Table S1. Influence of novel drugs targets for treatment of Alzheimer disease.

Targets	Class Type	Compounds	Direct and indirect effects	Publications/Clinical Trials
Amyloid-Beta and excitotoxicity	AChE inhibitors	Donepezil, Galantamine, Rivastigmine	Improvement in memory and cognitive and impairment as well as behaviour impairment	68
		Tacrine derivates (KT2D)	Neuroprotection against Aβ	70, 75
	NMDAR antagonist	Memantine	↓ Excitotoxicity, improvement in memory and cognitive impairment	68
		Sirt1 enhancer (A03)	↑ Sirt1 expression and memory improvement	78, 79, 80, 81, 82, 83, 84
	Immunotherapy (IMT)	Gantenerumab	Passive Immunization by ↓ Aβ spreading and aggregation, ↑ microglial activation and ↑ phagocytosis	71, 72 NCT03443973, NCT03444870, NCT02051608, NCT01224106, NCT01760005
		Crenezumab	Passive Immunization by ↓ Aβ spreading and aggregation, ↑ microglial activation and ↑ phagocytosis	71, 72, 73, NCT02353598, NCT01998841, NCT02670083, NCT03443973, NCT03491150),
		Aducanumab	Passive Immunization by ↓ Aβ spreading and aggregation, ↑ microglial activation and ↑ phagocytosis	71,72, NCT01677572, NCT02484547, NCT02477800, NCT03639987
	ETB receptor agonist	IRL-1620	↑ Clearance of ET-1 and Aβ, ↓ oxidative stress, ↑ neurogenesis and synaptogenesis improve memory deficiency	69, 91, 92, 93, 94
Mitochondria	Dopamine derived structure	DDQ	↑ Mitochondrial biogenesis, ↑ Mitochondrial fusion activity, ↓ mitochondrial fission activity, ↓ Aβ toxicity	95
Autophagy	CRMP2 modulator	LKE	Normalization of CRMP2 phosphorylation, ↓ Aβ-plaques load, ↓ phosphorylated tau, ↑ growth factor-dependent neurite outgrowth as well as autophagy related processes	99, 100
	Cyclin-dependent kinase modulator	Cdk5 inhibitors	↑ Autophagy by ↓ CRMP2 hyper-phosphorylation	103, 104
Neuroinflammation	Tetracycline antibiotic	Minocycline	↓ Proinflammatory (TNF-α and IL-1β)and ↑ anti-inflammatory cytokines (IL-10)	109
Neurogenesis and neuronal survival	Ciliary Neurotophic factor	P021	Inhibition of LIF signalling and ↑ the BDNF expression; ↑ neurogenesis by rescuing dendritic, synaptic and cognitive impairment; ↓ Aβ and tau mediated aggregation	110
	Natural disaccharide	Trehalose	↓ Aβ aggregation, ↑ hippocampal neurogenesis and synaptic plasticity, ↑ neuronal growth and survival	75, 111, 112, 113, 114
	Type II anti-diabetic	Metformin	↑ neurogenesis, ↓ oxidative stress, ↓ cognitive impairment	68, 116
	Allopregnanolones	BR297	↑ steroidogenesis, improving mitochondrial bioenergetics by ↑ cellular ATP production and ↓ oxidative stress, Preventing neuronal cell death	120, 121, 122
	Nurr1 activators	amodiaquine	↑ Dopaminergic neurogenesis, ↑ hippocampal neurogenesis ↓ Aβ plaques deposition, ↓ neuronal loss & microglia activation	207, 219
Metal ions homeostasis	Cu^{2+}, Zn^{2+}, Fe^{3+} chelators	PBT1 and PBT2	↓ Aβ-plaques load and ↓ cognitive impairment	65, 66, 117
	AChE inhibitor	BPT derivatives	Inhibition of Cu^{2+}- and Fe^{3+}-mediated Aβ aggregation	74, 75
	Fe2+ chelators	DFO	↓ α-Syn- and Aβ-mediated-iron load, ↓ cognitive impairment	117

Arrows indicates; (↑), increase and (↓), decrease. All abbreviation are explained in text.

