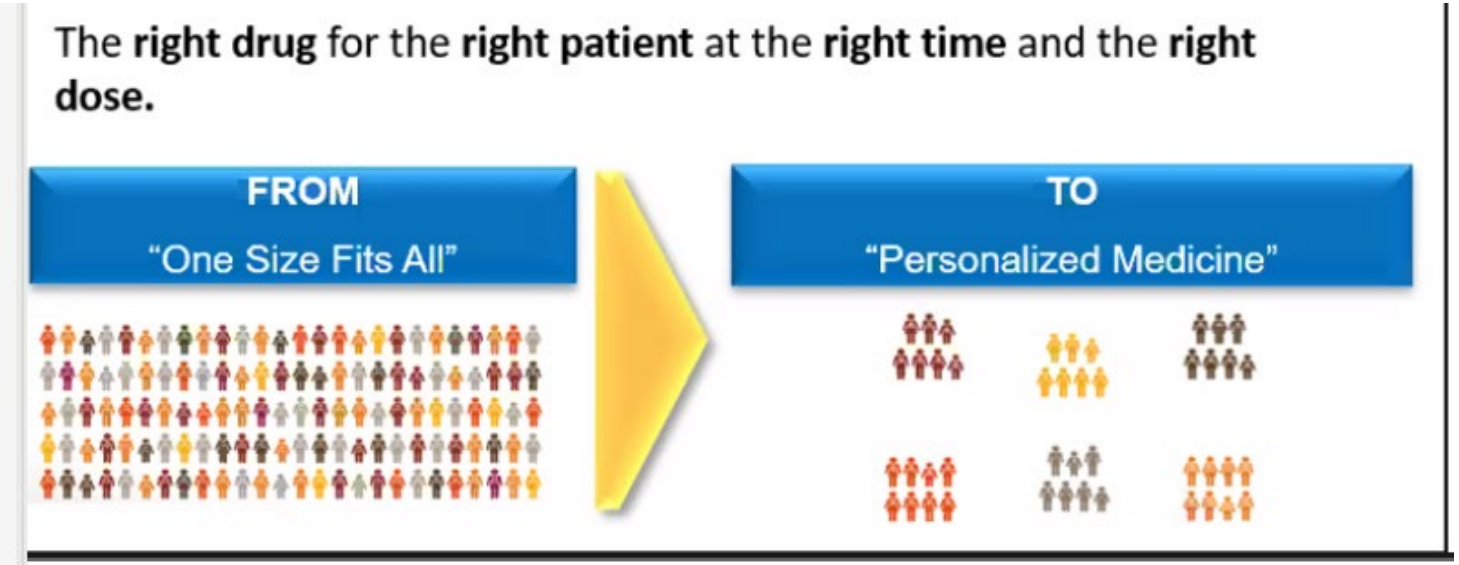
Uniting Data, the Patient Voice and Regulatory Strategies to Advance Treatments for Disorders of the Nervous System

:

Insights from Critical Path Institute

Transformation in the Neurosciences



nature reviews drug discovery
https://doi.org/10.1038/s41573-025-01165-w

Review article

Check for updates

Biomarker-guided decision making in clinical drug development for neurodegenerative disorders

Jeffrey L. Cummings[1], Charlotte E. Teunissen[2], Brian K. Fiske[3], Isabelle Le Ber[4], Kristin R. Wildsmith[5], Michael Schöll[6,7], Billy Dunn[3] & Philip Scheltens[8,9]

Nat Rev Drug Discov. 2025 Aug;24(8):589-609.

nature reviews neurology
https://doi.org/10.1038/s41582-024-01047-6

Perspective

Check for updates

Inclusion in neurological research: empowering people living with neurological diseases

Maria Teresa Ferretti[1], Maria Bonaria Uccheddu[2,3], Richelle Flanagan[4], Iracema Leroi[5,6] & Elena Moro[7,8]

Nature Reviews Neurology **volume 21**, pages159–170 (2025)

Role of Regulatory Agencies in Shaping Change

CRITICAL PATH INSTITUTE

www.nature.com/mp

Molecular Psychiatry

PERSPECTIVE OPEN

Check for updates

Precision psychiatry roadmap: towards a biology-informed framework for mental disorders

Martien J. H. Kas[1], Brenda W. J. H. Penninx[2], Gitte M. Knudsen[3], Bruce Cuthbert[4], Peter Falkai[5,6], Gary S. Sachs[7], Kerry J. Ressler[8], Ewa Bałkowiec-Iskra[9,10,11], Florence Butlen-Ducuing[12,13,14], Marion Leboyer[15], Hugh Marston[16], Johan Luthman[17] and Valentina Mantua[1]

A biological definition of neuronal α-synuclein disease: towards an integrated staging system for research

Tanya Simuni*, Lana M Chahine*, Kathleen Poston, Michael Brumm, Teresa Buracchio, Michelle Campbell, Rohini Chowdhury, Christopher Coffey, Luis Concha-Marambio, Tien Dam, Peter DiBiaso, Tatiana Foroud, Mark Frasier, Caroline Gochanour, Danna Jennings, Karl Kieburtz, Catherine M Kopil, Kalpana Merchant, Brit Mollenhauer, Thomas Montine, Kelly Nudelman, Gennaro Pagano, John Seibyl, Todd Sherer, Andrew Singleton, Diane Stephenson, Matthew Stern, Claudio Soto, Caroline M Tanner, Eduardo Tolosa, Daniel Weintraub, Yuge Xiao, Andrew Siderowf, Billy Dunn, Kenneth Marek

GUIDANCE DOCUMENT

Early Alzheimer's Disease: Developing Drugs for Treatment

MARCH 2024

Download the Draft Guidance Document | Read the Federal Register Notice

Draft | Level 1 Guidance

Not for implementation. Contains non-binding recommendations.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Alzheimer's disease

