Accelerating Medicines Partnership

Gene Therapy

August 26, 2020

FNIH
Foundation for the National Institutes of Health

Co-Leads:
Peter Marks, MD, PhD (CBER/FDA)
PJ Brooks, PhD (NCATS/NIH)
Gopa Raychaudhuri, PhD (CBER/FDA)
Seng H. Cheng, PhD (Pfizer)

Accelerating Medicines Partnership in Gene Therapy (AMP GT) - Program Plan and Partnering Webinar

General Goals

- Review and understand the scope, design, impact and deliverables of the AMP GT Program
- Understand the pre-competitive partnership opportunities to address the limited access to gene therapy for populations affected by ultra-rare diseases

The webinar is being recorded for archival purposes

- Slides will be made available following the Webinar

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Zoom Housekeeping Notes

Please mute yourself when not talking to reduce background noise. (You will be muted upon entering by the host, unless you're a speaker.) The mute/unmute button is on the task bar on the bottom to the far left.

Please submit your questions and comments using the "chat" feature. We will use these responses during the Q&A at the end of the primary program sessions. **Please be sure to send your chat to "everyone."**

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Today's Presenters

National Center for Advancing Translational Sciences

Dr. P.J. Brooks — Program Director, Office of Rare Diseases Research

FDA

Dr. Peter Marks — Director, Center for Biologics Evaluation and Research

FNIH
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Dr. Joseph Menetski — Associate Vice-President of Research Partnerships

Steve Hoffmann — Director, Inflammation and Immunology

Today's Agenda

11:30 AM – 11:35 AM	**Introduction and Webinar Overview**
11:35 AM – 11:45 AM	**Session 1: FNIH and the Accelerating Medicines Partnership**
11:45 AM – 12:45 PM	**Session 2: The AMP Gene Therapy Program**
12:45 PM – 1:05 PM	**Q&A**
1:05 PM – 1:15 PM	**Session 3: Communications and Partnering Opportunities**
1:15 PM – 1:25 PM	**Q&A**
1:25 PM – 1:30 PM	**Ongoing Actions, Timelines and Next Steps**

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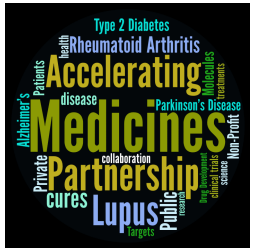
Session 1

FNIH and the Accelerating Medicines Partnership

FNIH
Foundation for the National Institutes of Health



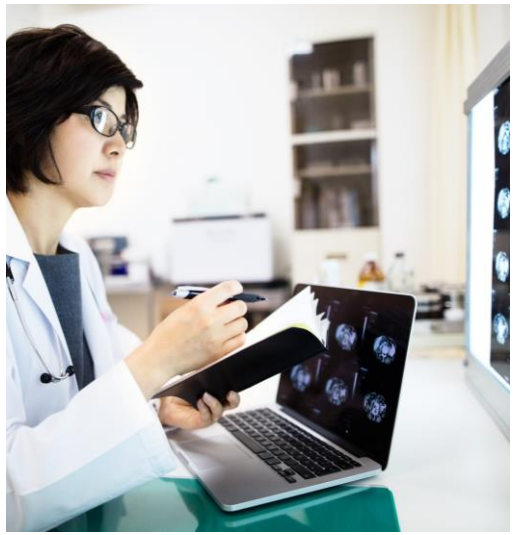
FNIH

Who are we?
What do we do?
How we achieve it?

AMP

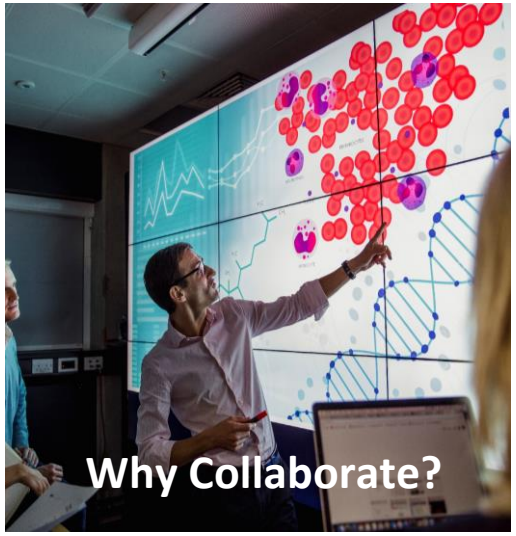
What is AMP?
How did we get here?

About the FNIH



The mission of the Foundation for the National Institutes of Health (FNIH) is to support the mission of the NIH. The FNIH creates and leads alliances and public-private partnerships that advance breakthrough biomedical discoveries and improve the quality of people's lives.

The FNIH was created by Congress in 1990 as a not-for-profit charitable organization. The Foundation began its work in 1996 to facilitate groundbreaking research at the U.S. National Institutes of Health (NIH) and worldwide.



- Attract and share resources
- Enable insight and innovation
- Establish standards
- Distribute expertise
- Create consensus
- Drive competitiveness in marketplace
- Disseminate knowledge
- Enhance credibility
- Reduce costs
- Support training & education
- Manage complexity

FNIH

By the Numbers

$1.2B raised to date

$0.90 of every dollar spent directly supports programs

600+ programs supported since inception

124 *active* research partnerships, scientific education/training, conferences/ events, capital programs

17 years of “exceeds or meets industry standards” rating by Charity Navigator

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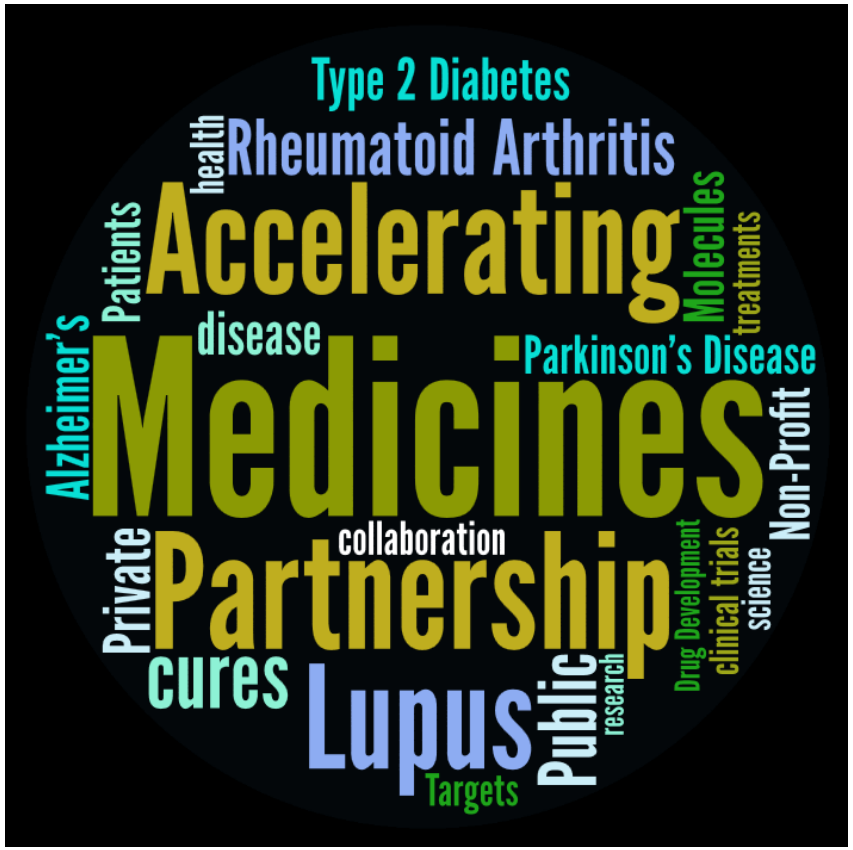
Select FNIH Partnerships

- **Accelerating Medicines Partnership** — **$302 million**
  NIH (OD), NIA, NIAMS, NIDDK, NINDS, 12 companies, 10 not-for-profit organizations
- **Partnership for Accelerating Cancer Therapies** — **$220 million**
  NCI, PhRMA, 12 pharmaceutical companies
- **Grand Challenges in Global Health (GCGH)** — **$201 million**
  Bill & Melinda Gates Foundation
- **Alzheimer's Disease Neuroimaging Initiative (ADNI)** — **$148 million**
  NIA, NIBIB, 25+ companies, 3 not-for-profit organizations
- **The Biomarkers Consortium** — **$95 million**
  FDA, NIH, CMS, PhRMA, BIO, pharmaceutical and nutrition companies, not-for-profit organizations
- **LungMAP: Master Lung Protocol Trial** — **$40 million**
  NCI (SWOG), FDA, Friends of Cancer Research, 10 companies to date
- **Helping End Addiction Long-Term (HEAL) Partnership Committee** — **$0.4 million**
  NIH contract

