View online at www.PDTrialTracker.info

Disease-modifying therapies in the PD trial pipeline: Addressing funding, staffing & recruiting needs

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Rallying to the Challenge
Sept. 27-28, 2017
VARI & CPT, Grand Rapids, Michigan

Project Goal

- Provide the patient community with an overview of all active and planned clinical trials of disease-modifying therapies for PD (treatments to slow, halt, or reverse progression).

- Facilitate patient/researcher collaboration to address funding, staffing, and recruiting needs for these trials in order to accelerate the path to a cure.

Project Motivation

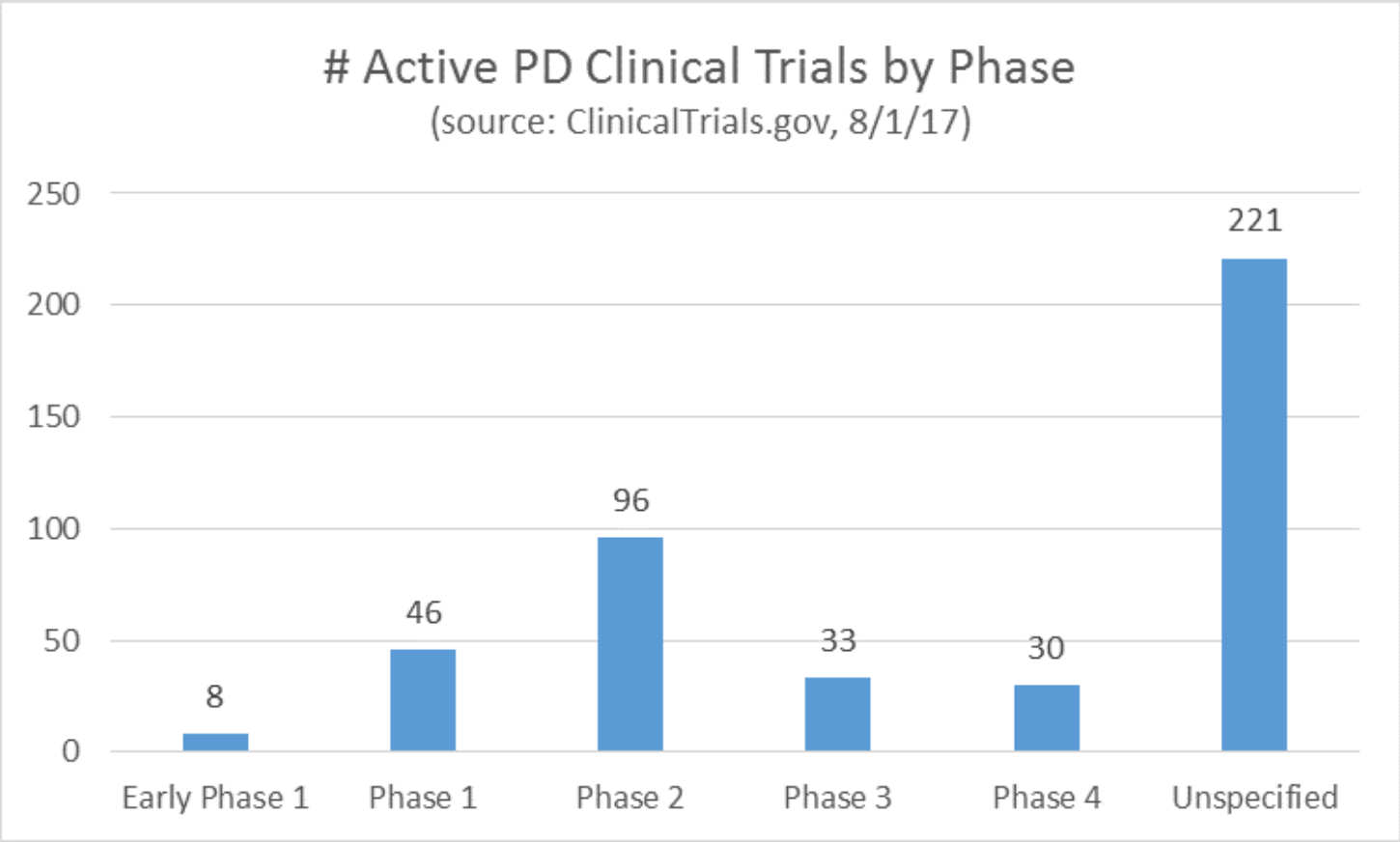
- Patient desire to help speed the path to a cure for PD.
- Journal articles
  - "Rising to the Challenges of Clinical Trial Improvement in Parkinson's Disease"