EU-IN Horizon Scanning Report

November 2024
EMA/540805/2024

Received: 14 May 2025 | Accepted: 15 May 2025

DOI: 10.1002/trc2.70113

Alzheimer's & Dementia® Translational Research & Clinical Interventions

PERSPECTIVE

Assessing clinical meaningfulness in clinical trials for Alzheimer's disease: A U.S. regulatory perspective

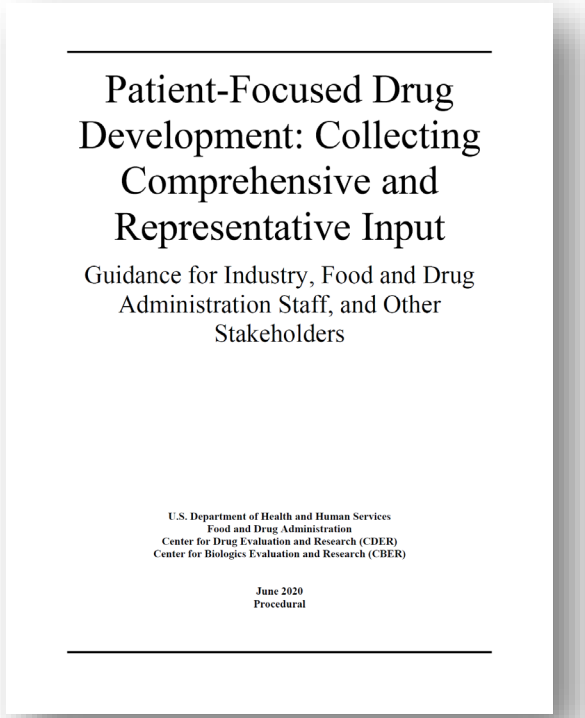
Teresa Buracchio | Michelle Campbell | Kevin Krudys

Case Example of Impact

Patient Focused Drug Development Guidance Series

CRITICAL PATH INSTITUTE

- "Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation."[1]

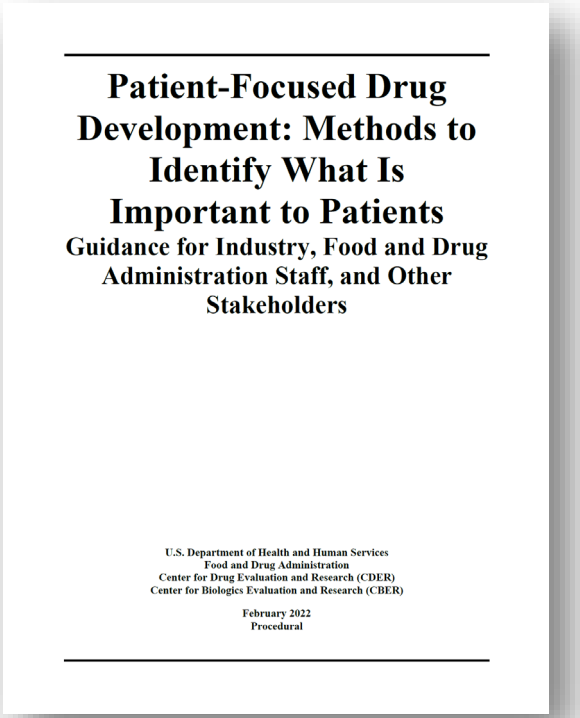


Patient-Focused Drug Development: Collecting Comprehensive and Representative Input

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

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

June 2020
Procedural

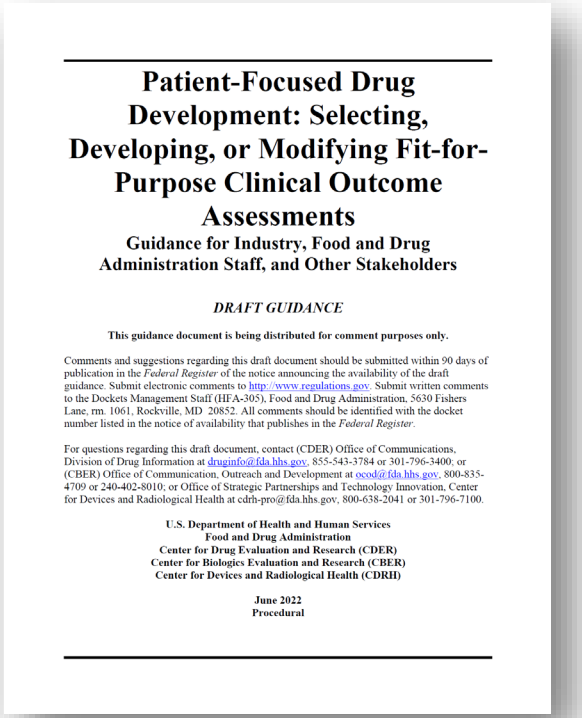


Patient-Focused Drug Development: Methods to Identify What Is Important to Patients

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

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

February 2022
Procedural



Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

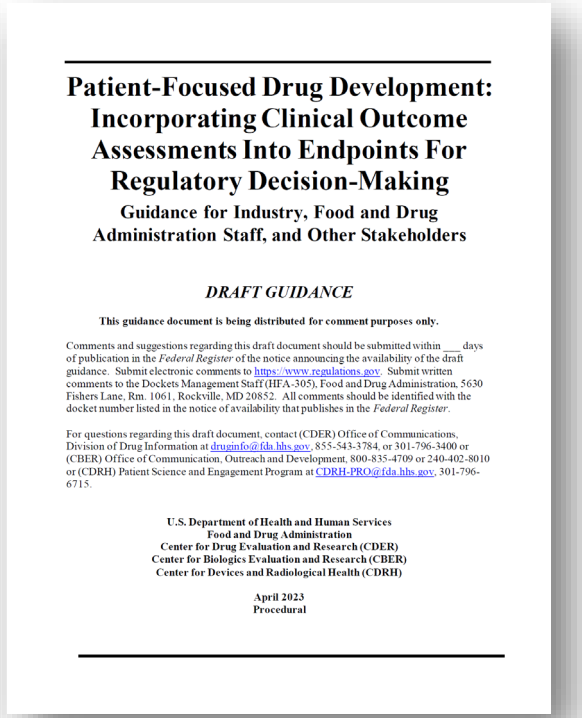
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Communications, Division of Drug Information at druginfo@fda.hhs.gov, 855-543-3784 or 301-796-3400; or (CBER) Office of Communication, Outreach and Development at ocod@fda.hhs.gov, 800-835-4709 or 240-402-8010; or Office of Strategic Partnerships and Technology Innovation, Center for Devices and Radiological Health at cdrh-pro@fda.hhs.gov, 800-638-2041 or 301-796-7100.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