Coordination and Programmatic Leadership
Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
GeneConvene Global Collaborative

FNIH

The Accelerating Medicines Partnership



AMP Overview and Scope

- **NIH partnered with FNIH, FDA, 10 biopharmaceutical firms, multiple non-profits (including patient advocacy groups), to:**
  - Increase the number of new diagnostics, therapies
  - Reduce time, cost of developing them
- **Investing >$350M in four projects (5-year initial commitment):**
  - Alzheimer's disease (launched in 2014)
  - Type 2 diabetes (2014)
  - Rheumatoid arthritis/Lupus (2014)
  - Parkinson's Disease (2018)
  - Schizophrenia (Sept 2020)
- **Project management provided by FNIH**

Developing continuing (2.0) programs:

- AD
- Common Metabolic Disease (CMD) and
- Autoimmune and Immune-Mediated Diseases (AIM)

New program:

- Gene Therapy

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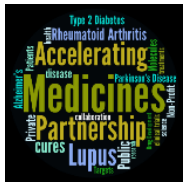
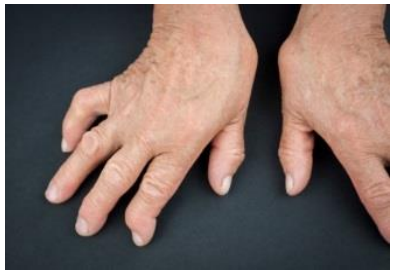


Alzheimer's Disease

Type 2 Diabetes



Autoimmune Diseases

Parkinson's Disease

Industry members

abbvie
Biogen
gsk
Lilly

Janssen
Lilly
MERCK
Pfizer
SANOFI

abbvie
Bristol-Myers Squibb
MERCK
Janssen
Pfizer
SANOFI
gsk
Takeda

Celgene
verily
gsk
Pfizer
SANOFI

Government members

NIH National Institute on Aging
NIH National Institute of Neurological Disorders and Stroke
FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Institute of Diabetes and Digestive and Kidney Diseases

NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH National Institute of Allergy and Infectious Diseases

NIH National Institute on Aging
NIH National Institute of Neurological Disorders and Stroke
FDA U.S. FOOD & DRUG ADMINISTRATION

Non-profit members

alzheimer's association
GEOFFREY BEENE
US Against Alzheimer's
we can stop it by 2020.
Alzheimer's Drug Discovery Foundation

American Diabetes Association.
JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

LUPUS RESEARCH ALLIANCE
LUPUS FOUNDATION OF AMERICA
Arthritis Foundation
Rheumatology Research Foundation
Advancing Treatment | Finding Cures

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

PhRMA
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Operating Principles of AMP

- **Simple governance:** Steering Committees under an overall Executive Committee
  - Steering Committee leadership by nominated co-chairs – one industry, one NIH or Academic
  - Firm rules on funding equity, in-kind contributions
  - Project management by FNIH to minimize overhead
- **Tight management of deliverables and timelines:** Concrete interim deliverables with *go/no go* on next phases based on interim findings
- **Industry engagement:** Participants ensure focus is on relevant, translatable research and provide contributions in-kind (e.g., relevant data)
- **Patient advocacy groups and foundations:** Ensure perspectives and needs of the disease patient populations contribute to project design and ongoing execution
- **Data Sharing:** Findings shared broadly and quickly, in the interest of patients and the public health
- **Pre-Competitive:** No pre-emptive patenting; broadest possible opportunity for commercialization

AMP Gene Therapy: Origins

Advanced Therapy Medicinal Products (ATMPs) development regarding host responses, persistence of efficacy, redosing, and safety

HEVER
Sr. Pharma Leadership

innovative medicines initiative

efpia

Workshop & Calls

ARDAT
Accelerating Research and Innovation for ATMPs

Today

Q3

Q2/Q3

2019

2020

FDA

Q3

Dec 9th

Q1/Q2

June

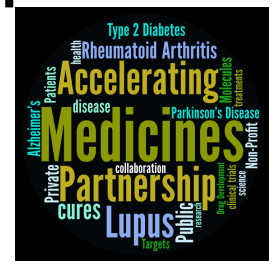
AMP Gene Therapy

Stakeholder Survey

F2F Mtg

Working Groups

Concept Approval



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Engaged Partnership with Strong Potential for Support

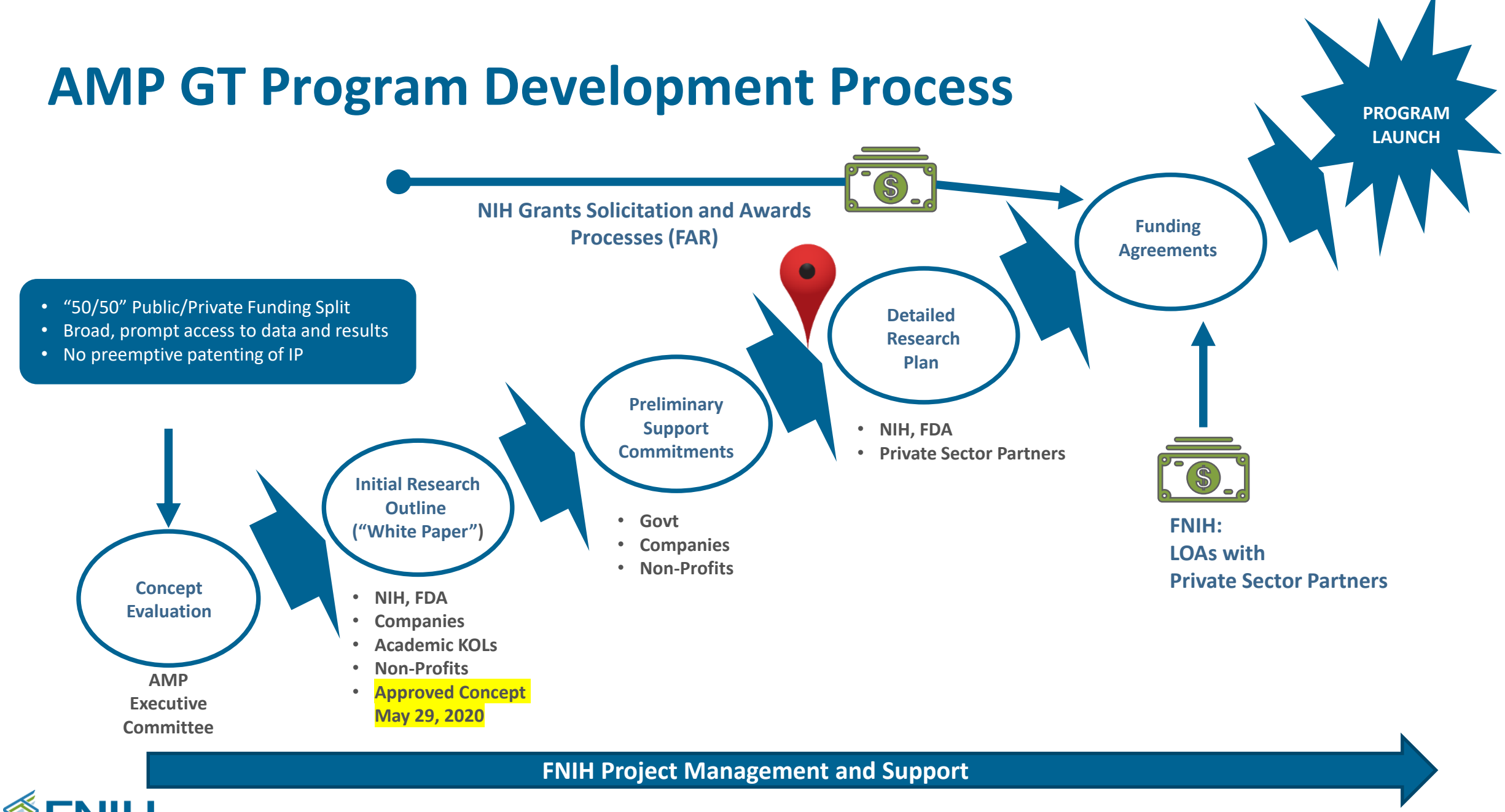
- **Strong involvement and leadership from multiple NIH ICs, FDA & leading academic KOLs and Institutions**

NCATS NINDS NHLBI NIMH FDA/CBER

- **Several pharma committed funds to support the design phase of the AMP-GT program**
- **Multiple representatives contributed expertise and experience to the core working groups**

AveXis / Novartis	BMS	Eli Lilly	Roche	UCB
Bayer	Boehringer-Ingelheim	Pfizer	Sanofi	Ultragenyx

