



PARKINSON'S PRIORITY THERAPEUTIC CLINICAL PIPELINE REPORT



Q1 2023

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Report Objectives

This report provides an overview of therapies currently in clinical development for Parkinson's disease. The program status and result information include updates until March 2023. Brief rationale and progress in several key areas of therapeutic interest are described along with a more detailed listing of specific therapies, current development status and, where appropriate, information about MJFF support (funding or non-funding).

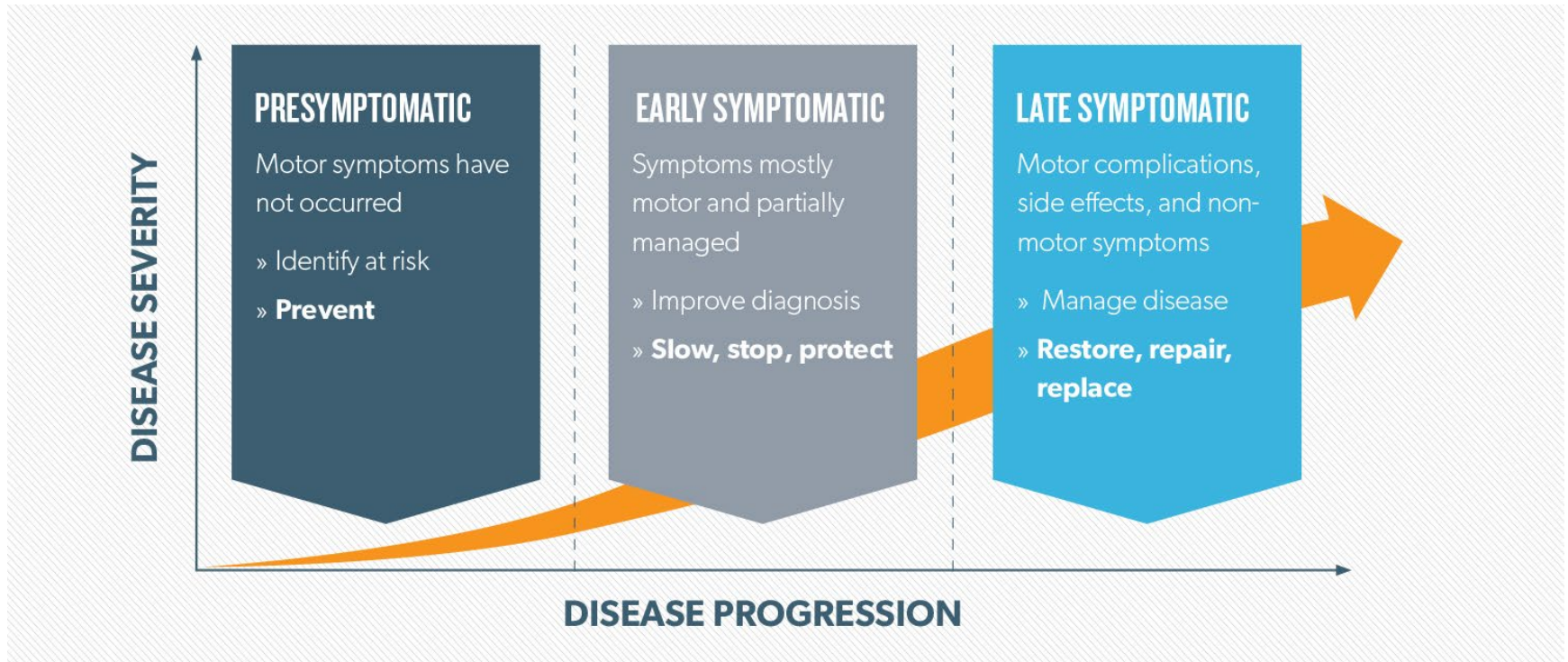
MJFF monitors numerous information sources to assess the therapeutic pipeline for Parkinson's disease. This report is not comprehensive of every approach or intervention being developed today, but represents treatments identified by MJFF research staff as important for monitoring given significance to the Parkinson's community and for understanding MJFF role and impact. The report is mostly focused on pharmacological and biologic therapies, while approaches such as exercise, alternative therapies and behavioral interventions are generally not included. In addition, clinical programs on neuromodulation and technology-enabled therapies represent active MJFF funded programs and are not a full listing of all approaches currently in development.

The report will be updated and distributed on an annual basis. Information in this report is not confidential and is intended only as a guide for communicating pipeline progress with our community stakeholders. Any errors or omissions are not intentional.

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THE PARKINSON'S CHALLENGE



- » Delivering better treatments and cures to people with Parkinson's disease requires developing
- » diverse therapies targeting **critical stages and symptoms**



PARKINSON'S PIPELINES WE MONITOR

Given the many approaches needed for treating the full spectrum of Parkinson's disease challenges, MJFF actively monitors clinical-stage therapeutic programs within the following key areas:

- Therapies targeting underlying Parkinson's disease biology that may over time slow, stop, reverse, or prevent the degenerative process and resulting symptom progression
- Therapies targeting brain chemistry and activity that aim to provide daily relief from disabling Parkinson's symptoms

This report includes program-specific information in some therapeutic areas (e.g., pharmacological and biological), while for other areas (e.g., technology-enabled therapeutics and neuromodulation) it includes higher-level trends and perspectives.

Parkinson's Disease Biology

Specific Priority Targets:

- Alpha-Synuclein
- LRRK2
- GBA1

Other Targets and Pathways:

- Mitochondrial Impairment
- Oxidative Stress
- Autophagy
- Inflammation
- Microbiome
- Cell Repair
- Cell Replacement
- Other targets

Brain Chemistry and Activity

- Acetylcholine
- Cannabinoid
- Dopamine
- GABA
- Glutamate
- Epinephrine/Norepinephrine
- Serotonin
- Phosphodiesterase
- Other targets

2022 IN REVIEW¹

3

Significant regulatory events:

- 3 NDAs filed for approval: IPX-203, SPN-830, ABBV-951
- 2 requiring additional data: SPN-830, ABBV-951

9

Therapies entered the clinic for PD²

- 7 novel treatments³
- 2 repurposed drugs⁴
- 1 new mechanism/target

6

Programs advanced in the clinic:

- Phase 1 → Phase 2
 - FAScinate Therapeutics | KM-819
 - Inhibikase | iKT148009
 - Vanda Pharma | Fanapt (Iloperidone)
 - CuraSen Therapeutics | CST-2032
- Phase 2 → Phase 3
 - Annovis Bio | Buntanetap (ANVS-401)
 - Denali & Biogen | DNL-151/BIIB-122

2

Key Agreements & Acquisitions:

- Janssen Pharmaceuticals acquired YTX-7739 from Yumanity
- ABL Bio entered licensing agreement with Sanofi for development of ABL-301

¹Excludes medical devices/neuromodulation, hypoxia therapy, and other non-biomedical therapies

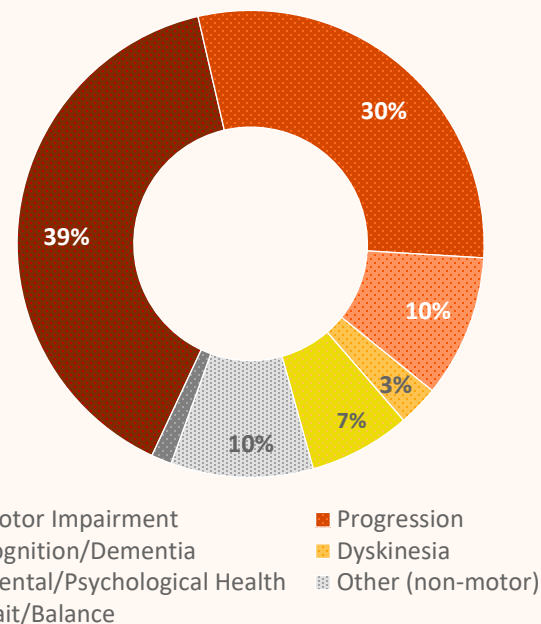
²ABL-301; ATH-1017; CX-8998 (entry after prior withdrawn/uninitiated trial); DGX-001; HNC-364; ISN-GSH (Glutathione/Insulin); KW-6002; NEU-723; STEM-PD

³Includes non-approved therapies that first entered the clinic prior to 2022 for a different disease indication. Excludes reformulations, repurposed drugs, Phase 4/other, natural medicine/supplement trials, and those that do not have a potential path for development in US/EU

⁴Includes approved drugs being explored as a PD treatment for the first time or for a new symptom

73 PD drug trials launched in 2022 focusing on a variety of indications. **Over a quarter of trials (n = 21)** targeted disease **progression** as the primary indication or in addition to a specific symptom (e.g., cognition)

Target Therapeutic Indications
2022 Initiated Trials



Phase 1-3 trials (n = 68) **launched** in 2022 exploring pharmacological interventions in PD (currently ongoing or completed). Includes trials that are actively registered on a clinical trial website but are not yet recruiting. Trials targeting more than one indication are counted multiple times (n = 3). Excludes trials for drugs with an unknown intended use (n = 5) or without a specified start date.

