



Parkinson's  
Progression  
Markers  
Initiative

# **PATH TO PREVENTION (P2P) THERAPEUTICS PLATFORM TRIAL IN EARLY NEURONAL SYNUCLEIN DISEASE (NSD)**

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ISCTM 2026 MEETING (FEB 2026)**



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# Coffey Disclosures

- Grant funding received from Michael J Fox Foundation, NIH NINDS, PCORI
- Consultant for QurALIS, Ionis Pharmaceuticals

# The Parkinson's Progression Markers Initiative (PPMI)

## Clinical Enrollment by Cohort as of 02Feb2026

	Consented	Screen Failed/Denied	Pending	Total Enrolled	Withdrawn/Completed	Active
PD	2037	472	39	1526	489	1038
HC	440	104	0	336	121	215
PRODROMAL	5523	2615	287	2621	264	2357
TOTAL	8000	3191	326	4483	874	3610

**\*4483\* Total Enrolled PPMI Clinical Participants**

**\*3610\* Active PPMI Clinical Participants!**

15+ years of natural history data – defining biological & clinical progression in PD

# PPMI 2023 Highlights: A New Biomarker!



## ‘Big step forward’: New lab tests may accelerate Parkinson’s diagnosis and research

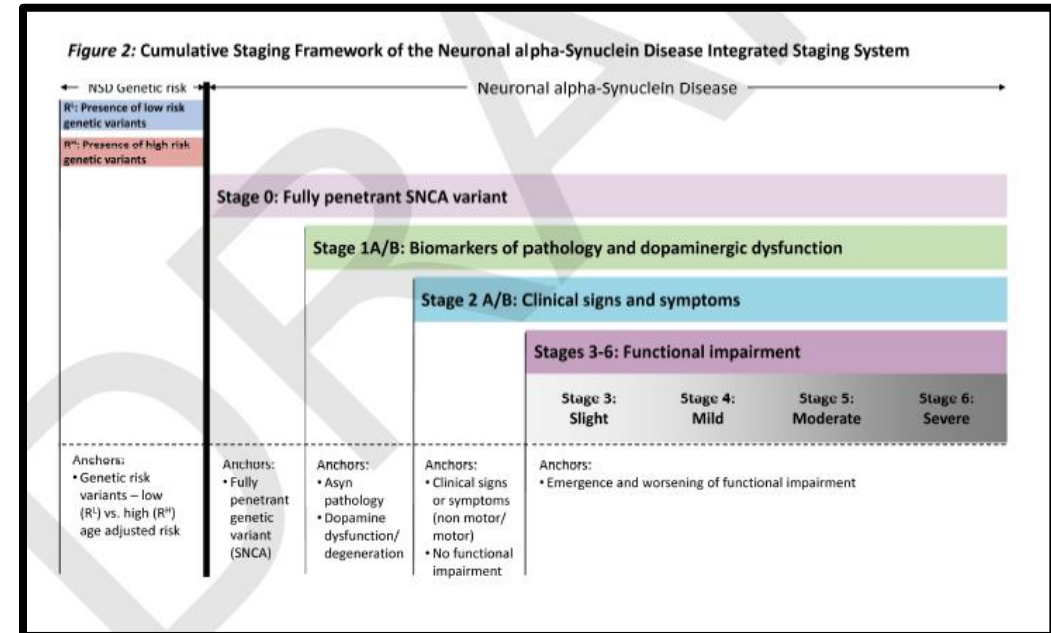
By Brenda Goodman, CNN  
© 6 minute read · Published 6:37 PM EDT, Thu April 13, 2023

## Michael J. Fox: Do you have Parkinson's? New test is 'breakthrough' in diagnosing disease.

*I'm involved with the work of The Michael J. Fox Foundation in many ways, but I come to this breakthrough first and foremost as a patient.*

