ACCELERATING DRUG DEVELOPMENT FOR RARE DISEASES: ESTABLISHING A CORNERSTONE THROUGH DATA SHARING

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Disclaimer: Dr. Budd Haeberlein is an employee of Biogen. The information in this presentation is based on the presenters’ expertise and experience, and represents the views of the presenter.
There is a pressing need for a better-informed basis on which to design clinical trials.

The need to quantitatively characterize diseases is particularly acute in rare disease drug development as the information upon which to do so is limited.
WHAT ARE THE CHALLENGES IN RARE DISEASE DRUG DEVELOPMENT?

SMALL HETEROGENEOUS POPULATIONS

▪ Lack of disease characterization / disease progression
▪ High heterogeneity leading to variability in disease presentation & course
▪ Lack of comprehensive scientific understanding / mechanisms in disease
▪ Challenges of clinical trial designs
▪ Limited patient number & Geographic dispersal
▪ Underinformed outcome assessments and endpoints
▪ Underinformed or absent biomarkers
▪ Evolving standard of care
CAN RARE DISEASE DEVELOPMENT BENEFIT FROM LESSONS FROM LARGER DEVELOPMENT PROGRAMS?

- These challenges are not unique to rare diseases, but are amplified in difficulty

- Smaller samples and paucity of data are also a challenge in early phases of drug development where critical go/no-go decisions are often based on:
  - Limited data, smaller numbers of patients, information gaps, evolving disease understanding, need for informed decisions for Phase 3 design
  - All in setting of limited information, information is often limited to what you have available internally
CNS DISORDERS PRESENT CHALLENGES FOR DRUG DEVELOPMENT...

### Potential Challenges

- **Uncertain target engagement**
  - Difficult to detect pharmacodynamic effects in CNS compartment

- **Population heterogeneity**
  - Syndromic classification

- **“Noisy readouts”**
  - Cognitive function, mood, psychosis, pain

- **Insidious onset and slow progression**

### Potential Pitfalls

- **Errors in dose selection**
- **Diagnostic uncertainty, imprecise staging of disease, Low responder rates**
- **Need large numbers to detect treatment effect, ↓ Data Quality**
- **Larger and longer trials, ↓ Data Quality, ↑ Missing data**

↑ Variability of data

↓ Ability to detect treatment effect
DATA SHARING PROVIDES THE KEY

- Data sharing, integration and quantification can de-risk decision-making by reducing uncertainty, across the drug development value chain (from translational, through early phase clinical development, to registration studies)
IMPACTFUL GLOBAL DATA ACCESS FOR INDUSTRY AND RESEARCHERS: ALZHEIMER’S CASE STUDY

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)

486* approved applicants from 385+ distinct institutions from 52 countries

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

* as of 8/25/2019
ALZHEIMER’S DISEASE CLINICAL TRIAL SIMULATOR: REGULATORY-ENDORSED TOOL MADE POSSIBLE BY DATA SHARING, COLLABORATION AND QUANTITATION

Disease progression: 75 year-old males, by APOE4 and baseline severity
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
C-PATH IS UNIQUELY FOCUSED ON DEVELOPMENT IN A PRE-COMPETITIVE ENVIRONMENT WITH SUPPORT OF INDUSTRY & 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 actionable and robust quantitative solutions across rare diseases

**Focus on Drug Development**

Potential to dramatically accelerate the evolution of the scientific understanding of rare diseases, reduce clinical trial costs, and thereby expedite drug development
RDCA-DAP: A RESOURCE FOR THE FUTURE OF DRUG DEVELOPMENT IN RARE DISEASES
The combination of C-Path and NORD, with each group’s expertise and vision, will establish the RDCA-DAP in order to facilitate disease-specific data sharing-informed disease characterization, at a quality level that will meet the development needs of industry and regulatory requirements.
By creating the RDCA-DAP, the need for one-off disease characterization efforts for every disease will be eliminated.

Instead we have a living, durable structure ready to establish in rapid order a data sharing database for any given rare disease:

- Minimize start up time
- Minimize development time
- Minimize delivery time of new therapeutics to patients
EARLY SUCCESSES OF RDCA-DAP IN DATA SHARING

Commitments to sharing key patient-level data

- Friedreich’s Ataxia Database
  - First data source for RDCA-DAP
- NORD’s IAMRARE™ Registries
  - Soon to be integrated
- Who wants to be next?
SUMMARY

- C-Path has an established track record and expertise in secure data sharing and integration
  - RDCA-DAP poses an exciting opportunity to grow and expand those capabilities

- NORD has an established track record and expertise in the generation of robust patient registries and patient outreach
  - RDCA-DAP poses an exciting opportunity to continuously expand and optimize such registries

- By working together, RDCA-DAP can transform the drug development landscape for rare diseases
THANK YOU
A SUCCESS STORY – REGULATORY FIRSTS

C-Path Regulatory Successes

**Alzheimer’s Disease**
- AD clinical trial database
- FDA & EMA endorsed AD clinical trial simulation tool
- EMA qualified AD biomarker
- FDA & EMA letters of support
  - Biomarkers & MCI model

**Parkinson’s Disease**
- FDA letter of support
  - PD biomarker
- EMA model-based qualified PD biomarker

**Multiple Sclerosis**
- EMA qualified Performance Outcome Measure*
  - Test battery for all forms of MS which could be used in conjunction with other performance measures and functional scales
  * in public comment phase

**Tuberculosis**
- EMA qualified in-vitro platform
- Pathogen genomics data platform
- PB/PK Model for pulmonary drug distribution received scientific advice

**Polycystic Kidney Disease**
- EMA & FDA model-based qualified Total Kidney Volume (TKV) imaging biomarker
- FDA letter of support
  - TKV imaging biomarker
- PKD clinical database

**Patient-Reported Outcomes**
- FDA clinical outcome assessment qualification
  - Symptoms of Major Depressive Disorder Scale
  - Non Small Cell Lung Cancer Symptom Assessment Questionnaire
  - Asthma Daytime and Nighttime Symptom Diaries

**Predictive Safety Testing**
- EMA/FDA/PMDA qualified non-clinical kidney safety biomarkers
- FDA qualified clinical kidney safety markers
- FDA & EMA letters of support
  - Biomarkers (kidney, skeletal muscle injury, liver)

**U.S. FOOD & DRUG ADMINISTRATION**
- 8 Qualification Decisions
  - Polycystic Kidney Disease
  - Predictive Safety Testing
  - Patient-Reported Outcome
- 1 Fit-for-Purpose Endorsement
- 7 Letters of Support

**EUROPEAN MEDICINES AGENCY**
- 7 Qualification Decisions
  - Polycystic Kidney Disease
  - Tuberculosis
  - Alzheimer’s
  - Predictive Safety Testing
  - Parkinson’s
  - Multiple Sclerosis
- 7 Letters of Support

**Pmda**
- 1 Qualification Decision
  - Predictive Safety Testing