Industry Data Sharing Initiative

Martha Brumfield, Critical Path Institute, Special Advisor and Past President & CEO
Samantha Budd Haeberlein, Biogen, C-Path Data Sharing Initiative Co-Chair
Billy Dunn, FDA, C-Path Data Sharing Initiative Co-Chair
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Description</th>
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</table>
| 9:15 – 9:30 a.m. | Perspectives on AD and related Dementias – FDA  
                   |   Billy Dunn (CDER)                                                                  |
| 9:30 – 9:45 a.m. | Perspectives on AD and related Dementias – EMA  
                   |   Maria Tome (EMA) – remotely presented                                              |
| 9:45 – 10:00 a.m. | Digital health tools and drug development - FDA  
                   |   Leonard Sacks (CDER)                                                               |
|               | **Break (15 min)**                                                                  |
| 10:15 – 10:40 a.m. | Can we detect and treat Alzheimer’s disease a decade before dementia?  
                   |   Reisa Sperling (Harvard)                                                         |
| 10:40 - 11:00 a.m. | "... and the Related Dementias" - Multiple Targets, Multiple Outcomes.  
                   |   Jeffrey Kaye (Oregon Health & Science University)                                |
| 11:00 a.m. – noon | **Panel Discussion – Aligning on Key Unmet Needs**  
                   |   Billy Dunn (FDA-CDER), Eric Bastings (FDA-CDER), Maria Tome (EMA),  
                   |   Leonard Sacks (FDA-CDER), Chris Leptak (FDA-CDER), Carlos Pena (FDA-CDER),  
                   |   Reisa Sperling (Harvard), Jeffrey Kaye (OHSU), Jim Hendrix  
                   |   (Alzheimer’s Association)                                                        |
**GENESIS (continued)**

Critical Path for Alzheimer’s Disease
2018 Annual Meeting & Regulatory Science Workshop

**November 13, 2018**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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| 9:15 – 9:30 a.m. | Vision for the Future: Strengthening Communication Across the AD Drug Development Community  
Samantha Budd-Haeberlein (Biogen, Vice-President and Head of Alzheimer’s Disease), and Billy Dunn (FDA, Director, Division of Neurology Products) |
| 1:20 – 2:50 p.m. | Working Roundtable Discussion  
All |

**SESSION IV:**
Solving Industry Needs Through Data Sharing: From Prevention to Treatment of Dementia
Moderators: *Klaus Romero (C-Path, Director, Clinical Pharmacology & Quantitative Medicine), Samantha Budd-Haeberlein (Biogen, Vice-President and Head of Alzheimer’s Disease), and Billy Dunn (FDA, Director, Division of Neurology Products)*
PROBLEM

- There is a pressing need for a better-informed basis on which to design clinical trials in neuroscience
- Science is directing us to conduct trials in even earlier stages of progressive neurological disease – the information upon which to do so is limited

VISION IN ALZHEIMER’S DISEASE AS A TEMPLATE FOR PROGRESSIVE NEUROLOGICAL DISEASES

- To provide a disease progression model across the entire continuum of Alzheimer’s disease (AD) – from the earliest stages to severe AD – providing an invaluable tool that will aid in optimizing trial design & execution, reduction of cost & time, and reduced patient burden
DISEASE PROGRESSION MODEL ACROSS THE ENTIRE AD CONTINUUM

**Input**

Studies
- AMARANTH
- BAN2401/Clarity AD
- Bapineuzumab
- CREAD
- EARLY
- EMERGE/ENGAGE
- EPOCH/APECS
- EXPEDITION
- GENERATION
- GRADUATE
- MissionAD
- TOMMORROW
- Others

**Output**

Understanding of progression
- Trajectory
- Rate
- Predictors
- Transform AD drug development
  - Cost
  - Time
  - Participants
THE CRITICAL PATH INSTITUTE

- Host of over fifteen global, pre-competitive, public-private partnerships with participation from industry, academia, advocacy groups, and regulators, with impact on regulatory science

Regulatory qualification of preclinical and clinical biomarkers for use in safety, efficacy, and trial enrichment

Development and qualification of clinical outcome assessment tools

Development of quantitative modeling and simulation tools

Regulatory acceptance of nonclinical tools for medical product development

Impact on regulatory science

Forming and managing large international consortia

Provision of large-scale data solutions for scientific research

Clinical data standards development

www.c-path.org
15 PUBLIC-PRIVATE-PARTNERSHIPS COLLABORATING WITH OVER 1500 SCIENTISTS & 90 ORGANIZATIONS WORLDWIDE
C-PATH’S DATA COLLABORATION CENTER

✓ Provides large-scale data solutions for scientific research
✓ Develops customized data platforms for improved collaborations
✓ Multisource data aggregation and standardization
✓ Curation and administration of data and its storage
✓ Robust security policies and framework
✓ Application of current regulations to ensure compliance

