Considerations for Participation in PPP Projects: Learnings from the Critical Path for Parkinson's Consortium

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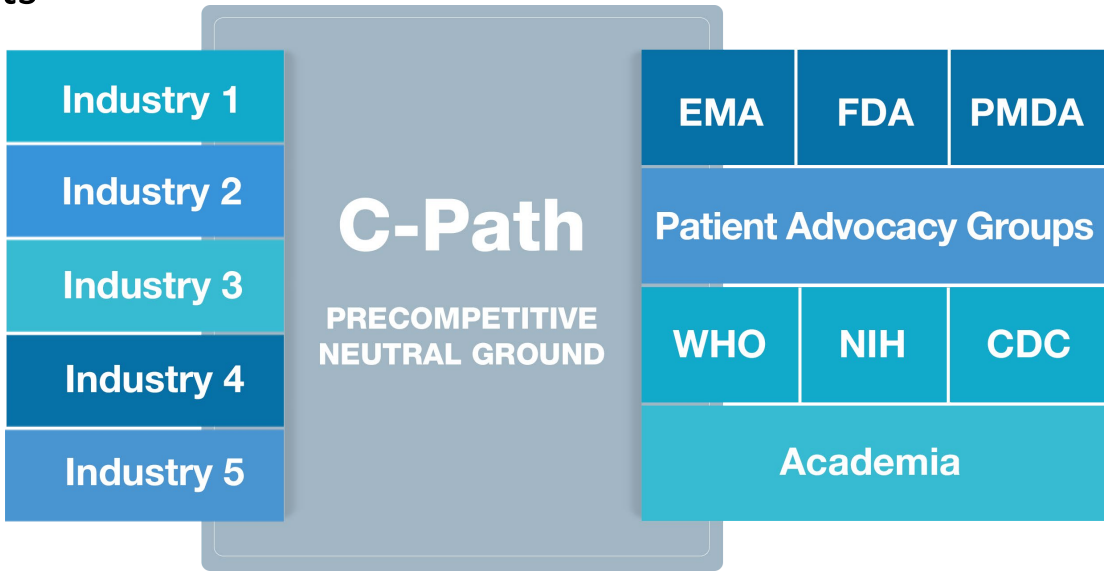
Critical Path Institute: A Public-Private Partnership

CRITICAL PATH INSTITUTE

- Acts as a trusted, neutral third party
- Convenes scientific consortia of industry, academia and government for sharing of data and expertise
  - ✓ The best science
  - ✓ The broadest experience
  - ✓ Active consensus building
  - ✓ Shared risk and costs
- Enable iterative FDA/EMA/PMDA participation in developing new methods to assess the safety and efficacy of medical products



Regulatory endorsement of novel methodologies and drug development tools

C-Path Public-Private Partnerships

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Active Consortia/Programs					
AKI/Neph	Acute Kidney Injury/ Nephrotoxicity	ePRO Consortium	Electronic Patient-Reported Outcome Consortium	PRO Consortium	Patient-Reported Outcome Consortium
BmDR	Biomarker Data Repository	FA-ICD	Friedreich's Ataxia Integrated Clinical Database	PSTC	Predictive Safety Testing Consortium
CDRC	CURE Drug Repurposing Collaboratory	HD-RSC	Huntington's Disease Regulatory Science Consortium	QuantMed	Quantitative Medicine
CPAD	Critical Path for Alzheimer's Disease	IBD	Inflammatory Bowel Disease	RDCA-DAP	Rare Disease Cures Accelerator – DAP
CPP	Critical Path for Parkinson's Disease	INC	International Neonatal Consortium	RD COAs	Rare Disease Clinical Outcome Assessments
CPTR	Critical Path to TB Drug Regiments	MSOAC	Multiple Sclerosis Outcome Assessment Consortium	T1D	Type 1 Diabetes Consortium
CP-SCD	Critical Path for Sickle Cell Disease	PKD	Polycystic Kidney Disease	TB-PACTS	TB-Platform for Aggregation of Clinical TB Studies
DCC	Data Collaboration Center	PMD	Pediatric Medical Devices	TOMI-T1D	Trial Outcome Markers Initiative in T1D Consortium
D-RSC	Duchenne Muscular Dystrophy Regulatory Science Consortium	PredicTox KE	PredicTox Knowledge Environment	TTC	Transplant Therapeutics Consortium

Critical Path Institute Regulatory Successes

C-PATH REGULATORY SUCCESSES

ALZHEIMER'S DISEASE
- FDA & EMA endorsed AD clinical trial simulation tool
- EMA qualified model-based AD biomarker
- FDA & EMA letters of support
  - Model-based AD biomarkers and pre-dementia clinical trial simulator