June 2022
Procedural



Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

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Comments and suggestions regarding this draft document should be submitted within ___ days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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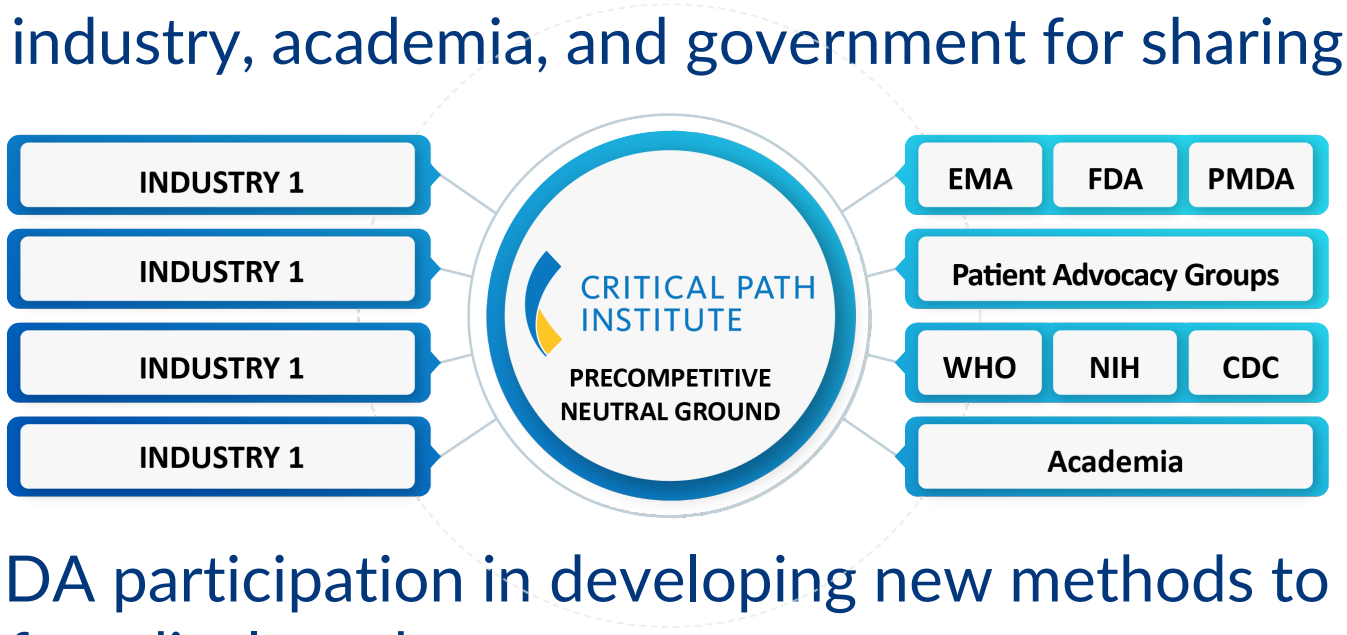
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

April 2023
Procedural

1. FDA CDER Patient-focused Drug Development, www.fda.gov

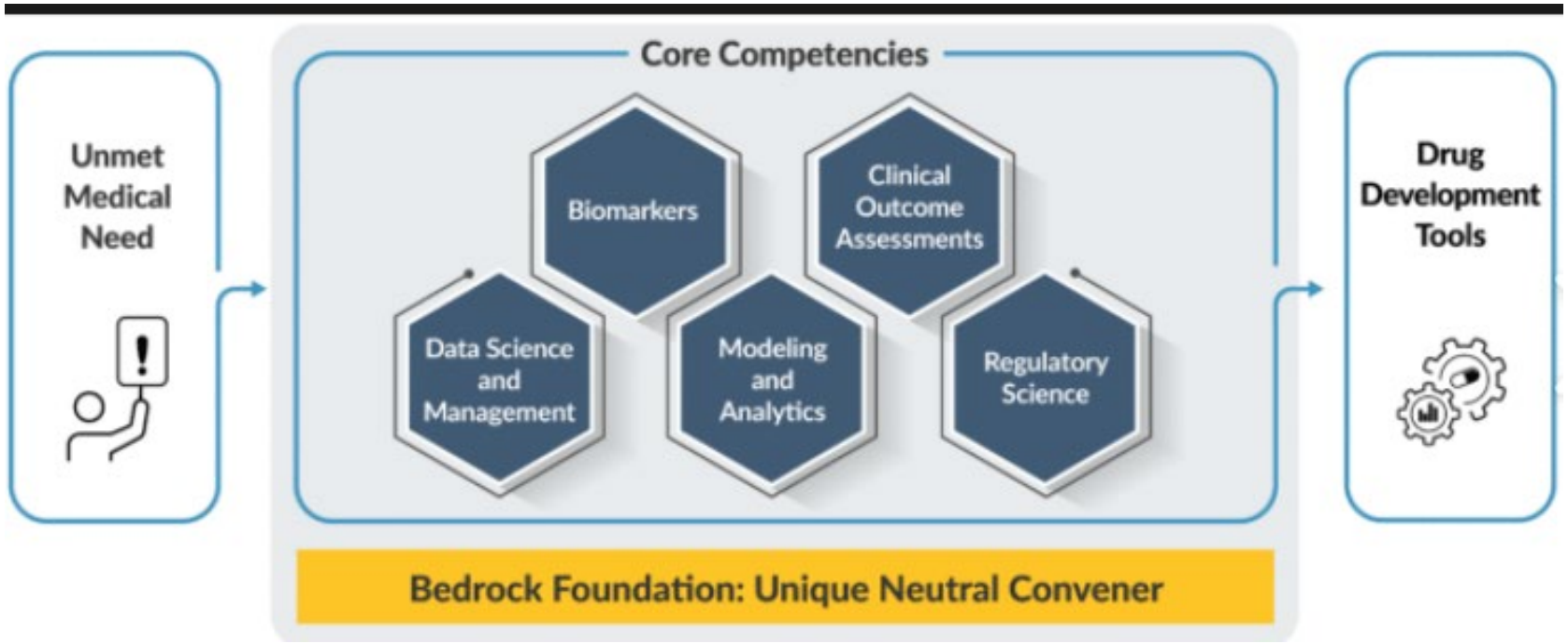
Critical Path Institute Leads Unique Public-Private Partnerships