CURRENT STATUS OF THE PARKINSON'S PIPELINE¹

A robust, diverse and rapidly advancing pipeline of therapies being tested in clinical trials is a key metric of progress toward our vision of new treatments and cures for people with Parkinson's disease. Below is a snapshot of the current state of the Parkinson's clinical pipelines we monitor:

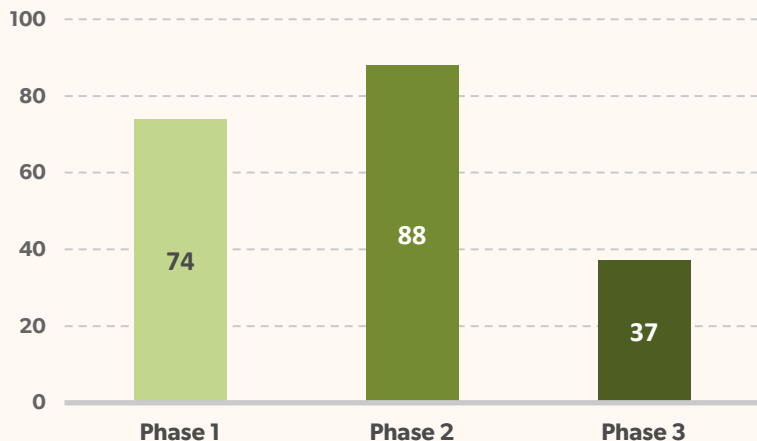


146 unique therapies in clinical testing monitored as potential new Parkinson's disease treatments*

*Number includes treatments with active trials or that have recently completed a phase of clinical testing and remain in active development for PD with commercial potential in US/EU. Reformulations and repurposed drugs are counted as unique therapies. Natural supplements and other dietary approaches are generally excluded unless there is a clear, biologically justified hypothesis being tested. Excludes preclinical programs expected to enter clinic this year, though such preclinical programs are listed under "Parkinson's Priority Program Pipelines".

Active Trials by Phase

March 2023

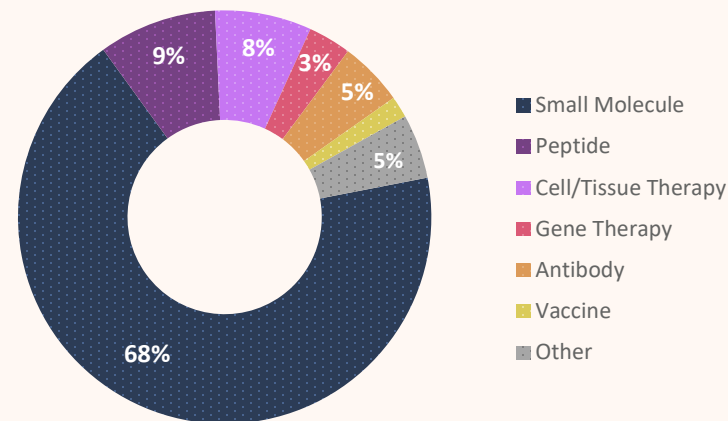


Total estimated number of active interventional drug trials by phase. Programs in "Phase 4" (post-approval) or other undefined stages of clinical development are not included. Total number of active trials is often greater than the number of unique therapies since a drug may be being used in multiple ongoing trials and/or is not considered a new PD therapy (e.g., generic drug development)

Source: Informa, data accessed March 2023

Therapeutic Approach by Program

March 2023



n = 119

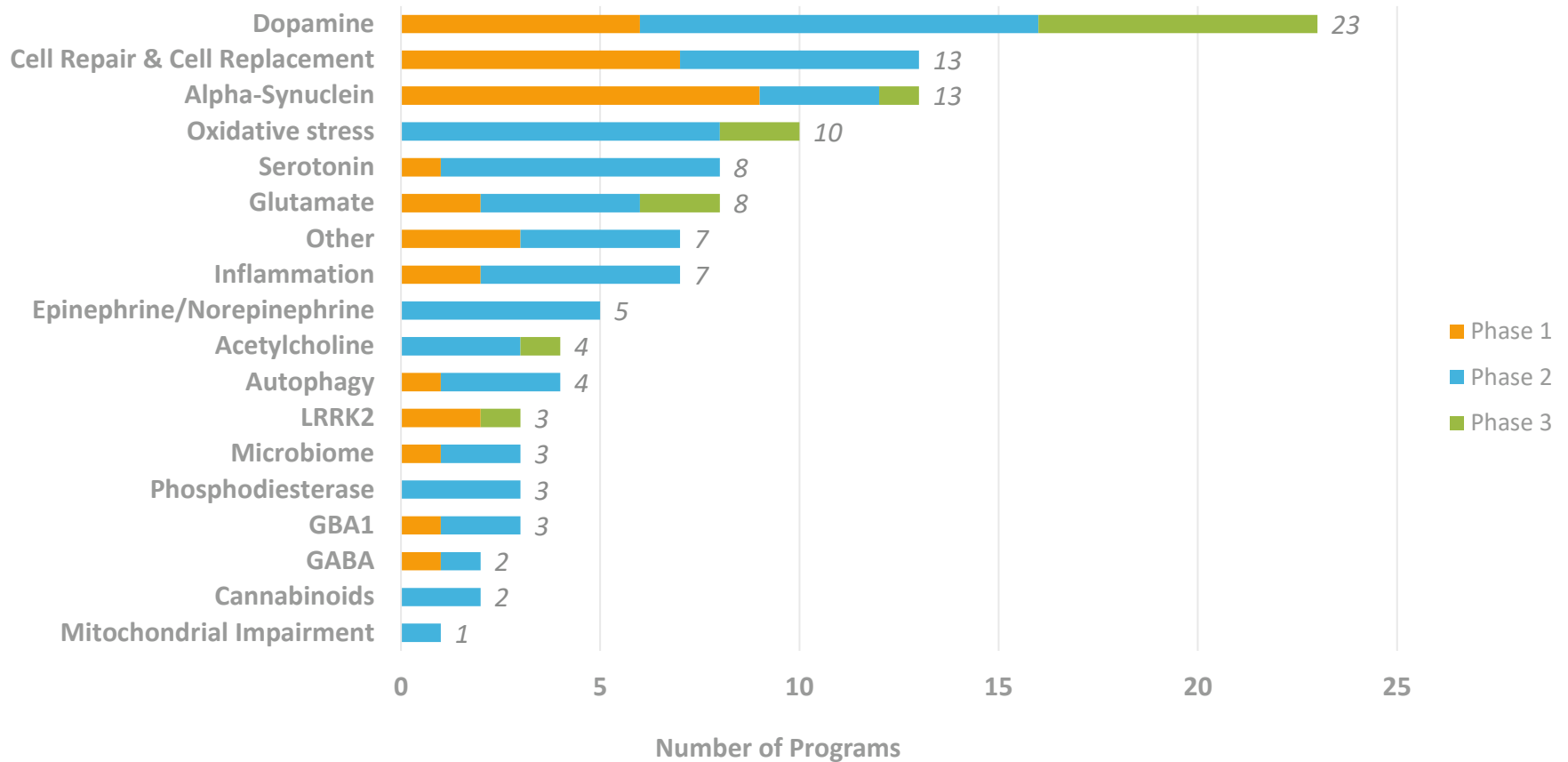
Breakdown of MJFF-monitored clinical programs by therapeutic approach. **Data include programs currently listed in this report and are not comprehensive of all active clinical programs in Parkinson's disease.** Different trials testing the same therapy (e.g., exenatide) are counted once, unless reformulation

¹Excludes medical devices/neuromodulation, hypoxia therapy, and other non-biomedical therapies

THE CLINICAL PIPELINE IS BEST BAROMETER OF PROGRESS¹

Several clinical-stage programs are targeting novel pathways addressing the underlying disease biology or brain chemistry targets addressing motor and non-motor symptoms. Below is an overview of programs included within this report by target and clinical trial stage.