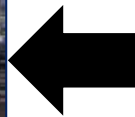
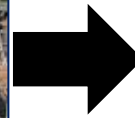
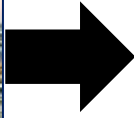
**Michael J. Fox** Opinion contributor  
Published 5:14 a.m. ET May 2, 2023

# PPMI 2024 Highlights: NSD-ISS Staging



# Master Protocols

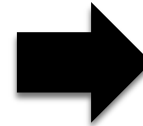
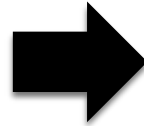
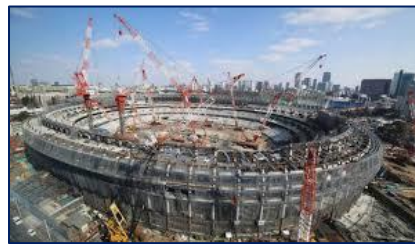
- Traditional approach to running a clinical trial....



# Master Protocols

## Platform trials bring efficiency

- Create one optimized trial infrastructure and use it to perpetually study multiple therapies



# Path to Prevention (P2P): A Platform Trial Embedded in PPMI



**Most efficient** way to test a number of therapeutics/mechanisms under a master protocol



Enables **rapid** testing with more flexible study designs

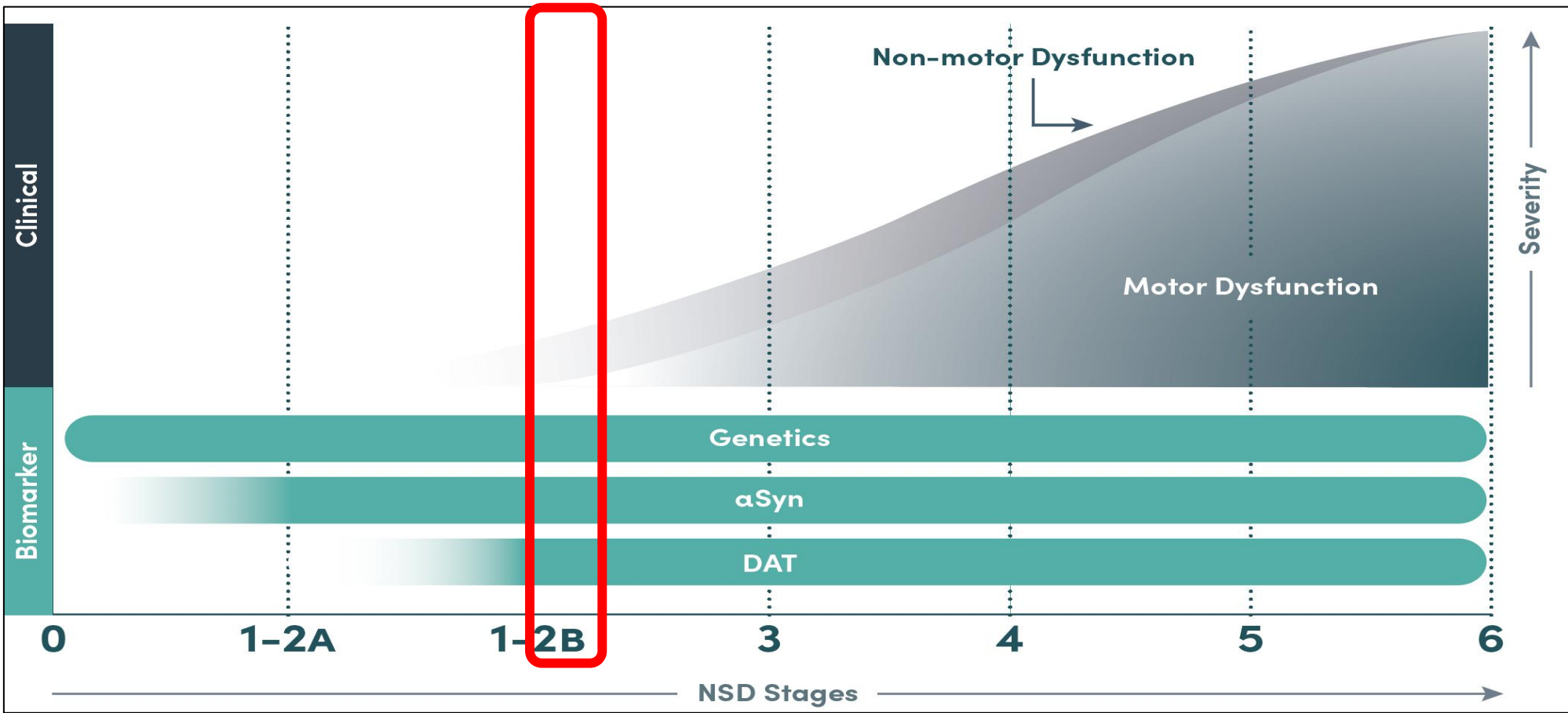


**Established success** in other disease areas offers value to industry partners invested in PD

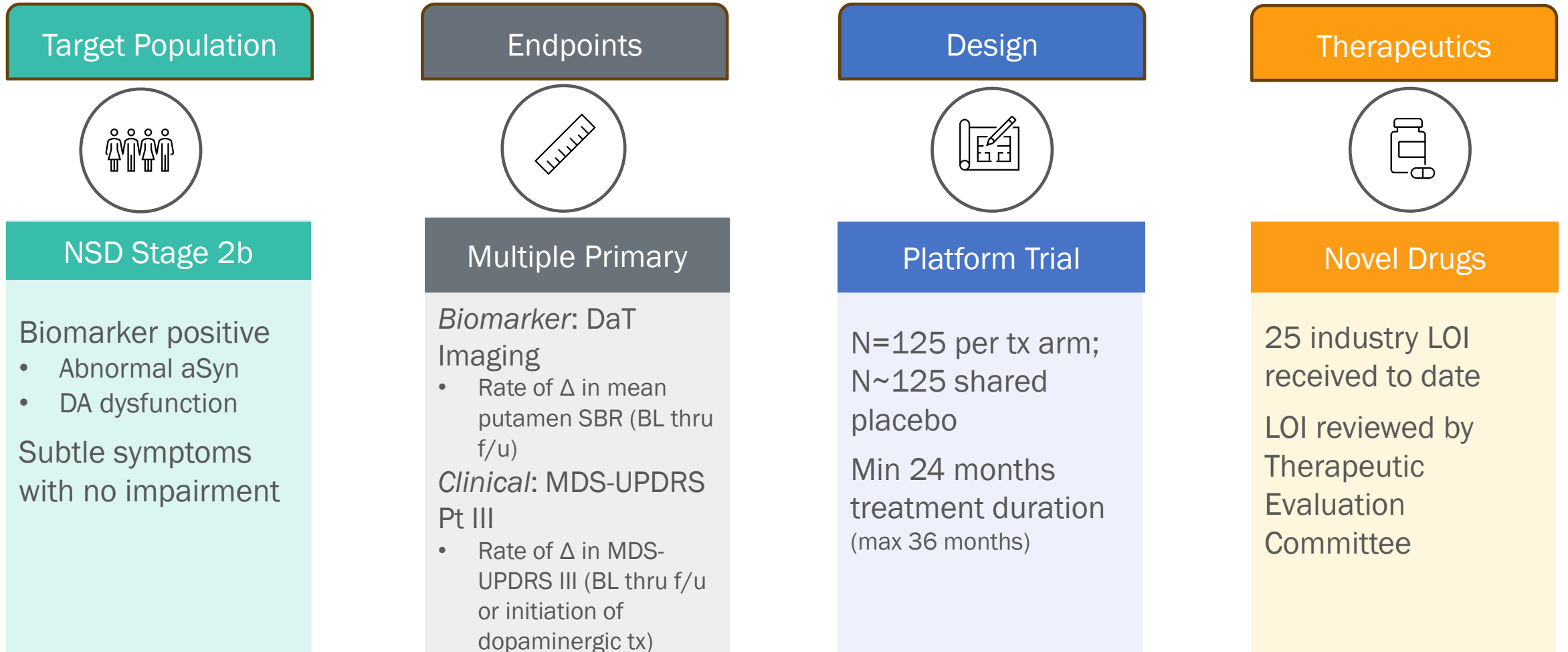
PPMI's prodromal cohort offers a **unique target population** that is otherwise challenging for individual sponsors to recruit

