# TABLES

**Table 1: General characteristics of clinical trials in DLB as of September 27, 2022**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Clinical trial phase | Number of clinical trials | Status | | | Classification | | Repurposed  Agents |
| Completed | Activea | Other status | DMT | Symptomatic |
| Phase3 | 7 (17.5%) | 6 (86%) | 1 (14%) | 0 | 0 | 7 (100%) | 7 (100%) |
| Phase 2 | 31 (77.5%) | 15 (48.4%) | 8 (25.8%) | 8b (25.8%) | 8 (25.8%) | 23 (74.2%) | 16 (51.6%) |
| Phase 1 | 2 (5%) | 0 | 0 | 2c (100%) | 2 (100%) | 0 | 2 (100%) |
| Total | 40 | 21 (52.5%) | 9 (22.5%) | 10 (27%) | 10 (25%) | 30 (75%) | 25 (65%) |

aRecruiting, Active/not recruiting

bWithdrawn=3, pending=2, not recruiting=2, terminated=1

cnot yet recruiting=2

**Table 2: Agents in phase 3 clinical trials for dementia with Lewy bodies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Agent | CADRO | Mechanism of action | Therapeutic purpose | Status | Registry source | Registry number | Start date | End date\* |
| Memantine | Neurotransmitter Receptors | Noncompetitive, low- to medium-affinity antagonist of NMDA glutamate receptors | Symptomatic | Recruiting | ICTPR | ISRCTN79794378 | March 2022 | April 2025 |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Completed | ICTPR | jRCTs041180125 | October 2017 | December 2020 |
| Pimavanserin | Neurotransmitter Receptors | Antagonist/inverse agonist at serotonin 5-HT2A receptors and less potent antagonist. Inverse agonist actions at 5-HT2C receptors | Symptomatic | Completed | CT.gov and EUdraCT | NCT03325556  2017-002227-13 | September 2017 | October 2019 |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Completed | ICTPR | JapicCTI-152839 | April 2015 | November 2017 |
| Donepezil | Neurotransmitter Receptors | Acetylcholinesterase inhibitor | Symptomatic | Completed | CT.gov and ICTPR | NCT01278407  NCT00598650 | January 2011 | March 2013 |
| Yokukansan (traditional Japanese Kampo medicine) | Multi-target | Prevents neurotoxicity induced by amyloid-associated oxidative stress. Improves glutamate uptake and inhibits glutamate-induced neuronal death. Partial agonistic effect on serotonin 5-HT1A receptors | Symptomatic | Completed | ICTPR | UMIN000001511 | August 2006 | March 2009 |
| Galantamine | Neurotransmitter Receptors | Acetylcholinesterase inhibitor | Symptomatic | Completed | CT.gov and ICTPR | NCT00230997 | December 2002 | August 2004 |

\*End date: actual end date or study completion date

**Table 3: Biomarkers use in clinical trials**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Biomarkers use | |  | Clinical trial phase | | |
| Total | Phase 3 | Phase 2 | Phase 1 |
| Inclusion criteria | DaTSCAN  MIBG  PSG | 5  2  3 |  | 4  2  3 | 1 |
| *Stratification* | Plasma Aβ42/40 ratio  CSF AD biomarkers  Genetic testing for APOE  Genetic testing for GBA | 1  1  1  1 |  | 1  1  1  1 |  |
| Outcome measure | Plasma HVA and DOPAC  Plasma AD biomarkers  Plasma Aβ42/40 ratio  Plasma α-synuclein  Serum ATP | 2  3  1  3  1 |  | 2  2  1  2 | 1  1  1 |
| CSF HVA  CSF DOPAC  CSF AD biomarkers  CSF α-synuclein  CSF cGMP  CSF NSE, S100B, phosphorylated neurofilaments and TREM-2 | 2  1  2  3  2  1 |  | 2  1  1  2  1  1 | 1  1  1 |
| Amyloid PET | 1 |  | 1 |  |
| EEG or qEEG  PSG or videoPSG | 3  2 |  | 3  2 |  |
| DaTSCAN  MIBG  FDG-PET | 2  1  2 | 1 | 2  1 | 1 |
| MRI volumetry  MRI spectroscopy | 2  1 |  | 1 | 1  1 |
| Digital biomarkers | 5 |  | 5 |  |

Abbreviations: DaTSCAN: Dopamine transporter single photon emission computerized tomography, MIBG: iodine-123 metaiodobenzylguanidine myocardial scintigraphy, PSG: polysomnography, Aβ: amyloid-β, AD: Alzheimer’s disease, APOE: apolipoprotein E, GBA: glucosylceramidase β, HVA: homovanillic acid, DOPAC: 3,4-Dihydroxyphenylacetic acid, ATP: adenosine triphosphate, cGMP: cyclic guanosine monophosphate, NSE: neuron-specific enolase, S100B: S100 calcium-binding protein B, TREM-2: triggering receptor expressed on myeloid cells 2, EEG: electroencephalogram, qEEG: quantitative electroencephalogram, PET: positron emission tomography, FDG-PET: fluodeoxiglucose positron emission tomography, MRI: magnetic resonance imaging.

