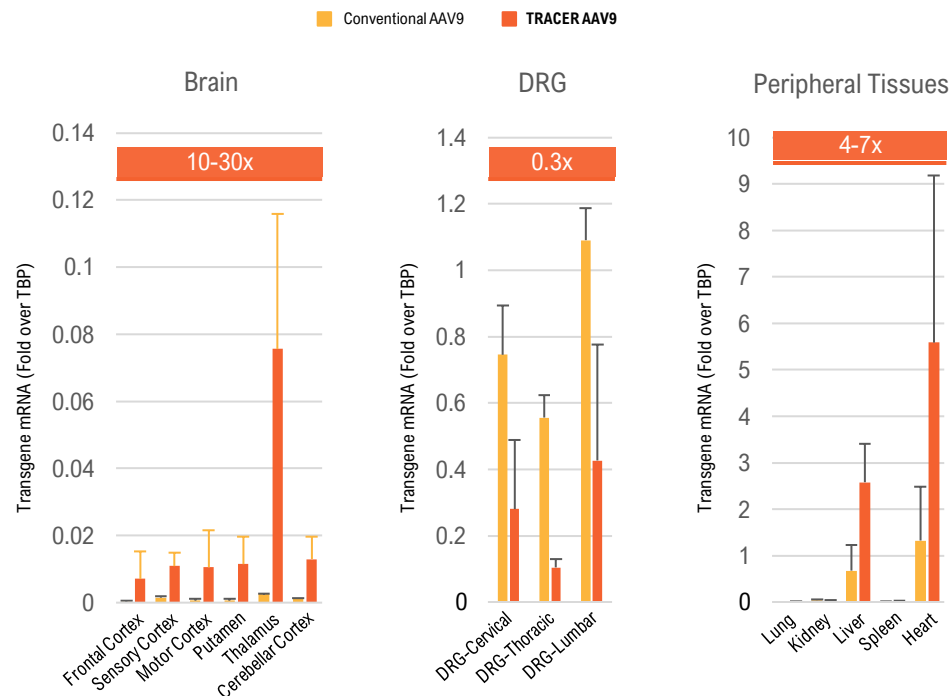


\*compared to conventional AAV9 dosed intravenously

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

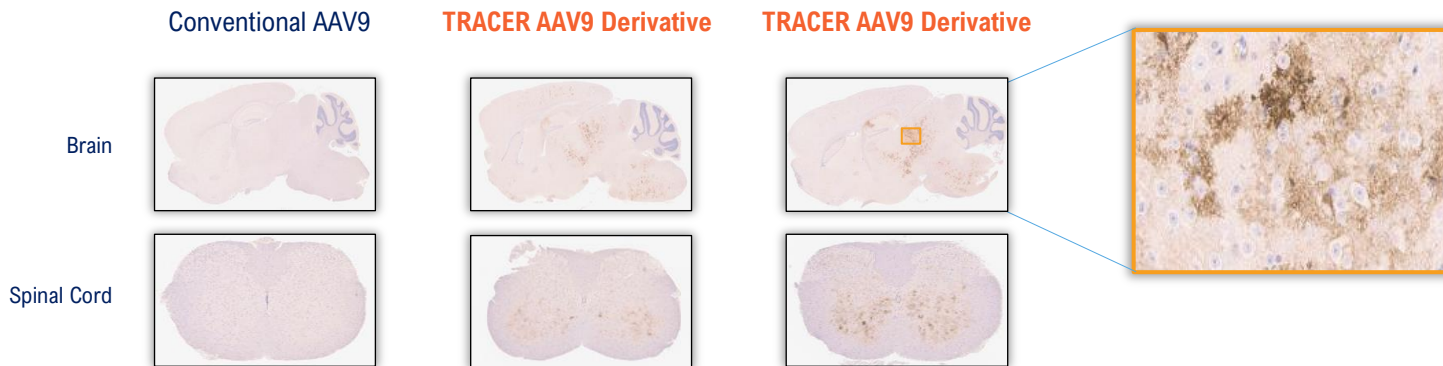


## TRACER-Derived AAV9 Transgene Expression Pattern in NHPs



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

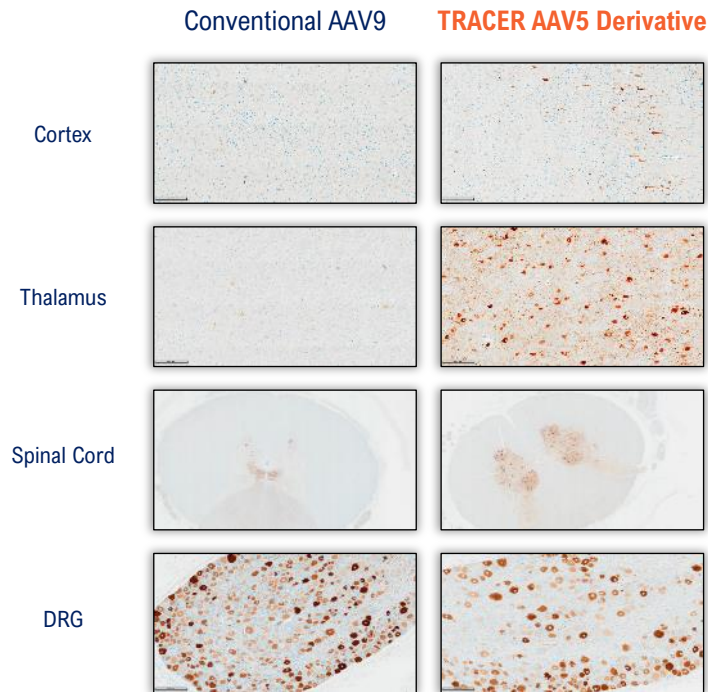
## CNS Tropism in Mouse



- ✓ 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 NHPs and rodents facilitating preclinical development



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



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

# TRACER capsids achieve unprecedented CNS transduction, strong cardiac transduction\*

## Expanding capsid library and further refining initial capsids to enhance desirable characteristics

**AAV9-derived capsid** from initial screening campaign demonstrated unprecedented levels of primate **CNS** transduction by IV dosing with no toxicities

**Separate AAV9-derived capsid** from initial screening campaign displayed strong **heart** transduction and partial DRG detargeting



TRACER