AMP GT Program Development Process



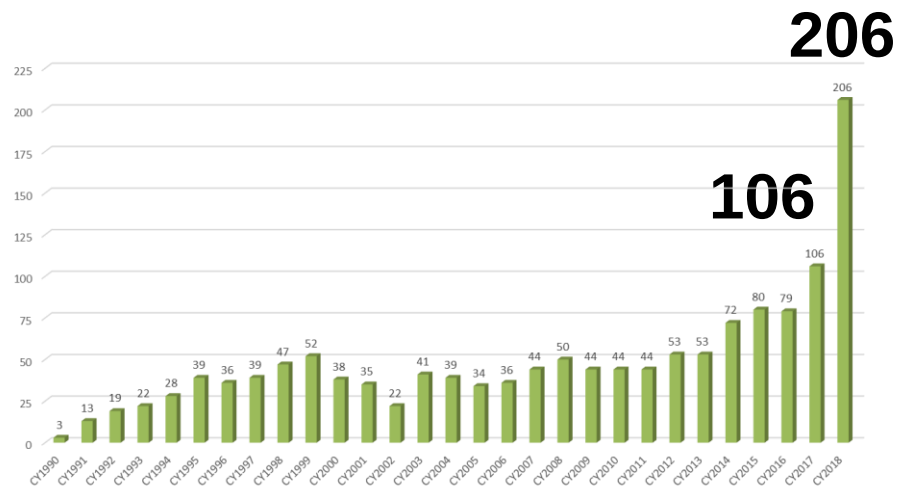
Session 2

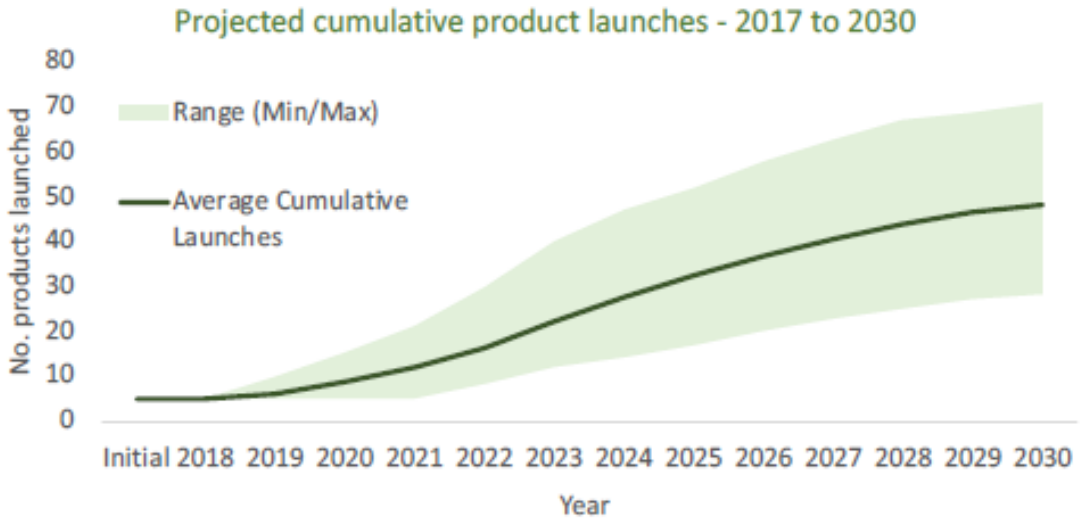
The AMP Gene Therapy Program (AMP GT)

Variation on a Theme

Increased Activity in Gene Therapy

Number of IND applications to FDA is increasing noticeably and there are over 900 active INDs as of Dec 31, 2019





Correlates with prediction of 40 to 60 product launches and more than 500,000 treated by 2030

Approved Gene Therapies

United States

- Tisagenlecleucel (2017)
- Axicabtagene ciloleucel (2017)
- Voretigene neparvovec-rzyl (2017)
- Onasemnogene abeparvovec-xioi (2019)

European Union

– Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence (2016)

– Tisagenlecleucel (2018)

– Axicabtagene ciloleucel (2018)

– Voretigene neparvovec-rzyl (2018)

– Autologous CD34+ cells encoding βA-T87Q-globin gene (2019)

Alipogene tiparvovec
(approved 2012, withdrawn 2017)

Challenges of Individualized Therapies

- Manufacturing
- Nonclinical development
- Clinical development
- Product access

Current manufacturing platforms limit gene therapy production

Can leveraging validated processes facilitate the development of new products?

Approximate Treatment Population Per Year	1-100	>100-10,000	>10,000

Benefits of AMP GT Partnership

- Makes adeno-associated virus (AAV) technology more accessible to a broader range of diseases
- Potential to streamline preclinical and product testing
- Facilitates scientific advances that will ultimately benefit entire field
- **Bring therapies to all individuals in need sooner**

Accelerating Medicine Partnership – Gene Therapy

AAV Basic Biology Translational Implications

Enhancing Vector Generation

Enhancing therapeutic gene expression in patients

Advancing Access to AAV Technologies and Vectors for Bespoke Clinical Applications

AAV vector manufacturing and analytics

Clinical Development

Bespoke Gene Therapy Consortium

AAV Basic Biology Working Groups

Vector Generation

Chris Frye	Eli Lilly
P. J. Brooks*	NIH/NCATS
Deanna Portero	NIH/NCATS
Chris Boshoff	NIH/NINDS
Dimitris Papanicolaou	Novartis
Otmane Boussif	Novartis
Samih Yagmour	Novartis
Tim Charlebois*	Pfizer
Markus Haindl	Roche
Karen Vincent	Sanofi
Marrah Lachowicz-Scroggins	NIH/NHLBI
Emmanuel Adu-Gyamfi	FDA/CBER
Bettina Buhring	NIH/NIMH
Enrique Michelotti	NIH/NIMH
Ingo Gorr	Boehringer-Ingelheim
Onur Kas	UCB
Tal Kramer	UCB

Gene Expression

Udo Maier*	Boehringer-Ingelheim
Feng Pan	Eli Lilly
Zhuo Cheng	Eli Lilly
P. J. Brooks*	NIH/NCATS
Deanna Portero	NIH/NCATS
Jill Morris	NIH/NINDS
Dimitris Papanicolaou	Novartis
Otmane Boussif	Novartis
Samih Yagmour	Novartis
Suryanarayan Somanathan	Pfizer
Joseph Rabinowitz*	Pfizer
Andreas Schaubmar	Roche
Catherine O-Riordan	Sanofi
Pankaj Qasba	NIH/NHLBI
Bettina Buhring	NIH/NIMH
Enrique Michelotti	NIH/NIMH
Onur Kas	UCB
Tal Kramer	UCB

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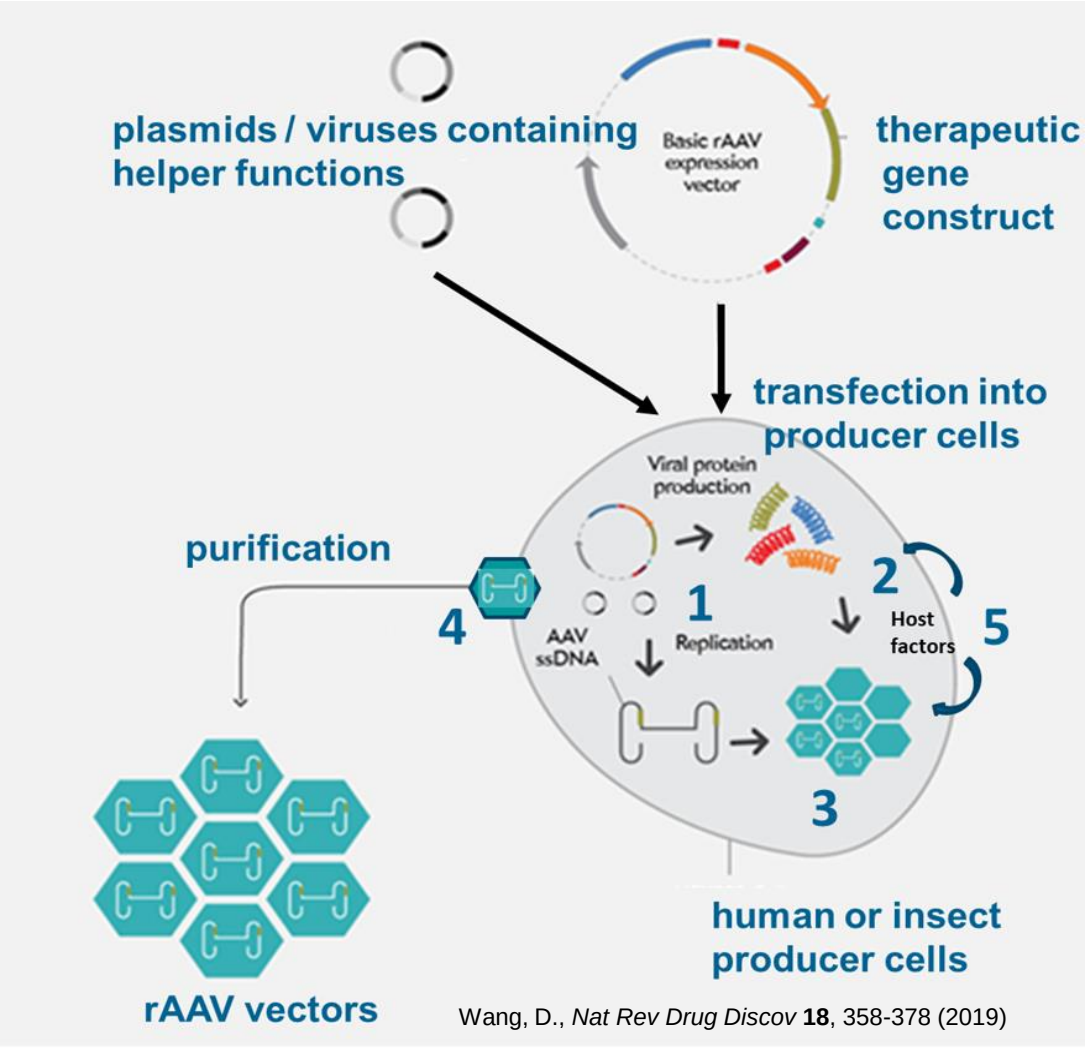
* WG Co-Chairs