MULTIPLE SCLEROSIS
- EMA qualified PerfO measure
  - Test battery for all forms of MS

POLYCYSTIC KIDNEY DISEASE
- EMA & FDA model-based qualified Total Kidney Volume (TKV) imaging biomarker
- FDA letter of support
  - TKV imaging biomarker
- FDA designated reasonably likely surrogate marker for PKD trials (TKV)

PREDICTIVE SAFETY TESTING
- EMA, FDA & PMDA qualified non-clinical kidney safety biomarkers
- FDA qualified clinical kidney safety markers
- Six FDA & EMA letters of support

PARKINSON'S DISEASE
- FDA letter of support
  - PD imaging biomarker
- EMA qualified model-based PD imaging biomarker

TUBERCULOSIS
- EMA qualified translational drug development platform

PATIENT-REPORTED OUTCOME MEASURES
- FDA COA qualification
- Symptoms of Major Depressive Disorder Scale
- Non-Small Cell Lung Cancer Symptom Assessment Questionnaire
- Asthma daytime and nighttime symptom diaries

TYPE 1 DIABETES
- EMA letter of support for model-based islet autoantibodies biomarker for trial enrichment

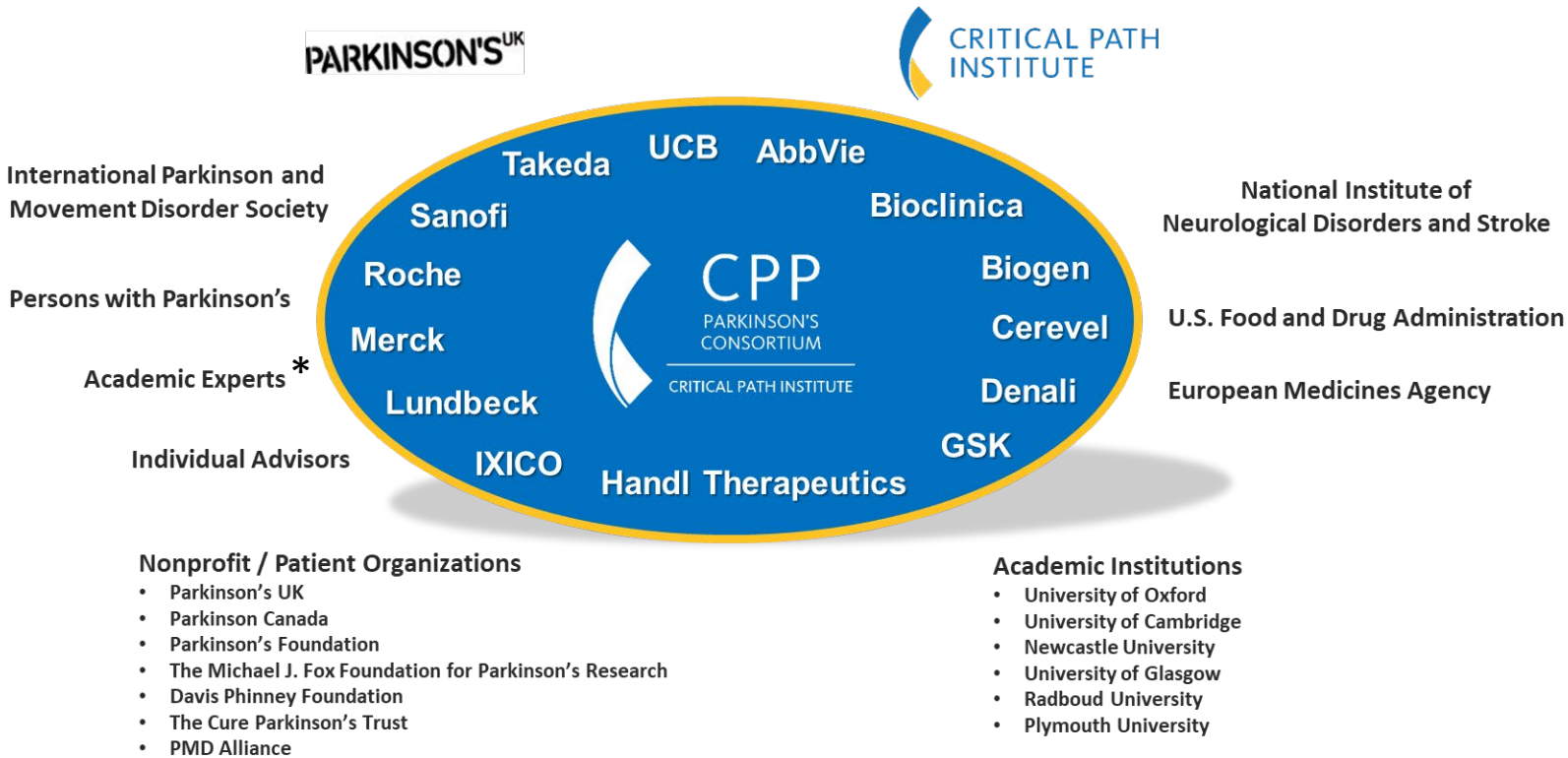
FDA
- 6 Qualification Decisions
- 1 Fit-for-Purpose Endorsement
- 7 Letters of Support