    Soania Mathur, Steve DeWitte, Israel Robledo, Tom Isaacs, Jon Stamford (Journal of PD vol. 5, 2015)

    Presents results from *Rallying to the Challenge 2014* survey:
    - Researchers cited funding/admin support/recruitment as key trial barriers.
    - Patients cited potential side effects and medication disruption as key trial participation barriers.
  - "Accelerating Drug Development for the Field: Building Clinical Trial Recruitment Infrastructure in Parkinson's" (Michael J. Fox Foundation article in Clinical Researcher, April 2014)
    - Cites importance of sales, marketing, and planning functions in recruiting process.
- Patient/family anecdotes regarding trial experience
  - Highlight greater need for trial information, improved communication, medical care access, trial follow-up. (marketing/customer service)

Overview of Current PD Trial Pipeline

413 Active Interventional PD Studies as of Aug. 1, 2017



Note 1: 21 of 413 trials are combined Phase 1/Phase 2 OR combined Phase 2/3.
Note 2: Total Active PD Studies = 413 Interventional + 139 Observational = 552, as of 8/1/17 on ClinicalTrials.gov.

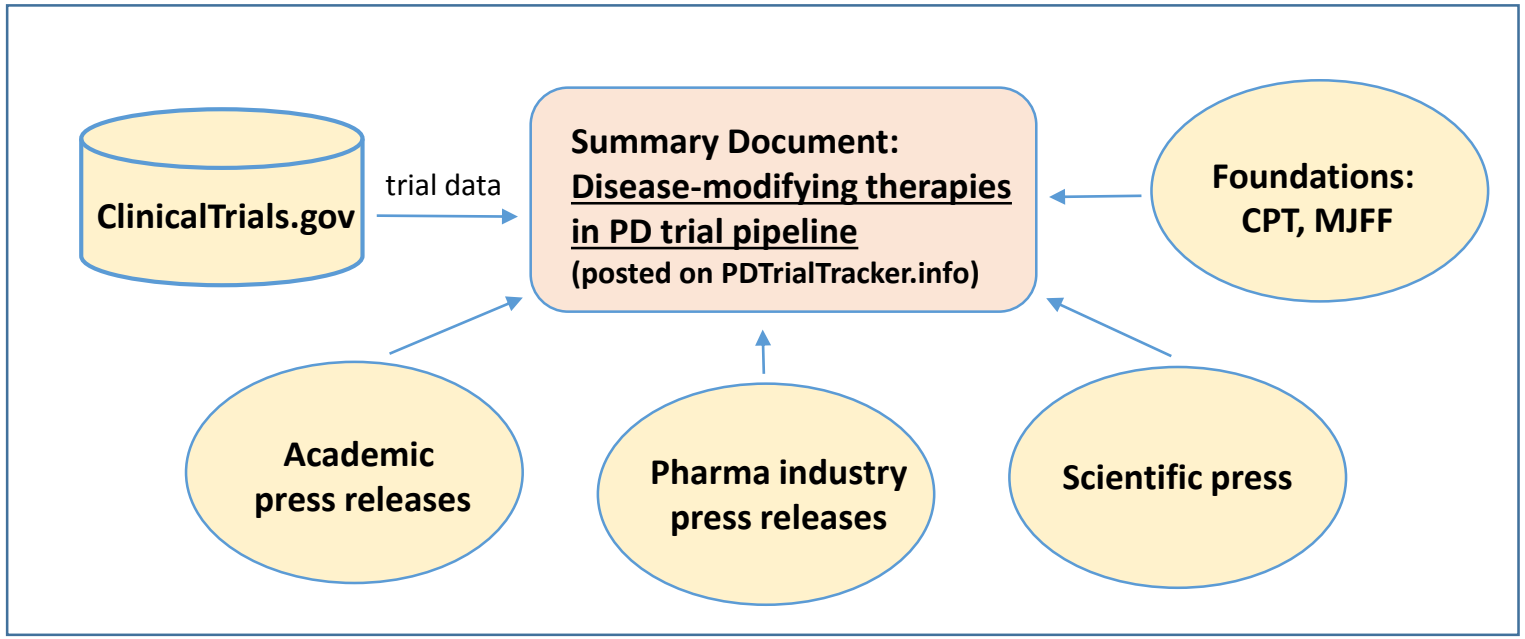
# Trials by Recruiting Status	
Recruiting:	269
Not yet recruiting:	56
Enrolling by invite:	25
No longer recruiting:	63
Total:	413

Trials by Therapy Focus

DBS: ~50
Exercise: ~50
Dyskinesia: ~15
Cognitive therapy: 7
Alpha-synuclein: 7
Gene therapy: 6

How many trials are evaluating disease-modifying therapies?