**New class of AAV9-derived capsids** showed strong tropism for glial cells; may enable more effective targeting of certain non-neuronal **CNS** diseases

**AAV5-derived capsid** displayed enhanced **CNS** tropism in NHPs, cross-species translatability among primates and rodents

# VECTORIZED ANTIBODY PLATFORM

---

# There are significant opportunities for innovation in CNS-targeted antibodies

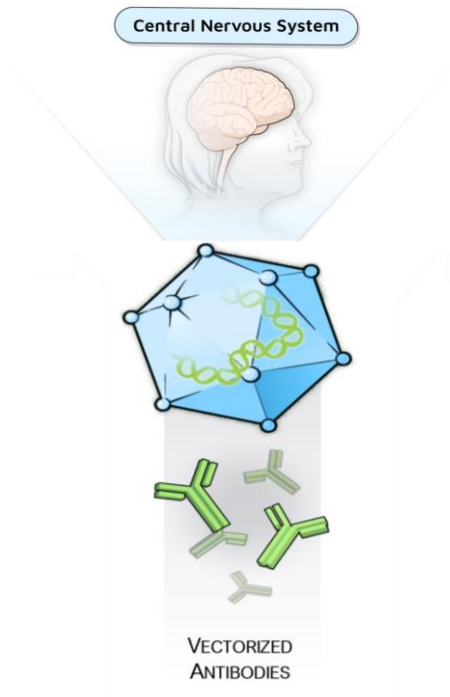
## Antibody therapies in neurological indications face significant challenges

- Delivery to CNS with passive immunotherapy is very limited
  - 0.1% of antibodies pass through the BBB
- Inability to target the intracellular proteome
- Pharmacokinetic liabilities associated with antibody fragments limit efficacy
- Potential for toxic, off-target effects with systemically-dosed antibodies
- Substantial manufacturing volumes and costs

