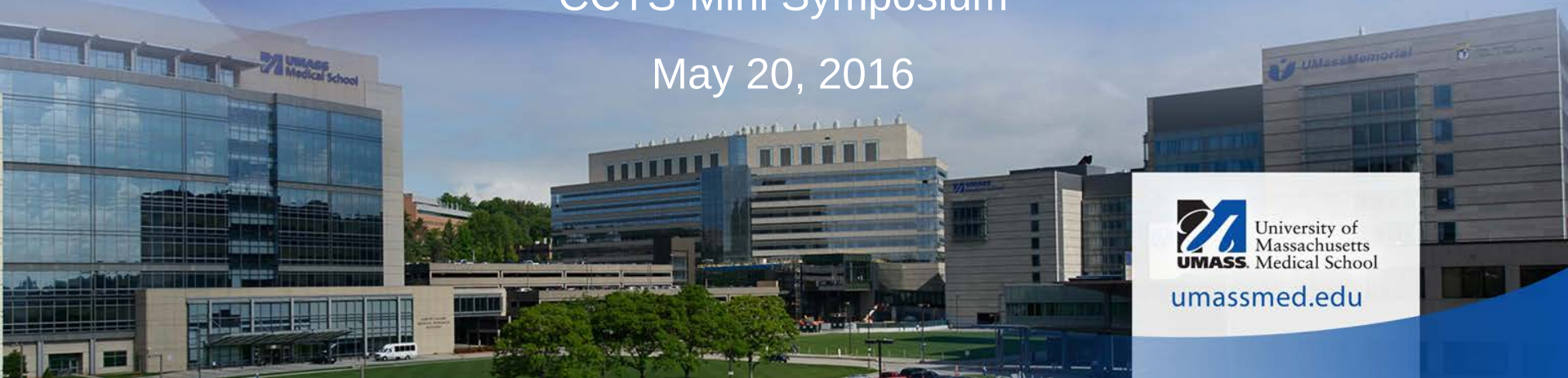
VOYAGER THERAPEUTICS

- A SPINOUT FROM UMASS GENE THERAPY AND RNAI TECHNOLOGIES

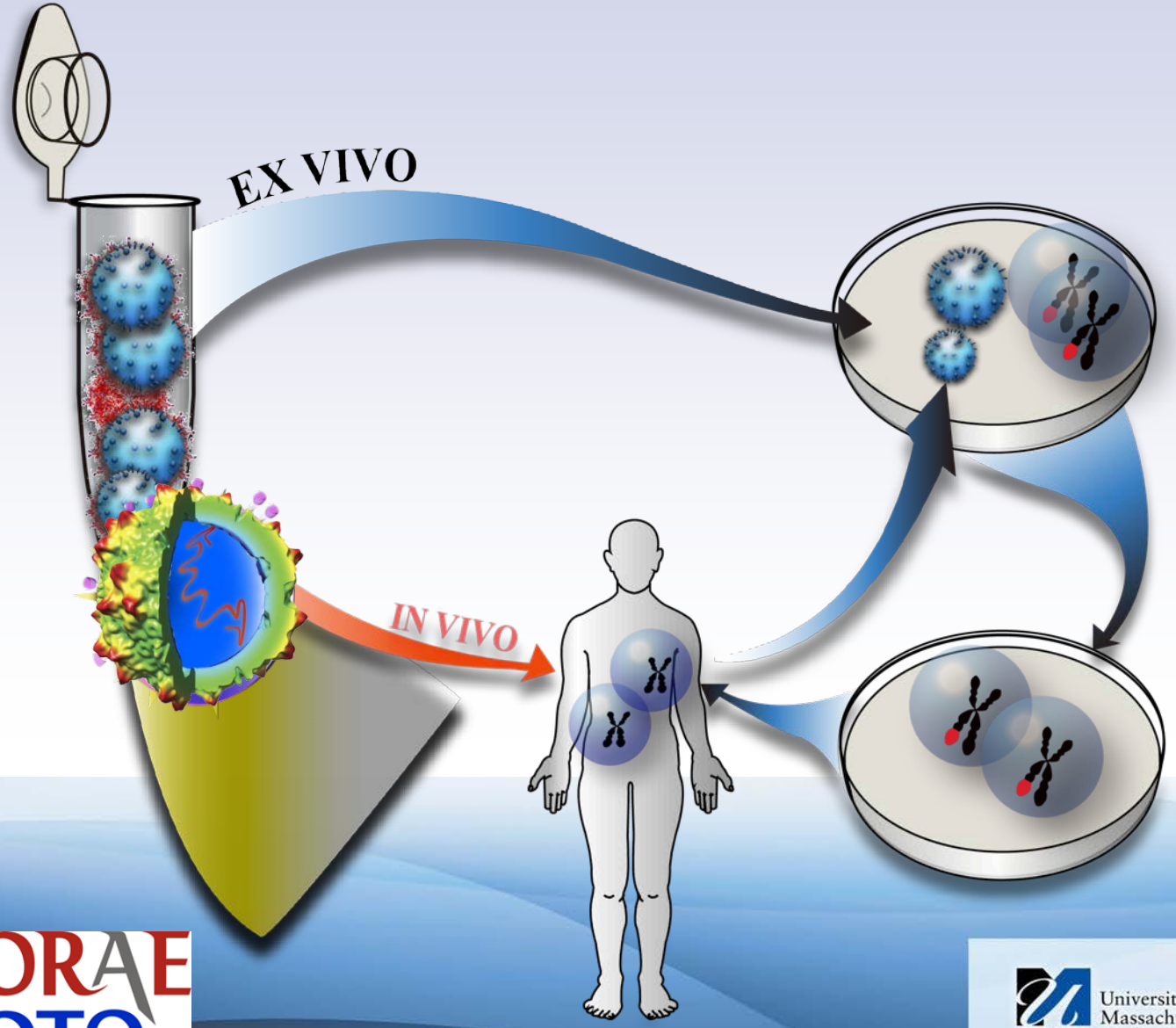
Guangping Gao, PhD