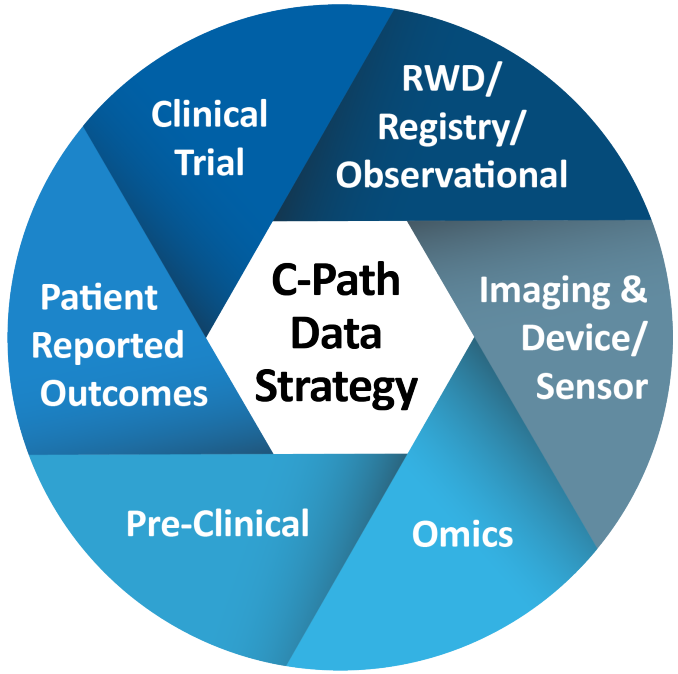
- Foster development of new evaluation tools to inform medical product development and regulatory decision-making
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise
  - ✓ **Active consensus building**
  - ✓ **Shared risk and costs**
  - ✓ **The best science**
  - ✓ **The broadest experience**



- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Obtain official regulatory endorsement of novel methodologies and drug development tools

C-Path's Five Core Competencies
grounded in data science and regulatory strategies





Impact of Data Sharing: Drug Development Tools for Nervous System Disorders

CRITICAL PATH INSTITUTE

Alzheimer's Disease

- AD drug disease trial model, AD predementia neuroimaging biomarker

Parkinson's Disease

- PD neuroimaging biomarker targeting early PD
- Disease progression model
- Synuclein SAA as susceptabiity/risk biomarker

Huntington's Disease

- Biologic staging of disease in collaboration with leaders and the community

Duchenne Muscular Dystrophy

- Modeling disease progression, simulation tools -- Stage specific outcome measures

Multiple Sclerosis

- Clinical outcome assessment battery for MS clinical trials

Traumatic Brain Injury

- Neuroimaging & fluid biomarkers for mild TBI

Stephenson et al., Neurotherapeutics 20(6):1682-169 2023

Biological Staging Paves the Way to Early Intervention Across Brain Disorders

A biological classification of Huntington's disease: the Integrated Staging System

Sarah J Tabrizi*, Scott Schobel*, Emily C Gantman, Alexandra Mansbach, Beth Borowsky, Pavlina Konstantinova, Tiago A Mestre, Jennifer Panagoulias, Christopher A Ross, Maurice Zauderer, Ariana P Mullin, Klaus Romero, Sudhir Sivakumaran, Emily C Turner, Jeffrey D Long, Cristina Sampaio, on behalf of the Huntington's Disease Regulatory Science Consortium (HD-RSC)†