Advancing the Understanding of AAV Biology

A. Enhancing Vector Generation

1. Viral genome replication and processing for virion packaging
2. Capsid production and assembly
3. Packaging of viral genome to generate productive viruses
4. Transport and release of virus
5. Host factors that influence the process of viral generation

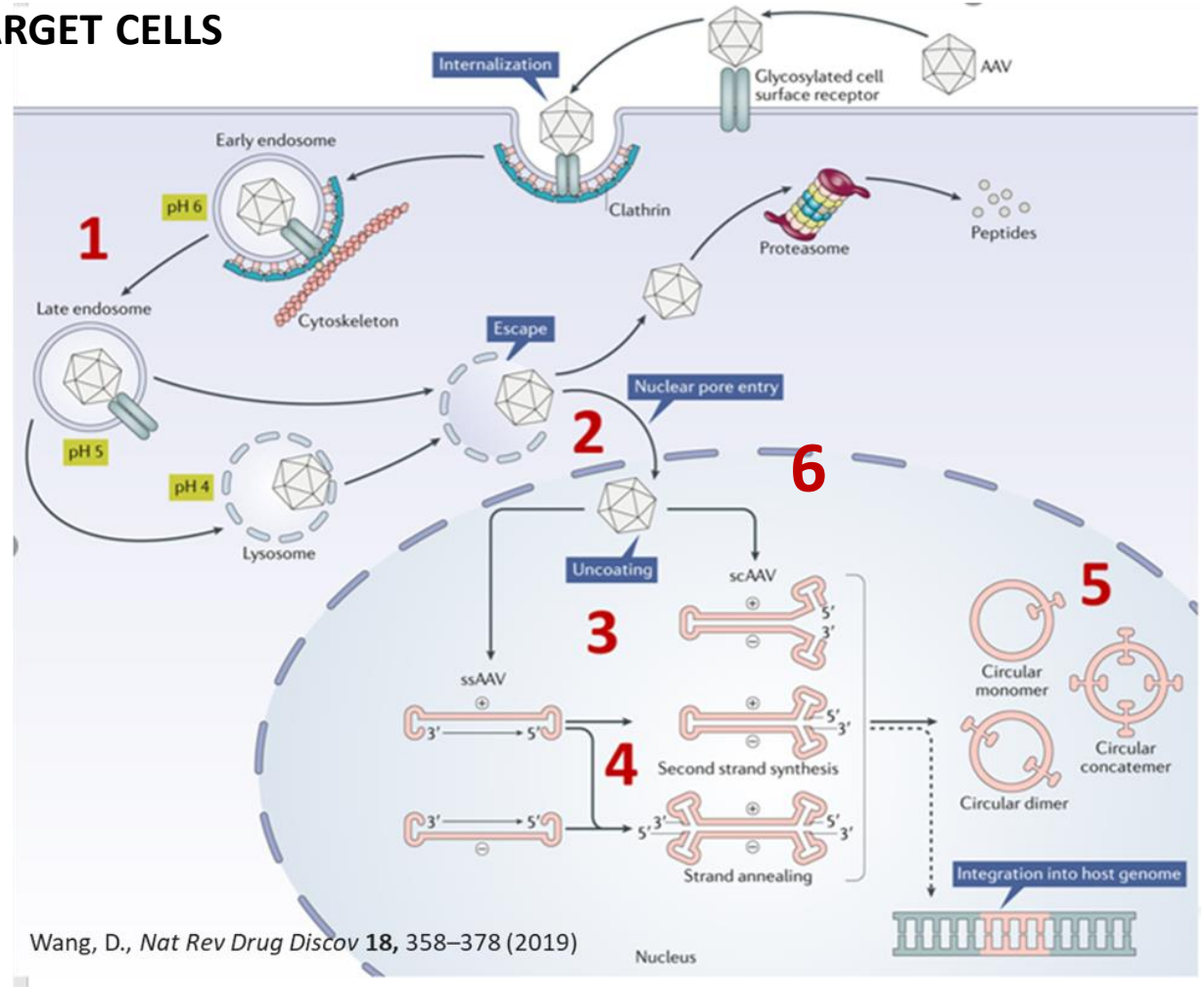


Wang, D., *Nat Rev Drug Discov* **18**, 358-378 (2019)

Advancing the Understanding of AAV Biology

B. Enhancing therapeutic gene expression in target cells

1. The endosomal state of the AAV virion
2. Trafficking to the nucleus
3. Uncoating in the nucleus
4. Second strand synthesis
5. Concatemerization of the viral genome
6. Post expression events

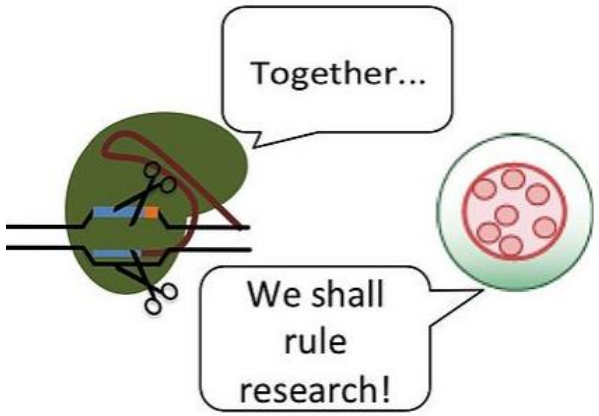


Wang, D., *Nat Rev Drug Discov* **18,** 358–378 (2019)

Proposed Approach to Advancing AAV Biology

Strategy:

- **Support high throughput functional genomic approaches and targeted funding opportunities:**
  - Assays for each step in AAV vector production and gene expression in target cells amenable to high-throughput screening (HTS)
    - Whole genome screening using siRNA, CRISPR
    - Library of approved drugs
    - Possibly using NCATS facility as a central testing site
  - Focused funding on specific questions that may not be covered by HTS approaches



Key Role of Gene Therapy Partners in AAV Biology

- Prioritize and weight questions and primary focus
- Shape the format and process for sharing results
- Continuous guidance of the research through periodic review of project(s)
- Suggest innovation to BGTC pilot program

Focus on the Bespoke Gene Therapy Pilot Program

Advancing Access to AAV Technologies and Vectors for Bespoke Clinical Applications

AAV vector manufacturing and analytics

Clinical Development

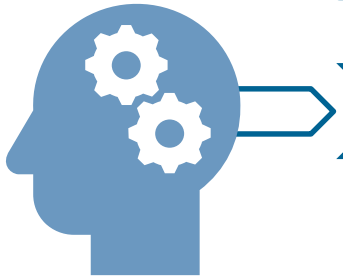
Bespoke Gene Therapy Consortium

Bespoke Gene Therapy Consortium (BGTC)

Non-profit umbrella organization

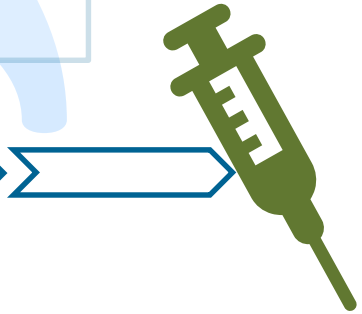
- Provide facilities for vector generation
- Central facility for small batch manufacture
- Improve manufacturing efficiency
- Facilitate out-licensing if appropriate

FDA to streamline regulatory requirements to facilitate access to these products
Establish Master File(s) for tools at the FDA for standard vector(s)