CCTS Mini Symposium

May 20, 2016



Gene Therapy Strategies: An Overview



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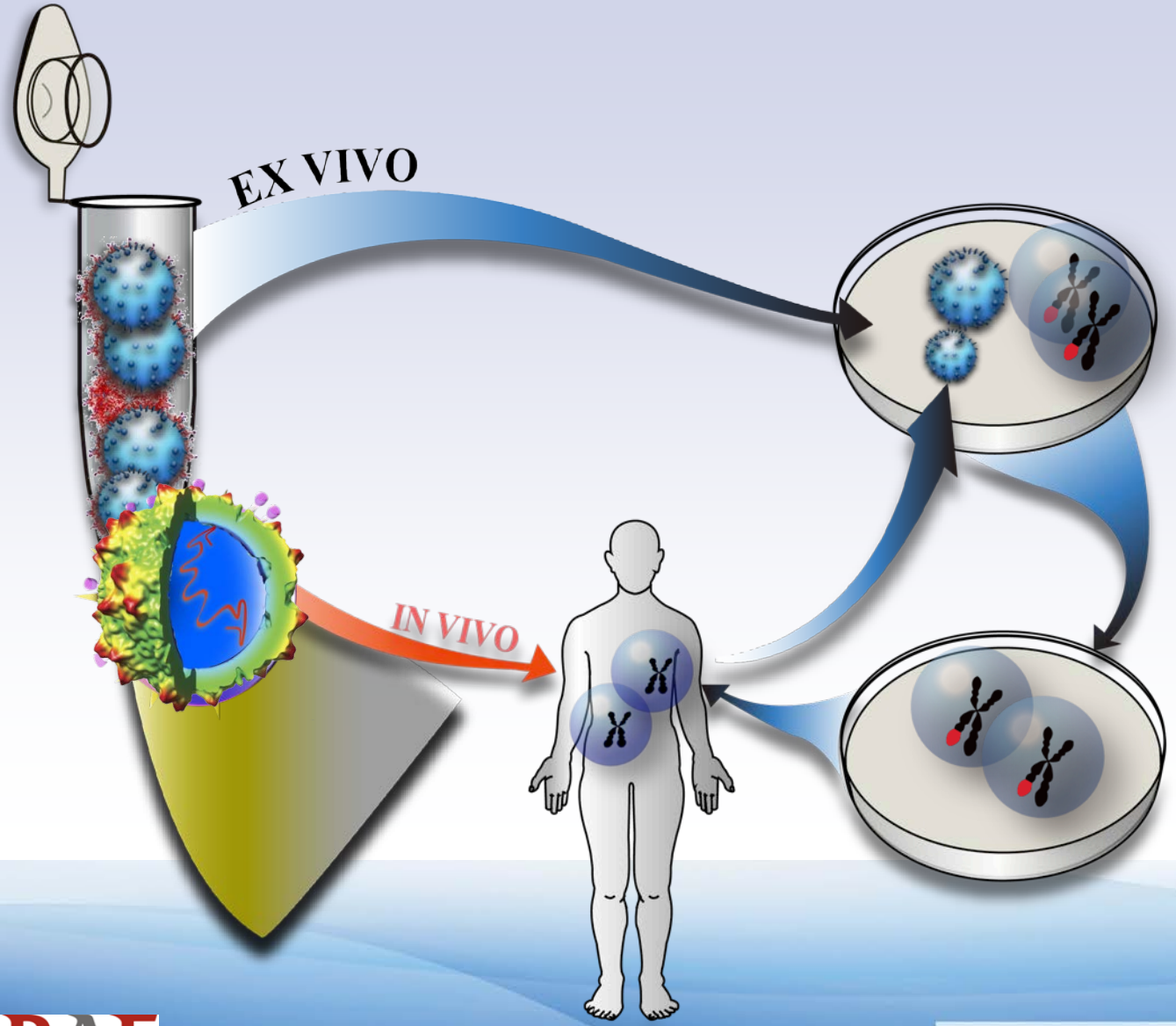
Disclosure