As of May 2019, the DCC’s data platform securely hosts data from 146 clinical studies and 179 nonclinical experiments, representing over 77,054 subjects, over 200 million data points and 12 different therapeutic areas.
CLINICAL DATA GROWTH

as of May 2019, clinical data: 146 studies / 77,054 subjects

C-Path’s Data Collaboration Center also manages:
- Non-clinical data from 179 studies involving 11,775 subjects
- Genotypic/phenotypic data for 9,215 tuberculosis isolates
C-PATH’S DATABASES ARE UNIQUELY FOCUSED ON ENABLING DRUG DEVELOPMENT SOLUTIONS

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<th>Feature</th>
<th>ADCS</th>
<th>Brain Commons</th>
<th>Clinical Study Data Request Consortium</th>
<th>C-Path</th>
<th>FNIH (Sage Bionetworks)</th>
<th>GAAIN</th>
<th>NACC</th>
<th>Vivli</th>
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CONTEMPORARY LARGE AND DEEP AD DATASETS PROVIDE AN UNPRECEDENTED OPPORTUNITY TO REALIZE THE VISION

The following datasets are of greatest relevance to the development of an early AD progression model:

- Biogen: EMERGE/ENGAGE, Aducanumab, 3,200+
- Eisai/Biogen: MissionAD1/MissionAD2, Elenbecestat, 1,900+
- Eisai/Biogen: BAN2401, 800
- Eisai/Biogen: Clarity AD, BAN2401, 1,500+
- Eli Lilly: EXPEDITION/EXPEDITION2/EXPEDITION3, Solanezumab, 4,100+
- Eli Lilly/AstraZeneca: AMARANTH/DAYBREAK-ALZ, Lanabecestat, 3,900+
- Janssen/Pfizer: Bapineuzumab, 3,300+
- Janssen: EARLY, Atabecstat, 500+
- Merck: EPOCH/APECS, Verubecestat, 3,600+
- Novartis/Amgen: GENERATION S1/GENERATION S2, Umibecestat, 1,600+
- Roche: CREAD/CREAD2, Crenezumab, 1,500+
- Roche: GRADUATE1/GRADUATE2, Gantenerumab, 1,500+
- Takeda/Zinfandel: TOMMORROW, Pioglitazone, 3,000+

>30,000 Additional patient-level records
Clinical Trial Transparency and Data Sharing

We are committed to sharing information about our clinical research with patients and researchers to enhance public health.

**BIOGEN CLINICAL TRIAL TRANSPARENCY AND DATA SHARING POLICY**

In alignment with global legal requirements, the Industry Trade Association Principles¹, and internal company policies, Biogen is committed to sharing information about our clinical research as follows:
EARLY SUCCESSES

- Since launch of this initiative, several organizations committed to sharing key trial data with CPAD
  - Lundbeck (*Idalopirdine* trials)
  - Novartis (GENERATION S1 and S2)
  - Takeda (TOMMORROW trial)
  - vTv Therapeutics (*STEADFAST* trial)
  - Washington University (DIAN study, NCT00869817)

>12,000 additional patient-level records from these sources; with this, the CPAD Data Repository could grow to >26,000 patient-level records in the short-term
# EARLY SUCCESSES – AD TRIALS TO BE SHARED WITH CPAD

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<tr>
<th>Sponsor</th>
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<td>vTv Therapeutics</td>
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GOALS AND DELIVERABLES

Key Industry Trials
- AMARANTH
- BAN2401
- Clarity AD
- Bapineuzumab
- CREAD
- EARLY
- EMERGE/ENGAGE
- EPOCH/APECS
- EXPEDITION
- GENERATION
- GRADUATE
- MissionAD
- TOMMORROW

Disease Progression Model

- Secure transfer
- Curation
- Quality control

Data Mapping

CPAD Repository

Impact
- Accelerate the evolution of the scientific understanding of the AD Continuum
- Reduce clinical trial costs
- Expedite drug development
- Reduce patient burden

AD Community
IMPACTFUL GLOBAL DATA ACCESS FOR INDUSTRY AND ALZHEIMER’S RESEARCHERS

38 AD studies with 14,583 individual anonymized patient records and more than 420,000 covariate measurements

(shared by Abbott Laboratories, AstraZeneca, Bellus Health, Eisai, Forest Laboratories, GlaxoSmithKline, Johnson & Johnson, Novartis, Pfizer, Sanofi, Servier, and ADCS)

496* approved applicants from 393 distinct institutions from 52 countries

- Pharmaceutical Industry
- Government Agencies
- Non-profit Organizations
- Academia
- Independent Researchers

