Advancing the Development of Bespoke Gene Therapies

Peter Marks, MD, PhD
AMP Meeting
February 6, 2024
Importance of Therapies for Disorders that are Rare

• Out of thousands of rare hereditary and acquired diseases there are hundreds of disorders affecting one to thousands per year that could be addressed with novel therapies
  – Addressing molecular defects may reduce some more common diseases to very rare diseases
FDA Approved Systemic Directly-Administered Gene Therapy

• **Onasemnogene abeparvovec-xioi** (Zolgensma): for the treatment of patients less than two years of age with spinal muscular atrophy (SMA) with confirmed biallelic mutations in the *survival motor neuron 1* (*SMN1*) gene
  
  – SMA Type 1 commonly presents with muscle weakness that is evident at birth or within the first few months of life


Evelyn with documented SMA1 treated with onasemnogene, now age 3 running around, something never seen in untreated children
Current Challenges

• Gene therapy is currently at a critical juncture due to a combination of factors
  – Manufacturing challenges
  – Clinical development timelines
  – Different global regulatory requirements
Actions at Center for Biologics

- Advancing manufacturing technologies for cell and gene therapy through research
- Application of platform technology provision
- Work to more clearly define the use of accelerated approval for gene therapy
- Exploring concurrent submission and product review with other regulatory authorities
- Communication pilot for rare diseases
Manufacturing

Current manufacturing platforms limit gene therapy production

Issues: Capacity Cost

Sweet Spot

Technologic Advances Needed

Approximate Treatment Population Per Year

1-100 >100-10,000 >10,000
Manufacturing Solutions

• Harmonization of manufacturing protocols
  – Standardized protocol use by academics and small companies would more easily facilitate transfer of process to contract manufacturing organizations

• Automation of manufacturing process
  – Development of automated or semi-automated fabrication devices for gene therapies based on a manufacturing machine-disposable paradigm
Premise

• In appropriate situations, non-clinical data and manufacturing information from one product may be able to be leveraged to another.
Omnibus Appropriations Act of 2023

• Section 2503. Platform Technologies
  – Sponsors may also “reference or rely upon data and information” from a previous application for a drug or biological product that incorporates or uses the same platform technology
  – Data must be submitted by the same sponsor or the sponsor relying on the data received permission from the sponsor who originally submitted the data
  – FDA will issue guidance relating to the program
Leveraging Accelerated Approval

The science inherent in the development of many gene therapies potentially facilitates the use of biomarkers as endpoints that are reasonably likely to predict clinical outcomes.

**Animal Models**
- Disease model reflects aspects of human pathology
- Administration of therapy associated with achievement of a specific protein level ameliorates disease

**Human Observations**
- Disease state is associated with protein levels above or below a certain range
- Certain protein levels are associated with disease absence or minimal disease

Demonstrate that equivalent protein levels can be achieved in humans affected by the disease.
Collaboration on **Gene Therapies Global (CoGenT Global) Pilot**

- Initial participation by Standing Regulatory Members of ICH
- Partners may participate in internal regulatory meetings and meetings that include the sponsor
- Specific regulatory reviews are shared and discussed with partners
- All meetings conducted and information shared under strict confidentiality agreements
- Goal is to increase the efficiency of the regulatory process, reducing time and cost for agencies and sponsors
Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot

• Further accelerate pace of development for products intended to address unmet medical needs in rare diseases or conditions likely to lead to significant disability or death

• Three CBER eligible products in the initial iteration to receive enhanced communications when selected for the pilot
  – An initial meeting to review features of the pilot program
  – Additional ad hoc email or live interactions on an as needed bases
  – Applications for requests to participate accepted through March 1, 2024

