Kristophe Diaz, PhD
Chief Executive Officer
325 Hudson Street, 4th Floor
New York, NY 10013
646-725-1453
diaz@curepsp.org

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National Institute of Neurological Disorders & Stroke (NINDS)
National Institutes of Health (NIH)
6001 Executive Boulevard
Rockville, MD 20852

Submitted electronically via email at NationalPDplan@nih.gov

Subject: NOT-NS-26-039: National Plan to End Parkinson's Request for Information (RFI) Strategy[1]

Dear Members of the Advisory Council on Parkinson's Research, Care, and Services (ACPRCS),

CurePSP appreciates the opportunity to provide perspectives on research, care, services, and supports for Parkinson's disease and related neurodegenerative parkinsonisms in response to this Request for Information (RFI).

Research:

The following research priorities are ordered based on the magnitude of the unmet need, their potential to accelerate progress toward effective treatments, opportunities for near-term action by leveraging resources and infrastructure, and the extent to which progress in one area can enable advances across the broader research pipeline. The order reflects these considerations rather than a determination that lower-ranked priorities are substantially less important.

Priority 1: Accelerate Earlier and More Accurate Diagnosis and Biomarker Development
Earlier and more accurate diagnosis is one of the most consequential unmet needs for PSP, CBD, and MSA because it directly affects clinical care, research participation, therapeutic development, and the ability for people living with these diseases and their families to plan for rapidly changing needs.

Early symptoms of PSP, CBD, and MSA can resemble Parkinson's disease or other neurologic disorders, contributing to misdiagnosis and diagnostic delay. By the time an accurate diagnosis is reached, disease progression may already have substantially affected mobility, cognition,

[1] https://grants.nih.gov/grants/guide/notice-files/NOT-NS-26-039.html

communication, autonomic function, or independence. Diagnostic delay can also narrow opportunities to participate in clinical trials and complicate efforts to test therapies at earlier stages of disease.

The National Plan should prioritize development, validation, and clinical translation of biomarkers capable of distinguishing PSP, CBD, and MSA from Parkinson's, Alzheimer's disease and related dementias, and from one another, as well as identifying relevant co-pathologies that may influence clinical presentation or therapeutic response. Promising approaches exist in the development of diagnostic tools such as fluid (e.g., neurofilament light chain and alpha-synuclein seed amplification assays), molecular, imaging, genetic, and multimodal biomarkers. Important limitations remain including differentiation among atypical parkinsonian disorders and performance of current alpha-synuclein assays in MSA. PSP and CBD continue to lack validated disease-specific biomarkers suitable for routine clinical use or as definitive research endpoints.

National investments should support a pragmatic diagnostic framework that integrates clinical assessment with validated molecular, fluid, imaging, and genetic tools and establish pathways for translating successful research biomarkers into clinical practice. Biomarker development should occur alongside efforts to improve clinical recognition and referral so that scientific advances result in earlier diagnosis for patients.

Priority 2: Advance Disease Biology and Therapeutic Development
There are currently no approved disease modifying therapies for PSP, CBD, and MSA. Although meaningful progress has been made in characterizing tau pathology in PSP and CBD and alpha-synuclein pathology in MSA, fundamental questions remain about disease initiation, propagation, selective neuronal vulnerability, heterogeneity, and the mechanisms that produce distinct clinical phenotypes.

The National Plan should support sustained investigation of molecular pathways driving tau and alpha-synuclein pathologies, genetic risk and resilience factors, and the causal mechanisms of protein aggregation. These efforts may reveal new therapeutic targets. Research should recognize both shared biology across neurodegenerative diseases and mechanisms that are specific to individual disorders rather than assuming findings in Parkinson's disease or one atypical parkinsonian disorder will translate directly to another.

Although the therapeutic pipeline for these diseases continues to advance, clinical trial challenges in tau- and alpha-synuclein-targeted therapies demonstrate the need to strengthen the translational pathway before and during large efficacy trials. Priorities should include validated target-engagement biomarkers, improved patient selection and disease staging, outcome measures capable of detecting clinically meaningful change over shorter trial durations, and greater exploration of therapeutic targets beyond downstream protein aggregation.

The relatively small and often underrecognized populations affected by PSP, CBD, and MSA create structural challenges for therapeutic development. Small patient populations, high development costs, and the expense and risk of late-stage neurodegeneration trials can limit

commercial incentives relative to more prevalent neurological diseases.[2] These market dynamics make sustained federal investments and public-private partnerships particularly important for advancing promising therapies through the translational pipeline, including approaches that may otherwise struggle to attract sufficient private investment.