EMA
- 7 Qualification Decisions
- 7 Letters of Support

PMDA
- 1 Qualification Decision

Critical Path for Parkinson's (CPP) Consortium

- CPP was launched in 2015 with a major goal to develop tools to quantify disease progression
- Successfully acquired and integrated patient level data from >11000 PD patients
- Qualification of imaging biomarker for enrichment of trials in early PD
- Current CPP focus is regulatory endorsement of PD drug disease trial model
- Digital Drug Development Tools (3DT) team was launched under CPP with the goal of advancing regulatory readiness of digital health technologies in early PD studies



**CPP includes 25 academic scientific advisors as partners*

CPP has Integrated Data from >11000 people with Parkinson's From Around the World

PARKINSON'S UK
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.

CPP Unified PD
Clinical database

Observational Cohorts

- PPMI
- Oxford Discovery PD
- Tracking Parkinson's
- ICICLE
- CamPaIGN

Randomized Controlled Clinical Trials

PRECEPT	CONFIDENT-PD	SUREPD3
DATATOP	SP-513 (Rotigotine)	STEADYPD3
ELLDOPA	SP-512 (Rotigotine)	LS-1 NETPD
ADAGIO	SUREPD-Ph2	
FS-1	FS-Too	

Future model of Parkinson's therapies

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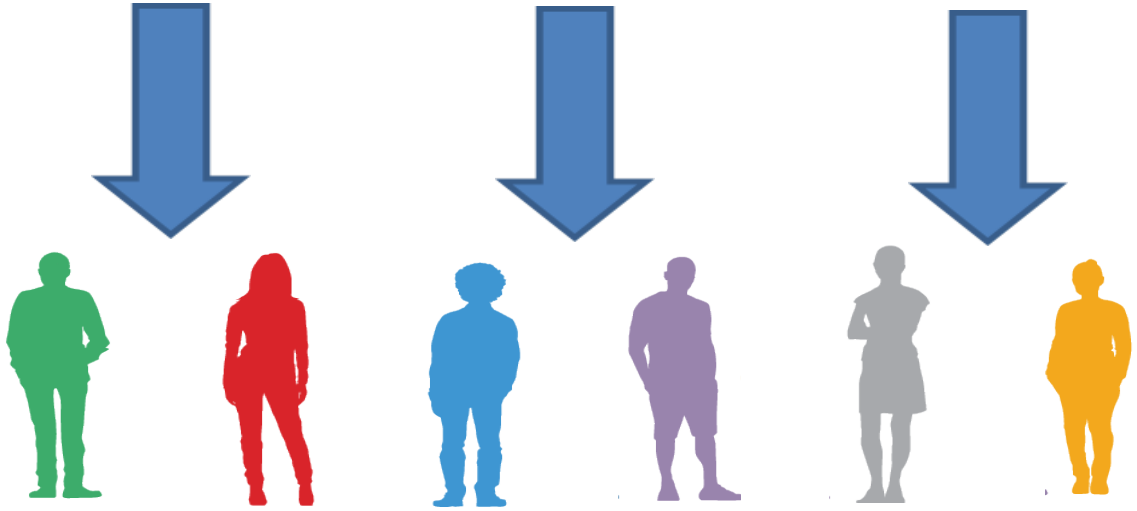
Parkinson's -
Not all one flavor

Personalized Medicine
targeted treatments



Case Example: Parkinson's Imaging Biomarker

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Qualification of novel methodologies for medicine development

Qualification opinion - Molecular neuroimaging of the dopamine transporter as biomarker to identify patients with early manifest Parkinsonism in Parkinson's disease