Idea for gene therapy target for rare disease

Vector generation → Manufacture of therapeutic → Clinical ability to treat patients



Therapies for patients

Standard vector menu:

- Instructions for use
- Tropism
- Ease of use for gene type
- Non-proprietary tools

Standard process menu:

- Known safety database
- Facilitate preclinical testing
- Leverage existing manufacturing processes and protocols

Standard delivery menu:

- Standard clinical protocols
- Known safety for non-proprietary vectors
- Standard delivery protocols

All results from treatments are reported back to the consortium for iterative learning

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Proposed Approach to Advancing Access by the Bespoke Gene Therapy Consortium

Strategy:

- Address the needs of getting a simple AAV generation/production manual ***(Maniatis for Gene Therapy)*** by coordinating and harmonizing the production of a set of vectors and processes that will allow rapid timelines and cost-effective delivery for the future:
  - Run 5-6 pilot projects for diseases with different prevalence, vector dose requirements, routes of administration (iv, it, subretinal)
  - Limited number (± 3) different AAV vector serotypes in the pilot
  - An algorithmic approach to identify appropriate target diseases by analysis of existing (and future) databases
  - Define and standardize vector quantitation, toxicity testing and lot release assays, in coordination with industry and academic manufacturers

BGTC Working Groups

Mfg & Analytics

Peter Marks*	FDA/CBER
P. J. Brooks*	NIH/NCATS
Gopa Raychaudhuri*	FDA/CBER
Jude Samulski	University of North Carolina
Tim Charlebois	Pfizer
Samih Yaghmour	Novartis/Avexis
Kelvin Lee	NIIMBL
Barry Byrne	University of Florida
Bettina Buhring	NIH/NIMH
Enrique Michelotti	NIH/NIMH
Deanna Portero	NIH/NCATS
Richard Synder	Thermo Fisher
Sandy MacCrae	Sangamo Therapeutics
Chris Boshoff	NIH/NINDS
Jill Morris	NIH/NINDS
Laetitia Malphettes	UCB
Stefanos Grammatikos	UCB
Onur Kas	UCB
Maen Qadan	Eli Lilly
Chris Frye	Eli Lilly
Scott May	Eli Lilly

Clinical Development

P. J. Brooks*	NIH/NCATS
Beverly Davidson*	CHOP
Cheryl McDonald	NIH/NHLBI
Deanna Portero	NIH/NCATS
Kevin A. Strauss	Clinic for Special Children
Yael Weiss	Ultragenyx
Steven Gray	UT Southwestern
Enrique Michelotti	NIH/NIMH
Bettina Buhring	NIH/NIMH
Peter Marks	FDA/CBER
Gopa Raychaudhuri	FDA/CBER
Rachel Sher	NORD
Vanessa Boulanger	NORD
Chris Boshoff	NIH/NINDS
Jill Morris	NIH/NINDS
Khara Ramos	NIH/NINDS
Johannes Streffer	UCB
Marina Braun	UCB
Marcel Brink	UCB
Maen Qadan	Eli Lilly
Chris Frye	Eli Lilly
Scott May	Eli Lilly

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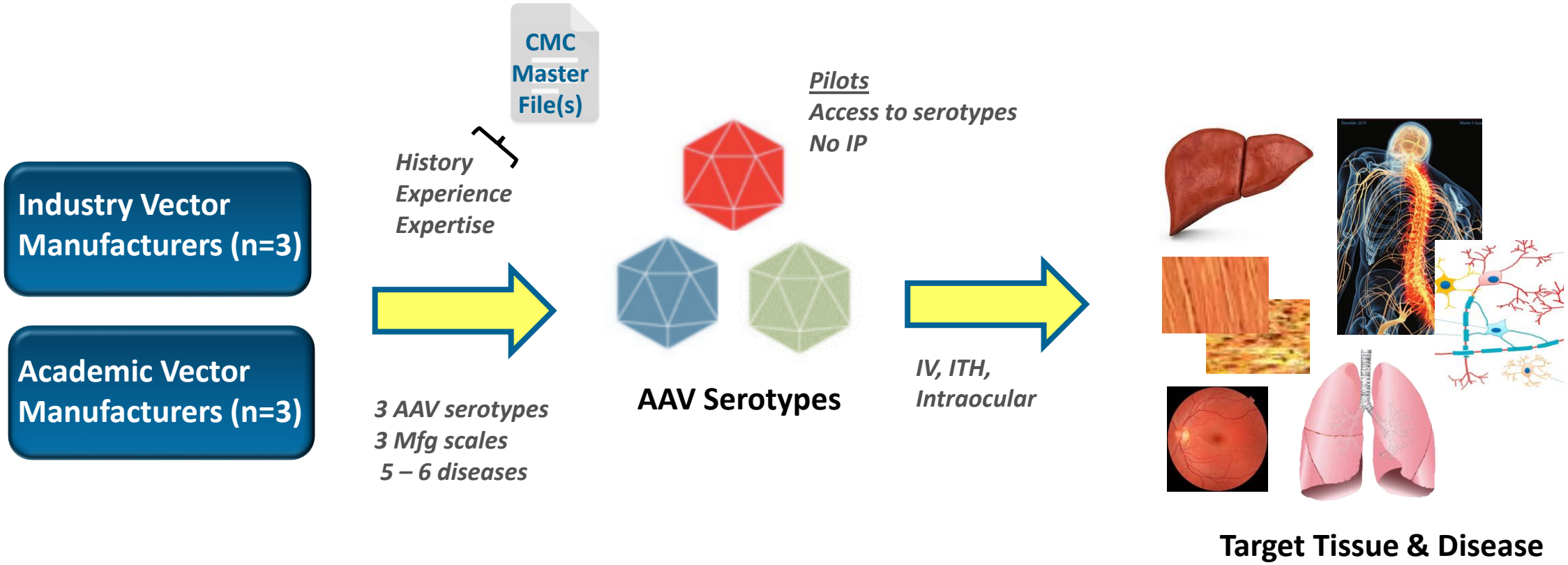
Strategy to Leverage Existing Expertise and Capacity to Manufacture Gene Therapy Product for the Pilots



GOAL: Transgene sequence is the only difference being introduced into an established manufacturing paradigm

Vector Manufacturing

- Manufacturer would prepare and test vector supplies for both preclinical/tox and clinical use
- Provide sufficient quantity of vector to supply treatment for clinical trial
  - Clinical indication matched and agreed upon in advance
  - Considerations: capacity, timelines, dose/patient, # of patients, storage stability → vector requirements met by one or two successful batches at the specified scale
    - 0-100 doses for intravenous administration (10^{15} vg/dose)
    - 0-100 doses for intrathecal administration (10^{14} vg/dose)
    - 0-100 doses for intraocular injection (10^{13} vg/dose)
- Manufacturer will supply vials (NIH to provide final labelling) and certificate of analysis (C of A)
  - No drug substance supply to be maintained (for simplicity)

Ongoing discussions with potential partners

Exploring Partner ability and willingness to manufacture and supply clinical vector as in-kind support for the pilot project

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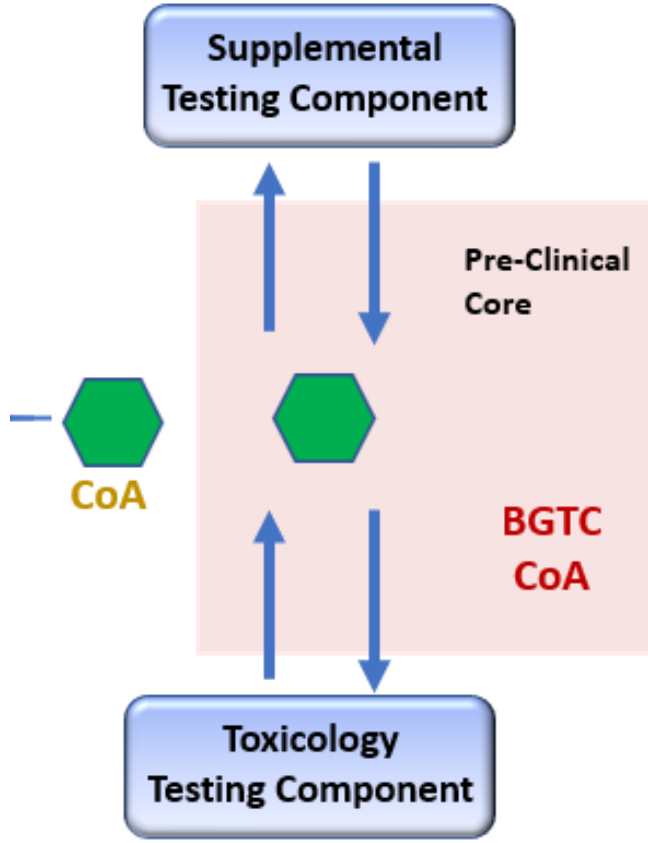
Release Testing and Specifications