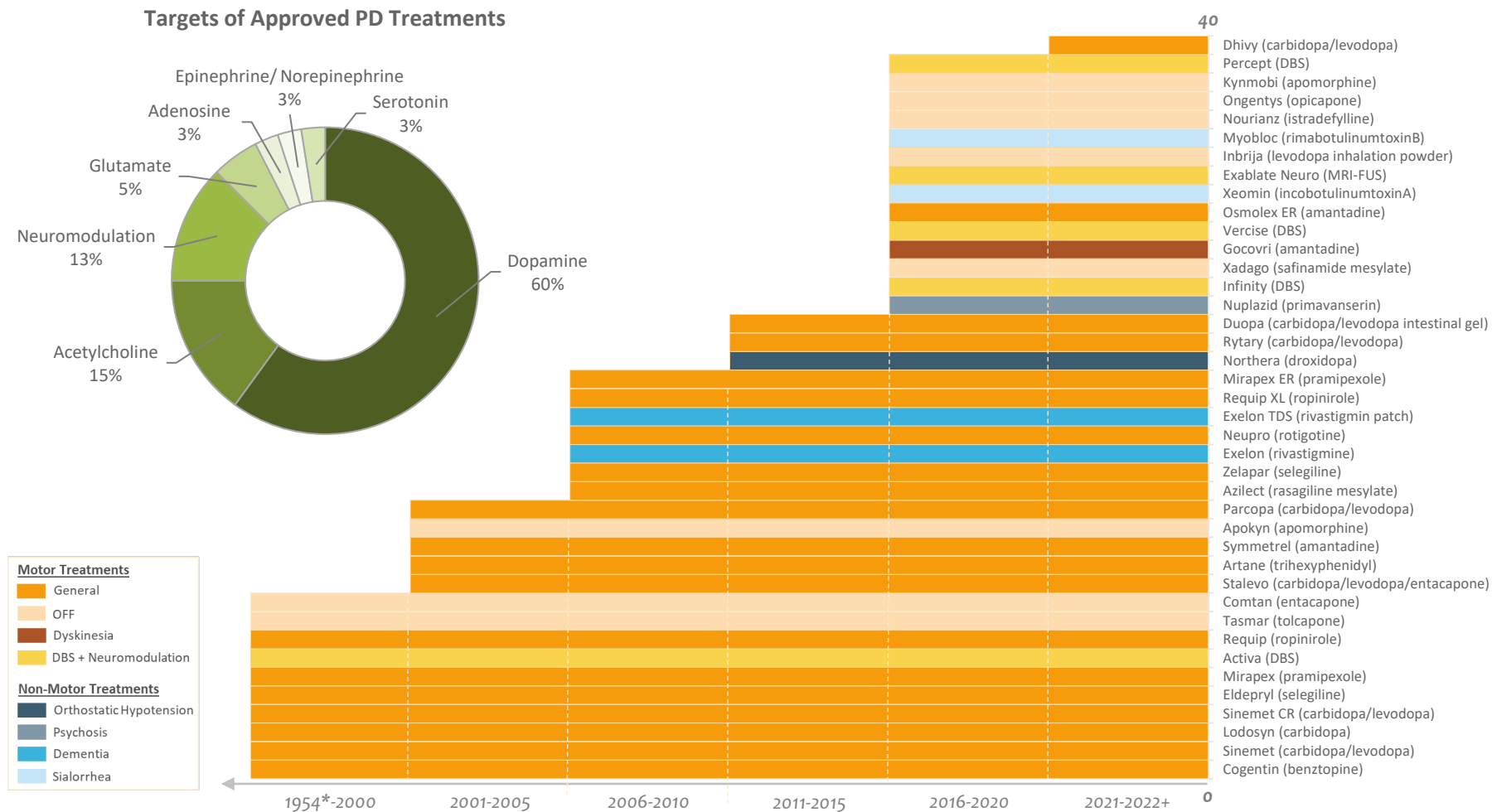
Clinical Programs by Target and Trial Stage



¹Excludes medical devices/neuromodulation, hypoxia therapy, and other non-biomedical therapies

APPROVED THERAPIES

As the clinical pipeline grows, we hope to see new and diverse therapies reach market and move into the hands of the patient. Below is a visual overview of Parkinson's drug approvals in the United States and an overview of those approved treatments by target



Total cumulative number of approved Parkinson's therapies over time with more than 30 drugs indicated for Parkinson's disease or related symptoms as of this report. Note that some treatments such as Xeomin and Myobloc are approved for general symptoms but were tested in a Parkinson's population and shown to have benefit. Several older drugs such as Eldepryl (Selegiline) and Symmetrel (Amantadine) have been discontinued, although there are generic and/or reformulation versions available on market.

*first therapy approved for Parkinson's



Parkinson's Priority Therapeutic Areas

TREATMENTS TARGETING ALPHA-SYNUCLEIN

Therapeutic Rationale

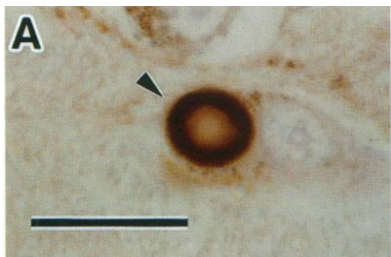
Genetic and pathological evidence strongly supports a critical role of the alpha-synuclein (aSyn) protein in PD. Presence of aSyn-containing aggregates called “Lewy bodies” (see image below) within certain brain cells of almost all people with PD—and evidence that this pathology may spread from cell to cell—provides strong rationale for seeking treatments that can target the production, spread and/or clearance of this abnormal toxic form of the protein.

Current Landscape & Looking Ahead

Treatments seek to target aSyn pathology in multiple ways. Some leverage the immune system and antibodies to specifically remove abnormal aSyn. Others target cellular mechanisms involved in handling or clearing aSyn or seek to reduce spread of aSyn pathology from cell to cell. Several leading programs are moving through mid (Phase 2) and advanced (Phase 3) testing.

MJFF Perspective and Role

Given its potentially central role in PD pathogenesis, MJFF’s efforts are multi-layered and seek to translate a diverse range of aSyn therapeutics into the clinic. Moreover, the Foundation has robust efforts in developing biomarkers and imaging methods for measuring aSyn that could support improved diagnosis, disease subtyping and measures of therapeutic target engagement. One particularly promising measurement is seen with advances in so-called aSyn seeding amplification assays (see right).



One of the first images published from the brain of a Parkinson’s patient of a Lewy body chemically stained to visualize the alpha-synuclein protein (Baba et al., *American Journal of Pathology* 1998)

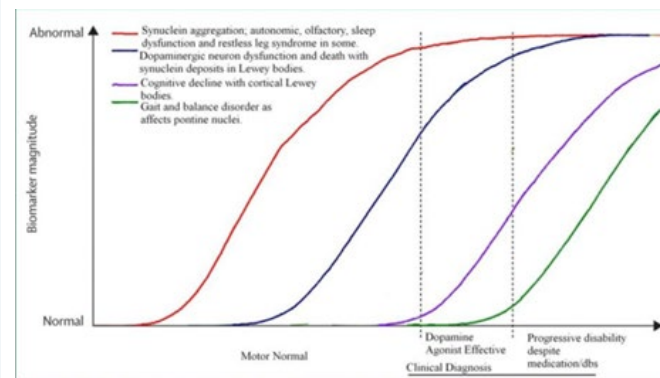
α -Synuclein seed amplification assay (SAA)

Accurate aSyn biomarkers are critically needed to identify individuals in early stages of α -synucleinopathy, for accurate diagnosis, and for target engagement of aSyn-targeted therapies.

α -Synuclein SAA is a novel biomarker that distinguishes PD from controls and reflects underlying pathology. This is a robust diagnostic tool that can reduce the time needed to diagnose Parkinson’s disease, help ensure biologic homogeneity in PD clinical trials and act as an enrichment tool for trials.

Results from a Parkinson’s Progression Markers Initiative (PPMI) study evaluating aSyn SAA performance in CSF samples from a large cohort of patients with PD, individuals at-risk for PD and healthy controls (n=1145) confirm that a-syn SAA accurately differentiates PD patients from healthy controls (see *Andrew Siderowf, et al. 2022. Zenodo. https://doi.org/10.5281/zenodo.7004865*).

Almost all prodromal PPMI participant with either hyposmia or RBD, plus DAT deficit were SAA positive, suggesting this is an early biomarker of disease pathology that precedes onsets of PD motor symptoms. Together, these results have important implications for how we think about the earliest stages of PD as well as how we may improve clinical trial design.

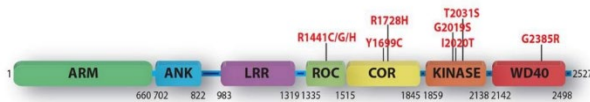


The ability to measure aSyn seeding offers the potential to capture some of the earliest progression stages of PD, possibly before the onset of dopamine cell loss and prior to the onset of the symptoms of PD

TREATMENTS TARGETING LRRK2

Therapeutic Rationale

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene explain 1-40% of cases of PD depending on the population studied. LRRK2 is a 'kinase': a protein that chemically modifies other proteins in the cell to regulate cellular processes, such as the endolysosomal pathway, a system critical for transporting, recycling and degrading cellular components. PD-associated mutations appear to increase this activity, although how this causes neurodegeneration is not known. Whether abnormal LRRK2 activity may explain cases of PD in people without mutations is an area of active investigation.



A schematic of the LRRK2 protein showing some of the most important mutations linked to PD (Image from Steger et al., eLife 2016.)

Current Landscape & Looking Ahead

Programs in clinical testing seek to reduce LRRK2's pathological function either by inhibiting its kinase activity or reducing production of the LRRK2 protein. Drug makers are testing benefits of inhibiting LRRK2 in people both with and without genetic mutations in the hope of exploring wider use of such approaches. The LRRK2 pipeline continues to grow as companies bring additional programs into clinical testing.

MJFF perspective

With strong genetic links to PD and compelling therapeutic rationale, MJFF has been a consistent supporter and funder of studies to facilitate translation of LRRK2 research into treatments for people with PD. MJFF uses highly collaborative models to support work around key challenges and barriers to progress (e.g., biomarkers, safety assessments, patient recruitment challenges) which have been instrumental in fueling the growing number of LRRK2 therapeutic programs in development.

