Consortia-Based Strategies in Neurodegenerative Diseases: Critical Path Institute’s Track Record in Collaborative Efforts

Martha A. Brumfield, PhD
President & CEO
Agenda

- C-Path Model for Collaboration and Where We Focus
- Innovative Drug Development Tools
- What Is In Scope for This Collaboration
- Critical Importance of Sharing Data
How C-Path Works: A Public-Private Partnership

• Act as a trusted, neutral third party
• Convene scientific consortia of industry, academia, and government for sharing of data/expertise
  ✓ The best science
  ✓ The broadest experience
• Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
• Official regulatory endorsement of novel methodologies and drug development tools
C-Path Consortia

- Coalition Against Major Diseases
  *Focusing on diseases of the brain*

- Coalition For Accelerating Standards and Therapies
  *Data standards*

- Critical Path for Parkinson’s Consortium
  *Enabling clinical trials in Parkinson’s Disease*

- Critical Path to TB Drug Regimens
  *Accelerating the development of TB drug regimens and diagnostics*

- Duchenne Regulatory Science Consortium
  *Duchenne Muscular Dystrophy*

- Huntington’s Disease Regulatory Science Consortium
  *Expediting approval of Huntington’s therapeutics*

- International Neonatal Consortium
  *Neonatal clinical trials*

- Multiple Sclerosis Outcome Assessments Consortium
  *Drug Effectiveness in MS*

- Polycystic Kidney Disease Outcomes Consortium
  *New imaging biomarker for PKD*

- Patient-Reported Outcome Consortium
  *Assessing treatment benefit*

- Electronic Patient-Reported Outcome Consortium
  *Electronic capture of treatment benefit*

- Predictive Safety Testing Consortium
  *Drug safety*

- Pediatric Trials Consortium
  *Developing effective therapies for children*

- Type 1 Diabetes Consortium
  *Qualifying biomarkers for type 1 diabetes*

- Transplant Therapeutics Consortium
  *New drug development tools for transplantation*
C-Path Regulatory Successes

<table>
<thead>
<tr>
<th>CAMD</th>
<th>AD clinical trial database</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFAST</td>
<td>AD clinical trial simulation tool</td>
</tr>
<tr>
<td>CPP</td>
<td>EMA qualified AD biomarker</td>
</tr>
<tr>
<td>CPTR</td>
<td>FDA Letters of Support - AD biomarkers</td>
</tr>
<tr>
<td>PKD</td>
<td>EMA/FDA/PMDA qualified non-clinical kidney safety biomarkers</td>
</tr>
<tr>
<td>PSTC</td>
<td>FDA and EMA letters of support:  - Kidney biomarkers  - Skeletal muscle injury biomarkers  - Drug-induced liver injury</td>
</tr>
</tbody>
</table>

- **CAMD**
  - AD clinical trial database
- **CFAST**
  - 30 therapeutic area users guides across 25 different disease areas, CDISC
- **CPP**
  - FDA and EMA letter of support - PD biomarker
- **CPTR**
  - EMA qualified Hollow Fiber System for Tuberculosis
  - ReSeqTB data platform
- **PKD**
  - Total Kidney Volume Imaging (TKV) biomarker qualified with EMA and FDA
  - FDA letter of support (TKV)
- **PSTC**
  - EMA/FDA/PMDA qualified non-clinical kidney safety biomarkers
  - FDA and EMA letters of support:  - Kidney biomarkers  - Skeletal muscle injury biomarkers  - Drug-induced liver injury
EXAMPLES OF HOW BIOMARKERS ARE USED IN DRUG DEVELOPMENT

- **Basic Research**
  - Mechanism of Action
  - Drug Target Selection

- **Prototype Design or Discovery**
  - Stratification
  - Patient Selection
  - Enrichment

- **Preclinical Development**
  - Dose Selection
  - Safety Assessment
  - Efficacy Assessment

- **Clinical Development**
  - Preclinical Safety Assessment
  - Mechanism of Action
  - Dose Selection

- **FDA Filing/Approval and Launch**

**Molecular Pathways Leading to Disease**

**Courtesy of Shashi Amur, Office of Translational Sciences, FDA CDER**
Some Enablers for Biomarker Development

- Data standards
- Data quality
- Data reproducibility
- Statistical considerations
- Assay/imaging considerations/validation
- Assay/imaging protocols
- Establishing cut points