Methodology for Identifying Disease-Modifying Therapies in the Pipeline



Result: Project has identified ~30 disease-modifying trials currently in Phase 1, 2, or 3 (~ 16% of 183 active Phase 1, 2, 3 clinical trials) and ~10 trials in design.

Disease-Modifying Therapies in PD Trial Pipeline: Summary Document (available online at PDTrialTracker.info)

Compiled info includes:

- Therapy under study
- Phase (pre-clinical, 1, 2, 3)
- Study title
- Recruiting status
- Study start date / End date
- Estimated enrollment
- Sponsor / collaborators
- Study locations & Eligibility
  via link to ClinicalTrials.gov id# (NCT#)
- More info: press releases, prior study results, funding needed

Potential Disease-Modifying Therapies in the PD Clinical Trial Pipeline: Active Trials, Trials in Design, Recently Completed Trials

Therapy (*=repurposed compound)	Description	Phase	Study Title (status)	Study start date	Est. study end date	Estimated Enrollment	Sponsor	Collaborators	Study Locations & Eligibility: see ClinicalTrials.gov	More Info	
Inosine*	Antioxidant / Nutritional supplement	Phase 3	Study of Urate Elevation in Parkinson's Disease, Phase 3 (SURE-PD3) (recruiting)	Jun-16	Aug-20	270	Michael Alan Schwarzschild, Massachusetts General Hospital	PSG, MJFF, UofRochester, NINDS	NCT02642393	MJFF Blog 9.1.15	Inosine Phase 2 completed 12/12 (NCT00833690)
Isradapine*	Calcium channel blocker	Phase 3	Efficacy of Isradipine in Early Parkinson Disease (STEADY-PD III) (not recruiting)	Sep-14	Mar-19	336	Univ. of Rochester	NINDS, MJFF, PSG	NCT02168842	MJFF Blog 6.29.16	MJFF website: Therapies in Development
EPI-589*	Treats childhood mitochondrial diseases	Phase 2A	Safety and Biomarker Study of EPI-589 in Parkinson's Disease (recruiting)	Mar-16	Jul-18	40	Edison Pharmaceuticals		NCT02462603	CPT - Linked Clinical Trial Initiative	
EPI-743	Targeted at mitochondrial and other neuro diseases	Phase 2B in design								Phase 2A completed (NCT01923584)	EdisonPharma.com/about-edison/
UDCA*	Used to treat liver disease. Acts to recover mitochondrial function.	Trial in design								CPT - Linked Clinical Trial Initiative: Trials Pending (seeking funding)	
Ambroxol*	Used to prevent build-up of excess mucous in respiratory diseases	Phase 2A	Ambroxol in Disease Modification in Parkinson Disease (AiM-PD) (not yet recruiting)	Dec-16	Dec-17	20	University College, London	CPT, PRO.MED.CS Praha a.s - Czech Republic	NCT02941822	CPT - Linked Clinical Trial Initiative	
Simvastatin*	Cholesterol-lowering drug	Phase 2	Simvastatin as a Neuroprotective Treatment for Moderate Parkinson's Disease (PD STAT) (recruiting)	Sep-15	Dec-19	198	Plymouth Hospitals NHS Trust	University of Plymouth	NCT02787590	CPT - Linked Clinical Trial Initiative	Funders: Plymouth Univ., JPM Moulton Trust, CPT
Deferiprone*	Used to reduce iron levels in blood after transfusions	Phase 2	Conservative Iron Chelation as a Disease-modifying Strategy in Parkinson's Disease (FAIRPARKII) (recruiting)	Feb-16	Dec-18	338	University Hospital, Lille	European Commission, ApoPharma	NCT02655315	CPT - Linked Clinical Trial Initiative	Funding received from EU Horizon 2020 research and innovation program.
Deferiprone*	Used to reduce iron levels in blood after transfusions	Phase 2	Study of Parkinson's Early Stage with Deferiprone (SKY) (recruiting)	Jul-16	Jul-18	140	ApoPharma		NCT02728843	CPT - Linked Clinical Trial Initiative	
Exenatide (Bydureon)*	Type 2 Diabetes drug (GLP-1 agonist)	Phase 2 completed. View results on CPT site.	Trial of Exenatide for Parkinson's Disease (EXENATIDE-PD) (completed)	Jun-14	Aug-16	60	University College, London		NCT01971242	CPT - Linked Clinical Trial Initiative	MJFF website: Therapies in Development

Study Funding Approach

- Based on identified funding requirements, PD advocates can partner with research teams to develop fundraising plans and timelines.
- PD advocates/researchers can jointly develop promotional materials stating study goals and funding needs. *(NAC trial example on next slide).*
- PD advocates can fundraise for a specific study (or group of studies) through events, online channels, etc.

