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

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GENE THERAPY STRATEGIES: AN OVERVIEW
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

EX VIVO

IN VIVO

HORAE

GTC

University of Massachusetts Medical School
**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)

First AAV for CFTR (November 1995)
First adenovirus for cystic fibrosis (1993)

1995

First lentivirus against HIV (2003)

Gao G entered The field (1994)

Discovery of AAV8 (2002)

2000

AAV8 to treat hemophilia B (2011)

First AAV for CFTR (November 1995)

2005

Glybera approved by EMA (2012)

AAV2 gene transfer to treat LCA (2008)

Clinical trial for X-linked ALD (2014)

2010

CAR-T-cell therapy (2011)

2015

AAV8 to treat hemophilia B (2011)
COMMERCIALIZATION OF GENE THERAPY
- RAPID TRANSFORMATION IN THE PAST FEW YEARS

- More Gene Tx companies founded and went public
- More and more investment $ into Gene Tx
- Year 2013 Year 2014 Q 1, 2015 Year 2015 Projektion
- GT Investment $ in billion

COMMERCIALIZATION OF GENE THERAPY
- RAPID TRANSFORMATION IN THE PAST FEW YEARS

- More than 200 gene therapy companies globally

- Imugene
- Phyllogica
- Protagonist Therapeutics
- Benitec Biopharma
- Susavon Biosciences
- Arizona Cancer Therapeutics
- Arbutus Biopharma
- ProNAI Therapeutics
- Bioneer
- Dynavax Technologies
- Lypro Biosciences
- ProNAI Therapeutics
- Incyte Pharmaceuticals
- 4D Molecular Therapeutics
- Quark Pharmaceuticals
- SGI-DNA (Synthetic Genomics)
- CALIMMUNE
- CytRx
- C3 Jian

- Pfizer
- Poseida Therapeutics
- Regulus Therapeutics
- Renova Therapeutics
- Solstice Biologics
- Theragen Pharmaceuticals
- Vical
- Audientes Therapeutics
- Avalanche Biotechnologies
- Artery Therapeutics
- Mello Biotechnology
- Circle Pharma
- Bachem
- MannKind
- Axcell
- Biomics Biotechnology
- Sirnaomics
- miRagen Therapeutics
- Quark Pharmaceuticals
- MannKind
- Zealand Pharma
- FTI Biotech
- AGTC
- iTherapeutics
- Genethon
- PeptiMimesis
- Transgene
- ENYO Pharma
- Transgene
- Lysogene
- Annarum
- Décion Pharmaceuticals
- GenSight Biologics
- InvivoGen Therapeutics
- Expression Therapeutics
- Silence Therapeutics
- Rigentec
- CureVac
- uniQure
- BioNTech
- CureVac
- AveXis
- Errant Gene Therapeutics
- Exicure
- Genaflow Technologies
- Norga Pharma
- BioCancell
- Medgenics
- Silenseed
- Atox Bio
- DNAVEC
- WaVe Life Sciences
- Takara Bio
- CanBas
- Esperance Pharmaceuticals
- Rhythm Pharmaceuticals
- WaVe Life Sciences
- Décion Pharmaceuticals
- Tarx Pharmaceuticals
- AGTC
- Alteron Therapeutics
- Akashi Therapeutics
- Aylam Pharmaceuticals
- AVROBIO
- bluebird bio
- Boston Biomedical
- CureVac
- Cydan
- Dicerna Pharmaceuticals
- Dimension Therapeutics
- Editas Medicine
- Elpidera (Moderna Therapeutics)
- ETAGEN Pharma
- Immunaset
- Intelia Therapeutics
- Moderna Therapeutics
- Onkaiyo Therapeutics
- Pronitut Bionics
- Ra Pharmaceuticals
- RaRNA Therapeutics
- Spark Therapeutics
- Valera (Modern Therapeutics)
- Voyager Therapeutics
- uniQure
- RX Pharmaceuticals
- Springbank Pharmaceuticals
- Lipimetix
- Antigen Express
- Zata Pharmaceuticals
- Asclepio Therapeutics
- GenVec
- Sirnaomics
- Transgene
- Regeneron
- ReGenX Biosciences
- Diapin Therapeutics
- ONL Therapeutics
- RetroSense Therapeutics
- ProNAI Therapeutics
- Discovery Genomics (ImmunoSoft)
- Trana Discovery
- Aeclles
- Qualiby
- Fennc Pharma
- uniQure
- Peptscan Therapeutics
- interRNA Technologies
- interRNA Technologies
- Vasade Biosciences
- MannKind
- SolaranRx
- TheraSource
- Dipexum Pharmaceuticals
- Alpha-1 Biologics
- iCell Gene Therapeutics
- Abenea Therapeutics
- Milo Biotechnology
- Teleta Therapeutics
- AVROBIO
- 13therapeutics
- Formula Pharmaceuticals
- Inovio Pharmaceuticals
- Spark Therapeutics
- Discovery Labs
- Medgenics
- Trasos Therapeutics
- Replicor
- Teleta Therapeutics
- Rhapsody Biologics
- BGN Pharmaceuticals
- Synteris
- Demagen
- Indep Pharmaceuticals
- Novaphen
- Clink Bioscience
- Bachem
- Xagen
- ArteGen
- Cardiofire
- Mima Therapeutics
- Agilis Biotherapeutics
- Chrysalis BioTherapeutics
- MultiVir
- Immunocore
- AmpliPhi Biosciences
- Bicycle Therapeutics
- Phio Therapeutics
- PolyTherics (Abzena)
- Mina Therapeutics
- NightstaRx
- ReGen Therapeutics
- Silence Therapeutics
- Oxford Biomedica
- AmpliPhi Biosciences
- Serpin Pharma
- AmpliPhi Biosciences
- Manna Pharma
- Halo Bio
- Immune Design
- PhaseRx
- Arrowhead Research
- Madison Vaccines
- Nano Oncology (PeptiMed)
- Circul Therapeutics
- CohBar
- Lumen Therapeutics
- Medicine
- Protagonist Therapeutics
- Arrowhead Research
- Genervon Biopharmaceuticals
- Toleron
- Ambrx Biotechnology
- Acterus Therapeutics
- BioMedica (Oxford BioMedica)
- Cidara Therapeutics
- Emsysce Biosciences
- Global Biotherapeutics
- IGE Therapeutics
- Inovio Pharmaceuticals
- Kalos Therapeutics