# NSD BASED DEFINITION OF POPULATION

Biologic definition for Neuronal Synuclein Disease (NSD) – encompasses PD and DLB

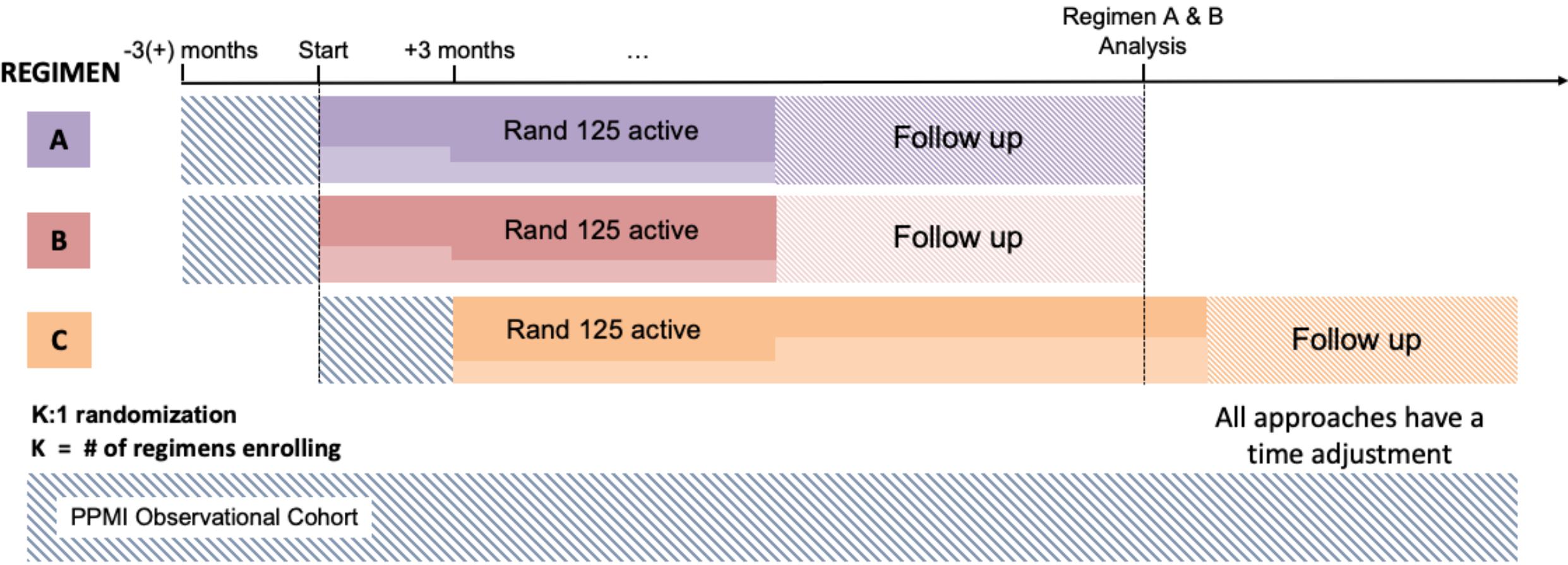


# PATH TO PREVENTION (P2P) STUDY SYNOPSIS



**Proof of concept learning Phase 2A** randomized double blind **platform study embedded in PPMI** to assess impact of putative NSD therapies in participants with Early Stage NSD on DAT SPECT imaging, clinical measures of symptom worsening, feasibility, safety, and tolerability.