Opportunities for Collaboration

Center for Biologics Evaluation and Research

AMP Bespoke Gene Therapy Consortium
Opportunities for Collaboration

Center for Biologics Evaluation and Research

AMP Bespoke Gene Therapy Consortium
Summary

• Working in collaboration with colleagues such as those in the Bespoke Gene Therapy Consortium, the Center for Biologics Evaluation and Research aims to make 2024 a breakout year addressing key challenges to the development of cell and gene therapies, especially for rare disorders
Accelerating Medicines Partnership® Bespoke Gene Therapy Consortium (BGTC)

https://fnih.org/our-programs/AMP/BGTC
BGTC and FNIH – Leadership and Management

• **Steering Committee Co-Chairs:**
  - PJ Brooks, PhD, NCATS/NIH
  - Timothy Miller, MD, Thermo Fisher Scientific
  - Peter Marks, MD, CBER/FDA (non-voting)

• **Program Management:**
  - Courtney Silverthorn, PhD, FNIH
  - Kira Gillett, MS, FNIH
  - Brad Garrison, MBA, PMP, FNIH
Presenters

**Steering Committee Co-Chairs:**
PJ Brooks, PhD, Deputy Director, DRDRI, NCATS, NIH
Timothy Miller, MD, Head, Enterprise Science & Innovation, Thermo Fisher Scientific

**Contract and Portfolio Management:**
Jean Dehdashti, MS, RAC, Program Officer, DRDRI, NCATS, NIH

**BGTC Coordination Center:**
Amritha Jaishankar, PhD, Executive Director, Cell & Gene Therapy Center, IQVIA
Carmen Sivakumaren, PhD, Manager, Enterprise Transformation Strategy, IQVIA
Jenny Fam, MBA, RAC, Director, Regulatory and Cell & Gene Therapy Center, IQVIA
BGTC program overview
- Unmet need and goals
- Consortium members
- Research and clinical program
- Project portfolio
- Structure and governance
- Regulatory Playbook version 1.0

BGTC Operations
- Challenges BGTC is addressing
- Key questions emerging
- Features of the BGTC program (and Coordination Center role)
- Early activities and outputs

Future directions
- Where we’re going
- Q&A
BGTC – Addressing an Unmet Need

- There are over 10,000 rare diseases affecting over 30 million Americans.

- For the estimated 80 percent of rare genetic diseases caused by a single defective gene, one promising therapeutic strategy is adeno-associated virus (AAV) gene therapy.

- Many of these diseases that could benefit from AAV gene therapy are so rare that they are of no current commercial interest.

- BGTC, coordinated by the FNIH, is a public-private partnership among the NIH, FDA CBER, pharmaceutical industry members, and patient organizations.
BGTC – Goals

• Improving AAV vector production and target gene expression

• Streamline preclinical and product testing
  ➢ Harmonize and validate minimum sets of manufacturing and preclinical testing requirements, while maintaining patient safety

• Streamline navigation of the regulatory pathway and product development AAV gene therapies that will ultimately benefit the entire field
  ➢ Standardized regulatory submission package templates
  ➢ The BGTC Regulatory Playbook to help advance future AAV gene therapies for rare diseases

• Change the consideration of diseases of commercial interest

• Deliver the promise of gene therapy to all patients & families
BGTC combines resources from a broad set of public & private partners

Public commitments: $39.5M
Private donations: $35.3M
Private in-kind contributions: $27.9M++
BGTC is comprised of research and clinical workstreams

1. **AAV BASIC BIOLOGY TRANSLATIONAL IMPLICATIONS**

   - Enhancing Vector Generation
   - Enhancing Therapeutic Gene Expression

2. **ADVANCING ACCESS TO AAV TECHNOLOGIES AND VECTORS FOR BESPOKE CLINICAL APPLICATIONS**

   - **CREATE & BUILD CAPACITY**
     - Manufacture of therapeutic
   - **HARMONIZE BEST PRACTICES**
     - Pre-clinical testing
   - **STREAMLINE REGULATORY PATHS**
     - Clinical ability to treat patients