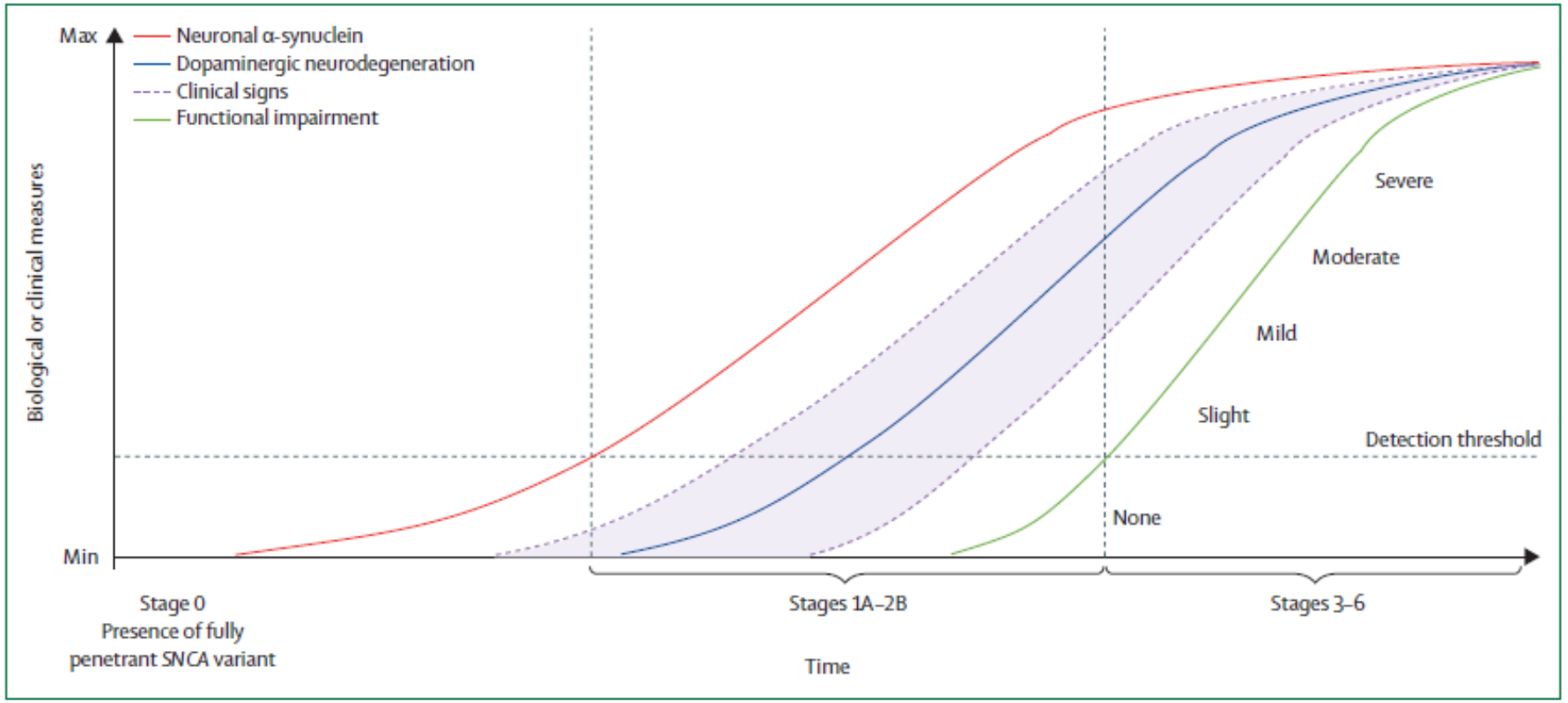
Lancet Neurol 2022; 21: 632–44

A biological definition of neuronal α-synuclein disease: towards an integrated staging system for research

Tanya Simuni*, Lana M Chahine*, Kathleen Poston, Michael Brumm, Teresa Buracchio, Michelle Campbell, Sohini Chowdhury, Christopher Coffey, Luis Concha-Marambio, Tien Dam, Peter DiBiaso, Tatiana Foroud, Mark Frasier, Caroline Gochanour, Danna Jennings, Karl Kieburtz, Catherine M Kopil, Kalpana Merchant, Brit Mollenhauer, Thomas Montine, Kelly Nudelman, Gennaro Pagano, John Seibyl, Todd Sherer, Andrew Singleton, Diane Stephenson, Matthew Stern, Claudio Soto, Caroline M Tanner, Eduardo Tolosa, Daniel Weintraub, Yuge Xiao, Andrew Siderowf, Billy Dunn, Kenneth Marek

Lancet Neurol 2024; 23: 178–90

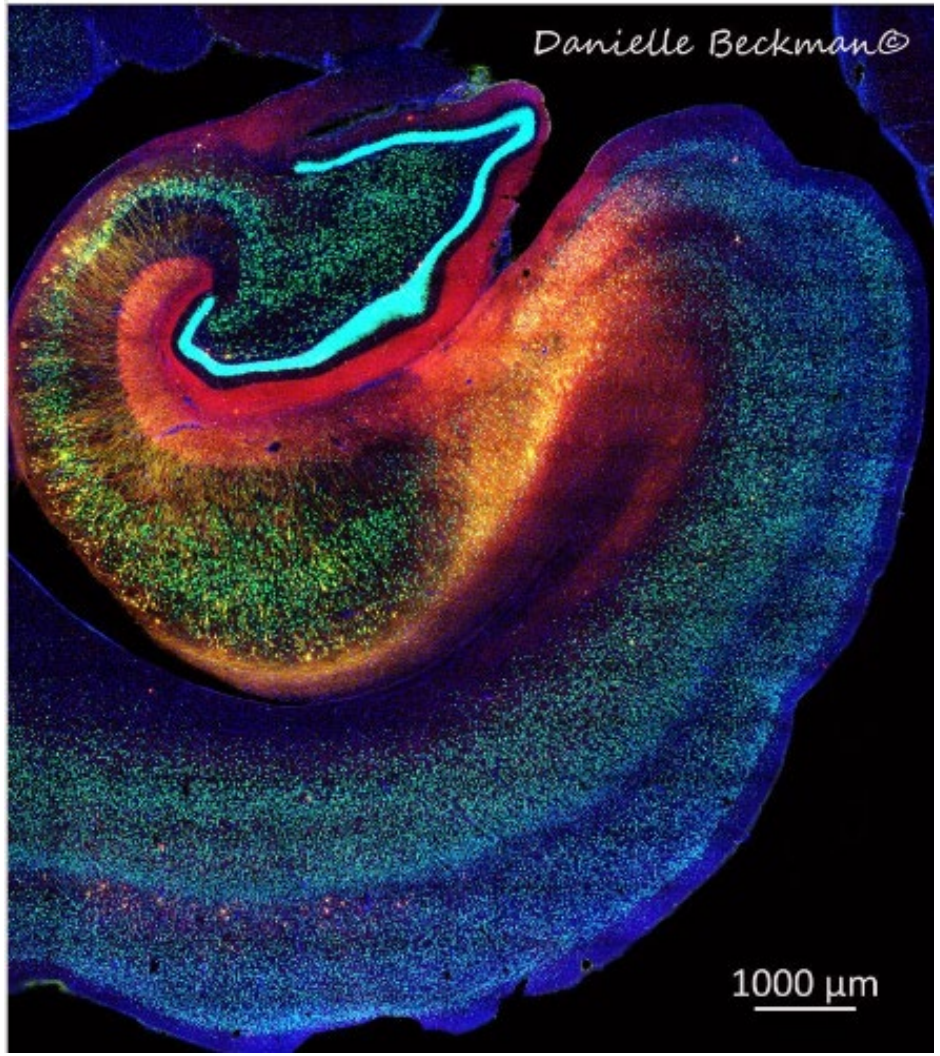
Disease progression modeling,
robust, reliable biomarkers lead the way