# P2P STUDY DESIGN: PERPETUAL PLATFORM TRIAL



All controls: used for current power calculations.

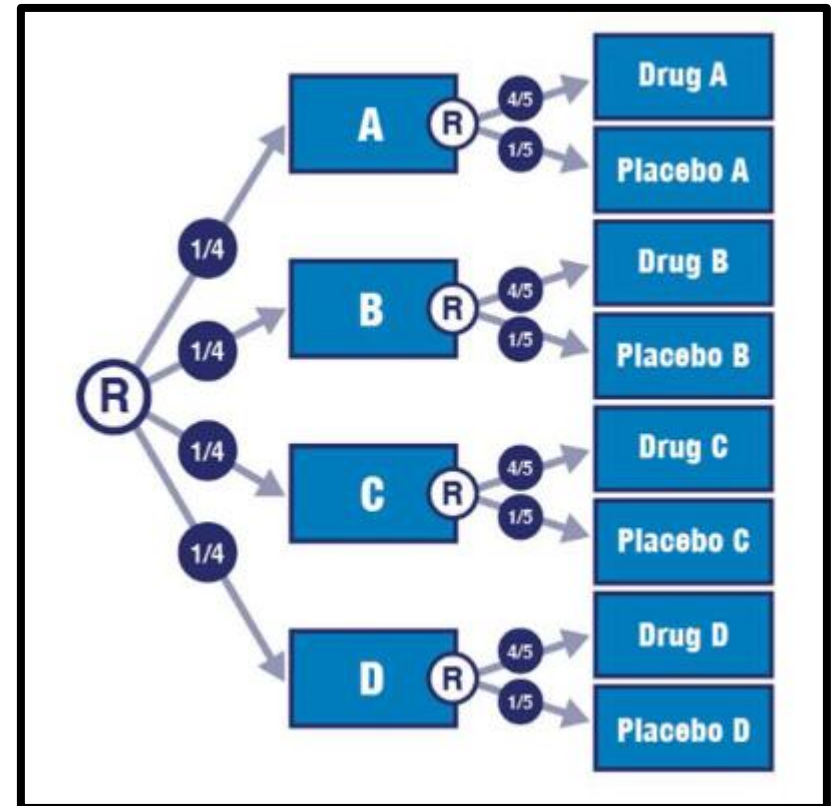


# P2P TWO-STAGE RANDOMIZATION

Participants identified as potentially eligible from PPMI.

**Randomization 1:** Participants invited to master protocol screening visit, and if qualified and consent, will be randomly assigned to one of K available regimens for which they are eligible (in equal manner).

**Randomization 2:** If all additional regimen-specific eligibility requirements are met, participants will be randomized to either active drug or placebo in a K:1 manner within regimen.



# MULTIPLE PRIMARY ENDPOINTS

**Biomarker:** Impact of interventions on DAT imaging

- As measured by the rate of progression in the mean putamen Specific Binding Ratio (SBR) from baseline through follow-up.

**Clinical:** Impact of interventions on the clinical outcome

- As defined by the rate of progression in the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score from baseline through end of follow-up or the initiation of dopaminergic treatment.