TREATMENTS TARGETING GBA1

Therapeutic Rationale

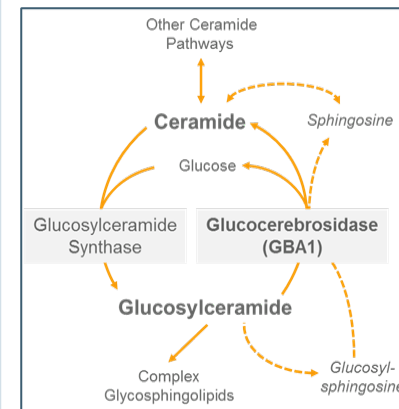
Genetic variation in the GBA1 gene are common risk factors for PD. The protein encoded by the gene (known as glucocerebrosidase or "GCase") regulates metabolism of important lipid molecules in cells, but when dysfunctional may lead to toxic accumulation of these lipids. Mutations in GBA1 are also linked to Gaucher disease and people with this disorder are at higher risk for PD. PD patients with GBA1-associated gene changes often have an earlier age of disease onset, more frequent cognitive issues and may progress more rapidly. Whether altered GCase activity explains PD cases without GBA1 mutations is an area of active study.

Current Landscape & Looking Ahead

Drug makers are primarily seeking to enhance GCase activity or reduce accumulated lipids as potential ways of treating this form of PD. Approaches include using gene therapy to deliver functional copies of the gene or using small molecule drugs to enhance GCase activity.

MJFF perspective

MJFF efforts have focused on identifying factors that may influence GCase and its impact on the lysosomal pathway. Through this work, the Foundation hopes to nominate additional targets with therapeutic potential and refine patient enrichment strategies for identifying people at-risk for this form of PD.

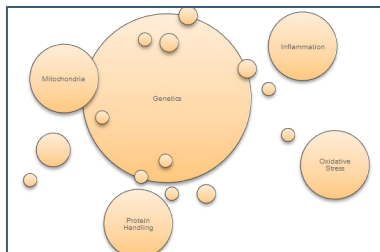


Schematic of the complex lipid pathway in which GBA1 functions. Impaired GBA1 can lead to accumulation of glucosylceramide which may underlie toxicity in Parkinson's disease in people with this impairment.

OTHER TREATMENTS TARGETING DISEASE BIOLOGY

Therapeutic Rationale

Increased understanding of biological processes disrupted in PD—including data from genetic studies—points to a host of molecular targets and pathways that could offer hope for slowing disease. Cellular mechanisms linked to mitochondrial function, oxidative stress, inflammation and processes involved in handling and degrading misfolded proteins all represent promising avenues for therapeutic development.



A range of biological factors may influence the cause and progression of PD and are areas of active research and treatment development.

Current Landscape & Looking Ahead

A robust pipeline of drugs are targeting various hypothesized mechanisms contributing to PD. Quite often, investigators test so-called ‘repurposed’ therapies: therapies approved for other indications which are then tried in a new disease such as PD. As these treatments already have safety and other data, they can often be moved quickly into clinical testing. However, these approaches can also be challenging to interpret as drugs may have variety of effects. As biological understanding of PD improves, companies can develop more targeted and optimized therapies.

MJFF perspective

MJFF supports work to expand biological understanding of PD (including implementation of ASAP initiatives like the Collaborative Research Network and the Global Parkinson’s Genetics Program). With this insight, we then seek to validate emerging targets and novel therapeutic approaches. A major challenge in advancing drugs against these mechanisms is lack of pathway-specific biomarkers that can help inform patient stratification and therapeutic’s target engagement, making interpretation of trial results challenging. This also drives major effort from MJFF to discover and validate better measurement of disease biology.

CELL REPAIR AND REPLACEMENT

Therapeutic Rationale

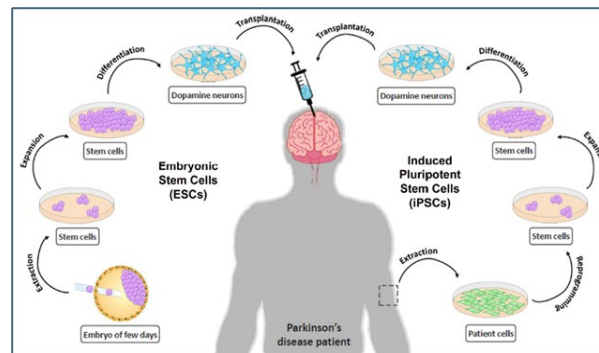
The isolation of human stem cells in the late 1990s led to an explosion of research to generate replacement cells for disorders like Parkinson’s disease. Moreover, identification of growth factors (natural chemical ‘fertilizer’ important for growing brain cells) have also pointed to ways to possibly protect or restore brain regions impacted by Parkinson’s disease. These approaches are generally agnostic to disease cause making them potentially beneficial to all people with Parkinson’s.

Current Landscape & Looking Ahead

Early trials with fetal tissue transplantation or delivery of growth factors were not successful, but newer approaches using improved methods and advanced technologies are underway to either protect and repair existing cells or replace damaged dopamine cells which may improve motor function. A major challenge is that some clinics are offering unregulated ‘stem cell therapies’ directly to patients with limited information on what is being delivered or long-term safety and benefits. (For this report, MJFF monitors programs reporting clinical trials but are unable to monitor these unregulated clinics.)

MJFF perspective

With newer programs entering the clinic, MJFF is closely monitoring progress and opportunistically supporting studies that may inform this promising pipeline.



Two major approaches to replacing lost dopamine cells in Parkinson’s disease using cells derived from different types of stem cells (image from <https://bit.ly/2GInjv>)

TREATMENTS TO ADDRESS MOTOR SYMPTOMS

Therapeutic Rationale

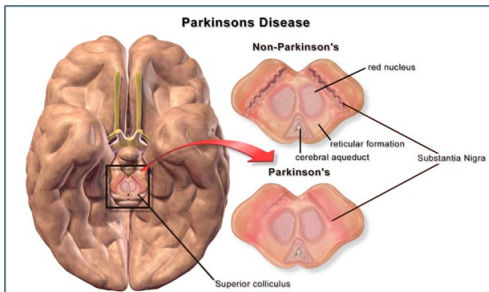
Slow movement, limb rigidity and rest tremor represent early diagnostic symptom hallmarks of PD. Additional challenges with posture, gait and balance may also exist. Loss of dopamine-producing neurons in the substantia nigra region of the brain are a primary (although not entire) cause of many of these movement-related symptoms. This discovery led to the use of dopamine replacement—in particular levodopa—as first-line therapy for people with Parkinson’s.

Current Landscape & Looking Ahead

A major focus of the pipeline is to optimize delivery of dopamine medications to address issues that arise as the disease advances (e.g., sudden OFF periods and dyskinesias). Other brain chemicals involved in regulating aspects of movement are also increasingly being explored (glutamate, serotonin, etc.). Surgical interventions such as deep brain stimulation (DBS) or Focused Ultrasound remain an option for some at later stages of disease and continue to be optimized. (See separate summary in this report.) Some late-stage (Phase 3) dopamine-targeting programs with positive, clinically meaningful results, are in discussion with FDA for approval.

MJFF perspective

Motor impairment remains a key driver of PD symptom management. Addressing more complicated motor symptoms such as gait disturbances (e.g., balance issues linked to falls, freezing) is still a challenging unmet need and focus of MJFF. Advances in use of technology (including DBS) offers new ways to address these symptoms.

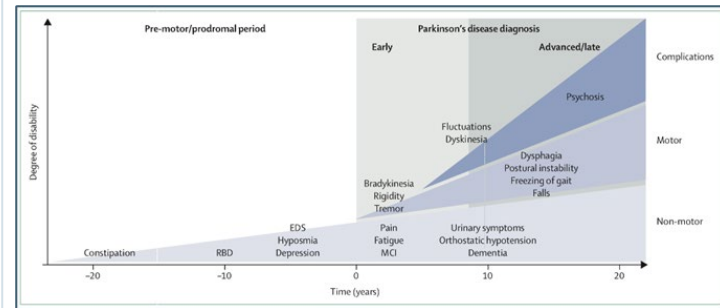


Loss of dopamine cells in the substantia nigra underlie Parkinson’s motor symptoms (image <https://bit.ly/2BV03XH>)

TREATMENTS TO ADDRESS NON-MOTOR SYMPTOMS

Therapeutic Rationale

While motor symptoms are a primary feature of PD, non-motor symptoms are often the most burdensome. These symptoms include cognitive impairment and dementia, psychiatric challenges, mood disorders, sleep issues and constipation, to name a few. Not everyone exhibits all symptoms or suffers them at the same time during the disease course which points to the complex nature of PD. Moreover, the underlying pathology leading to these non-motor symptoms is often less understood, hindering new treatment development.



Timing and diversity of non-motor symptoms represent an important aspect impacting quality of life for people with Parkinson’s disease. (Image from Kalia et al., Lancet 2015)

Current Landscape & Looking Ahead

Treating non-motor symptoms has historically been through use of existing medicines that target these symptoms non-specifically. In recent years, approvals for drugs to treat PD-specific non-motor features such as psychosis (Nuplazid) and orthostatic hypotension (Northera) reveal a growing interest among companies to develop drugs for these critical needs. Therapies targeting cognitive issues are a common focus in the pipeline, but potential treatments for a variety of mood disorders and psychological/mental health symptoms are also being explored. Many of these treatments focus on non-dopamine brain chemical signaling pathways (e.g., acetylcholine, serotonin, etc).

MJFF perspective

Understanding and treating non-motor features such as cognitive changes is an important focus for MJFF. Support seeks to advance trial designs as well as clinical outcome assessments and measures.