**Goal:** Optimized vector generation and gene expression for AAV gene therapy

**Therapies for patients**

**Goal:** A streamlined regulatory process that supports cost-efficient and high-quality vector production

**Gene therapy target for rare disease**
BGTC selected 8 awards for AAV biology research

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<thead>
<tr>
<th>PI</th>
<th>Institution</th>
<th>Project Title</th>
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<tr>
<td>Alan Davis</td>
<td>Baylor College of Medicine</td>
<td>Rep, Cap, and adenovirus synthetic RNAs for manufacturing recombinant adeno-associated virus vectors</td>
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<tr>
<td>Fred Bunz</td>
<td>Johns Hopkins University</td>
<td>Stable adeno-associated virus vectors for human gene therapy</td>
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<tr>
<td>Michael Chapman</td>
<td>University of Missouri</td>
<td>Bottlenecks in AAV cellular entry, trafficking and nuclear delivery</td>
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<tr>
<td>Antonella deMatteis</td>
<td>Telethon Institute of Genetics &amp; Medicine</td>
<td>Dissecting and piloting the intracellular trafficking of AAVs</td>
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<tr>
<td>Anna Kajaste-Rudnitski</td>
<td>San Raffaele Telethon Institute for Gene Therapy</td>
<td>Investigating innate sensing and antiviral restriction of AAV vectors in the human central nervous system</td>
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<tr>
<td>Brian Davis</td>
<td>GE Research</td>
<td>Characterizing the impact of CpG methylation on AAV genome packaging, expression, and the innate immune response toward improved gene therapy vector production</td>
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<td>Leah Byrne</td>
<td>University of Pittsburgh</td>
<td>Quantification of AAV dose-response with single cell resolution</td>
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<tr>
<td>Anna Maurer</td>
<td>UC Berkeley</td>
<td>Increasing rAAV transgene size by host factor modulation</td>
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**BGTC – Clinical Program**

62 disease nominations received

- Open submission process for clinical, research, patient communities

14 candidates announced July 2022

- Down-selection based on required and preferred criteria, request full clinical trial proposals

Final selection Announced May 2023

- 8 diseases selected

Paired with vector manufacturing for first-in-human clinical trial

- Paired with vector manufacturing for first-in-human clinical trial

**Factors Considered**

- Disease/disorder info
- Patient demographics
- Clinical presentation
- Pre-clinical and clinical research history

- Monogenic disorder
- No commercial business case
- Sufficient information to run a successful clinical trial
- Currently assembled patient group

- Cost
- Ability to secure AAV manufacturing
- Modest requirements for testing and follow-up
- Patient/program diversity

- Manufacturing by existing BGTC partners
- Leverage prior work where possible
Ocular
- Congenital Hereditary Endothelial Dystrophy (CHED)
- Retinal Degeneration (NPHP5)
- Retinitis pigmentosa 45 (CNGB1)

Neurological
- Multiple Sulfatase Deficiency (MSD)
- Charcot Marie Tooth disease type 4J (CMT4J)
- Spastic Paraplegia type 50 (SPG50)

Systemic
- Propionic Acidemia (PA-PCCB)
- Morquio A syndrome (Mucopolysaccharidosis IVA)
Ocular indications in the BGTC clinical portfolio

**Congenital Hereditary Endothelial Dystrophy (CHED)**
- PI: Anthony Aldave, UCLA
- SLC4A11 gene, AAV8
- ROA: intracorneal injection
- Bilateral corneal edema and opacification at birth or presenting in the first decade of life
- Significant bilateral visual impairment and deprivation amblyopia and nystagmus

**Retinal Degeneration (NPHP5)**
- PI: Tomas Aleman, University of Pennsylvania
- NPHP5 gene, AAV5
- ROA: subretinal injection
- Early onset, severe form of Leber congenital amaurosis (LCA) group of dystrophies
- Rapid degeneration of rod cells used for night vision, with unexpected preservation of poorly functioning cone cells used for day vision