Qualification opinion on dopamine transporter imaging as an enrichment biomarker for Parkinson's disease clinical trials in patients with early Parkinsonian symptoms (PDF/762.14 KB)

Adopted

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

29 May 2018
EMA/CHMP/SAWP/765041/2017
Committee for Medicinal Products for Human Use (CHMP)

Qualification opinion on dopamine transporter imaging as an enrichment biomarker for Parkinson's disease clinical trials in patients with early Parkinsonian symptoms

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Drugs

Home › Drugs › Development & Approval Process (Drugs) › Drug Development Tools Qualification Programs › Biomarker Qualification Program

Biomarker Qualification Program

Letter of Support (LOS) Initiative

C-Path, CAMD	Molecular Neuroimaging Biomarker: Dopamine Transporter (DAT)	Exploratory Prognostic Biomarkers for Enrichment in Early Stage Parkinson's Disease Clinical Trials	3/16/2015: Letter of Support (PDF)

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NETWORKING FOR A CURE

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FDA Gives a Nod for Alzheimer's and Parkinson's Biomarkers

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03 Apr 2015 In the age of the Internet, don't you love it when you get a real letter? Especially a letter

CPP is changing the landscape

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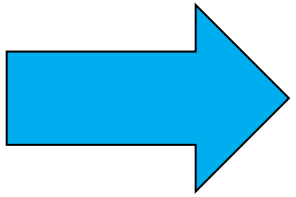
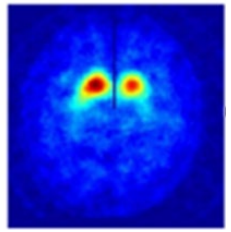
- Before





Now

Selecting more appropriate subjects for clinical trials will reduce the numbers needed and make trials more efficient.

~20% reduction in sample size by excluding biomarker negative subjects

Biomarker Strategies for Regulatory Success

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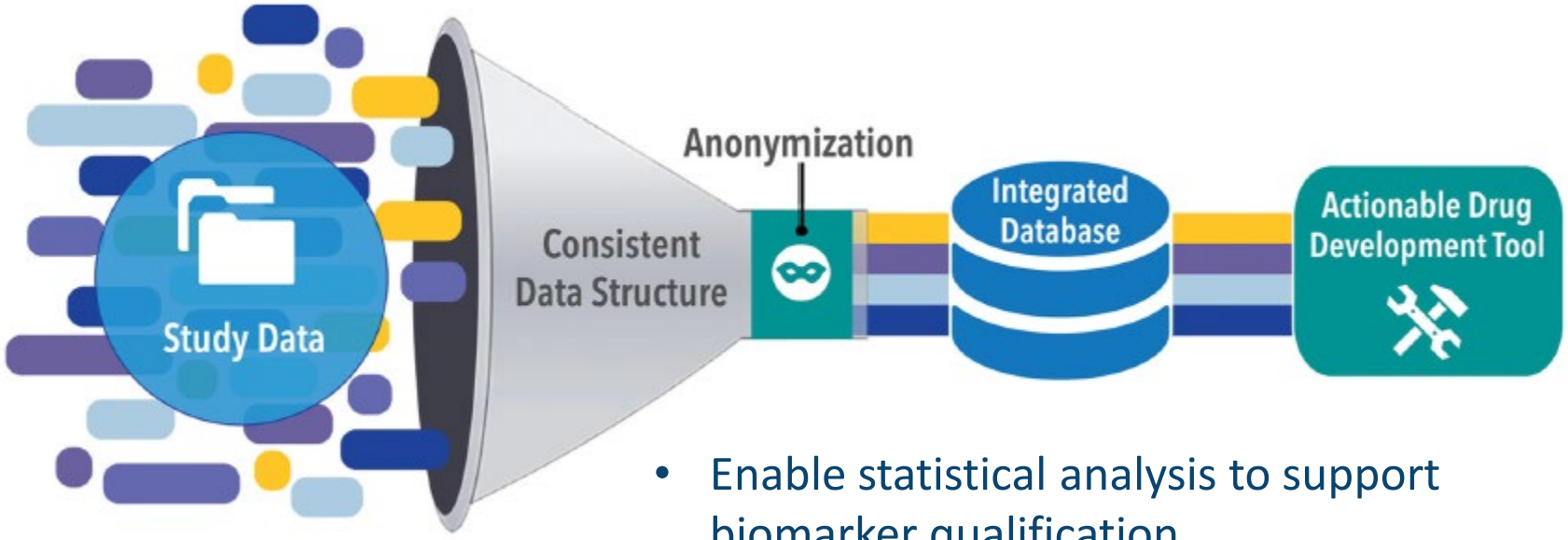
Retrospective data collection with **Prospective** biomarker data analysis