**Success** is defined as a statistically significant change associated with treatment shown for **either endpoint**.

# CONNECTIVITY BETWEEN PPMI AND P2P LEADS TO INCREASED EFFICIENCIES

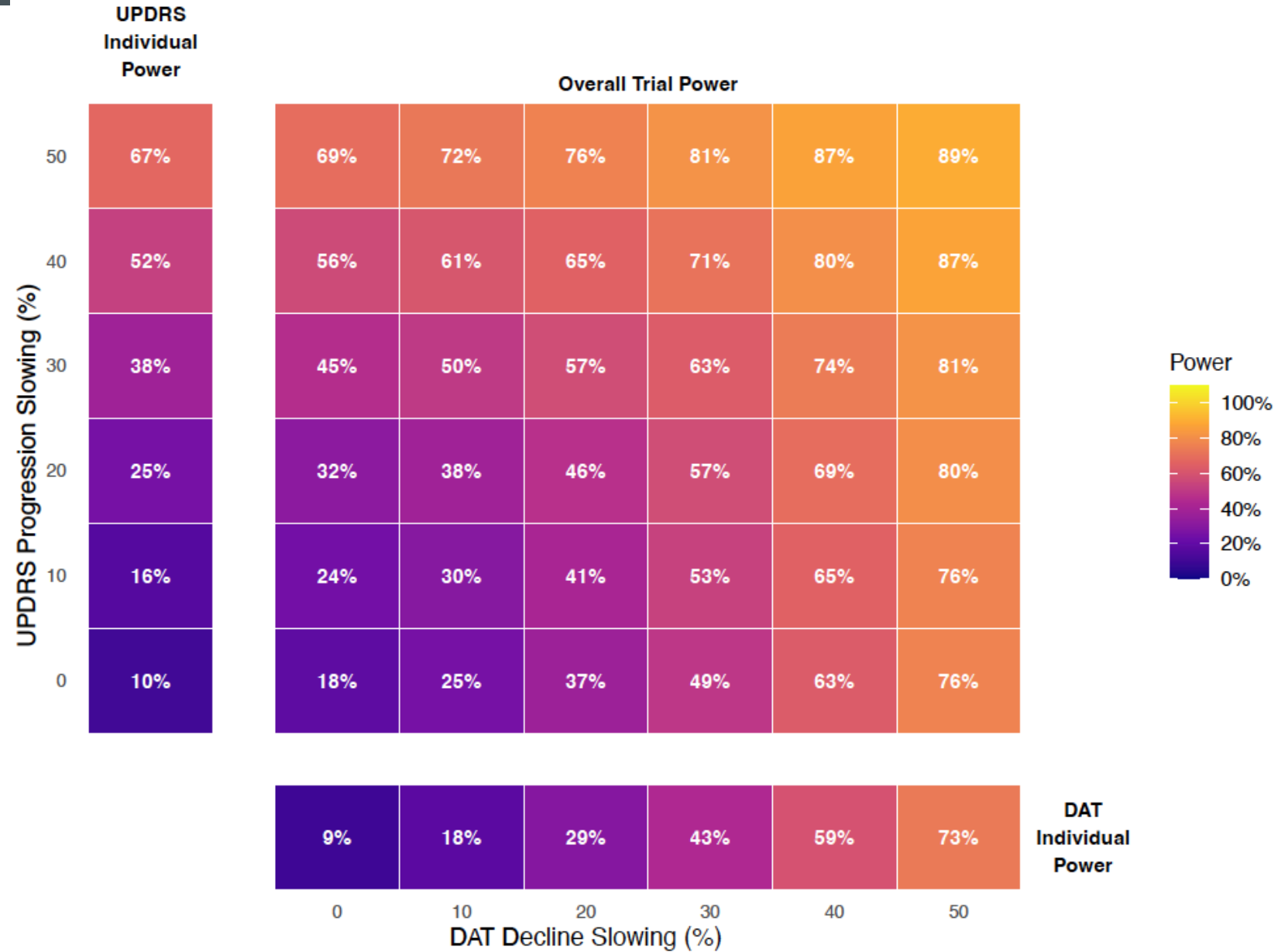
- P2P interventional cohorts recruited from PPMI
- P2P participants will continue contributing key data to PPMI (per PPMI cadence of visits)
- Upon completion of P2P interventional protocol, participants will continue to be followed in PPMI enabling long-term follow up
- *P2P can leverage additional natural history data from PPMI cohorts to inform progression modeling*



Embedding the platform trial within PPMI increases the primary analysis power to **80%** for 40%/40% slowing.