- Identify critical attributes that must be evaluated
  - Examples: Vg titer, purity, capsid identity and concentration, full:empty, potency, endotoxin & sterility
  - Provide scientific rationale and justification for why these tests are most critical
  - Consider what may be leveraged from the manufacturer's experience with the reference product, and whether reduced testing can be considered (scientifically justified) based on past experience/data
- Provide description of tests to be performed by the manufacturer (or Supplemental Testing Component, where applicable)



Assay Standardization and Harmonization

- Overall goal is to standardize testing, where possible
  - One specific goal is to standardize testing for vector copy number
- Current Perspectives
  - Manufacturers will test vector using their existing processes
  - Industry and academic manufacturing partners may need additional support to fulfil the testing requirements
  - NIH will establish a centralized testing facility to conduct supplemental testing, and also support product-specific testing (e.g., potency)

As the IND holder, NIH will be responsible for the CoA that is submitted to FDA to support the clinical trial

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Engagement with FDA

- Consider establishing Master Files
- Early engagement with FDA staff for feedback on specific issues e.g., testing requirements for AAV-based gene therapy products
  - Focus on principles so feedback is generally applicable (not product-specific)
- Explore streamlining regulatory requirements – examples:
  - Leveraging pre-clinical and CMC data based on past experience with vector or similar GT product, if scientifically justified, to reduce testing of future iterations of a similar product
  - Innovative clinical trial design for bespoke products
- Full spectrum of formal FDA meetings available to support product development
  - e.g., CATT, INTERACT, pre-IND meetings etc.
- Pathway to licensure?

BGTC – Mfg/Analytics Process

Diseases + researchers

Vector Producer A1

Vector Producer A2

Vector Producer I1

Vector Producer I2

CoA

Supplemental Testing Component

Toxicology Testing Component

Pre-Clinical Core

Clinical Trials Core

Regulatory Core

IND

BGTC CoA

Central IRB

Clinical sites

outcomes SAEs

Data Management and Analysis Core

BGTC Coordination Center

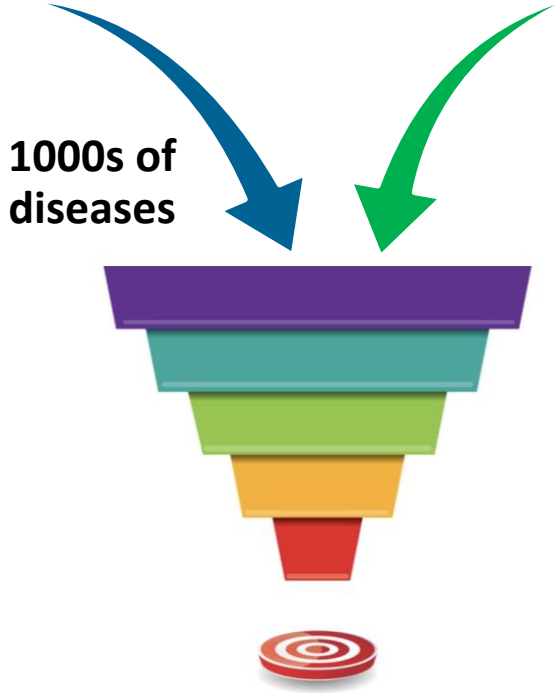
NIH National Center for Advancing Translational Sciences

A= academic, I= industry = clinical AAV vector

FDA U.S. FOOD & DRUG ADMINISTRATION

How to Prioritize Rare Diseases in the BGTC?

Evidentiary and Ethics Criteria for Disease Selection



Manageable for manual review & final selection

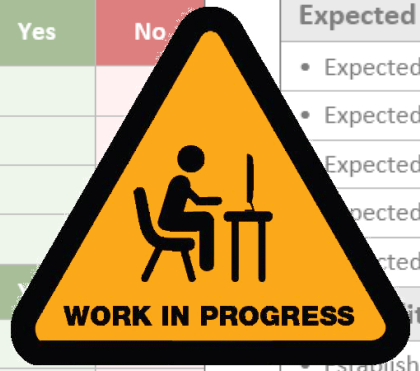
- Draft criteria were developed and revised by representatives from gov't, industry, academia, bioethics and patient advocacy
- Goal of establishing a complementary set of diseases, to allow maximum generalizability and potential benefit to the field
- Partners will have direct input and role in the final disease selection
- Highlight → this is a PILOT
  - Learning through the program
  - Improve as it matures

FNIH

BGTC Pilot Disease Selection Criteria

Pre-Clinical Screening Template		
Invariant Criteria	**Yes**	**No**
U.S. prevalence <1 per 100,000		
Established genotype-phenotype association		
Amenable to AAV-mediated gene *replacement* (i.e. AR, X-linked)		
Therapeutically relevant protein product <666 amino acids		
Variant Criteria		
Robust clinical trial endpoints (*patient-centered outcomes, biomarkers)*		
Valid animal model (e.g. mouse, swine, domestic, etc.)		
Proof-of-concept data in animal model (i.e. *efficacy*)		
Safety *and/or* overexpression data in animal model (*toxicology*)		
No known commercial interest		

Extra Queries for BGTC Pilot Only



BGTC Pilot Study: *Additional Screening Considerations*		
Expected Magnitude of Benefit	**Yes**	**No**
• Expected benefit represents substantial improvement over current therapies		
• Expected benefit substantially improves event-free survival		
• Expected benefit substantially reduces psychomotor disability		
• pected benefit restores primary sensory modality (e.g., vision, hearing)		
• cted benefit prevents end-stage organ failure (e.g., heart, liver, kidney)		
ity of Success	**Yes**	**No**
• Established network of key opinion leaders to facilitate trial design		
• Established patient advocacy *and/or* support group		
• Existing patient registry		
• Concentrated regional subject representation(s); e.g. *ethnic groups*		
• Expected meaningful change of functional endpoint (e.g., gait) within ≤1 year		
• Expected meaningful change of biomarker (e.g., analyte) within ≤1 year		
• Appropriate study *power:* expected benefit significant with *N* treated subjects		
Disadvantaged Populations	**Yes**	**No**
• Impacts newborns, infants, or young children		
• Impacts non-Caucasian individuals		
• Impacts socioeconomically disadvantaged populations		
• Impacts medically uninsured individuals		

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Getting to Final Selections

- Continued input and expertise from members of the Clinical Development WG
- Engagement and vetting of criteria and process with NIH Division of Ethics
- Transparency, clarity of process and program education will be an essential piece of the associated Communications efforts for AMP GT

Core Ethical Values for Clinical Research Priority-Setting

Social Value	Acceptable Risk-Benefit Ratio for Individual Participants	Procedural Fairness	Complexities in implementing a "Selection Algorithm"
• Magnitude of benefits • Probability of success • Disadvantages	• Diseases/Trials - acceptable risk (AAV exposure) vs. benefit calculus • Consider multiple levels: high risk/high reward; low risk/low reward selections	• selection be logical and transparent • Impartial and not conflict of interest by decision-makers	• Multiple criteria may not work well for (Y/N) • e.g. items within social value

Clinical Trial Design and Development

- Wherever possible, leverage already existing NIH funded clinical trial programs
  - Rare Diseases Clinical Research Network (RDCRN) https://www.rarediseasesnetwork.org/
  - NINDS NeuroNext https://neuronext.org/
  - CTSA Program https://ncats.nih.gov/ctsa
  - Other
- A single BGTC IRB
- Include board of expert clinicians in AAV GT trials to guide treatment and learning
- Pilot testing of visiting research nurses to allow administration of gene therapy in areas outside of major academic medical centers

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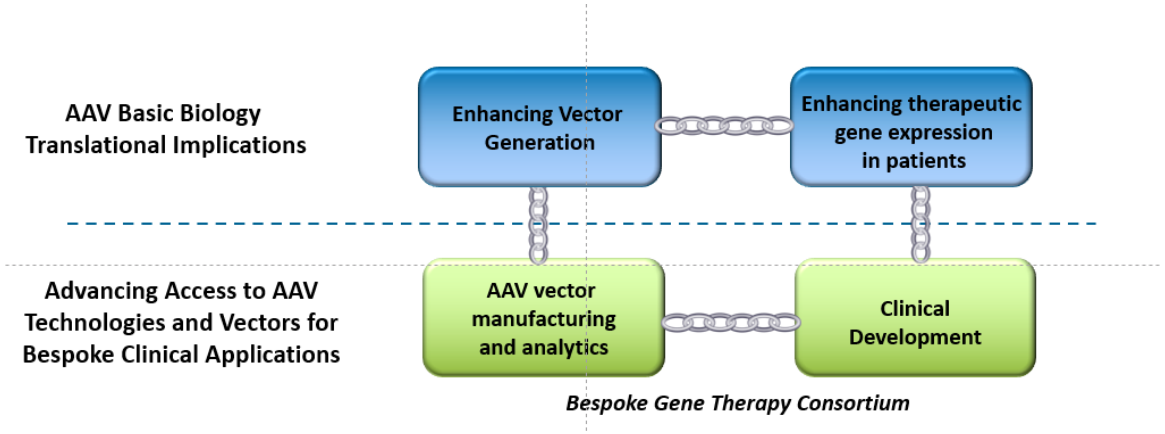
Key Deliverables of the BGTC