Consortium Collects:

- Key patient-level data
- Including clinical trials, registries, and longitudinal observational studies
- From academic laboratories, industry, and/or government agencies



- Enable statistical analysis to support biomarker qualification
- May also be used to develop quantitative drug development platforms

Newest example of CPP's impact

Digital Biomarkers

DOI: 10.1159/000512500
Received: July 29, 2020
Accepted: October 23, 2020
Published online: November 26, 2020

Maturation

Digit Biomark. 2020 Nov 26;4(Suppl 1):28-49.

Precompetitive Consensus Building to Facilitate the Use of Digital Health Technologies to Support Parkinson Disease Drug Development through Regulatory Science

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Neta Zach[b] on behalf of the Critical Path for Parkinson's Consortium

CPP Digital Drug Development Tool (3DT) Objective:
Advance regulatory maturity for The use of DHTs in PD clinical trials

https://www.karger.com/Article/FullText/512500

Engage Regulatory Agencies Early and Often

U.S. FOOD & DRUG ADMINISTRATION

Memorandum

Date: 7/10/2019

Subject: Critical Path Innovation Meeting: Parkinson's Disease Digital Drug Development Tools

Date of meeting: 5/14/2019

Requestor: Critical Path Institute, Critical Path for Parkinson's

Note: Discussions at Critical Path Innovation Meetings are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants.

FDA Representatives

Center for Drug Evaluation and Research
Office of Business Informatics (OBI)

EMA initiatives to support drug development

EUROPEAN MEDICINES AGENCY

What do we provide?

2. Innovation Task Force (ITF) platform and meetings

5 August 2019

ITF Briefing Meeting Report

Critical Path Institute Ltd, Critical Path for Parkinson's (CPP) Consortium

Briefing meeting held at the European Medicines Agency (EMA) on 15th July 2019.

The objective of the ITF briefing meetings is to provide for a preparatory discussion on scientific and regulatory topics relevant to the development of new medicinal products and technologies complementing and reinforcing existing formal procedures.

U.S. FOOD & DRUG ADMINISTRATION

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Critical Path Innovation Meetings (CPIM)

EMA: Innovative Task Force suggested taking a stepwise approach. Identify a small, well-defined meaningful measure and come back to them with a focused data-driven path for a future Scientific Advice and potential for qualification.

FDA: The appropriate FDA review divisions will continue to have iterative, disease-specific discussions with CPP, including strategies for establishing meaningful clinical endpoints.

What is Needed for Success in the Future?

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Current state

Medical practitioners aspire for prodromal diagnosis

Clinicians & drug developers aspire to enrol large diverse patient cohorts at minimal cost to validate studies

Patients want to increase their quality of life

Stakeholders

Voice of the patient

Regulators

Clinicians

Device vendors

Engineers, data scientists, statisticians

Success

Patient-centric outcomes

- Improved quality of life
- Patient centric digital biomarker

Data sharing

- Reduce duplication of effort
- Clinical and technical validation through data harmonisation

Data Standards

- Increase data interoperability and data management
- Data used beyond its purpose of collection

Global Collaboration

- Reduce discrepancy between research utility & clinical value

Stephenson et al., Digital Progression Biomarkers as Novel Endpoints in Clinical Trials: A Multistakeholder Perspective, J. Parkinson's Disease, *in press*

Summary

- Addressing gaps in new treatments for diseases of high unmet need require precompetitive collaborations and focus on regulatory science
- To enable improved success, efficiency and sense of urgency it has been suggested that new WARP SPEED strategies are needed for success in age related neurodegenerative diseases
  - Enhanced global collaboration
  - Data sharing has to be transformed and far easier than now
  - Focus on patients needs to be front and center
  - All stakeholders need to be fully onboard with collaboration
  - Expanding the term precompetitive beyond where it is now

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- Critical Path Institute Drug Development Tool team (3DT)

  Regulatory leads: Katrin Rupalla, Lauren Oliva

- Parkinson's UK, CPP advisors
- Bastiaan Bloem, Ray Dorsey
- Food and Drug Administration, CDER

  Dr. Billy Dunn, Dr. Michelle Campbell, Dr. Eric Bastings, Dr. Gerald Podskalny,

- European Medicines Agency

  Maria Tome, Corrine de Vries, Spiros Vamvakas

- People living with Parkinson's, the hidden pandemic