Trial funding approach: Fundraising for specific studies

Example: CPT's **NAC trial** promotional materials highlighting study goals & funding needs

★ FUNDING NEEDED – N-Acetyl Cysteine Trial★

What is N-Acetyl Cysteine (NAC)?

N-Acetyl Cysteine (NAC) is a readily available health supplement, which in its clinical strength, is currently used to treat paracetamol overdose and to loosen thick mucus in conditions like cystic fibrosis.

Why test it in Parkinson's?

NAC increases the amount of cysteine (an amino acid) which is available to the brain, which in turn increases the amount of glutathione (GSH) – a major antioxidant. Cells use GSH to speed up the chemical reactions which relieve toxic stress and reduce cell death, and past research has indicated that when there are decreased amounts of GSH these chemical reactions can't happen. The hypothesis is that NAC reduces dopamine neuron cell death by increasing GSH levels, so reducing toxic stress so NAC could potentially **slow down the progression of Parkinson's.**

What are the aims of this project?

1. The primary goal of the project is to prove that NAC is safe to use long-term with people with Parkinson's, at a higher than usual dose to increase the likelihood of affecting the disease, without negative side-effects

2. To study how NAC affects Parkinson's symptoms – both motor (movement-related) and non-motor (sleep, fatigue etc)

How will we measure outcomes?

Patient reported outcomes and Parkinson's patient-specific measures will be used to investigate any effect of NAC on symptoms. In addition, samples of serum and cerebrospinal fluid will be collected prior to and at the end of the trial, which will be analysed to measure the effect of NAC on oxidative stress biomarkers.

What is the design of the trial?

Led by Professor Caroline Tanner, this will be a double-blinded, randomised, placebo-controlled trial (which means that neither the patients nor the researchers know who is receiving NAC or the placebo). involving 60 patients with early to moderate stages of Parkinson's, across five centres in California over a period of 14 months.

Costs

The total cost of this project is US$1,913,674 (approximately £1,500,000 subject to exchange rate) – any VAT costs are included in this figure. Please see below for a breakdown of the budget.

ITEM	DETAILS	TOTAL COST $
Personnel	Includes salaries of the Principle and Co Investigators, Project Manager, Research Coordinator, Senior Nurse Coordinator, Data Manager, Medical Safety Monitor and Postward Staff	873,309
Consultant costs	Steering Committee: $6,000 Data/Safety Monitoring Committee: $1,800 People with Parkinson's: $2,400	10,200
Supplies	Includes office supplies and Cost of NAC: $62,881 Compounding and preparation: $506,920 Biomarker collection processing and storage: $59,200	636,859
Travel	Includes travel costs for patients, committee members and monitor visits	34,500
Other	Includes start-up costs, subject evaluation, insurance and Medrio EDC software	358,806
	TOTAL	$1,913,674

Fundraising Strategy

We are requesting £60,000 a year for three years (£180,000 total – approximately $300,000 towards this project) from The Clive & Sylvia Richards Charity to support the NAC trial.

Funding source	Target	Confirmed	Notes
Van Andel Research Institute (VARI)	$400,000	$400,000	VARI is partnered with CPT on the LCT programme, and has pledged support
The Cure Parkinson's Trust (CPT)	$400,000	$400,000	CPT's Trustees have pledged to match VARI's pledge of $400,000 towards this trial.
Trusts and Foundations	$600,000		We are approaching a number of targeted Trusts and Foundations in both the UK and the US, many of whom we have a close connection with or who are regular supporters of our work.
Major Donors	$200,000		We plan to hold a number of events for our high net worth supporters – we piloted this in 2016 and it has been extremely successful in raising funds for specific projects.
Individuals	$13,674		We will direct funds raised from individual challenge events (e.g. London Marathon 2017) towards this trial.
TOTAL	$1,913,674	$800,000	

Trial Recruitment & Participation

- Encourage adoption of Clinical Trials Best Practices to ensure Participant understanding of:
  - Trial purpose
  - Trial methodology (intervention, timeframe, …)
  - Trial risks and benefits
  - Any changes to existing medication regimen
  - Communication channel with trial team
  - How trial team will coordinate care with participant's existing physicians
  - How to access prompt medical care during and after trial if needed

  See CPT's Charter for Clinical Trials in Parkinson's describing standards of practice for Patients and Researchers.