**Retinitis pigmentosa 45 (CNGB1)**
- PI: Steve Tsang, Columbia University
- CNGB1 gene, AAV5
- Subretinal injection
- Night blindness due to rod photoreceptor dysfunction. Progressive secondary loss of cone photoreceptors with vision loss and blindness

**Legend:**
- PI: Principal Investigator
- ROA: Route of Administration

**Funding provided by CIRM**
Neurological indications in the BGTC clinical portfolio

**Neurological**

**Multiple Sulfatase Deficiency**
- PI: Rebecca Ahrens-Nicklas & Laura Adang, CHOP
- SUMF1 gene, AAV9
- ROA: Intracisternal magna
- Lysosomal storage disorder (LSD) characterized by a functional deficiency of all sulfatase enzymes
- Devastating, progressive, multi-systemic pediatric neurologic disorder, among other complications

**Charcot Marie Tooth disease type 4J**
- PI: Susan Iannaccone, UTSW
- FIG4 gene, AAV9
- ROA: Intrathecal
- Motor sensory neuropathy, mainly PNS
- Progressive weakness in both distal and proximal extremities, accompanied by areflexia or reduced reflexes. Wheelchair dependence is common

**Spastic Paraplegia type 50**
- PI: Steven Gray, UTSW
- AP4M1 gene, AAV9
- ROA: Intrathecal
- Delayed motor and global development
- Progressive pyramidal tract dysfunction with spasticity and weakness of the legs and loss of ambulation

Elpida Therapeutics raising funds and applying to CIRM
Systemic indications in the BGTC clinical portfolio

Propionic Acidemia
- PI: Chuck Venditti, NHGRI
- PCCB gene, AAV9
- ROA: IV
- Propionyl CoA carboxylase (PCC), mitochondrial enzyme deficiency
- Life-threatening metabolic crisis in the neonatal period, multisystemic complications for survivors

Mucopolysaccharidosis IVA (Morquio A Syndrome)
- PI: Shunji Tomatsu, Nemours Children’s Health
- GALNS gene, AAV8
- ROA: IV
- Lysosomal storage disease characterized by intracellular accumulation of keratan sulfate and chondroitin-6-sulfate.
- Short stature, skeletal dysplasia, dental anomalies, and corneal clouding

Legend:
- Trial to be conducted at NIH Clinical Center
• BGTC CC established *Oct 2023* through an NCATS lead government contract – Jean Dehdashti and PJ Brooks

• Black Canyon Consulting (BCC) prime contractor and IQVIA is the sub-contractor

• BGTC CC consists of:
  - Program Management Operations (BGTC CC PMO)
  - Four Support Cores:
    - Pre-clinical
    - Clinical
    - Regulatory and Quality Assurance
    - Data Management and Analysis
BGTC CC Supporting Teams

**Regulatory Affairs & Quality Assurance Core**
+ BGTC Sub-team Reps
  - Jenny Fam
  - Jan Pierre
  - Michael Hidock
  - Charles Shih

**Data Management & Analytics Core**
+ BGTC Sub-team Reps
  - Tracy Mayer
  - Tamara Pinkett
  - James Ferguson

**Pre-Clinical Core**
+ BGTC Sub-team Reps
  - Laura Lopez Fuentes
  - Mei-Fei Yueh
  - Mihret Amare

**Clinical Core**
+ BGTC Sub-team Reps
  - Erin Finot
  - Jin Chen
  - Griselda Sanchez
  - Sherin Meloni
  - Alex Secora

**Innovation**
- Amritha Jaishankar
- Barbara Arone

**Program Management Operations and Playbook**
- Adrian McKemey
- Carmen Sivakumaren
- James Noll
- Charles Vizzini
- Greg Plante
- Oluoma Agu
- Leah Herbert
- Kelley Coaier
- Joyce Liu
- David Hoekzema
- Vadim Sapiro
- Robin Douglas
- Brennan Miller
- Hanna Savran
- Lauren Taylor