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



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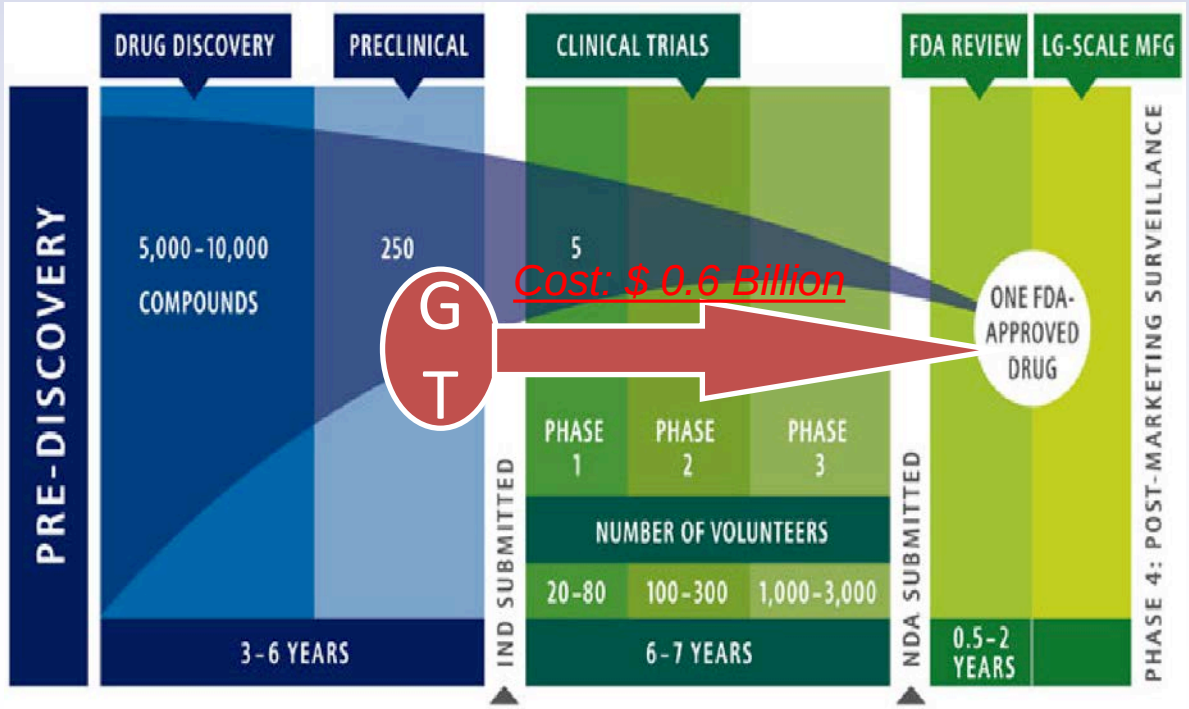
DRUG DEVELOPMENT
- *CONVENTIONAL VERSUS GENE TX*

Cost: $3 Billions



GT drug development:

- starts with a specific therapeutic agent
- skips the drug discovery phase

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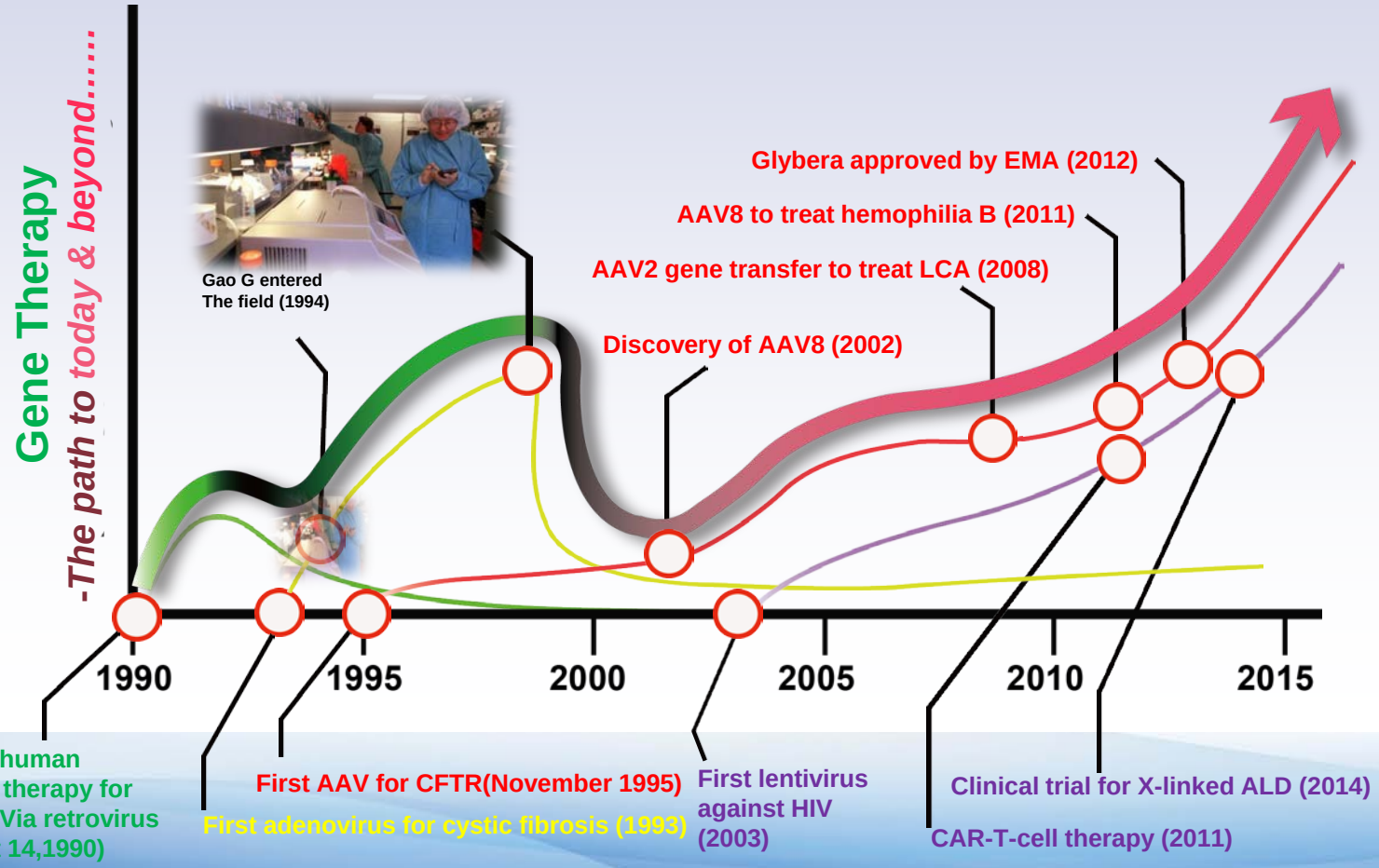
PROGRESS IN GENE THERAPY
- *DRIVEN BY VECTOR PLATFORM DEVELOPMENT*



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COMMERCIALIZATION OF GENE THERAPY

- RAPID TRANSFORMATION IN THE PAST FEW YEARS

Imugene
Phylogica
Protagonist Therapeutics
Benitec Biopharma
Susavion Biosciences
Arizona Cancer Therapeutics
Arbutus Biopharma
ProNAi Therapeutics
Bioneer
Dynavax Technologies
Lypro Biosciences
ProNAi Therapeutics
Ionis Pharmaceuticals
4D Molecular Therapeutics
Quark Pharmaceuticals
SGI-DNA (Synthetic Genomics)
CALiMMUNE
CytRx
C3 Jian