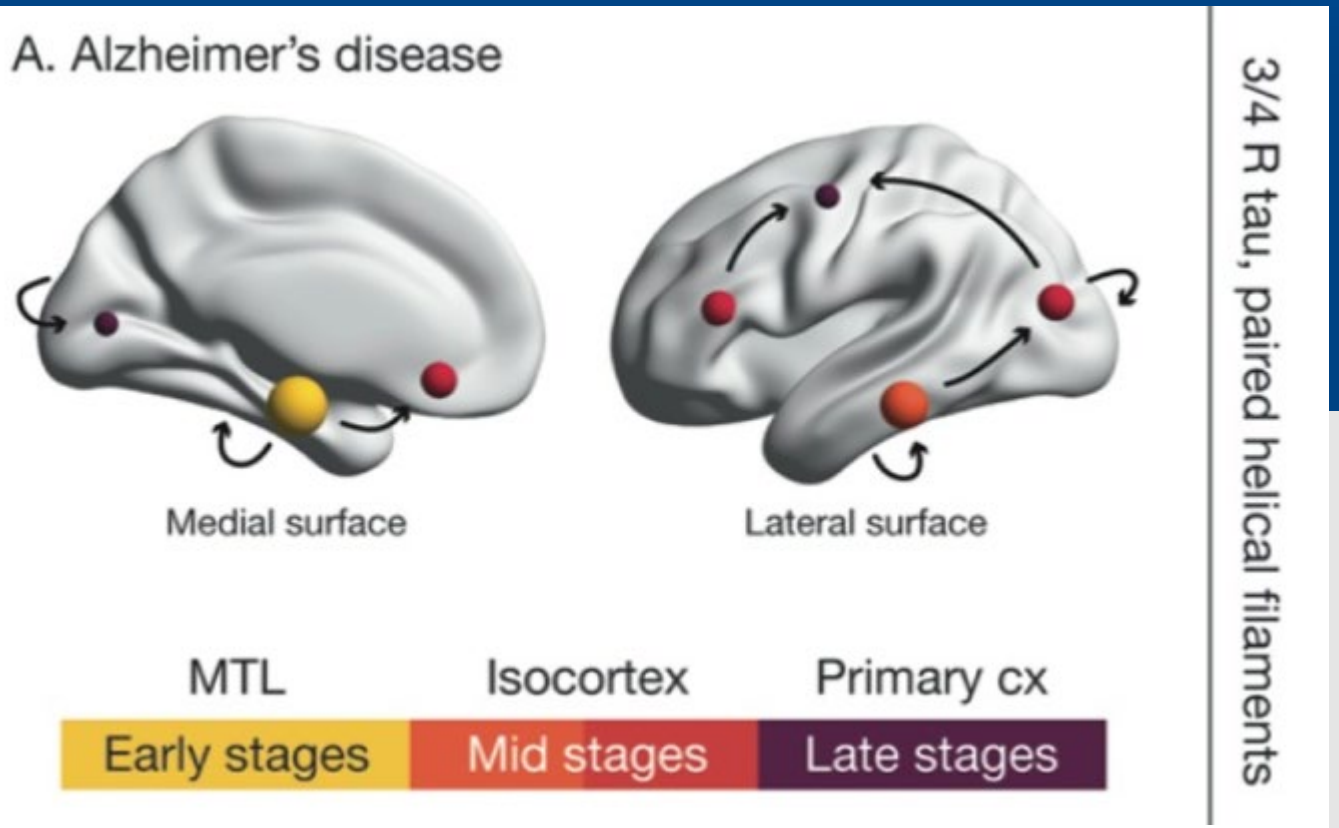


Neuronal Synuclein Disease

Hypothetical model of dynamic biomarkers of the neuronal α-synuclein disease-integrated staging system
Simuni et al., Lancet Neurol , 2024

Alzheimer's disease , Tau neuroimaging biomarkers





Leuzy et al., TauPET imaging in tauopathies, still a challenge, Molecular Psychiatry 24(8) 1112, 2019

Alzheimer's Disease/CPAD: Multistakeholder consensus for TauPET imaging methodologies

Received: 7 November 2023 | Revised: 15 March 2024 | Accepted: 18 March 2024

DOI: 10.1002/alz.13908

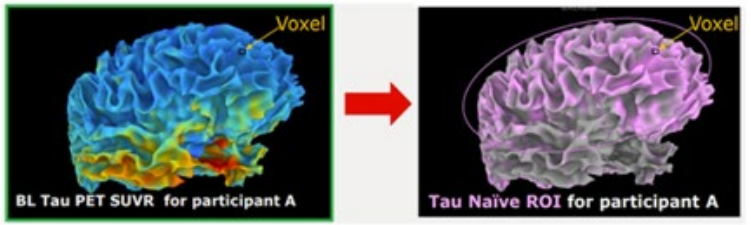
Alzheimer's & Dementia
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE

Harmonizing tau positron emission tomography in Alzheimer's disease: The CenTauR scale and the joint propagation model

Antoine Leuzy[1,2,3] | Lars Lau Raket[1,4] | Victor L. Villemagne[5,6,7] | Gregory Klein[8] | Matteo Tonietto[8] | Emily Olafson[9] | Suzanne Baker[10] | Ziad S. Saad[11] | Santiago Bullich[12] | Brian Lopresti[13] | Sandra Sanabria Bohorquez[9] | Mercè Boada[14,15] | Tobey J. Betthauser[16,17,18] | Arnaud Charil[19] | Emily C. Collins[4] | Jessica A. Collins[20] | Nicholas Cullen[2] | Roger N. Gunn[21,22] | Makoto Higuchi[23] | Eric Hostetler[24] | R. Matthew Hutchison[20] | Leonardo Iaccarino[4] | Philip S. Insel[25] | Michael C. Irizarry[16] | Clifford R. Jack Jr[26] | William J. Jagust[27] | Keith A. Johnson[28,29] | Sterling C. Johnson[16,17,18] | Yashmin Karten[2] | Marta Marquié[17,18] | Sulantha Mathotaarachchi[3] | Mark A. Mintun[4] | Rik Ossenkoppele[1,30] | Ioannis Pappas[31,32] | Ronald C. Petersen[33] | Gil D. Rabinovici[34,35] | Pedro Rosa-Neto[36,37] | Christopher G. Schwarz[26] | Ruben Smith[1,38] | Andrew W. Stephens[12] | Alex Whittington[21] | Maria C. Carrillo[39] | Michael J. Pontecorvo[4] | Samantha Budd Haeberlein[3] | Billy Dunn[40] | Hartmuth C. Kolb[3] | Sudhir Sivakumaran[2] | Christopher C. Rowe[6,7,41] | Oskar Hansson[1,42] | Vincent Doré[7,43]

Tau spreading as priority methodology for tracking and quantifying drug effects in central compartment In parallel with cognitive / functional decline



Alzforum April 2025

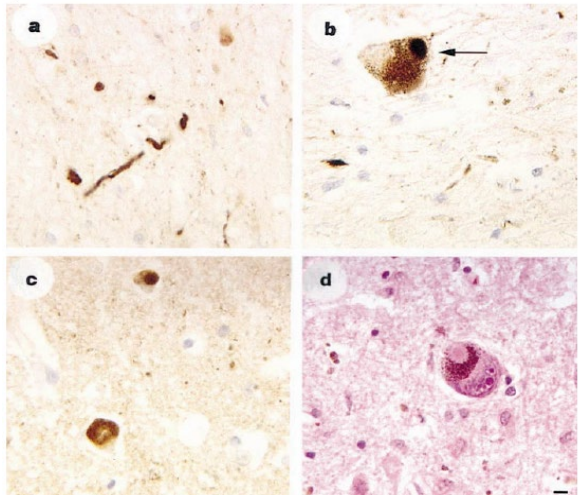
CPAD led Abstract for submission to TauGlobal mtg, May 2026

Advancing Spatial Tau PET Endpoints in a Pre-Competitive Effort Led by the Critical Path for Alzheimer's Disease Consortium

Antoine Leuzy[1], Alexis Moscoso Rial[1], **Yashmin Karten**[1], Tammie Benzinger[2], Gérard Bischof[3], Christopher A. Brown[4], Sandhitsu R. Das[4], Emma M. Coomans[5], Stephanie S. Doering[2], Elena Doering[6], Nicolai Franzmeier[7], Thomas Gérard[8], Bernard Hanseeuw[8], Clifford R. Jack Jr.[9], Keith Johnson[10] Hartmuth C. Kolb[11], Renaud Lhommel[8], Paul Maguire[12], Rik Ossenkoppele[5], Ziad Saad[13], Christopher G. Schwarz[9], Victor L. Villemagne[14], Gregory Klein[15], Nadine Tatton[16], Diane Stephenson[16].

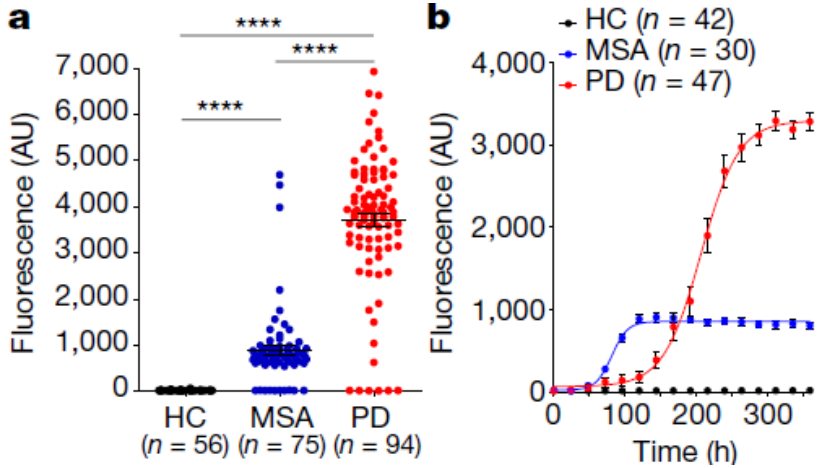
Synuclein Pathology –
Synuclein seed amplification

Lewy (1912) described concentric inclusion bodies especially in the nucleus basalis, the substantia inomminata and the dorsal motor nucleus of the vagus



Spillantini, Schmidt, Lee, Trojanowski, Jakes and Goedert, Nature 1997

SAA Florescence: PD>MSA>HC



For now!