- A menu of AAV vector and vector generation processes
- A harmonized set of vector quantitation and lot release assays
- A process for disease selection for trials
- Manual for AAV gene therapy using select AAV serotype vectors
- Establish board of expert clinicians in AAV GT trials to guide treatment and learning
- Framework to manage IND & legal liabilities; pilot studies for shared learning and future processes
- Implementation of results from Advancing the Understanding of AAV Biology component

Key Role of Gene Therapy Partners in BGTC Pilot

- Participate in the BGTC: learn first-hand and guide the pilot as program moves forward
- Engage on subteam(s) that are directly involved in the development and standardization and harmonization of testing processes, assays and regulatory interactions
- Continuous guidance of BGTC progress through periodic review of project
- Incorporate the innovations and understanding from the AAV biology research



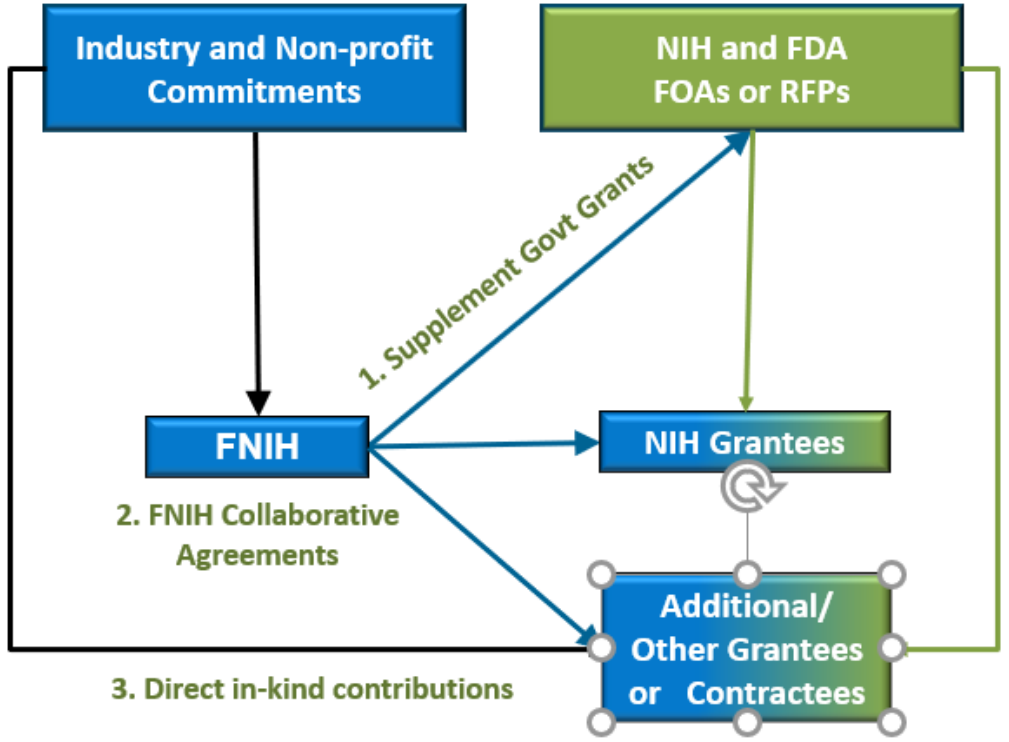
Proposed Budget

AMP-GT program	Annual costs
Whole host and viral genome high throughput screening and additional targeted specific grants and contracts	$10M direct and indirect costs
Cost of goods for manufacture and delivery of 5-6 gene therapies (~10 Pts/trial)	$8M direct and indirect costs
FNIH Project management, meetings, and travel; includes outgoing research indirects	$2.5M direct and indirect costs
Total Estimated Costs	$102.5M

The AMP-GT partnership seeks co-investment (50:50) of public and private sector partners: funding to supplement federal support from NIH and FDA.

Decisions, Support and Partner Engagement

- Project Plan will expand on these key questions and how they interrelate → RFPs
- Proposals may be supported through multiple funding mechanisms (grants, contracts, collaborative and in-kind agreements); managed by NIH, FDA or FNIH
- **AMP GT stakeholder representatives will have a meaningful role (e.g., subteam, decisions) to review, prioritize, select best proposals and outline the appropriate levels of support**

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Session 3

Communications and Partnering Opportunities

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Communications

Help advance education and engagement strategies relating to gene therapy

1. **Fund and help develop special outreach to external stakeholders:**
   - Patient and research communities, regulatory authorities, industry, academia and other nonprofits
   - Dissemination of materials about the science of Gene Therapy
     - Infographics, FAQs, announcements, project results
     - Symposia (regional or national conferences), publications, commentaries, workshops, webinar(s), print and/or web materials or videos

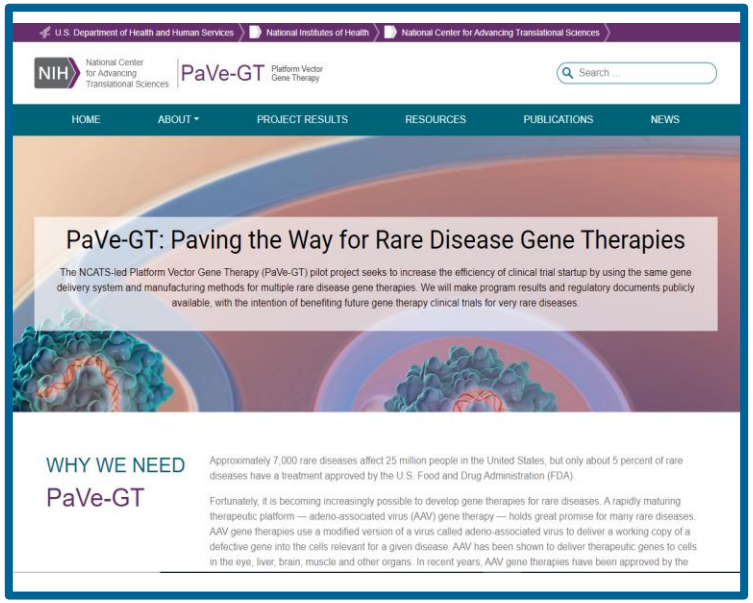
2. **Fund and help develop materials to support internal stakeholders (project partners) in communicating about AMP-GT**
   - e.g., talking points, internal Q&A, preparation notes for speaking with media

3. **Support development of internal and external communications activities through an AMP-GT Outreach Working Group**
   - Share patient/family perspective(s) with scientific project team/SC

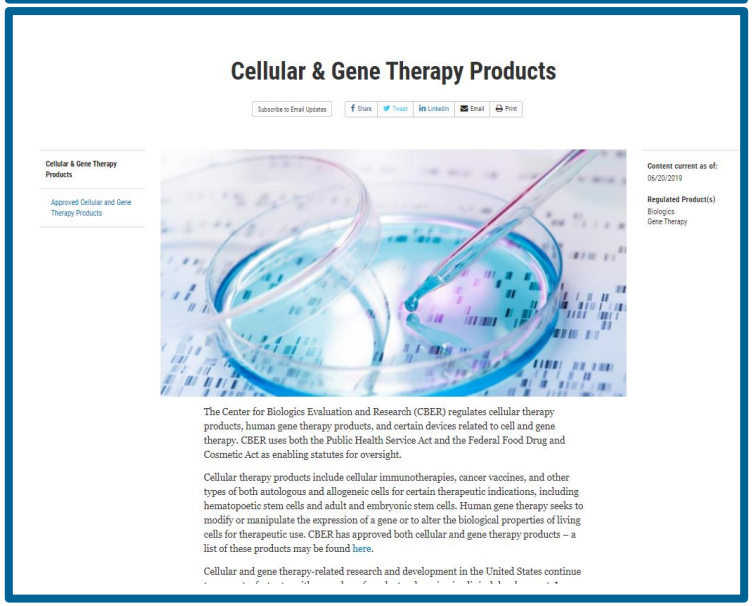
4. **Help with patient recruitment as necessary**