Courtesy of Shashi Amur, Office of Translational Sciences, CDER
Our work involves multi-stakeholder collaboration in a pre-competitive space. Clarity regarding what is in and out of scope is very important. Here are high-level principles:

- Promote development of innovative drug development tools to be incorporated into regulatory approaches critical for advancing safe and effective HD therapies
- Enable protected mechanisms for information and data sharing in the collaboration among industry, academic centers, patients, regulatory and other government agencies
- Foster awareness of the importance of data standardization and the need to focus on early stage of disease
- Focus on needs of people with HD, needs of therapeutic developers, needs of regulators
Huntington’s Disease Regulatory Science Consortium: Scope

OUT OF SCOPE

• Discussions, evaluations, analysis, etc. that pertain to specific:
  • Products or therapeutics in development
  • Clinical trials specific to a single therapeutic
  • Protocols specific to a single trial
  • Vendors
  • Research sites
  • Investigators
  • HD-RSC Members
  • Government advocacy

• Discovery of/basic research regarding new biomarkers and other clinical development tools; rather, we focus on assuring appropriate analytical and clinical validation and adequate evidence gathering to support their use in drug development
Critical Factors That Enable Collaboration

• Member Legal Agreement
• Governance
• Scientific, Regulatory, and Project Management Expertise
• Data Collaboration Center
  − Data Contribution & Data Use Agreements
Past

- Data sharing among industry was extremely rare
- Academics misconstrued publishing of trial summary results as “data sharing”
- Trial participants always assumed their data were being shared
History and Evolution of Data Sharing

### Present

- Many databases with patient-level data exist, from both industry and academic sources
- Trial participants are now adamant their data be shared
- ICMJE and many funders require that actual data be published
- Big data initiatives promise much, but can they deliver?
- Smart data can lead to more insights and answers

DATA COLLABORATION

NEUTRAL SPACE
The Emerging Future

• Disease-specific databases containing 10,000+ patient-level data fields that can be tapped to inform decisions
• Databases containing data from safety biomarkers, collected across multiple diseases, from multiple INDs, NDAs, that inform our learning
• Real-world data structured in a consistent manner
C-Path Data Mapping and Integration Process
Therapeutic Area Data Standards:
Key to Combining Datasets

Therapeutic Area User Guide for Huntington's Disease
Version 1.0 (Draft)
Prepared by the
CFAST Huntington's Disease Standards Team

Therapeutic Area User Guide for Polycystic Kidney Disease
and Mild Cognitive Impairment
Version 2.0
Prepared by the
CFAST Alzheimer's Development Team
Clinical Data Contributed to C-Path

Clinical data: 97 studies
54,044 subjects

Note: nonclinical 119 studies. 6296 subjects.
ReSeqTB: 5628 Individual Isolates
Successful C-Path Data Collaboration Projects

1. AD placebo arm, patient-level data

   - PKD database: Used to develop disease progression model and clinical trial simulation tool
   - PKD database: Used for regulatory qualification of prognostic biomarker

2. PTCL (TB clinical and preclinical data aggregation)

   - CPTR: Used to support modelling and simulation development

3. MS placebo arm, patient-level data

   - Parkinson’s disease database (in progress)
   - Parkinson’s disease database (in progress)

4. Duchenne muscular dystrophy database (in progress)

   - In support of Fit for Purpose disease model
   - In support of Fit for Purpose disease model
As the products of these partnerships mature, it is incumbent upon all stakeholders to share the collective knowledge and impact from integrating the deliverables into drug development programs. Cataloguing and sharing these experiences and successes publicly will enable further learning and encourage the adoption of these novel approaches to achieve unmet public health needs. With continued partnership, multisector collaborations can continue to advance innovations in medical product development and the health of all Americans.
Thank You

www.c-path.org
C-Path Core Competencies

- Regulatory qualification of preclinical and clinical biomarkers for safety, efficacy, and trial enrichment
- Outcome assessment instrument development
- Comprehensive modeling & simulation programs
- Novel *in vitro* tools to expedite proof-of-concept
- Clinical data standards development
- Secure data management, standardization, curation, database development, and hosting for external use
- Forming and managing large international consortia
- Forming collaborations with non-C-Path consortia (e.g., IMI, FNIH)