Adaptive platform trials, such as the PSP Trial Platform,[3] and appropriately designed basket trials may provide more efficient approaches for testing multiple therapies or biologically related hypotheses in relatively small patient populations. These approaches should complement other pathways for therapeutic development. Federal agencies, private sector, and non-governmental organizations should support a range of trial designs and public-private partnerships that reduce barriers and create incentives to test promising mechanisms in PSP, CBD, and MSA, while allowing sufficient flexibility in patient selection, endpoints, and study design to reflect the needs of individual therapies.

Priority 3: Strengthening Research Tools, Infrastructure, and Participation
The relatively small populations currently identified with PSP, CBD, and MSA make shared research infrastructure particularly important. Small, disconnected cohorts and inconsistent methods can limit statistical power, reproducibility, validation, and translation.

The National Plan should support coordinated infrastructure that includes longitudinal natural history cohorts; standardized biospecimen collection and neuropathology resources; validated cellular and animal models; harmonized imaging, clinical, and biomarker protocols; shared data and research tools; and strong coordination among federal agencies, academic centers, biofluid and brain banks, patient organizations, industry, and people with lived experience.

Research infrastructure should also be designed around the realities of participation in rapidly progressing diseases. People with PSP, CBD, and MSA may experience early and profound mobility limitations, cognitive or communication changes, swallowing difficulty, autonomic symptoms, or other impairments that make conventional research participation difficult. Care partners frequently provide transportation and logistical support while already carrying substantial caregiving responsibilities. Restrictive eligibility criteria can further exclude people later in the disease course.

Clinical trials should incorporate decentralized or hybrid participation where appropriate, reduce unnecessary travel and visit burden, support care partner participation, and reassess unnecessarily restrictive eligibility criteria. Research should also systematically incorporate patient experience data, including patient-reported outcomes, care partner input, and real-world functional assessments, to complement clinical measures and ensure that endpoints capture changes that are meaningful to people living with these diseases and their families.

Priority 4: Identify and Address Gaps in Representation, Access, and Data
Disparities in diagnosis, research participation, and access to specialty care are increasingly documented in Parkinson's disease, but comparable data for PSP, CBD, and MSA remain

[2] https://www.drugtargetreview.com/why-tau-still-lacks-treatments-and-how-funders-are-responding/681835.article
[3] https://www.psp.org/ptp

extremely limited. The absence of data should be treated as an important research gap rather than interpreted as evidence that disparities do not exist.

Registries and observational cohorts for atypical parkinsonian disorders are often recruited through specialty academic centers and may not adequately capture people who live far from major medical centers, have lower socioeconomic resources, experience advanced disability, or face language and other barriers to participation.

The National Plan should support collection and reporting of demographic, geographic, socioeconomic, diagnostic, and healthcare-access data for PSP, CBD, and MSA; research examining how these factors affect diagnostic accuracy, diagnostic delay, specialty care, and research participation; and community-partnered approaches to identifying barriers that may not be visible in existing datasets.

Research opportunities should also be made more accessible through linguistically and culturally appropriate materials, partnerships between specialty centers, community providers, and organizations, and recruitment strategies designed to reach populations historically absent from specialty-center research.

Priority 5: Build a Disease-Specific Evidence Base for Environmental Risk
Environmental risk research is substantially less developed for PSP, CBD, and MSA compared to Parkinson's disease. Existing studies have raised hypotheses regarding occupational, chemical, pesticide, metal, and other exposures, but evidence varies considerably by disease and is often limited by small samples, retrospective exposure assessment, and inconsistent definitions.

The National Plan should support adequately powered, longitudinal research examining environmental and occupational exposures, gene-environment interactions, and geographic patterns across individual parkinsonian disorders. Findings from Parkinson's disease may provide useful hypotheses, particularly where biological pathways overlap, but environmental associations should not be generalized from Parkinson's disease to PSP, CBD, or MSA, or from one atypical parkinsonian disorder to another, without disease specific evidence.

Care Services Supports:

The following care, services, and supports priorities are ordered based on the urgency and impact of the unmet need, as well as opportunities for the National Plan to catalyze actionable improvements in care, support, and services based on existing resources and infrastructure. The order reflects these considerations rather than a determination that lower-ranked priorities are substantially less important.