* as of 9/30/2019
EARLY SUCCESSES – SHARING WITH OTHER C-PATH COLLABORATIONS

- Several key datasets were recently shared with other C-Path consortia:
  - Duchenne Muscular Dystrophy - Regulatory Science Consortium (D-RSC)
    - 14 datasets (6 from industry) with 4,930 individual subjects
    - 1 additional dataset was recently received; 1 additional dataset is in process to be shared
  - Huntington’s Disease - Regulatory Science Consortium (HD-RSC)
    - 3 datasets (observational studies) with 8,600 individual subjects
    - 5 additional datasets (2 clinical trials) in process to be shared (15,500 individual subjects)
  - Critical Path for Parkinson’s Disease (CPP)
    - 14 datasets (9 clinical trials; 5 observational studies) with 8,200 individual subjects
  - Friedreich’s Ataxia (5 datasets in house; 3 datasets are under discussion; total of 1,350 subjects)
Drugs for Treatment of Partial Onset Seizures: Full Extrapolation of Efficacy from Adults to Pediatric Patients 2 Years of Age and Older Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 7, Room 2040
Silver Spring, MD 20993-0002
Phone: 888-463-6332 or 888-382-3462; Fax: 888-382-4142; Email: DruginfoFDAserv@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidance-drugs

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

September 2019
Clinical Pharmacology/Clinical
“Systematic and quantitative analyses conducted by FDA, using data from clinical trials of drugs approved for the treatment of POS in both adults and pediatric patients 2 years of age and older, have shown that the relationship between exposure and response (reduction in seizure frequency) is similar in adults and pediatric patients 2 years of age and older.”
SUCCESS – THE POWER OF DATA SHARING

- 2/16/18 Draft Guidance published

- Approvals
  - 9/13/17 Aptiom (eslicarbazepine)
  - 11/3/17 Vimpat (lacosamide)
  - 5/3/18 Lyrica (pregabalin)
  - 5/10/18 Briviact (brivaracetam)
  - 9/27/18 Fycompa (perampanel)

- Under review
  - 11/21/18 application for new drug
  - 3/25/19 supplement submitted for additional drug

- Pending
  - 5/16/18, 8/28/18, 12/10/18, and 4/26/19 discussions with sponsors of four additional drugs
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<th>Age range</th>
<th>Length of follow up</th>
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<td>5-14</td>
<td>52 weeks</td>
<td>Functional measures.</td>
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</table>

In analysis dataset (not all data):
TOTAL Number of Individual Patients: 1,137
TOTAL Number of Observations: 23,305
LESSONS FROM THE DUCHENNE MUSCULAR DYSTROPHY
REGULATORY SCIENCE CONSORTIUM

Challenge

How to quantitatively describe the longitudinal disease continuum of Duchenne muscular dystrophy?

Opportunity

Identify relevant measures across the disease continuum, captured across the integrated datasets.

Solution

Develop a sophisticated quantitative clinical trial simulator that captured all the identified relevant measures across the disease continuum of Duchenne muscular dystrophy.
D-RSC SUMMARY OF CONTEXT-OF-USE STATEMENT

**General Description**

A disease progression model-based clinical trial simulation (CTS) tool designed to optimize clinical trial enrichment and design of studies to investigate efficacy of potential therapies for Duchenne Muscular Dystrophy (DMD)

**Measures of disease progression**

- North Star Ambulatory Assessment
- Velocities of completion of the supine-stand test, 4-stair climb test, 10-meter walk/run test and 30-foot walk/run test
- Forced vital capacity
- Brooke scale

**Target Population for use**

Individuals with DMD 4 years and older (endpoint-dependent), regardless of stage of disease
NOT ALL MEASURES NEED TO BE PRESENT IN ALL DATA SOURCES

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Baseline covariates proposed to be included in the analyses: Age, BMI, RACE, Steroid use, Age at start of steroid use, Genetic mutation, Study type

The power of numbers: 1139 individuals with DMD with a total of 24210 (non-missing) observations of the selected measures, from 4 to 34 years of age
LESSONS LEARNED AND ENVISIONED IMPACT

Application of the DMD quantitative tool

To help inform, through simulations, the selection of inclusion/exclusion criteria, enrichment strategies, stratification approaches, timing and selection of clinical assessments, trial duration and sample size for studies evaluating therapeutic candidates for DMD.

How could things look like for AD?

Determine relevant common-denominator measures across the targeted datasets and structure a quantitative plan to develop a comprehensive model of disease dynamics across such measures.
C-PATH IS UNIQUELY FOCUSED ON DEVELOPMENT IN A TRULY NEUTRAL PRE-COMPETITIVE ENVIRONMENT WITH ESTABLISHED SUPPORT OF BOTH INDUSTRY AND REGULATORS

Advanced Data Management

Extant technical expertise and infrastructure to obtain, integrate and make accessible high quality patient-level datasets suitable for queries and analyses

Advanced Analytics to Generate Solutions

Data-based ability to generate a disease progression model across the entire continuum of Alzheimer’s disease (AD) – from earliest stages to severe AD

Focus on Drug Development

Potential to dramatically accelerate the evolution of the scientific understanding of AD, reduce clinical trial costs, and thereby expedite drug development
SUMMARY

- C-Path has established an AD clinical trial repository of 38 trials and ~14,000 individual patient records
- However, more contemporary datasets across the entire disease spectrum are needed
- C-Path is urging all consortium industry members to pre-competitively share high-value, contemporary trial data allowing for expansion of this knowledgebase
- C-Path has generated a trial inventory of relevant data that will transform the entire AD space and how future trials are being executed through the creation and regulatory endorsement of novel tools