At AMP Symposium
BGTC Regulatory Playbook Version 1.0

**OBJECTIVE: DOCUMENT BEST PRACTICES FOR GENE THERAPY PRODUCT DEVELOPMENT, INCORPORATING BGTC MINIMUM STANDARDS AND EXPERT ADVICE**

- Version 1.0 released today for viewing/download using QR code below
- Serves as an initial framework
- Subsequent versions (v2.0+) will incorporate learnings from BGTC, including:
  - minimal CQAs and experiences gained
  - minimum animal toxicology and experiences gained
  - streamlined approaches to regulatory submissions
Acknowledgement

We would like to acknowledge all BGTC members and contractors for their continued dedication, support and expertise that have shaped the program, with the goal of moving our portfolio of AAV projects into the clinic – THANK YOU!
Next session covers the why, what, & how of executing the program

**BGTC program overview**
- Unmet need and goals
- Consortium members
- Research and clinical program
- Project portfolio
- Structure and governance
- Regulatory Playbook version 1.0

**BGTC Operations**
- Challenges BGTC is addressing
- Key questions emerging
- Features of the BGTC program (and Coordination Center role)
- Early activities and outputs

**Future directions**
- Where we’re going
- Q&A
BGTC is unique in simultaneously addressing key challenges

*Potential to be a “pathfinder” within a complex, evolving regulatory environment*

- Imperative for patient group engagement in development pathway
- Supporting IND holders to fulfill their regulatory responsibilities
- Streamlining product development and navigation of the regulatory pathway through bolstering limited clinical infrastructure
- Incorporating broad multidisciplinary expertise from across the government and industry

AMP Symposium | February 2024
Several key questions have arisen in designing the right solution

How do we meet the needs of each asset in a dedicated, comprehensive way?

How do we efficiently navigate the regulatory pathway and accelerate development of these gene therapies in rare diseases?

How do we devise a robust systematized data collection and management approach?

How do we bring common asset-level findings to the program level?

How do we develop a mechanism for evolving and sharing learnings?

How does the sponsor demonstrate accountability and regulatory compliance/quality?

How do we manage communication and triage feedback among stakeholders?

How do we demonstrate a model that is repeatable for other disease areas and therapeutic modalities?

How do we enable long-term monitoring and sustainability?

How do we bring common asset-level findings to the program level?
Several key questions have arisen in designing the right solution

Cross-Functional Project Team Engagement and BGTC Expertise

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**Data Management & Analysis (DMA)**
- How do we devise a robust systematized data collection and management approach?

**Quality Management System (QMS)**
- How does the sponsor demonstrate accountability and regulatory compliance/quality?

**Long-Term Follow-Up (LTFU)**
- How do we enable long-term monitoring and sustainability?

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**Regulatory Playbook**

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BGTC Coordination Center

Cross-Functional Project Team Engagement

Data Management & Analysis (DMA)

Quality Management System (QMS)

BGTC Regulatory Playbook

Long-Term Follow Up (LTFU)
Focus of early activity was on assessing project team readiness
Readiness assessments lead to formalized go-forward strategies

General format:
Summary of observations with detailed sections:
- Significant factors and assessed impact
- Conclusions and implications for next steps

Detailed sections for:
- Non-clinical
- Clinical
- CMC
- Regulatory
- Quality
- Data Mgmt. & Analysis
- LTFU

Readiness assessments:
- Evaluate assets against next milestone (e.g., IND, Pre-IND)
- Are consistent with the BGTC approach and best practices
- Will be repeated for every key milestone over next 3 years
Seven emerging considerations for IND readiness