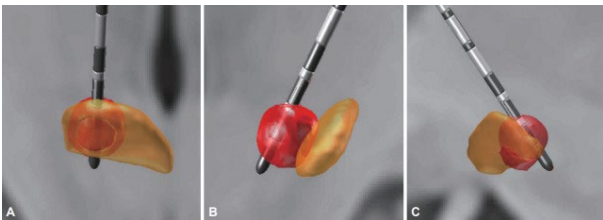
NEUROMODULATION

Therapeutic Rationale

Over time, standard medications may become less effective at controlling symptoms or associate with increasingly disabling complications, such as dyskinesia. Approaches to directly target abnormal brain activity can offer alternative options for people with PD.

Current Landscape & Looking Ahead

Deep brain stimulation (DBS) is a leading approved treatment option for some patients and can reduce medication requirements. By surgically implanting electrodes to stimulate specific brain regions and adjusting this stimulation, a trained clinician can help people improve motor function. In addition, focused ultrasound (FUS) ablation therapy may also improve function by lesioning (with focused sound waves) a small part of the brain circuitry impacted by PD. Both DBS and FUS continue to be optimized in ways to improve possible benefits to people with PD, including exploring their use in earlier stages of the disease, creating ‘smarter’ DBS that can dynamically respond to someone’s clinical state, or assessing impact on non-motor features. In addition, a variety of other neuromodulatory approaches (e.g., various electrical or magnetic stimulation strategies) are being explored that may offer less-invasive ways to target brain activity.



Some researchers are exploring better ways to direct DBS stimulation in the brain to improve ability to impact symptoms (Paff M, et. al. J Mov Disord. 2020 Sep;13(3):185-198.

MJFF perspective

MJFF has supported research to advance novel DBS systems and programming as well as supporting earlier clinical exploration of FUS. For this report, we have included examples of studies MJFF has funded but have not tracked all studies exploring neuromodulation given the breadth and complexity of this pipeline.

TECHNOLOGY-ENABLED THERAPIES

Therapeutic Rationale

The use of digital health technologies is emerging as an important part of medical care and research. These technologies refer to a wide range of applications, such as wearable devices, smartphone applications and other technology-enabled solutions to improve existing care and rehabilitative therapy or to assist people in minimizing the impact of symptoms.

Current Landscape & Looking Ahead

A growing number of groups are testing technologies to improve motor (e.g., cueing devices improving freezing of gait) and non-motor symptoms (e.g., adapting healthy sleep patterns with light therapy), support the delivery of care for a more personalized on-demand intervention (e.g., speech training applications) or optimize clinical and/or self-care management (e.g., medication adherence smartphone applications). Based on the intended use and associated risk of those therapies, regulatory requirement and clinical development paths can vary. Importantly, clinical adoption and utility of these technologies remains an open question, requiring more real-world data to be collected.



Digital Closed Loop Gait Training Therapeutic (Ellis TD, Earhart GM, 2021;11(s1):S95-S101. doi: 10.3233/JPD-202407. PMID: 33646177; PMCID: PMC8292155.











MJFF perspective

MJFF supports better use of technology for treatment and measurement of PD and monitors this sector to better understand the utility of these technologies, regulatory and policy challenges, and infrastructures needed to utilize these new types of therapies. While we do not formally track all technologies in clinical testing, we include a few MJFF-funded programs in this report.



Parkinson's Priority Program Pipelines


ALPHA-SYNUCLEIN


Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Alterity Therapeutics	ATH-434 ¹	aSyn disaggregator		Progression	1	\$	Phase 1 trial pending
BioArctic	BAN-0805 ²	aSyn disaggregator		Progression	1	-	Phase 2 trial pending
AstraZeneca & Takeda	MEDI-1341/ TAK-341	aSyn disaggregator		Progression	1	-	Phase 1 results pending
UCB	UCB-7853	aSyn disaggregator		Progression	1	-	Phase 1 results pending Q3 2023
Vaxxinity	UB-312	aSyn disaggregator		Progression	1	\$	Phase 1 results pending H1 2023
ABL Bio & Sanofi	ABL-301	aSyn inhibitor		Progression	1	-	Phase 1 results pending H2 2023
Janssen Pharmaceutical	YTX-7739 ³	Stearoyl-CoA desaturase + aSyn toxicity inhibitor		Progression	1	\$	Pending update following acquisition
AC Immune	ACI-7104	aSyn disaggregator		Progression	1b	\$	Update on planned phase 2 trial in H2 2023
MODAG & Teva	Anle-138b	aSyn disaggregator		Progression	1b	\$	Phase 1b results pending H1 2023
Novartis & UCB	UCB-0599	aSyn inhibitor		Progression	2a	\$, Other	Phase 2a results pending H2 2024

¹MSA prioritized for initial development. Future plans include proof-of-concept study in PD.

²AbbVie terminated collaboration with BioArctic on aSyn portfolio despite Phase 1 results supporting continued development of ABBV-0805. BioArctic is currently seeking partners.

³YTX-7739, previously a Yumanity program, was acquired by Janssen Pharmaceutical in 2022.

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 







^aHashed cells represent programs that are new to MJFF monitoring or have made advances since the last report. Discontinued programs (shaded grey) and pending programs can be found in the appendix.

^bRoles include direct funding at any stage of development (\$ = historical, \$ = active) or additional support (Other) such as recruitment or protocol advice. While not every company receives direct funding or other support, MJFF continuously engages with companies to understand challenges/opportunities, and this may not be fully reflected in this report.

^cDates of expected results are estimates derived from publicly available press releases or estimated study completion dates.


ALPHA-SYNUCLEIN CONT'D


Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Enterin	Kenterin ¹ (ENT-01)	aSyn inhibitor		Cognition/Dementia	1	-	Phase 2a trial pending 2023
				Psychosis	1	-	Phase 2a trial pending 2023
				Constipation	2b	-	Pending update
Prothena & Roche	Prasinezumab	aSyn disaggregator		Progression	2b	Other	Phase 2b topline results pending 2024
University of Tübingen	Prasinezumab ²	aSyn disaggregator		Cognition/Dementia	2b	\$	Phase 2b trial launch pending Q4 2023
Annovis Bio	Buntanetap ³ (ANVS-401)	Amyloid + tau + aSyn inhibitor ³		Progression	3	\$	Phase 3 interim analysis pending Q2 2023

¹Development for specific PD symptoms, potential effect on overall disease progression

²Investigator initiated study is testing Prasinezumab (Roche's aSyn disaggregator mAb) in patients with GBA mutations to evaluate effectiveness in cognition. Study is planned to start recruitment in Q4 2023.

³Annovis ANVS-401 currently has potential to target multiple proteins, including aSyn, to improve axonal transport.


Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage






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LRRK2

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Biogen	BIIB-094	LRRK2 gene expression inhibitor (Antisense oligonucleotides)	Other	Progression	1	\$, Other	Phase 1 results pending Q4 2023-Q1 2024
Neuron23	NEU-723	LRRK2 kinase inhibitor		Progression	1	-	Phase 1 results pending Q3 2023
Denali & Biogen	DNL-151/ BIIB-122	LRRK2 kinase inhibitor		Progression	3	Other	Phase 3 results pending 2031

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage








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GBA1

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Bial Biotech	BIA 28-6156/ LTI-291	Glucocerebrosidase enhancer		Progression	1	\$, Other	Pending update
Prevail Therapeutics (Eli Lilly) & Regenxbio	PR-001	GCase restoration		Progression	1 2	Other	Phase 1/2 results pending 2028
IRCCS National Neurological Institute	Ambroxol	Glucocerebrosidase enhancer		Progression	2	-	Phase 2 results pending Q2-Q3 2024
Lawson Health Research Institute	Ambroxol	Glucocerebrosidase enhancer		Progression	2	-	Phase 2 results pending Q4 2023 - Q1 2024
University College, London	Ambroxol	Glucocerebrosidase enhancer		Progression	2	-	Phase 3 trial launch pending H2 2023

MITOCHONDRIAL IMPAIRMENT

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Sheffield Teaching Hospital	Ursodiol (UDCA)	Mitochondrial enhancer		Progression	2	\$	Phase 2 results - primary endpoint not met. Publication pending

Vaccine 

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Peptide 

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OXIDATIVE STRESS

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
University of Florida & NINDS	Exenatide	GLP-1 agonist		Progression	1	-	Phase 1 results pending
Radbound University	Hypoxia Therapy	Hypoxic preconditioning	Other	Progression	1	2	Phase 1 results pending Q2 2023 Phase 2a trial launch pending Q3 2023
FASciate Therapeutics (Kainos Medicine)	KM-819	FAF1 antagonist		Progression	2	-	Phase 2 results pending Q4 2025 - Q1 2026
Stockholm Health Care Services	Exenatide	GLP-1 agonist		Progression	2	-	Phase 2 results pending Q4 2023
Cedars-Sinai Medical Center & Novo Nordisk	Liraglutide	GLP-1 agonist		Progression	2	-	Phase 2 positive results. Press release
University Hospital, Toulouse & Sanofi	Lixisenatide	GLP-1 agonist		Progression	2	-	Phase 2 results pending 2023
Neuraly	NLY-01 (pegylated exenatide)	GLP-1 agonist		Progression	2	-	Phase 2 topline results - primary endpoint not met. Further analysis pending. Press release
Invex & Peptron	PT-320 (exenatide SR)	GLP-1 agonist		Progression	2	-	Phase 2 trial ongoing
Oslo University & Novo Nordisk	Semaglutide	GLP-1 agonist		Progression	2	-	Phase 2 results pending Q4 2024 - Q1 2025
Gateway Institute	ISN-GSH (insulin-glutathione)	Insulin receptor agonist + reducing agent		Cognition/Dementia	2	-	Phase 2 results pending H2 2024