Priority 1: Improve Timely Diagnosis and Access to Specialized Care
For people living with PSP, CBD and MSA, the diagnostic journey is itself a major care challenge. Symptoms may initially resemble Parkinson's disease or other neurological conditions, while limited familiarity with atypical parkinsonian disorders among nonspecialist providers and long wait times for neurology appointments alongside patients with slower disease progressions can contribute to repeated referrals and delayed diagnosis that can span over two to three years. Because PSP, CBD, and MSA generally progress more rapidly than

Parkinson's disease, the years spent seeking a diagnosis and an appropriate treatment plan can represent a substantial portion of the disease course. This prolonged diagnostic and care journey can also impose avoidable financial burdens on the individuals, families, and the healthcare system through repeated clinical visits, extensive diagnostic testing, and treatment trials before an accurate diagnosis is reached.

The National Plan should improve recognition of atypical parkinsonian disorders across primary care, general neurology, rehabilitation, emergency care, and other settings; establish clearer referral pathways to movement disorder and other appropriate specialists; and expand the workforce capable of recognizing and managing these diseases. Earlier recognition and more efficient referral pathways can also reduce unnecessary healthcare utilization and cost associated with a prolonged diagnostic journey.

Earlier diagnosis should be treated as a shared research and care objective. Better biomarkers will improve diagnostic accuracy, while provider education, specialist capacity, and referral pathways are necessary to ensure that diagnostic advances reach people living with the diseases.

Priority 2: Establish Coordinated, Disease Appropriate Care Pathways

People living with PSP, CBD, and MSA require care from multiple disciplines (e.g., neurology, nursing, clinical social work, urology, sleep, rehabilitation, palliative care) regularly and at different points in their diseases. PSP and CBD may require expertise spanning movement disorders, cognitive neurology, and neuropsychology. MSA may require movement disorders and autonomic expertise. Responsibility for coordinating care frequently falls to the patients themselves and their families.

Multidisciplinary models that integrate clinicians from across different areas of healthcare, while ensuring the goals of care are centered around the patient and family, provide an important foundation for comprehensive care. CurePSP's Centers of Care network is an example that demonstrates how specialized centers can connect people living with PSP, CBD, and MSA to clinical expertise, supportive services, education, and research.[4]

Of note, care models should be customized beyond the Parkinson's framework to diseases with different trajectories. PSP, CBD, and MSA can involve symptoms observed earlier than Parkinson's, such as falls, dysphagia, communication impairment, cognitive and behavior changes, or severe autonomic dysfunction, resulting in earlier and more significant disability. Many Parkinson's medications (e.g., carbidopa-levodopa, amantadine) may offer less robust or sustained benefit for people living with PSP, CBD, or MSA. Other Parkinson's medications (e.g., dopamine agonists) and advanced or surgical interventions used in Parkinson's treatment (e.g., deep brain stimulation, focused ultrasound, carbidopa-levodopa enteral gel) are not made available for people living with PSP, CBD, and MSA due to little to no benefit or contraindications. Care pathways should anticipate these disease-specific needs and introduce rehabilitation, baseline and preventative testing (e.g., swallow evaluation), safety planning, assistive equipment, palliative care, and advanced care planning at clinically appropriate points in the disease course.

[4] https://www.psp.org/centers-of-care

National efforts should identify, evaluate, and scale effective models of coordinated care, including expanded access to telehealth and hub and spoke approaches that extend specialty expertise into communities without neurology subspecialists. Existing delivery models should be examined for approaches that can be adapted across healthcare systems rather than creating duplicative disease-specific infrastructure.

Priority 3: Address Care Partner Burden and Support Needs
PSP, CBD, and MSA create substantial physical, emotional, social, and financial consequences not only for the person living with disease but also for family members and care partners. Rapid progression can lead to early loss of mobility and functional independence, risk of complications, communication impairment, hospitalization, and increasing dependence on both paid and unpaid care. Care partners frequently assume responsibility for physical care, transportation, appointment management, healthcare navigation, financial and legal planning, and coordination across multiple providers. This burden can affect their own health, employment, finances, and social connections.

Care partners should be recognized as integral members of the care team. The National Plan should support care partner-inclusive care planning, anticipatory education, respite and navigation services, mental health and bereavement supports, and interventions addressing the physical and psychological toll of caregiving. Policies should also recognize the economic effects of reduced work, workforce departure, and unpaid caregiving. Alongside these interventions, dedicated research is needed to better characterize the trajectory and drivers of care partner burden in PSP, CBD, and MSA, and develop meaningful measures of physical, psychological, and economic impact that can inform effective supports and policy.