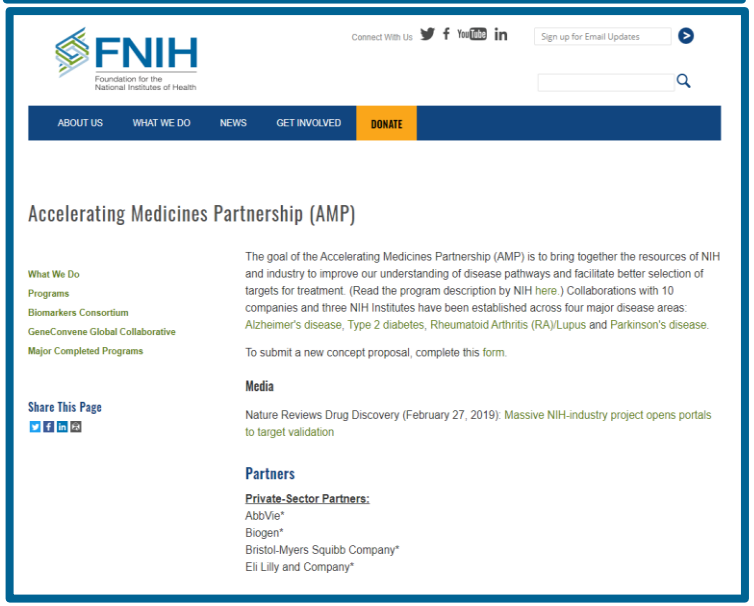
Development of AMP GT Webpage(s)

Good model in NCATS PaVe-GT
https://pave-gt.ncats.nih.gov/



Goal: Complement and link resources and information from multiple sources





Alignment and Scientific Sharing with Other Consortia

- Many pharma partners are also investing in complementary efforts
  - ARDAT – Accelerating Research and Innovation of ATMPs
    - Advanced Therapy Medicinal Products (ATMPs) development regarding host responses, persistence of efficacy, redosing, and safety

- AMP GT will work with ARDAT and IMI leads to coordinate regular exchanges between the two programs (e.g., at conferences, F2F mtgs)
- Opportunity to bring greater visibility, involvement and expertise across programs

Proposed Industry Investment

Funding Support

- Proposed budget for AMP GT scientific program = $102.5M
- NIH/FDA anticipated support for 50% of budget
- Private sector desired support = the other 50% (~$50M)
- Seeking a minimum of 10 large Pharma partners: ~$1M / year over 5 years
- Tiered levels of investment of additional partners based on R&D budget

Representation

- R&D Stakeholders may appoint one representative as a *full* **voting member** of the SC
- Opportunities to nominate representatives with specific expertise and experience for subteams or special purpose groups are expected to be necessary in the program
  - Regulatory manufacturing, communications, etc.

Proposed Not-for-Profit, Philanthropist & Advocacy Organization Investment

Funding Support

- Key contributors: nonprofit, advocacy leaders, and philanthropists
- Join the Steering Committee as a Stakeholder and serve as a *full* **voting member** with a financial commitment of $100,000 or more per year
- Organizations and individuals donating between $99,999 and $25,000 annually may join the Steering Committee as **non-voting members**

Representation

- Stakeholders may appoint one representative as a *full* **voting member** of the SC
- Opportunities to nominate representatives with required expertise and experience for subteams or special purpose groups may emerge

AMP GT Steering Committee: Voting

- **NIH, FDA, and not-for-profit organizations will have votes that will not exceed 50% of total**
- **Industry Partners will have the other 50% of the votes**
- Academic investigators, whether provided funding by the project or not, may be added at the Steering Committee's discretion. To avoid potential conflicts of interest, such academic members would not be voting members

Time Commitments and Meetings

- Monthly SC teleconferences
- 1 – 2 face-to-face meetings of the SC per year
- The SC may elect to form Working Groups to advise the full Steering Committee on scientific, operational or technical issues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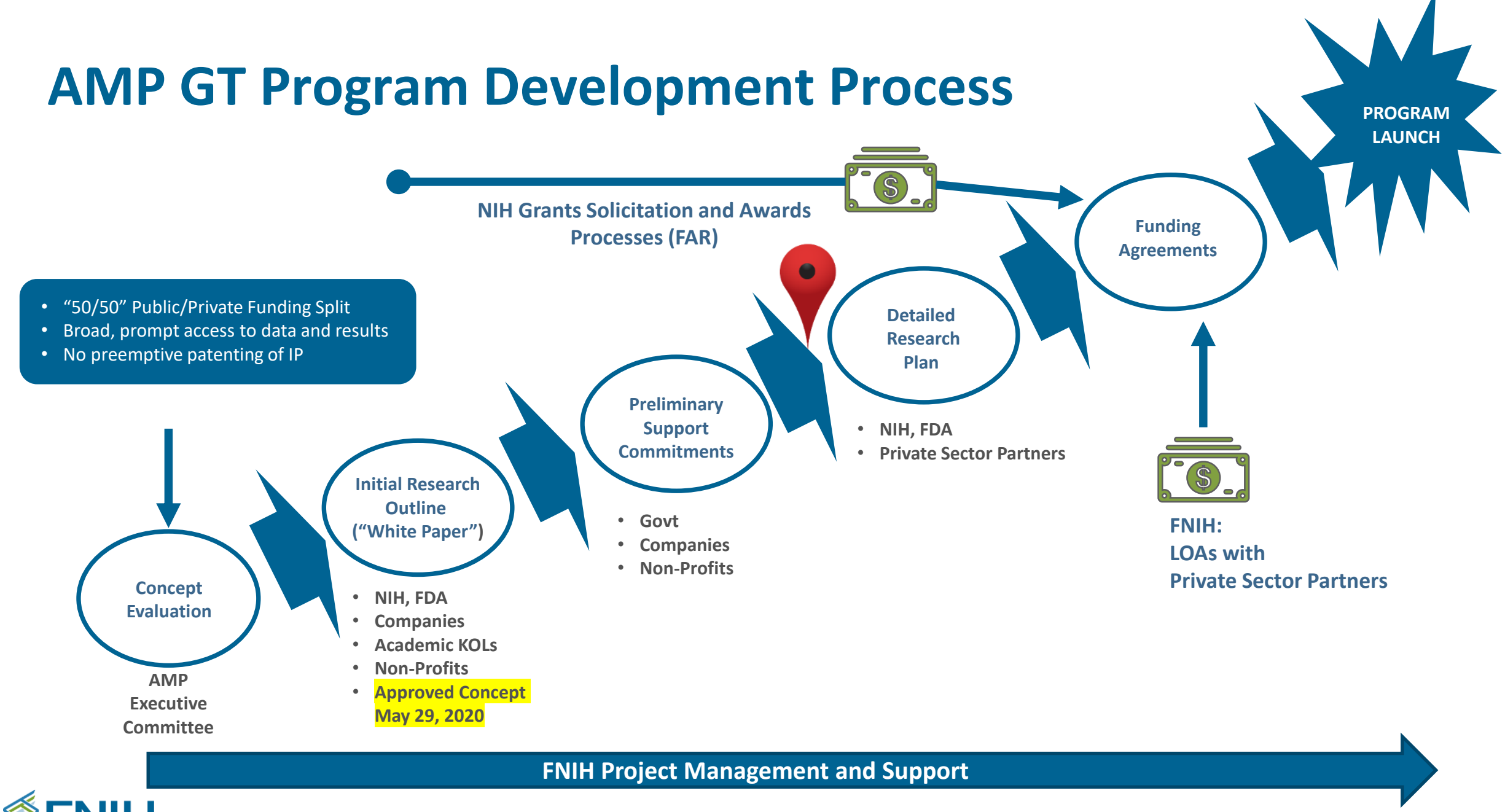
Timelines and Next Steps

AMP GT Program Development Process



Ongoing Actions & Next Steps

- Collate questions and comments from Webinar (chat, follow-up emails, direct conversations) → ✉ **send additional questions to FNIH**
- Finalize the Project Plan (Q3 2020)
  - White paper and outline of pilot manufacturing process and engagement with BGTC Coordinating Center & FDA
  - Refinement of disease selection criteria
  - Continued development of a strategic plan for Communication efforts
- Formal Letters of Agreement sent to potential partners (Q4 2020)

Contact Information

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THANKS FOR YOUR
ATTENTION

Back-up Slides

AMP GT: Complementing and Expanding on NCATS PaVe-GT

PaVe-GT and FDA-NCATS-FNIH Public-Private Partnership

	PaVe-GT	FDA-NCATS-FNIH Public-Private Partnership
Diseases	Four rare diseases selected	TBD # of diseases
AAV Source	Single manufacturer	Consortium ?
Regulatory	Make public all FDA communications and submissions	Adapt PaVe-GT templates ?
Clinical Sites	NIH Clinical Center	Multiple clinical sites ?
AAV Serotypes	Single serotype	Multiple serotypes ?

NIH National Center for Advancing Translational Sciences

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