

Molecular target	Mechanism of action	Drug(s)	Mode of Administration	Primary outcomes	Current status
Neuroinflammation	Inhibition of microglial activation	Minocycline	Oral	Time to initiation of symptomatic pharmaceutical treatment	Negative Phase 2 trial; NCT00063193
	Altered T-cell lineage	Sargramostim	Intravenous	Safety & tolerability	Completed & ongoing Phase 1 trials; NCT01882010 NCT03790670
	Enzyme myeloperoxidase (MPO) inhibition	AZD3241	Oral	Safety & tolerability Pharmacokinetics PET binding	Ongoing Phase 2 trials; NCT01603069 NCT01457807 NCT01527695
	NLR family pyrin domain containing 3" (NLRP3) inflammasome inhibition	Inzomelid	Oral	Safety & tolerability, Pharmacokinetics & Pharmacodynamics	Completed (results pending) Phase 1 trial; NCT04015076
	3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) inhibition	Simvastatin	Oral	MDS-UPDRS part III (OFF)	Ongoing phase 2 trial; NCT02787590
	Inhibition of nucleic acid synthesis, reduced lymphocyte proliferation	Azathioprine	Oral	MDS-UPDRS part III (OFF)	Ongoing phase 2 trial; EudraCT Number: 2018-003089-14
Alpha-Synuclein	Inhibition of α -synuclein aggregation	Nilotinib	Oral	Safety & tolerability	Phase 2 trial Completed; NCT02954978

	(autophagy-cAbl inhibitors)	Nilotinib	Oral	Safety & tolerability/ MDS-UPDRS Part III	Phase 2 trial Completed negative; NCT03205488
		Radotinib	Oral	Safety & tolerability	Phase 2 trial Completed; NCT04691661
		K0706	Oral	Safety & tolerability	Ongoing Phase 2 trial; NCT03655236
Insulin resistance	GLP-1 receptor agonists (reduced insulin resistance, reduced inflammation and alpha-synuclein aggregation)	Exenatide	Subcutaneous injections	MDS-UPDRS Part 3	Ongoing Phase 3 trial; NCT04232969 Ongoing Phase 2; NCT04154072
		NLY01		MDS-UPDRS Part 2 +3	
		Liraglutide	Subcutaneous injections	MDS-UPDRS Part 3, NMSS& MADRS-2	Ongoing Phase 2 trial; NCT02953665
		Lixisenatide	Subcutaneous injections	MDS-UPDRS Part 3	Ongoing Phase 2 trial; NCT03439943
		Semaglutide	Subcutaneous injections	MDS-UPDRS Part 3 OFF medication	Ongoing Phase 2 trial; NCT03659682
Gut microbiota	Altered gut microbiota population	Faecal microbiota transplantation	Naso-jenjunal		Ongoing Phase 2 trial; NCT03808389
Neurotrophic factors	GDNF	GDNF	Bilateral stereotactic putaminal injections	Safety & tolerability/ MDS-UPDRS Part III	Phase 2 trial Completed;

					NCT03652363
		Recombinant-Methionyl Human GDNF	Continuous implanted catheter putaminal infusion	Safety & tolerability	Phase 1 trial Completed; NCT00006488
		AAV2-GDNF	Bilateral stereotactic putaminal injections	Safety & tolerability	Phase 1 trial Completed; NCT01621581
				Safety & tolerability	Ongoing Phase 1 trial; NCT04167540
		Neurturin (AAV2-neurturin/CER E-120)	Bilateral stereotactic putaminal injections	Safety & tolerability	Phase 1 Completed; NCT00252850
				MDS-UPDRS Part III	Phase 1 Completed; NCT00252850
					Phase 2 Completed negative; NCT00400634
	CDNF	GDNF homologue	Continuous implanted catheter putaminal infusion	Safety & tolerability	Phase 1 Completed; NCT03775538
				Safety & tolerability	
				Safety & tolerability	Phase 1 Completed; NCT03295786

					Phase 1+2 Ongoing; NCT04228653
	PDGF	sNN0031	Intracerebroventricular infusion	Safety & tolerability	Phase 1+2 Completed; NCT00866502

Table 1 Summary of clinical trials exploring different novel therapeutic targets