Table S2. Influence of novel drugs targets for treatment of Parkinson's disease.

Targets	Compounds	Direct and indirect effects	Publications/Clinical Trials
α-Syn and LRRK2	Antisense oligonucleotides	↓ α-Syn synthesis and ↓ LRRK2 synthesis	129, 213
	DLN201	Inhibition of LRRK2 kinase activity	NCT03710707
	GZ/SAR40261	GCS inhibitor, ↑ α-Syn degradation and ↑ lysosomal activity	130, NCT02906020
	Ambroxol	GBA activator, ↑ α-Syn degradation, ↑ lysosomal activity	NCT02941822
	Caspase-1 inhibitor	↓ C-terminal truncation and ↓ α-Syn cleavage and toxicity	132, 133
	Anle138 and SynuClean-D	Stabilization of α-Syn structure and prevention oligomerization by ↓ α-Syn misfolding and aggregation	134
	NTP200-11		NCT02906020
	Nilotinib	Inhibition of c-Abl kinase activity, ↓ α-Syn aggregation	136, NCT03205488
	PRX002 and BIIB054	Passive Immunization by ↓ α-Syn spreading	NCT02157714, NCT03318523
	PD01A and PD03A	Active Immunization by ↓ α-Syn spreading	NCT02216188, NCT02267434
Mitochondria	STI-571	↑ Parkin-mediated mitophagy	144
	NIX	Mitochondrial autophagy receptor Nip3-like protein X restores mitophagy	140
	USP30 inhibitors	↑ Parkin-mediated mitophagy	147
	BG12	↑ Mitochondrial biogenesis by activation of Nrf2	148
	Quercetin	↑ Mitochondrial biogenesis by activation of PGC1α	150, 151
Autophagy	TFEB	↑ Autophagy	160, 162, 163
	KYP-2047	↑ Beclin-1 mediated autophagy by inhibition of PREP	168
	PLGA-aNPs	↑ Autophagy by ↑ lysosomal activity	169
	NCGC607	↑ Autophagy by ↑ chaperone-GCase mediated lysosomal activity	165, 170, 171
Ca^{2+} homeostasis	Israpidine	Inhibition of Ca^{2+} channels, ↓ mitochondrial oxidative stress	173, 175, NCT02168842
Neuroinflammation	Maxadilan	↑ PACAP activity by cAMP, ↓ microglial pro-inflammatory cytokines	180, 181, 182
	S14	PDE7 inhibition, ↑ adult neurogenesis and ↑ anti-inflammatory responses	185, 186, 187, 209
	Glitazones derivatives	↑ PPARγ activation, ↑ neuroprotection, ↓ microglial pro-inflammatory cytokines	189, 190, 191, 192, 193
Neurogenesis and neuronal survival	CDNF and MANF	Protection and repair of dopaminergic neurons	202, NCT03775538
	PDGF-BB	↑ Dopaminergic neurogenesis in the subventricular zone	205, 206
	Nurr1 activators	↑ Dopaminergic neurogenesis, ↑ hippocampal neurogenesis ↓ Aβ plaques deposition, ↓ neuronal loss & microglia activation	207, 219
	CREB activator (Rolipram)	↑ Dopamine neurogenesis by ↑ of dendritic outgrowth	208
	Tideglusib	↑ Neurogenesis in the dentate gyrus of the hippocampus by inhibition of GSK-3	210
	IPS cells transplantation	↑ Dopaminergic cells	211
Metal ions homeostasis	PBT1 and PBT2	Cu^{2+}, Zn^{2+}, Fe^{3+} chelators; ↓ Aβ-plaques load and ↓ cognitive impairment	65, 66, 117
	DFO and DFP	Fe^{2+} chelators, ↓ α-Syn- and Aβ-mediated-iron load, ↓ motor & cognitive impairment	117

Arrows indicates; (↑), increase and (↓), decrease. All abbreviations are explained in text.