<table>
<thead>
<tr>
<th>Category</th>
<th>Early observations</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturing</td>
<td>Manufacturing schedule to meet CMC requirements TBD</td>
<td>Sync contracts, quality agreements, audits to regulatory milestones</td>
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<tr>
<td>Quality</td>
<td>Disparate and various approaches to quality compliance</td>
<td>Recommend instituting a centralized quality management system (QMS)</td>
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<tr>
<td>Regulatory</td>
<td>Very early stage of planning FDA meetings and request guidance on regulatory pathway</td>
<td>Create templated project plans/milestones for each team as key tool for status tracking and governance decisions</td>
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<tr>
<td>Data Management</td>
<td>Natural history studies as comparator or run-in for clinical – many in non-Part 11 compliant systems</td>
<td>A centralized EDC/eCOA approach would help conform data to CDISC standards to submission quality and make consistent with clinical eCRFs</td>
</tr>
<tr>
<td>Clinical</td>
<td>Project teams have questions on relevance and applicability of their endpoints</td>
<td>Benefit in providing high level guidelines to the program on requirements and any flexibility for endpoints</td>
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<td>Program</td>
<td>Questions on roles &amp; responsibilities of PI vs BGTC emerging, particularly around the assets where NIH holds the IND</td>
<td>Developing a ‘DARE’ framework to enable NIH to fulfill responsibilities of IND holder</td>
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<td></td>
<td>Although patient advocacy group (PAG) engagement commenced, at early stage to leverage the full potential</td>
<td>Early, programmatic PAG engagement on protocol and LTFU responsibilities to de-risk clinical study enrollment and loss to follow up</td>
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</table>
Both immutable and variable drivers can influence asset timelines

**Immutable Drivers of Timelines**

- GMP Production is critical and rate limiting:
  - IND enabling pre-clinical studies should be conducted using GMP-like materials (referred to as Tox-grade). Scheduling of these studies is dependent on manufacturing schedule.
  - A GMP batch must be completed before IND submission (Module 3 must reflect GMP production information and sample batch record provided).
  - Plan for adequate time between Pre-IND and IND to incorporate feedback/evidence into IND.
  - Receipt of a Study May Proceed (SMP) letter/email from FDA for Study Start Up (IRBs require this).

**Variable Drivers of Timelines**

- INTERACT is an optional meeting (and not guaranteed to be granted) and is not necessary for all assets. BGTC will advise whether types of questions merit INTERACT.
  - GMP “like” materials may be used in some cases for some pre-clinical studies (e.g., pilot studies). This approach may be considered to optimize timelines, while weighing risks.
  - We assumed 1-1.5 years between Pre-IND and IND based on experience however this time is not fixed and can change (shorter or longer) depending on resources.
  - Opportunity for harmonization between milestone-driven projects.
  - Institutional dependent processes for specific activities (e.g. vendor management).
Asset-level findings surface synergies at the program level

Asset commonalities
- Animal models
- Vector backbone
- Manufacturers and vendors
- Prior FDA interactions
- Electronic data capture for natural history study
- Concerns with patient retention

Potential program accelerators
- Shared learnings from FDA meetings from one asset to another
- Minimum requirements for study design
- Standardized, centralized, and harmonized data management system across trials
- Efficiencies in process, qualification, testing
- Patient engagement and input from protocol design through LTFU
- Leveraging natural history programs for comparative data and to optimize LTFU efficiency

Pre-/Non-clinical
CMC Capabilities
Clinical
Access
LTFU
INTERACT/Pre-IND
IND
First-in-human
Portfolio progress to continue being reported at program level

<table>
<thead>
<tr>
<th>Affected Organ System</th>
<th>Program</th>
<th>Readiness Assessment</th>
<th>INTERACT Meeting</th>
<th>Pre-IND Meeting</th>
<th>Testing and GMP Production</th>
<th>Pivotal Preclinical Studies</th>
<th>IND Filing and Clearance</th>
<th>IRB Approval</th>
<th>DSMB Contract</th>
<th>Study Site Setup</th>
<th>Clinical Trial Start</th>
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<tbody>
<tr>
<td>Ocular</td>
<td>Retinitis pigmentosa 45 (CNGB1)</td>
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<td>Ocular</td>
<td>NPHPS-5 Retinal Degeneration (NPHPS5)</td>
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<td>Neurological</td>
<td>Multiple Sulphatase Deficiency (MDS)</td>
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<td>Systemic</td>
<td>Propionic Acidemia (PA)</td>
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<tr>
<td>Systemic</td>
<td>Morquio A (Mucopolysaccharidosis IVA, MPS IVA)</td>
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*Complete*, *On track*, *Minor delays*, *Significant delays*, *Not started / Not applicable*
Data management needs emerged as key factor for asset timelines
Benefits / risk reduction through a centralized data ecosystem
Sponsor responsibilities requires a quality management system
QMS model defines framework for quality & regulatory compliance