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage






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OXIDATIVE STRESS CONT'D

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c	
HealthPartners Institute	Novolin R (intranasal insulin)	Insulin receptor agonist		Multiple Symptoms	2	-	Phase 2 results pending Q3 2023	
Zhejiang University School of Medicine	Idebenone	Reducing agent		Progression	2	3	-	Phase 2/3 results pending H1 2023
University College London	Exenatide	GLP-1 agonist		Progression	3	\$	Phase 3 results pending Q2-Q3 2024	

AUTOPHAGY

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
1 st Biotherapeutics	1 st -102 (FB-101)	c-Abl kinase inhibitor		Progression	1	-	Phase 1 results pending
Inhibikase	ikT-148009	c-Abl kinase inhibitor		Progression	2	\$	Phase 1 positive results Press release Phase 2 results pending Q4 2023
II-Yang Pharmaceutical	Radotinib	c-Abl kinase inhibitor		Progression	2	-	Phase 2 results pending Q2-Q3 2025
SPARC	Vodobatinib (K-0706)	c-Abl kinase inhibitor		Progression	2	Other	Phase 2 results pending H1 2023

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Peptide 

Development Stage











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INFLAMMATION

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Neuramedy Co. Ltd.	NM-101 ¹	Toll-like receptor 2 antagonist		Progression	1	-	Phase 1 trial launch pending Q2 2023
Longevity Biotech	LBT-3627 ¹	Vasoactive intestinal polypeptide agonist		Progression	1	\$	Phase 1 trial pending Q3 2023
The Scripps Research Institute	PDM608 ¹	Granulocyte macrophage colony stimulating factor	Biologic	Progression	1	\$	Phase 1 trial launch pending Q2 2023
Partner Therapeutics	Sargramostim	Granulocyte macrophage colony stimulating factor	Biologic	Progression	1b	-	Phase 1 results pending Q4 2024 - Q1 2025
Roche	RO-7486967	NLRP3 inhibitor		Progression	1b	Other	Phase 1b results pending Q4 2023
BioVie	NE-3107	ERK1/2 inhibitor		Motor Impairment, Progression	1 2	-	Phase 1/2 positive results Press release
Alkahest	GRF-6021 ²	Blood plasma fraction		Cognition/Dementia	2	\$, Other	Pending update
Alkahest	AKST-4290 ²	Chemokine antagonist		Progression	2	\$	Pending update
University of Cambridge	Azathioprine	Immunosuppressant		Progression	2	-	Phase 2 results pending H1 2024
Stockholm Health Care Services	Montelukast	Leukotriene antagonist		Progression	2	-	Phase 2 results pending

¹In preclinical stage, expected to enter Phase 1 in 2023

²No recent updates on development plans following Alkahest acquisition by Grifols in 2021

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage




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MICROBIOME

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a		MJFF Role ^b	Status or Results Expected ^c
University of Texas	PRIM-DJ2727	Fecal microbiota (microbiome modulator)	Other	Motor Impairment	1		-	Phase 1 results pending H1 2023
4D Pharma	MRx-0005 ¹ MRx-0029 ²	Inflammation inhibitor (microbiome modulator)	Other	Progression	1	2	Other	Phase 1/2 trial pending
University of California San Francisco	Rifaximin	Antibiotic		Motor Impairment	1	2	-	Phase 1/2 results pending Q4 2023-Q1 2024
Medical University of Warsaw	Fecal transfer	Fecal microbiota (microbiome modulator)	Other	Motor Impairment, Progression	1	2	-	Phase 1/2 results pending Q4 2024-Q1 2025

^{1,2}In preclinical stage, expected to enter Phase 1 in 2023

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 













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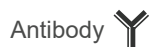
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CELL REPAIR

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c	
Taiwan Mitochondrial Applied Technology Co.	MitoCell ¹	Adipose-Derived Mesenchymal Stem Cells		Progression	1	-	Phase 1 trial launch pending H1 2023	
Herantis	HER-096 ¹ (xCDNF)	CDNF agonist		Progression	1	-	Phase 1 trial launch pending H1 2023	
InnoMedica	Talineuren (GM1)	Neural regeneration	Other	Progression	1	-	Phase 1 pending update	
Hebei Newtherapy Bio-Pharma	Allogeneic MSCs	Umbilical cord-derived mesenchymal stem cells		Progression	1	-	Phase 1 results pending	
IMAC Holdings	MSCTC-0010	Umbilical cord-derived mesenchymal stem cells		Bradykinesia	1	-	Phase 1 results pending	
Asklepios Bio (Bayer)	AAV2-GDNF	GDNF agonist		Progression	1b	-	Phase 1b results pending Q2-Q3 2027	
Herantis	HER-902 (rhCDNF)	CDNF agonist		Progression	1	2	Other	Pending update
University of Texas	Allogeneic MSCs	Bone marrow-derived mesenchymal stem cell		Progression	2a	\$	Phase 2a results pending H2 2023	
Hope Biosciences	HB-adMSC	Adipose-derived mesenchymal stem cells		Progression	2	-	Phase 2 results pending Q2-Q3 2023	
Athira Pharma	ATH-1017	HGF agonist		Cognition/Dementia	2	Other	Phase 2 results pending Q2 2023	
Living Cell Technologies	NTCell	Pig choroid plexus cells		Progression	2b	-	Phase 3 trial pending H1 2024	

¹In preclinical stage, expected to enter Phase 1 in 2023



Development Stage









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CELL REPLACEMENT

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
BlueRock Therapeutics	MSK-DA01	Dopamine cell replacement (derived from hESCs)		Motor Impairment	1	\$	Phase 1 interim results pending Q3-Q4 2023
Region Skåne, Lund University & University of Cambridge	STEM-PD	Dopamine cell replacement (derived from hESCs)		Motor Impairment	1	-	Phase 1 results pending 2027
International Stem Cell Corporation	ISC-hpNSC	Dopamine cell replacement (derived from hPSCs)		Motor Impairment	1	-	Pending update
ASU-Banner Neuro Research Center	Allogeneic DA progenitor cells ¹	Dopamine cell replacement (derived from iPSCs)		Progression	1b	\$	Phase 1b trial launch pending Q2 2023
Aspen Neuro	ANPD-001 ¹	Dopamine cell replacement (derived from iPSCs)		Progression	1 2	-	Phase 1/2 trial pending
Kyoto University & Sumitomo Dainippon	iPSC-DA Transplants	Dopamine cell replacement (derived from iPSCs)		Motor Impairment	1 2	\$	Phase 1/2 results pending Q4 2023 - Q1 2024 U.S. trial pending 2024

¹In preclinical stage, expected to enter Phase 1 in 2023

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 












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DOPAMINE

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Dizlin Pharmaceuticals	Infudopa (LD/CD)	Dopamine receptor agonist		Motor Impairment	1	-	Pending update
Lundbeck	Lu-AF28996	Dopamine receptor agonist		Motor Impairment, OFF	1	-	Phase 1 results pending Q3-Q4 2023
Serina Therapeutics	SER-214 (rotigotine)	Dopamine receptor agonist		Motor Impairment	1	-	Phase 1 results pending
Luye Pharma Group	LY-03009	Dopamine stimulation		Motor Impairment	1	-	Pending next trial
UCB	UCB-0022	D1 positive allosteric modulators D1 PAM		Motor Impairment	1	-	Phase 1 results pending H1 2023
Guangzhou Henovcom Bioscience	HNC-364	MAO-B		Motor Impairment	1	-	Phase 1 results pending Q2 2023
Sinopia Biosciences	SB-0110 ¹	Dopamine receptor pathway modulator		Dyskinesia, Motor Impairment	1b	\$	Phase 1b trial launch pending Q2 2023
University Hospital, Lille & InBrain Pharma	A-dopamine	Dopamine receptor agonist		Motor Impairment	1 2	-	Phase 1/2 results pending Q3-Q4 2023
Oxford BioMedica	AXO-Lenti-PD ²	Dopamine synthesis		Motor Impairment	1 2	Other	Pending update

¹SB-0110 is in preclinical stage, expected to enter Phase 1 in 2023

²Sio Gene Therapies discontinued development in 2022 after several manufacturing and development challenges. Rights were returned to Oxford BioMedica, who plans to out-license the program to a suitable partner

