

CLAIMS

1. Use of a monoclonal antibody capable of specifically binding to human alpha-synuclein, wherein said antibody binds an epitope within amino acids 112-117 (**SEQ ID NO:9** (ILEDMP)) of human alpha-synuclein (**SEQ ID NO:10**), or antigen-binding
5 fragment thereof that binds said epitope, wherein the antibody, or antigen-binding fragment thereof is selected from the group consisting of antibody (1)-(15):

Antibody (1) or an antigen-binding fragment thereof, comprises:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
(b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:2**;
10 (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
(d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
(e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
(f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**;

- 15 Antibody (2) comprises the heavy chain variable domain of **SEQ ID NO:7** or the light chain variable domain of **SEQ ID NO:8**;

Antibody (3) comprises a heavy chain consisting of a variable domain of **SEQ ID NO:7** and a light chain consisting of a variable domain of **SEQ ID NO:8**;

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Antibody (4) or an antigen-binding fragment thereof, comprises:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
(b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:33**;
(c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
25 (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
(e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
(f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**;

- 30 Antibody (5) comprises the heavy chain variable domain of **SEQ ID NO:30** or the light chain variable domain of **SEQ ID NO:8**;

Antibody (6) comprises a heavy chain consisting of a variable domain of **SEQ ID NO:30** and a light chain consisting of a variable domain of **SEQ ID NO:8**;

- Antibody (7) or an antigen-binding fragment thereof, comprises:
- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
 - (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:34**;
 - 5 (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
 - (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
 - (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
 - (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**;
- 10 Antibody (8) comprises the heavy chain variable domain of **SEQ ID NO:31** or the light chain variable domain of **SEQ ID NO:8**;
- Antibody (9) comprises a heavy chain consisting of a variable domain of **SEQ ID NO:31** and a variable domain of **SEQ ID NO:8**;
- 15 Antibody (10) or an antigen-binding fragment thereof, comprises:
- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
 - (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:35**;
 - (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
 - 20 (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
 - (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
 - (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**;
- Antibody (11) comprises the heavy chain variable domain of **SEQ ID NO:32** or the light chain variable domain of **SEQ ID NO:8**;
- 25 Antibody (12) comprises a heavy chain consisting of a variable domain of **SEQ ID NO:32** and a variable domain of **SEQ ID NO:8**;
- 30 Antibody (13) or an antigen-binding fragment thereof, comprises:
- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:20**;
 - (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:21**;
 - (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:22**;
 - (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:23**;

- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:24**;
and
(f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:25**;
- 5 Antibody (14) comprises a heavy chain variable domain of **SEQ ID NO:26** or the light chain variable domain of **SEQ ID NO:27**;
- Antibody (15) comprises a heavy chain consisting of a variable domain of **SEQ ID NO:26** and a variable domain of **SEQ ID NO:27**;
- 10 in the manufacture of a medicament for treatment together with an additional medicament selected from the group comprising dopamine, caspase inhibitors, calpain inhibitors, LRRK2 inhibitors, BACE1 inhibitors, aggregation inhibitors, antibodies against any form of A β peptides, inflammation inhibitors, LAG-3 antibodies, Isradipine, molecules reversing alpha-synuclein induced reduction in
- 15 phagocytic activity of microglia, nicotine, caffeine, modulators of GCase, MAO-B inhibitors, Levodopa/carbidopa, Dopamine agonists, COMT inhibitors and A₂A antagonists wherein said treatment is of Parkinson's disease (including idiopathic and inherited forms of Parkinson's disease), Gauchers Disease (GD), Diffuse Lewy Body Disease (DLBD), Lewy body variant of Alzheimer's disease
- 20 (LBV), Combined Alzheimer's and Parkinson's disease, pure autonomic failure and multiple system atrophy in a subject in need thereof.
2. The use according to claim 1, wherein said additional medicament is selected from the group comprising pramipexole, Pralnacasan, Alicapistat, PF-06447475, NB-360, Neuropore NPT100-18A, NPT200-11, epigallocatechin gallate,
- 25 Bapineuzemab, Solanezumab, Gantenerumab, Crenezumab, Aducanumab, Relatimab, GSK2831781, IMP321, ELN484228, NCGC607, Miglustat, Eliglustat, Rasagiline, Eldepryl, Zelapar, Ropinerole, Bromocriptine, Comtess, Tasmar and Istradefyline, or a pharmaceutically acceptable salt thereof.
3. The use according to any one of the preceding claims, wherein the antibody is a
- 30 human, humanized, recombinant or chimeric antibody.
4. The use according to claim 1, wherein the treatment is chronic.

5. The use according to claim 1, wherein the chronic treatment is for at least 2 weeks.
6. The use according to claim 1, wherein the subject is human.
7. The use according to claims 1-6 wherein said monoclonal antibody and additional medicament are to be administered approximately simultaneously or wherein the medicaments are to be taken separately.
8. A kit comprising an antibody as defined in the previous claims and a medicament selected from the group comprising dopamine, caspase inhibitors, calpain inhibitors, LRRK2 inhibitors, BACE inhibitors, aggregation inhibitors, antibodies against A β , inflammation inhibitors, LAG-3 antibodies, Isradipine, molecules reversing alpha-synuclein induced reduction in phagocytic activity of microglia, nicotine, caffeine, and modulators of GCase, MAO-B inhibitors, Levodopa/carbidopa, Dopamine agonists, COMT inhibitors and A₂A antagonists
9. The kit according to claim 8 wherein said medicament is selected from the group comprising pramipexole, Pralnacasan, Alicapistat, PF-06447475, NB-360, Neuropore NPT100-18A, NPT200-11, epigallocatechin gallate, Bapineuzemab, Solanezumab, Gantenerumab, Crenezumab, Aducanumab, Relatlimab, GSK2831781, IMP321, ELN484228, NCGC607, Miglustat, Eliglustat, Rasagiline, Eldepryl, Zelapar, Ropinerole, Bromocriptine, Comtess, Tasmar and Istradefylin, or a pharmaceutically acceptable salt thereof.

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