Voyager Therapeutics - A Spinout from UMass Gene Therapy and RNAi Technologies

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GENE THERAPY STRATEGIES: AN OVERVIEW

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University of Massachusetts Medical School
DISCLOSURE

1. G. Gao is a cofounder of Voyager Therapeutics, a biopharmaceutical company and holds equity in the company.

2. G. Gao is an inventor on patents with potential royalties licensed to Voyager and other biopharmaceutical companies.
GENE THERAPY STRATEGIES: AN OVERVIEW
**Drug Development**

- **Conventional versus Gene Tx**

**Cost:** $3 Billions

**GT drug development:**
- starts with a specific therapeutic agent
- skips the drug discovery phase
PROGRESS IN GENE THERAPY - DRIVEN BY VECTOR PLATFORM DEVELOPMENT

- The path to today & beyond.....

1990
First human gene therapy for ADA Via retrovirus (Sept 14, 1990)

1995
First AAV for CFTR (November 1995)
First adenovirus for cystic fibrosis (1995)

2000
AAV2 gene transfer to treat LCA (2008)
Discovery of AAV8 (2002)

2005
AAV8 to treat hemophilia B (2011)
Gau G entered the field (1994)

2010
Clinical trial for X-linked ALD (2014)

2015
Glybera approved by EMA (2012)
CAR-T-cell therapy (2011)
COMMERCIALIZATION OF GENE THERAPY
- RAPID TRANSFORMATION IN THE PAST FEW YEARS

More than 200 gene therapy companies globally
WHY UMMS?

- A WORLD LEADER IN RNAi, DEGENERATIVE NEUROLOGICAL DISEASE RESEARCH & AAV GENE THERAPY

• Our faculty have made key advances
  – World leading scientists in RNAi research (Mello, Ambros, & Zamore)
  – World leading physician scientists in neurodegenerative disorders
    Ø Brown for Amyotrophic Lateral Sclerosis
    Ø Aronin for Huntington Disease
  – World leading rAAV gene therapy scientists
    Ø First to discover novel primate AAVs for efficient and stable gene transfer (Gao, 2002)
    Ø First to use AAV gene therapy in patients with 4 INDs (Flotte 1995)

• Horae Gene Therapy Center
  – A >12,000 Ft² state-of-art research facility on the 6th floor of Albert Sherman Building
  – Research home for 15 faculty and affiliated faculty members, > 60 trainees and staff
**Important Milestones in Founding & Growing of Voyager**

- **2009**: Initially approached by 3rd Rock Venture
- **2012**: Re-engagement by 3rd Rock Venture
- **2013**: Continued discussions w/t 3RV on “AAVian”
- **2014**: Voyager signed license agreement w/ UMMS for RNAi and rAAV technology platforms
- **2015**: $845 M committed by Sanofi/Genzyme for strategic collaboration w/t Voyager in CNS gene therapy
- **2016**: Voyager secured $60 M series B funding from “Crossover” investors
- **2016**: Voyager IPO $225 M cash
Voyager was founded by world leaders in the fields of AAV gene therapy, expressed RNA interference and neuroscience.

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Kinetics Foundation Chair in Translational Research and Professor in Residence of Neurological Surgery and Neurology, University of California at San Francisco

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Phillip Zamore, Ph.D.  
Howard Hughes Medical Institute Investigator; Gretchen Stone Cook Chair of Biomedical Sciences, Professor of Biochemistry and Molecular Pharmacology, and Co-Director of the RNA Therapeutics Institute, University of Massachusetts Medical School (UMMS)
Company Highlights

Robust product engine to engineer, optimize, manufacture and deliver AAV gene therapies

Pipeline of five programs for severe CNS diseases

Lead program, VY-AADC01, for advanced Parkinson’s disease with human POC expected in H2:2016

Strategic collaboration with Genzyme — gene therapy “know-how”

Strong financial position with ~$225 million of cash following IPO in November 2015, no debt

Management team and scientific founders that have pioneered significant advances in AAV gene therapy and neuroscience, and have extensive CNS drug development expertise (Steve Paul, MD, CEO)
Treating Severe CNS Diseases with AAV Gene Therapy

**Why CNS?**
- Significant unmet medical need
- Genetically-validated targets
- Targeted delivery to regions of the brain & broader delivery to the spinal cord is achievable
- Durable transgene expression as CNS cells are terminally differentiated
- Immune-privileged site

**Why AAV?**
- Ability to target a variety of tissue & cell types within the CNS
- >1,300 patients (200 in CNS) treated, no AAV-related SAEs to date
- AAV does not readily integrate into the target cell genome, reducing potential for oncogenesis
- Ability to manufacture at commercial quality and scale
Product Engine Driving Pipeline of AAV Gene Therapies

**Product Engine**
- Dosing & Delivery Techniques
- Vector Engineering & Optimization
- Process R&D & Manufacturing

**Pipeline of 5 Programs**

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<tr>
<th>Program</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Commercial Rights</th>
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<tbody>
<tr>
<td>VY-AADC01</td>
<td>Advanced Parkinson’s Disease</td>
<td></td>
<td>U.S. (Voyager®)</td>
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<tr>
<td>VY-SOD101</td>
<td>Monogenic Form of ALS</td>
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<td>U.S. (Voyager®)</td>
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<td>VY-FXN01</td>
<td>Friedreich’s Ataxia</td>
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<td>VY-HTT01</td>
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<td>VY-SMN101</td>
<td>Spinal Muscular Atrophy</td>
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<td>U.S. (Voyager®)</td>
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Commercial Scale AAV Manufacturing Capabilities

**Process R&D**
- Process R&D center at Voyager’s headquarters
- Research grade baculovirus / Sf9 production system
- Up to 250L bioreactor capacity
- Proprietary reagents for new capsids and constructs

**Large Scale Research Capacity**
- Collaboration with UMass Medical School
- Research grade baculovirus / Sf9 production system
- Up to 500L bioreactor capacity

**Commercial Scale cGMP Capacity**
- Collaboration with MassBiologics
- cGMP baculovirus / Sf9 production system
- Up to 1,000L bioreactor capacity
- Voyager retains IP and key process know-how
Robust Strategic Collaboration with UMMS

Voyager and UMMS collaborate under a broad strategic partnership to advance AAV gene therapy research, manufacturing and education

**Research Collaboration**
- Pilot grant program focused on understanding & optimizing AAV vectors for therapeutic use
- Licenses and sponsored research focused on novel AAV technology
- Opportunities for UMMS participation in Voyager clinical trials

**Production & Manufacturing**
- AAV vector supply from the UMMS Gene Therapy Vector Core to support Voyager research projects
- Partnership with MassBiologics to advance AAV process development & GMP production for Voyager product programs

**Educational Support**
- Postdoctoral training program
- Sponsorship of annual lecture series on AAV-mediated gene therapy
- Opportunities for Voyager to support graduate fellowships in the area of central nervous system AAV gene therapy