Pfizer
Poseida Therapeutics
Regulus Therapeutics
Renova Therapeutics
Solstice Biologics
Theragene Pharmaceuticals
Vical
Audentes Therapeutics
Avalanche Biotechnologies
Artery Therapeutics
Mello Biotechnlogy
Circle Pharma
Bachem
MannKind
Ascletis
Biomics Biotechnology
Sirnaomics
miRagen Therapeutics
Quark Pharmaceuticals
MannKind
Zealand Pharma
FIT Biotech
AGTC
iTherapeutics
Genethon
PeptiMimesis
Transgene
ENYO Pharma
Transgene
Lysogene
Annapurna
Déclion Pharmaceuticals
GenSight Biologics
InvivoGen Therapeutics
Expression Therapeutics
Silence Therapeutics

Rigontec
CureVac
uniQure
BioNTech
CureVac
AveXis
Errant Gene Therapeutics
Exicure
Genable Technologies
Nogra Pharma
BioCancell
Medgenics
Silenseed
Atox Bio
DNAVEC
WaVe Life Sciences
Takara Bio
CanBas
Esperance Pharmaceuticals
Rhythm Pharmaceuticals
WaVe Life Sciences
Déclion Pharmaceuticals
Tarix Pharmaceuticals
AGTC
Aileron Therapeutics
Akashi Therapeutics
Alnylam Pharmaceuticals
AVROBIO
bluebird bio
Boston Biomedical
CureVac
Cydan
Dicerna Pharmaceuticals
Dimension Therapeutics
Editas Medicine
Elpidera (Moderna Therapeutics)

ETAGEN Pharma
ImmusanT
Intellia Therapeutics
Moderna Therapeutics
Onkaido Therapeutics
Pronutria Biosciences
Ra Pharmaceuticals
RaNA Therapeutics
Spark Therapeutics
Valera (Moderna Therapeutics)
Voyager Therapeutics
uniQure
RXi Pharmaceuticals
Spring Bank Pharmaceuticals
LipimetiX
Antigen Express
Zata Pharmaceuticals
AsclepiX Therapeutics
GenVec
Sirnaomics
Transgene
RegeneRx
ReGenX Biosciences
Diapin Therapeutics
ONL Therapeutics
RetroSense Therapeutics
ProNAi Therapeutics
Discovery Genomics (Immusoft)
Trana Discovery
Ascletis
Qualiber
Fennec Pharma
uniQure
Pepscan Therapeutics
InteRNA Technologies
InteRNA Technologies

Vasade Biosciences
MannKind
SolaranRx
TheraSource
Dipexium Pharmaceuticals
Alpha-1 Biologics
iCell Gene Therapeutics
Abeona Therapeutics
Milo Biotechnology
Telesta Therapeutics
AVROBIO
13therapeutics
Formula Pharmaceuticals
Inovio Pharmaceuticals
Spark Therapeutics
Discovery Labs
Medgenics
Thrasos Therapeutics
Replicor
Telesta Therapeutics
Rhapsody Biologics
BCN Peptides
Sylentis
Dermagen
InDex Pharmaceuticals
Novahep
Olink Bioscience
Bachem
Xigen
ArisGen
Cardiorentis
Mirna Therapeutics
Agilis Biotherapeutics
Chrysalis BioTherapeutics
MultiVir
Immunocore

AmpliPhi Biosciences
Bicycle Therapeutics
Phico Therapeutics
PolyTherics (Abzena)
MiNA Therapeutics
NightstaRx
ReGen Therapeutics
Silence Therapeutics
Oxford Biomedica
AmpliPhi Biosciences
Serpin Pharma
AmpliPhi Biosciences
Marina Biotech
Halo-Bio
Immune Design
PhaseRx
Arrowhead Research
Madison Vaccines
Nano Oncology (PeptiMed)
Circuit Therapeutics
CohBar
Lumen Therapeutics
Medikine
Protagonist Therapeutics
Arrowhead Research
Genervon Biopharmaceuticals
Tolerion
Ambryx Biotechnology
Arcturus Therapeutics
BioMedica (Oxford BioMedica)
Cidara Therapeutics
Ensysce 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 Ft^2 state-of-art research facility on the 6^{th} floor of Albert Sherman Building
  - Research home for 15 faculty and affiliated faculty members, > 60 trainees and staff