- SEPTEMBER 2025 DATA CUT
- DYNAMIC BORROWING OF NON-RANDOMIZED PATIENTS

**P2P Platform Trial Power**  
with 100 non-randomized P2P-eligible PPMI participants



Simulated platform power is averaged across the first 3 regimens without any non-randomized P2P-eligible PPMI participants. It assumes that two regimens enter together, followed by a third one year later. Overall trial power uses a one-sided overall alpha of 0.20. Individual endpoint powers use a one-sided alpha of 0.10.

# P2P READINESS? PPMI BASELINE NSD STATUS

	<b>PD (N = 1525)</b>	<b>HC (N = 336)</b>	<b>Prodromal (N = 2621)</b>
NSD	<b>1177 (85%)</b>	22 (7%)	1546 (64%)
Not NSD	206 (15%)	<b>294 (93%)</b>	878 (36%)
Missing / Not Evaluable	142	20	197

# P2P READINESS? PPMI BASELINE NSD-ISS

NSD-ISS Stage	PD (N = 1177)	HC (N = 22)	Prodromal (N = 1546)
Stage 0	0	0	5 (<1%)
Stage 1A	0	6 (27%)	21 (1%)
Stage 1B	1 (<1%)	0	9 (1%)
Stage 2A	29 (3%)	15 (68%)	746 (50%)
Stage 2B	225 (20%)	1 (5%)	<b>497 (33%)</b>
Stage 3	689 (62%)	0	122 (8%)
Stage 4	156 (14%)	0	91 (6%)
Stage 5	8 (1%)	0	1 (<1%)
Stage 6	1 (<1%)	0	0
Not Stageable	68	0	54



# P2P READINESS? PPMI ELIGIBILITY TRACKER

Download Date	Eligible	Added	Removed
04/28/2025	276	-	-
05/27/2025	286	19	9
06/30/2025	318	43	11
08/04/2025	325	15	8
08/25/2025	328	11	8
09/29/2025	332	17	13
10/27/2025	344	26	14
11/24/2025	359	26	11
12/29/2025	385	34	8
<b>01/29/2026</b>	<b>385</b>	<b>8</b>	<b>8</b>



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## P2P READINESS: REGULATORY

Master protocol and first RSSP were submitted to FDA and received IND for NSD Stage 2B defined population

- Revised master protocol will be submitted with next RSSP
- Annual progress report submitted 01/30/2026

Engaged with EMA country-based SA meeting

- Received favorable feedback regarding study design & biologically defined population



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# P2P READINESS? KEY LEARNINGS FROM REGULATORY INTERACTIONS

- Stage 2B NSD population is acceptable for inclusion in this phase 2 POC study
- Multiple primary endpoints (DAT-SPECT, MDS-UPDRS III) acceptable with clear threshold
- Platform trial design is acceptable
- Randomization plan is acceptable but requires careful management of concurrent vs. non-concurrent placebo controls
- SAA data use does not require IVDR compliance for this exploratory trial (EU focused discussion)



# P2P READINESS: SUMMARY

## Clinical Sites

- High enthusiasm from PPMI clinical site investigators and coordinators

## Participants

- Strong PPMI volunteer interest reported in interviews; survey pending confirmation
- Modeling supports feasibility of recruiting 2-3 arms from PPMI cohort in the US for **Q4 2026 launch**

## Regulators

- FDA supportive, including a positive Type C meetings and open IND
- Positive scientific advice in 2 key European countries

## Biopharma Partners

- 25 letters of interest received to date
- **In contracting with 2 companies;**
- Additional therapeutic candidate under consideration

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# COLLABORATORS

- Tanya Simuni
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- Caroline Tanner