✓ 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
    ➢ Brown for Amyotrophic Lateral Sclerosis
    ➢ Aronin for Huntington Disease
  – World leading rAAV gene therapy scientists
    ➢ First to discover novel primate AAVs for efficient and stable gene transfer (Gao, 2002)
    ➢ 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 with 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**: $45 M series A funding by 3RV & formally launching of Voyager
- **2016**: Voyager secured $60 M series B funding from “Crossover” investors
- **2016**: Voyager IPO $225 M cash
Company Founders

Voyager was founded by world leaders in the fields of AAV gene therapy, expressed RNA interference and neuroscience.

Krystof Bankiewicz, M.D., Ph.D.
Kinetics Foundation Chair in Translational Research and Professor in Residence of Neurological Surgery and Neurology, University of California at San Francisco

Guangping Gao, Ph.D.
Director, University of Massachusetts Medical School (UMMS) Gene Therapy Center & Vector Core; Scientific Director, UMMS-China Program Office; Professor of Molecular Genetics and Microbiology, UMMS

Mark Kay, M.D., Ph.D.
Dennis Farrey Family Professor, Head, Division of Human Gene Therapy, Departments of Pediatrics and Genetics, Stanford University School of Medicine

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

<table>
<thead>
<tr>
<th>Program</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>VY-AADC01</td>
<td>Advanced Parkinson’s Disease</td>
<td></td>
<td>U.S.: Voyager® Genzyme (option)</td>
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<tr>
<td>VY-SOD101</td>
<td>Monogenic Form of ALS</td>
<td></td>
<td>Ex-U.S.: Genzyme (option)</td>
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<tr>
<td>VY-FXN01</td>
<td>Friedreich’s Ataxia</td>
<td></td>
<td>Genzyme (option)</td>
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<tr>
<td>VY-HTT01</td>
<td>Huntington’s Disease</td>
<td></td>
<td>Genzyme (option)</td>
</tr>
<tr>
<td>VY-SMN101</td>
<td>Spinal Muscular Atrophy</td>
<td></td>
<td>Genzyme (option to worldwide)</td>
</tr>
</tbody>
</table>
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
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