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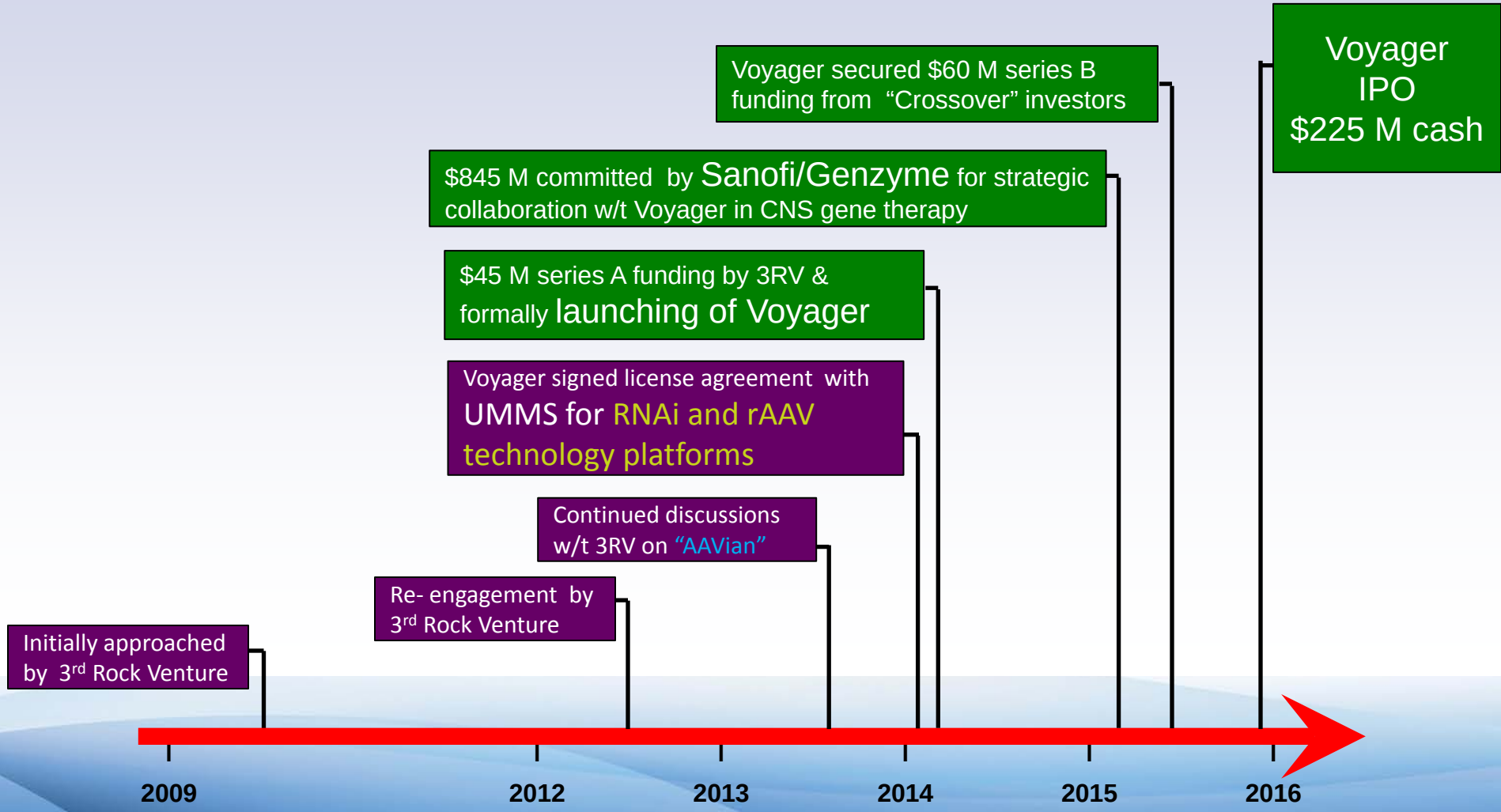
Important milestones in founding & growing of Voyager



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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

Program	Preclinical	Phase 1	Commercial Rights: U.S.	Commercial Rights: Ex-U.S.
VY-AADC01	Advanced Parkinson's Disease		Voyager® THERAPEUTICS	Genzyme *(option)*
VY-SOD101	Monogenic Form of ALS		Voyager® THERAPEUTICS	
VY-FXN01	Friedreich's Ataxia		Voyager® THERAPEUTICS	Genzyme *(option)*
VY-HTT01	Huntington's Disease		Voyager® THERAPEUTICS Genzyme *(option to co-U.S.)*	Genzyme *(option)*
VY-SMN101	Spinal Muscular Atrophy		Genzyme *(option to worldwide)*	

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