- Enhance trial outreach/marketing
  - Ensure latest trial data is on ClinicalTrials.gov (e.g., recruiting status)
  - Publish active trial info, with NCT#, on each trial location's website.
- Optimize participant experience/customer service
  - Staff training and continuity
  - Timely response to phone calls/emails (before/during/after trial)
  - Access to medical care as needed
  - Coordination with participant's physicians
  - Insurance for related medical care post-trial.
  - Share published results of trial.

Next Steps

- Share project with patients/researchers/pharma/foundations & collect feedback.
- Add project resources to:
  - Maintain listing of active disease-modifying trials.
  - Liaison with patient/research/pharma/foundation communities.
  - Develop and implement fundraising plans.
  - Facilitate adoption of clinical trials charter to enhance communication, recruitment, participation, and outcomes.
  - Expand project to include patient involvement in trial planning and design.
    - Consistent with PCORI efforts
    - Related blogs/articles (e.g., Parkinsons Movement: Patients must help design clinical trials, PDF article: Patient Engagement in PD Research)
- Expand project to include symptomatic trials in the pipeline.

Conclusion

- A review of disease-modifying therapies in the PD trial pipeline is available online at www.PDTrialTracker.info.
- Document is maintained by PD advocates to highlight study funding & recruiting needs for high-priority research towards a cure.
- Patient and research communities can work together to address funding and recruiting goals through
  - targeted fundraising approaches
  - adoption of clinical trials charter (best practices for pre-trial/during trial/post-trial) to improve recruitment and participation.

To learn more about this project, contact us at:

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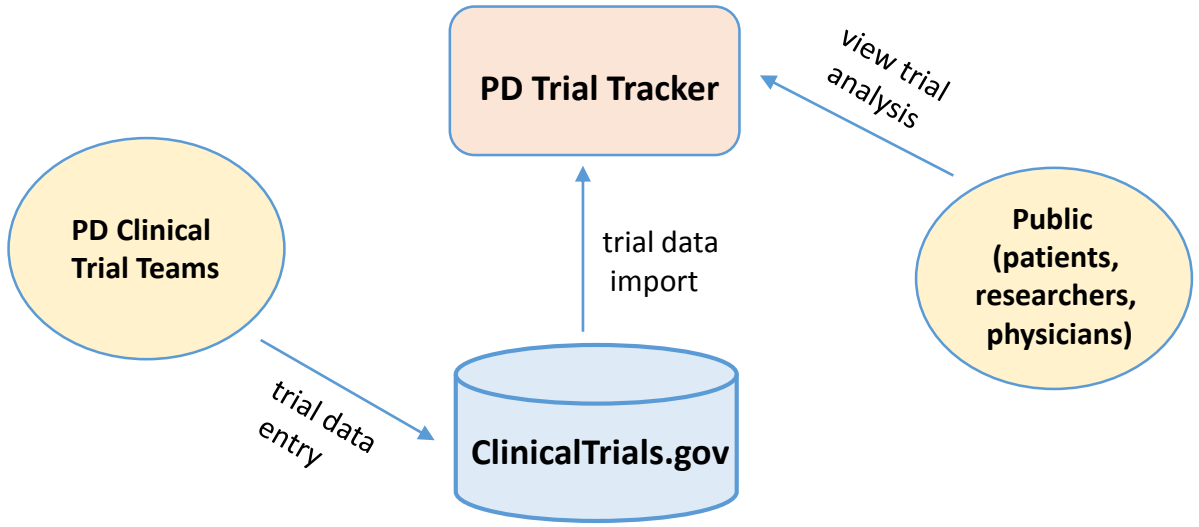
Appendix 1

PDTrialTracker.info: tracking the status of active PD clinical trials.

PDTrialTracker flowchart



About ClinicalTrials.gov

- Launched in 2000 by the NIH.
- Open access, free to public.
- Standards-based.
- FDA reqs. surrounding it use.
- 255,000+ studies WW listed, as of 9/17.
- 1800+ PD studies listed (500+ active)
- Search, filter, download features.

PDTrialTracker highlights

- Presents PD clinical trial data from ClinicalTrials.gov database.
- Filters, slices and dices, analyzes trial data.
- Presents canned, out-of-the-box data analysis via charts, graphs, tables.
- Allows for easy interpretation, yields new insights, suggests action plans.