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage













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DOPAMINE CONT'D

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Chase Therapeutics	CTC-413 (pramipexole ER)	Dopamine receptor agonist, NK-1 receptor antagonist		Motor Impairment, Progression	2	-	Phase 2 results pending Q4 2023 - Q1 2024
SynAgile	DopaFuse (CD/LD)	Dopamine receptor agonist		Motor Impairment	2	-	Phase 2 positive topline results Press release
Intrance Medical Systems	Lecigon ¹ (CD/LD/entacapone pump)	Dopamine agonist, COMT inhibitor		Motor Impairment	2	-	Phase 3 trial pending
Eli Lilly	Mevidalen ² (LY-3154207)	Dopamine receptor agonist		Cognition/Dementia	2	Other	Pending next trial
PureIMS	PIMS-703 (inhaled levodopa)	Dopamine receptor agonist		OFF	2	-	Pending update
Cerevance	CVN-424	Dopamine signaling modulator		Motor Impairment, OFF	2	-	Phase 2/3 trial launch pending Q2 2023
Kissei Pharma & Affamed	KDT-3594	Dopamine receptor agonist		Motor Impairment	2b	-	Ongoing phase 2b trial
IRLAB Therapeutics & Ipsen	Mesdopetam (IRL-790)	Dopamine receptor antagonist		Dyskinesia	2b	-	Phase 2b topline results - primary endpoint not met; Further analysis pending Press release
Luye Pharma Group	LY-03003 (rotigotine ER)	Dopamine receptor agonist		Motor Impairment	3	-	Pending update
Neuroderm (MT Pharma)	ND-0612 (CD/LD pump)	Dopamine receptor agonist		Motor Impairment	3	\$, Other	Phase 3 positive results Press release

¹Lecigon is available across Europe. Currently awaiting FDA approval to initiate pivotal Phase 3 trial in the US

²Development is indicated for Symptomatic LBD. Previous trials have included LBD associated with idiopathic PD

Vaccine 

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DOPAMINE CONT'D

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Cerevel Therapeutics	Tavapadon (PF-06649751)	Dopamine receptor agonist		Motor Impairment	3	Other	Phase 3 results pending Q2-Q3 2024
Pharma Two B	P2B-001 (pramipexole /rasagiline)	Dopamine agonist, MAO-B inhibitor		Motor Impairment	3	-	Phase 3 positive results Press release
AbbVie	ABBV-951 (LCD/LDP infusion)	Dopamine receptor agonist		Motor Impairment	3	-	Negative NDA decision, resubmission pending Press release
Amneal	IPX-203 (CD/LD)	Dopamine receptor agonist		Motor Impairment	3	-	NDA decision pending Q3 2023
Supernus Pharmaceuticals	SPN-830 (apomorphine infusion)	Dopamine receptor agonist		OFF	3	-	Negative NDA decision, resubmission pending Press release

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage







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ACETYLCHOLINE

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
University of Queensland	Levetiracetam	Acetylcholine receptor agonist		Cognition/Dementia	2	-	Phase 2 results pending Q4 2023 - Q1 2024
Takeda	TAK-071	Muscarinic M1 receptor agonist		Cognition/Dementia, Gait/Balance	2	\$, Other	Phase 2 results pending H1 2023
Anavex Life Sciences	Blarcamesine (ANAVEX-2-73)	Sigma-1 receptor agonist, Acetylcholine receptor antagonist		Cognition/Dementia, Progression	2	\$, Other	Phase 2 positive results Press release
NHS & University of Bristol	Rivastigmine	Acetylcholinesterase inhibitor		Gait/Balance	3	-	Phase 3 results pending Q4 2023

CANNABINOIDS

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Parkinson's UK & King's College London	Cannabidiol (CBD)	Cannabinoid receptor agonist		Psychosis	2	-	Phase 2 results pending Q1 2024
University of Colorado	Cannabidiol (CBD)	Cannabinoid receptor agonist		Motor Impairment	2	-	Phase 2 results pending
University Health Network, Toronto	Cannabis Oil	Cannabinoid receptor agonist		Pain	2	-	Phase 2 results pending H1 2023


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Small Molecule 

Cell/Tissue Therapy 

Peptide 





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GABA

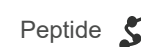
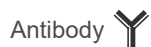
Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Sage Therapeutics & Biogen	SAGE-324 ¹	GABAA receptor agonist		Motor Impairment	1	-	Pending next trial
MeiraGTx	AAV-GAD	Glutamate decarboxylase stimulant		Motor Impairment	1 2	\$, Other	Phase 1/2 results pending H1 2024

¹Ongoing Phase 2 in essential tremor, next steps for further clinical development in PD pending

GLUTAMATE

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Appello Pharma	AP-472	Glutamate receptor agonist		Dyskinesia, Motor Impairment	1a	\$	Pending update
VistaGen	AV-101	AMPA receptor agonist, NMDA antagonist		Dyskinesia	1b	-	Phase 1b results pending H1 2023
Sage Therapeutics	SAGE-718	NMDA receptor agonist		Cognition/Dementia	2	Other	Phase 2 results pending Q3-Q4 2023
BrainX Corporation	Ceftriaxone	Cell wall synthesis inhibitor		Cognition/Dementia	2	-	Phase 2 results pending Q4 2023 - Q1 2024
Yale University	Ketamine	NMDA receptor antagonist		Depression	2	\$	Phase 2 results pending H2 2024
Pharmather	PT-001 (Ketamine)	NMDA receptor antagonist		Dyskinesia	2	-	Phase 3 trial pending
Addex Therapeutics	Dipraglurant (ADX-48621)	Glutamate receptor antagonist		Dyskinesia	2 3	\$	Pending update
Wayne State University	Memantine ¹	NMDA receptor antagonist		Progression	3	-	Phase 3 results pending Q3 2023

¹Possible aSyn transmission inhibition









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EPINEPHRINE/NOREPINEPHRINE

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
University of Iowa	Terazosin	Alpha-1 adrenergic antagonist		Progression	1	\$	Phase 1 results pending H1 2023
Cedars-Sinai Medical Center	Terazosin	Alpha-1 adrenergic antagonist		Progression	2	-	Phase 2 results pending Q4 2025-Q1 2026
CuraSen Therapeutics	CST-2032	Adrenoreceptor agonist		Cognition/Dementia	2a	-	Phase 2a results pending Q4 2023 - Q1 2024
Cedars-Sinai Medical Center	Carvedilol	Adrenoreceptor antagonist (putative antioxidant actions)		Progression	2	-	Phase 2 results pending Q2 2023
CuraSen Therapeutics	Clenbuterol (CST-103)	Adrenoreceptor agonist		Multiple Symptoms, Progression	2	-	Phase 2 positive topline results Press release
IRLAB Therapeutics	Pirepemat (IRL-752)	Adrenoreceptor antagonist, Serotonin antagonist		Cognition/Dementia, Gait/Balance	2b	-	Phase 2b topline results pending H1 2024

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage












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^cDates of expected results are estimates derived from publicly available press releases or estimated study completion dates.

SEROTONIN


Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Sumitomo Dainippon (DS Pharma)	DSP-9632P	Serotonin receptor agonist		Dyskinesia	1	-	Phase 1 results pending H2 2023
Neurolinx	Befiradol (NLX-112)	Serotonin receptor agonist		Dyskinesia	2a	\$, Other	Phase 2a positive results Press release
Vanda Pharma	Fanapt (Iloperidone)	Dopamine antagonist; Serotonin antagonist		Psychosis	2	-	Phase 2 results pending Q4 2023
Silo Pharma & UCSF	Psilocybin	Serotonin receptor agonist		Anxiety, Depression	2	-	Phase 2 results pending Q2-Q3 2023
University College, London	Ondansetron	Serotonin receptor antagonist		Hallucinations	2	-	Phase 2 results pending H1 2025
University Hospital of Strasbourg	Pimavanserin (Nuplazid)	Serotonin receptor antagonist		Impulse	2	-	Phase 2 results pending Q3 2023
University of Michigan & NIA	Citalopram	Serotonin reuptake inhibitor		Cognition/Dementia, Progression	2	-	Phase 2 results pending H2 2025
Silo Pharma & Maastricht University	Ketamine & Psilocybin	NMDA receptor antagonist; Serotonin receptor agonist		Cognition/Dementia, Mood	2b	-	Phase 2b trial ongoing
Bukwang Pharmaceutical	JM-010	Serotonin receptor agonist		Dyskinesia	2b	Other	Phase 2b results pending Q4 2023-Q1 2024


Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 







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PHOSPHODIESTERASE

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Celon Pharma	CPL-36	Phosphodiesterase 10A inhibitor		Dyskinesia	2	-	Phase 2 results pending H1 2023
Eisai	Irsonontrine (E-2027)	Phosphodiesterase 9A inhibitor		Cognition/Dementia	2	-	Phase 2 results - primary endpoint not met. Results report
Intra-Cellular Therapies	Lenrispodun (ITI-214)	Phosphodiesterase 1 inhibitor		Motor Impairment	2	\$, Other	Phase 2 results pending Q4 2024-Q1 2025