Establishes Standards Index

- For associated activities linked to current R&D standards for product development and testing
- Also demonstrates activities not required per regulations but "good practices" per guidance documents

Describes regulatory and quality documents

- These documents individually and collectively permit the evaluation of the R&D/non-R&D activity and those responsible (per the RACI) for the quality of the data produced

Enables sponsor decision-making

- Allows sponsor to demonstrate decision-making around research activities through the organization and set up of systems, process and procedures identified for each regulated area i.e., GLP, GMP and GCP

Ensures proper documentation

- Involves development of documentation along with accountability structure that assures evidence collection and standardization in operations
- Considers unknowns and lack of standards (controls) due to the bespoke nature of the program
Each GxP component requires three levels of quality measures

- **QMS**: Compliance, Accountability for IND holder
  - Reporting and signoff
- **QA**: Planned activities to ensure safety and quality
  - Audits, systems, standards
- **QC**: Ensure that the product meets the required quality standards
  - Contracts, structure, systematic set of processes

**GMP**

**GCP**

**GLP**
With AAV gene therapies, LTFU and its challenges are top of mind.
BGTC opens up opportunities for a common LTFU framework

Key Study Design Questions
1. Roll-up multiple trials into a single follow-up program?
2. Which delivery options to consider at each phase?
3. How quickly to transition to a new phase?
4. How far to transition along the phases?
5. Can a central PI model be adopted?
The Playbook is the first public output from the BGTC program.
The Playbook will incorporate BGTC learnings

Streamlining product development and navigation of regulatory pathway

Simplified roadmap to increase likelihood of success and accessibility to patients sooner

To be piloted with 8 BGTC assets and designed to be broadly applicable for other AAV gene therapies

Study may proceed

IND submission
Pre-IND Meeting
INTERACT Meeting

Milestone
Hurdle

BGTC Regulatory Playbook

Version 1.0
Ready for download!

AMP Symposium | February 2024

Ready for download!
Conclusion

BGTC program overview
- Unmet need and goals
- Consortium members
- Research and clinical program
- Project portfolio
- Structure and governance
- Regulatory Playbook version 1.0

BGTC Operations
- Challenges BGTC is addressing
- Key questions emerging
- Features of the BGTC program (and Coordination Center role)
- Early activities and outputs

Future directions
- Where we’re going
- Q&A
Where we’re going

**Q4 2023**
- Initiate program management activities
- Understand assets’ current status
- Assess “readiness” for next milestone(s)
- Identify next steps for key activities

**Q1 2024**
- Establish portfolio dashboard and asset-level project plans
- Begin steady-state asset engagement
- Design and implement centralized DMA approach components

**Q2 2024**
- Track / report asset development progress
- Establish QMS program / framework
- Facilitate BGTC best practices

**H2 2024 onwards**
- Continued advisory expertise to support development activities
- Contingency and continuation planning, LTFU / sustainability
- Centralized capture of learnings in playbook

**Outcome**
- BGTC portfolio assets reaching IND and first-in-human (FIH) trials
- Roadmap for similar developers in rare disease
- Model that is extensible to other therapeutic areas and modalities

**Feedback loop and learning system**
**Toolkit for project teams and broader community**
**Series of best practices for a platform approach**
Thank you and we would like to open the floor to questions!