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



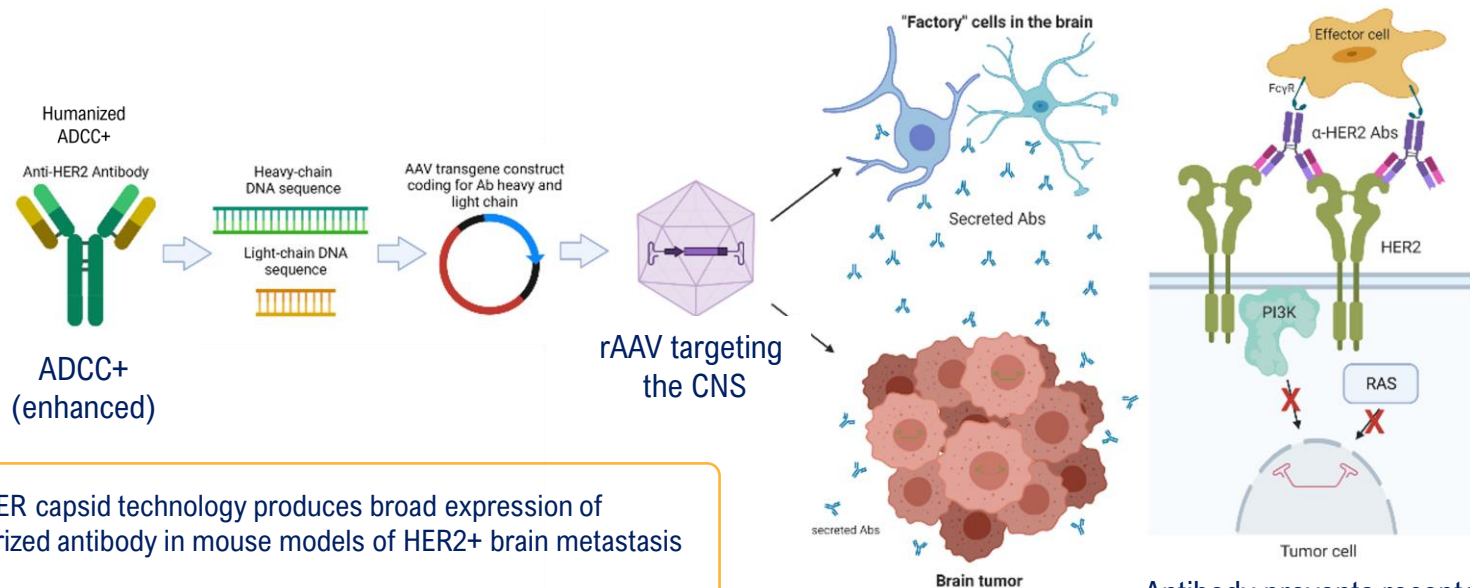
# Vectorized antibody approach allows for production of antibodies in affected brain regions



- ✓ Proprietary technology to enable expression of functional antibodies *in vivo*, incorporating multiple peptide chains with assembly, folding, and transport within the cell
- ✓ Active research in drugging intracellular proteome through vectorized intrabodies, nanobodies, degraders
- ✓ Potential for single dosing for continuous expression in target CNS cells to eliminate need for repeated passive administration of antibodies at high doses

# Vectorized anti-HER2 antibody program designed to activate innate immune system to destroy metastatic breast cancer tumors and inhibit tumor progression in CNS

## Strategy employs brain cells as antibody factories through AAV-mediated gene therapy



- ✓ TRACER capsid technology produces broad expression of vectorized antibody in mouse models of HER2+ brain metastasis
- ✓ IV administration of a TRACER AAV vector encoding an ADCC enhanced anti-HER2 antibody conferred ~40% survival benefit\*

Antibody prevents receptor dimerization & promotes ADCC

# Vectorized Tau program showcases single-dose vectorized antibody approach

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

- Modularly designed cassettes are arranged to optimize expression of fully-functional antibodies
- Payloads designed to deliver more therapeutically-relevant antibodies directly to critical brain regions associated with disease progression
- Vectorized antibodies demonstrate efficacy in multiple animal tauopathy models
- Vectorized antibody platform delivers high levels of antibody to the CNS; shows reduction of pathological tau and durable CNS 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.
  - 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.



# PRODUCT DEVELOPMENT

---



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



# Partnerships expand number of programs that may leverage TRACER capsids

TARGET	PARTNER	DEVELOPMENT STAGE
CNS	 NOVARTIS	Undisclosed
CNS	 NOVARTIS	Undisclosed
CNS	 NOVARTIS	Undisclosed
CNS	 Pfizer	Undisclosed
Cardiovascular	 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

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

# SUMMARY

---

# Powering the Next Generation of AAV Gene Therapy

- Growing franchise of novel TRACER capsids with potential to overcome delivery and toxicity limitations of first-gen AAV vectors\*
- Validating capsid license option deals signed with Novartis and Pfizer, significant potential for additional business development opportunities
- Highly differentiated and integrated AAV gene therapy product engine
  - Industry-leading capabilities across delivery, vector engineering, and process/analytical development for manufacturing
- Internal pipeline and partners' programs utilizing our capsids feature best-in-class potential





**[investors@voyagertherapeutics.com](mailto:investors@voyagertherapeutics.com)**

**[voyagertherapeutics.com](http://voyagertherapeutics.com)**