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage










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OTHER TARGETS

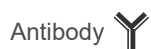
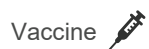
Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
<u>Adenosine</u>							
Kyowa Kirin	Istradefylline (KW-6002)	Adenosine receptor antagonist		Cognition/Dementia	2	-	Phase 2 results pending H2 2025
<u>Nurr1</u>							
NurrOn Pharmaceuticals	ATH-399A ¹	Synthetic ligand of Nurr1 agonists		Progression	1	\$	Phase 1 trial launch pending Q3 2023
<u>Progranulin (PGRN)</u>							
Alector & GSK	AL-101	Sortilin inhibitor		Progression	1a	-	Phase 1a positive results Press release
<u>Other/Multiple</u>							
Digestome Therapeutics	DGX-001	Vagal nerve stimulator		Non-motor Symptoms	1	-	Phase 1 results pending H1 2023
Praxis Precision Medicines	PRAX-944 ²	Calcium channel antagonist		Motor Impairment	1	Other	Phase 2 trial launch pending H1 2023
University of Sydney ³	Alogliptin, Albuterol, Nilvadipine	DPP-4 inhibitor, Calcium channel antagonist, Adrenoreceptor agonist		Motor Impairment, Progression	2	-	Phase 2 results pending
Clene Nanomedicine	CNM-Au8	Gold nanocrystals, bioenergetics	Other	Progression	2	\$	Phase 2 trial pending H1 2023
Jazz Pharma	CX-8998 ⁴	T-type calcium channel antagonist		Motor Impairment	2	-	Phase 2 results pending Q2-Q3 2024

¹ATH-399A is in preclinical stage, expected to enter Phase 1 in 2023

²PRAX-944 is in clinic for essential tremor (ET). Expected to enter Phase 2 for PD in 2023

³Treatments are being studied in parallel as part of a single trial platform effort

⁴Prior Phase 2 trial was withdrawn prior to initiation. New Phase 2 trial initiated in Dec. 2022. For purposes of this report, classifying as moving into clinic and Phase 2 for the first time



Development Stage



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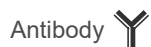
Programs included on this slide represent active MJFF-funded programs supporting technology-enabled therapeutics and neuromodulation and are not a full listing of all approaches currently in development.

DEVICES AND TECHNOLOGIES

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Newel Health	Soturi app	Digital therapeutic for medication optimization	Other	Motor Impairment, Treatment Plan Optimization	2	\$	Phase 2 trial launch pending Q2 2023
Shirley Ryan AbilityLab	Wearable Airbag Technology	Fall detection and mitigation	Other	Motor Impairment	2	\$	Phase 2 results pending Q1 2024
Queensland University of Technology	Photoreceptor Enhanced Light Therapy (PELT)	Melanopsin dysfunction	Other	Motor Impairment, Quality of Life, Sleep	2	\$	Phase 2 results pending H1 2024
Long Island University	Understand Me for Life App	Speech intelligibility app	Other	Speech	2	\$	Phase 2 results pending H1 2026
Sibel Health	ADAM+ platform	Swallowing and drooling digital therapeutic	Other	Dysphagia, Sialorrhea	3	\$	Phase 3 results pending H1 2025

NEUROMODULATION

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
The Regents of the University of California, San Francisco	Bidirectional neurostimulator	Adaptive DBS	Other	Motor Impairment	1	\$	Phase 1 results pending H1 2024
Wake Forest School of Medicine	Brainstem Neuromodulation Device	Non-invasive vestibular stimulation (tvCVS)	Other	Motor Impairment	2	\$	Phase 2 results pending H1 2024
Cleveland Clinic	V-GAIT platform	STN-DBS neural signatures, DBS programming	Other	Motor Impairment	2	\$	Phase 2 results pending H1 2025



Development Stage



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Programs included on this slide represent active MJFF-funded non-pharmacological programs and are not a full listing of all approaches currently in development.

OTHER NON-PHARMACOLOGICAL

Sponsor	Therapeutic	Mechanism	Approach	Indication	Stage ^a	MJFF Role ^b	Status or Results Expected ^c
Leiden University Medical Center	Head-up tilt during sleep (HUTS)	Autonomic dysfunction	Other	Orthostatic Hypotension, Supine Hypertension	2	\$	Phase 2 results pending H1 2024

Vaccine 

Antibody 

Gene Therapy 

Small Molecule 

Cell/Tissue Therapy 

Peptide 

Development Stage



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Appendix

PENDING AND DISCONTINUED PROGRAMS

Programs included on the following slides have been removed from active monitoring due to lack of progress, uncertainty in current development status or announced discontinuation. Trials will be removed from this section after one year if there are no additional updates (press release, website update, etc.). If further development can be confirmed, a program will be moved back to the main section of this report.

Sponsor	Therapeutic	Indication	Stage ^a	MJFF Role ^b	Status
<u>Industry</u>					
Cortexyme	Atuzaginstat (COR-388)	Progression	1	-	Development discontinued. FDA placed a clinical hold on COR-388 and company announced any future development will be in other indications
Alexza Pharmaceuticals	AZ-009 (apomorphine)	OFF	1	-	No updates on development or next steps since completion of phase 1 trial in 3/2020
Biogen	BIIB-118	Sleep	1	-	Development discontinued based on strategic review
Collaborative Medicinal	Cu(II)ATSM	Progression	1	\$	Active development for ALS but no significant progress in PD since 2019. Further activity in PD possible, but assume development has been deprioritized
Sunovion	DSP-6745	Psychosis	1	Other	Development discontinued
E-Scape Bio	ESB-1609	Progression	1	-	Development discontinued (<i>company ceasing operations</i>)
International Stem Cell Corporation	ISC-hpNSC	Motor Impairment	1	-	No recent update on next steps. Phase 1 trial ended in 6/2020
Lundbeck	Lu-AF82422	Progression	1	-	MSA has been prioritized with no immediate plans for continued development in PD
Adhera Therapeutics	MLR-1019 (armesocarb)	Dyskinesia	1	-	No update since press release regarding planned 2021 phase 2 trial
Nobilis Therapeutics	NBTX-001 (Xenon gas)	Anxiety, Energy, Pain	1	-	Phase 1 trial was expected to end in 12/2021 and is likely completed. No update since 2021
Neuropore	NPT-520-34	Progression	1	-	Phase 1 trial completed in 2019. No update since press release stating intent for exploring another study in 1/2020.
PTC Therapeutics	PTC-857	Progression	1	-	Completed Phase 1 trial, prioritizing PTC-857 as a treatment for ALS, no further development plans for PD GBA

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PENDING AND DISCONTINUED PROGRAMS

Sponsor	Therapeutic	Indication	Stage ^a	MJFF Role ^b	Status
<u>Industry</u>					
Atlantic Healthcare	Renzapride (ATL-1251)	Gastroparesis	1	-	No update since listed as Phase 1 on company pipeline in 2020
RaQualia Pharma	RQ-10	Constipation	1	\$	No further clinical development in multiple years; interest in out-licensing compound for additional studies
King's College London & AstraZeneca	Saracatinib	Psychosis	1	-	No recent updates – assume development has been deprioritized
XW Pharma	Valiloxylate (XW-10172)	Sleep	1	-	No update since announcing plans for Phase 2 trial in 2021 press release
Xoc Pharmaceuticals	XC-130	Motor Impairment	1	-	Phase 1 trial was expected to close in 4/2022 but no update since 9/2021
AstraZeneca & King's College London	AZD-0328	Cognition/Dementia	2a	\$	Phase 2 trial was terminated prior to recruitment start. No further development planned
Impel NeuroPharma	INP-107 (CD/LD)	Motor Impairment, OFF	2a	-	No recent updates. Planned study in 3/2022 did not start. Completion of Phase 1 trial in 2019
Theranexus	THN-102 (flecainide/modafinil)	Sleep	2a	-	Development discontinued after failure to find potential partner for development
Seelos Therapeutics	Aplindore (SLS-006)	Motor Impairment	2		Not in active development. Company continuing to evaluate next steps
B&A Therapeutics	Bumetanide	Gait/Balance, Motor Impairment	2	-	Development discontinued (<i>company ceasing operations</i>)
Cortexyme	Atuzaginstat (COR-388)	Progression	2	-	No update since completion of phase 2 trial in 2019
Alexza Pharmaceuticals	AZ-009 (apomorphine)	OFF	2	\$	Vivifi is seeking out partners to move towards another trial as of October 2022
Aptinyx	NYX-458	Cognition/Dementia	2	Other	Negative read-out of phase 2 in February 2023 - program discontinued

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PENDING AND DISCONTINUED PROGRAMS

Sponsor	Therapeutic	Indication	Stage ^a	MJFF Role ^b	Status	
<i>Industry</i>						
Sunovion	Ulotaront (SEP-363856)	Psychosis	2	Other	Phase 2 study completed in 2020. No updates on next steps for PD psychosis - schizophrenia appears to be prioritized	
Kyowa	KW-6356	Motor Impairment	2b	-	Development discontinued	
B&A Therapeutics	Bumetanide	Gait/Balance, Motor Impairment	2	-	Development discontinued (<i>company ceasing operations</i>)	
<i>Academic & Research Institutions</i>						
NIH/NINDS	AAV2-GDNF	Progression	1	-	Phase 1 trial completed in 2/2022, but no updates on results or next steps are currently available	
University of Minnesota	Ursodiol (UDCA)	Progression	1	-	Found to be reasonably safe and well tolerated, but small cohort (n=5) and variable pharmacokinetic results. Suggested larger studies needed to gather additional clinical data, but did not indicate plans to do so	
University of Jordan	Allogeneic MSCs	Multiple Symptoms	1	2	-	Phase 1/2 trial was supposed to end in 2021 and is likely complete. No update since 2021
NINDS	Flumazenil	Motor Impairment	1	2	-	No updates on next steps. Phase 1/2 trials ended in 2021
Hospices Civils de Lyon	Clonidine	Impulse	2	-	Last phase 2 trial was completed in 2021, but no results or next steps shared	

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