Luis Concha
Claudio Soto
Amprion

Patients (#)	CTRL (#)	Max Sens	Max Spec	Reference
PD (20)	HC (20)	95%	100%	Fairfoul et al. (2016)
PD (12)	HC (28)	92%	100%	Groveman et al. (2018)
PD (105)	HC (79)	96%	90%	Kang et al. (2019)
PD (15)	HC (11)	100%	100%	Manne et al. (2019)
PD (108)	HC (85)	97%	87%	Orru` et al. (2020)
PD (88)	HC (56)	94%	100%	Shahnawaz et al. (2020)
PD (116)	HC (35)	91%	97%	Quadalti et al. (2021)
PD (30)	HC (30)	96%[a]	100%	Russo et al. (2021)
PD (74)	HC (55)	89%	96%	Poggiolini et al. (2021)
PD (235)	HC (26)	89%	99%	Brockman et al. (2021)

Adapted from: Bellomo G et al. α-Synuclein Seed Amplification Assays for Diagnosing Synucleinopathies: The Way Forward. Neurology; 2022: 99(5)

FDA Supports Enrichment Biomarker: α-Synuclein
Critical Path for Parkinson's consortium

CRITICAL PATH INSTITUTE

U.S. FOOD & DRUG ADMINISTRATION

DRUG DEVELOPMENT TOOL
LETTER OF SUPPORT
DDT-BMQ-000157

August 19, 2024

We support Critical Path for Parkinson's consortium in issuing a Letter of Support for the application of binary assessment of α-syn SAA as an enrichment biomarker for patient selection in clinical trials investigating therapies that are intended to treat, prevent, or delay neurodegenerative disorders characterized by a common synuclein biology. The timing for this letter aligns with the growing number of disease-modifying candidates in development including innovative trial designs focused on prevention.

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Parkinson's Progression Markers Initiative

About ▾ Study Design ▾ Data & Specimens ▾ Publications & Presentations

Critical Path Institute's Regulatory endorsed biomarkers Enable the first ever Platfom trial for presymptomatic stage Parkinson's disease

Path to Prevention Platform Trial

PPMI is primed to advance innovative trial design for Parkinson's prevention. Join us.

Given advances in PD science, an increasingly robust pipeline of promising therapeutics, and an expanded infrastructure within PPMI, the field has an unprecedented opportunity to pioneer interventional trials in prodromal Parkinson's.

P2P Protocol Synopsis

P2P SOA

Target population: NSD Stage 2b

Tanya Simuni, Ken Marek, Michael J Fox Foundation and more

Regulatory Strategies that are Paving the Way for the Future -- C-Path alliances

CRITICAL PATH INSTITUTE

DHTs

GUIDANCE DOCUMENT

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

DECEMBER 2023

Download the Final Guidance Document | Read the Federal Register Notice

frontiers | Frontiers in Digital Health

November 2025

Aligning with regulatory agencies for the use of digital health technologies in drug development: a case study from Parkinson's disease

WATCH-PD

Women's health

Jan 2025

U.S. FOOD & DRUG ADMINISTRATION

Home / Regulatory Information / Search for FDA Guidance Documents / Evaluation of Sex Differences in Clinical Investigations

INFORMATION SHEET

Evaluation of Sex Differences in Clinical Investigations

Guidance for Industry

JANUARY 2025

January 2026

Commentary | **Articles** | January 16, 2026

Applied Clinical Trials

Applied Clinical Trials-02-01-2026 | Volume **35** | Issue **1**

Women as the Missing Voice in Parkinson's Disease

Author(s) Bola Grace, PhD, MBA; Ragasudha Botta, MBBS, PhD, MMSc; and Diane Stephenson, PhD

GEM-PD

Mechanistic Modeling

Oct 2025

Call for expression of interest to participate in the EMA multi-stakeholder workshop on reporting and qualification of mechanistic models for regulatory assessment October 2025

English (EN) (128.68 KB - PDF)

First published: 25/03/2025 **Last updated:** 01/04/2025

View

Editorial

https://doi.org/10.1038/s41591-026-04258-0

Neurodegenerative diseases need more mechanism-informed trials

Artificial Intelligence

Jan 2026

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Medicines | Human regulatory | Veterinary regulatory | Committees | News & events | Partners & networks

Home > News > EMA and FDA set common principles for AI in medicine development

EMA and FDA set common principles for AI in medicine development

14 January 2026

Advancing safe, ethical and aligned AI practices across the medicines lifecycle

CTS Clinical and Translational Science
An Official Journal of ASCPT
Open Access

December 2025

Clin Transl Sci. 2025 Dec 3;18(12):e70434. doi: 10.1111/cts.70434

How AI Transforms Regulatory Submission: Current Clinical Implementation and Future Prospects

Jagdeep T Podichetty [1,✉], Anna-Marika Bauer [1], Rachel Xu [1], Nick Henscheid [1], Wes Anderson [1], Ayan Khan [1], Shu Chin Ma [1], Huong Huynh [1], Klaus Romero [1]

Near term horizon opportunities….
Phoenix Arizona, May 2026

CRITICAL PATH INSTITUTE

Planning for Prevention of Parkinson's Meeting, May 22-23

Michael Schwarszchild, Grace Crotty; Mass General

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7th World PARKINSON CONGRESS Phoenix, AZ, USA

May 24-27th, 2026
Phoenix

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ABOUT PROGRAM ABSTRACTS REGISTRATION TRAVEL & HOTELS SUPPORT & EXHIBIT

Acknowledgements

- Critical Path Institute Staff, Cecile Olivier, Klaus Romero, Cheryl Coon
- Parkinson's UK, Michael J Fox Foundation
- Critical Path for Parkinson's Consortium Industry Members
- CPP scientific advisors and academic collaborators
- University of Rochester CHeT team
- CPP industry codirectors & Fatta Nahab, Gennaro Pagano;
- CPAD industry members and advisors; CPAD codirector: Greg Klein
- European Medicines Agency
- Food and Drug Administration, CDER

Michelle Campbell, Kevin Krudys, Teresa Buracchio, Emily Freilich

Research study volunteers and clinical trial participants

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