Priority 4: Reduce Financial and Coverage Barriers to Essential Services
The economic consequences of Parkinson's disease and atypical parkinsonism extend well beyond direct medical spending. A 2026 economic burden analysis estimated the total U.S. cost of Parkinson's disease and atypical parkinsonism at $82.2 billion in 2024, including $23.8 billion in direct medical costs and $58.4 billion in indirect and nonmedical costs such as lost income, disability-related expenses, and unpaid caregiving.[5] The analysis also highlighted the substantial pre-diagnostic and diagnostic-period costs incurred during often prolonged paths to an accurate diagnosis, including repeated clinical evaluations, misdiagnoses, unnecessary or duplicative testing, and delayed access to appropriate specialty care, supports, and services.

For people with rapidly progressing diseases, gaps in coverage or delays in eligibility can be particularly consequential. For example, although PSP, CBD, and MSA are included in the Social Security Administration's (SSA) Compassion Allowances program, expedited disability determinations do not eliminate statutory waiting periods that may delay Social Security Disability Insurance (SSDI) and Supplemental Security Income (SSI) eligibility.

The National Plan should examine opportunities that can have the potential to reduce financial

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5 https://www.michaeljfox.org/sites/default/files/media/document/Economic%20Burden%20of%20Parkinson%E2%80%99s%20and%20Atypical%20Parkinsonism%20in%20the%20United%20States_0.pdf

burden by improving coverage and timely access to rehabilitation, mobility and communication devices, dysphagia management, home-based services, respite care, and other supports that help people remain safe and independent. It should also examine care partner income protections and access to financial and legal planning resources.

Where feasible and appropriate, the National Plan should prioritize adapting or extending existing programs, benefits, payment models, and community-support infrastructure to people living with PSP, CBD, MSA, other atypical parkinsonian disorders, and Parkinson's disease, rather than creatin duplicative systems.

Priority 5: Identify and Address Disparities in Care and Services Delivery
The evidence base describing disparities in PSP, CBD, and MSA remains limited. The National Plan should prioritize identifying who is not being reached by existing diagnostic, specialty care, research, and support systems and the root cause behind it.

Potential barriers include geographic distance from specialty centers, inadequate specialist supply, limited access to telehealth, insurance coverage, financial constraints, language barriers, limited health literacy, transportation, and the substantial time required to coordinate fragmented care. These barriers may compound one another as disease progresses.

Interventions should be developed in partnership with affected communities and should incorporate lessons from established models in other areas of medicine (e.g., stroke systems of care, cancer patient navigation programs, HIV care continuum frameworks, multidisciplinary clinic models). It should also prioritize outreach and education for primary care and general neurology providers, streamlined specialist referral pathways, cultural and linguistically appropriate patient resources, telehealth and regional consultation models, and stronger connections between specialty centers and community-based providers.

Importantly, the limited demographic and access data available for PSP, CBD, and MSA should not prevent action. The National Plan should simultaneously improve data collection and test interventions capable of reaching populations currently missing from specialty care and research.

Cross Cutting Recommendations

Across research, care, services, and supports, CurePSP encourages the Advisory Council to consider several principles when developing the National Plan.

- **Explicitly include PSP, CBD, and MSA in federal strategies, datasets, programs, and implementation activities.** Inclusion should be intentional rather than assumed under the broader term "Parkinson's disease and related disorders."
- **Invest in shared infrastructure while preserving disease-specific research and care needs.** Biomarkers, trial networks, data platforms, workforce investments, and care delivery models can benefit the broader Parkinsonian community, but their performance and applicability should be evaluated for individual diseases.
- **Treat earlier and more accurate diagnosis as a bridge between research and care.** Biomarker discovery, clinical recognition, specialist training, referral pathways, and

research enrollment should be developed as complementary components of the same strategy.

- **Design research and services around the realities of rapidly progressive diseases.** Trial participation, rehabilitation, palliative care, care partner support, transportation, telehealth, and assistive services should account for declining mobility and independence over a compressed disease trajectory.
- **Leverage and evaluate infrastructure before creating parallel systems.** Federal programs, nonprofit, academic, healthcare, and community models should be assessed for opportunities to expand access and scale effective approaches.
- **Connect recommendations to implementation.** The National Plan should identify responsible federal and nongovernmental partners to translate recommendations into timely, feasible, sustained, actionable results in accelerating research, diagnosis, treatment, care, and quality of life.

Sincerely,

Kristophe Diaz, PhD
Chief Executive Officer
CurePSP