**Table 4: Agents in phase 2 clinical trials for dementia with Lewy bodies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Agent | CADRO | Mechanism of action | Therapeutic purpose | Status | Registry source | Registry number | Start date | End date\* |
| CT1812 | Synaptic Plasticity/Neuroprotection | σ-2 receptor modulator | DMT | Recruiting | CT.gov and ICTPR | NCT05225415 | June 2022 | April 2024 |
| Fosgonimeton (ATH-1017) | Growth factors and hormones | Activates signaling via the hepatocyte growth factor (HGF) | DMT | Recruiting | CT.gov and ICTPR | NCT04831281 | January 2022 | November 2023 |
| Ondansetron | Neurotransmitter Receptors | Selective antagonist of serotonin 5-HT3 receptors | Symptomatic | Recruiting | CT.gov and ICTPR | NCT04167813 | October 2021 | January 2025 |
| CST-103, CST-107 | Neurotransmitter Receptors | CST-103: β-2 adrenoceptor agonist  CST-107: β blocker with minimal brain penetration | Symptomatic | Active, not recruiting | CT.gov, ICTPR, EudraCT | NCT04739423  2020-006067-28 | June 2021 | August 2022 |
| Ambroxol | Proteostasis/Proteinopathies | Increases lysosomal fraction and the enzymatic activity of glucocerebrosidase | DMT | Recruiting | CT.gov and EUdraCT | NCT04588285  2019-002855-41 | May 2021 | December 2023 |
| Irsenontrine | Synaptic Plasticity/Neuroprotection | Active and selective phosphodiesterase 9 (PDE9) inhibitor | Symptomatic | Completed | CT.gov and ICTPR | NCT04764669 | February 2021 | January 2022 |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Not recruiting | ICTPR | jRCTs041190126 | February 2021 | Missing data |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Not recruiting | ICTPR | jRCTs051200054 | September 2020 | Missing data |
| NYX-458 | Neurotransmitter Receptors | NMDAR receptor modulator that enhances synaptic plasticity | Symptomatic | Recruiting | CT.gov and ICTPR | NCT04148391 | November 2019 | December 2022 |
| Neflamapimod | Synaptic Plasticity/Neuroprotection | ATP competitive inhibitor of p38α kinase | DMT | Completed | CT.gov and EUdraCT | NCT04001517  2019-001566-15 | September 2019 | June 2020 |
| Nilotinib | Proteostasis/Proteinopathies | Tyrosine kinase inhibitor | DMT | Recruiting | CT.gov and ICTPR | NCT04002674 | July 2019 | April 2023 |
| HTL0018318 | Neurotransmitter Receptors | Selective muscarinic M1 receptor partial agonist | Symptomatic | Withdrawn | CT.gov and ICTPR | NCT03592862  JapicCTI-183989 | July 2019 | September 2019 |
| Bosutinib | Proteostasis/Proteinopathies | Tyrosine kinase inhibitor | DMT | Completed | CT.gov and ICTPR | NCT03888222 | April 2019 | April 2021 |
| Irsenontrine | Synaptic Plasticity/Neuroprotection | Active and selective phosphodiesterase 9 (PDE9) inhibitor | Symptomatic | Completed | CT.gov, ICTPR, EudraCT | NCT03467152  JapicCTI-183932  2017-003728-64 | May 2018 | April 2020 |
| LY3154207 (Mevidalen) | Neurotransmitter Receptors | Positive allosteric modulator of the dopamine receptor D1 | Symptomatic | Completed | CT.gov and ICTPR | NCT03305809 | November 2017 | July 2020 |
| Intepirdine | Neurotransmitter Receptors | Selective 5-HT6 receptor antagonist | Symptomatic | Completed | CT.gov and ICTPR | NCT02910102 | October 2016 | November 2017 |
| Vodobatinib (K0706) | Proteostasis/Proteinopathies | Tyrosine kinase inhibitor | DMT | Recruiting | CT.gov and ICTPR | NCT03996460 | September 2016 | October 2023 |
| Galantamine | Neurotransmitter Receptors | Acetylcholinesterase inhibitor | Symptomatic | Pending | ICTPR | UMIN000022860 | September 2016 | Missing data |
| Nelotanserin | Neurotransmitter Receptors | Selective antagonist of the 5-HT2A serotonin receptor | Symptomatic | Completed | CT.gov and ICTPR | NCT02708186 | March 2016 | May 2018 |
| Intepirdine | Neurotransmitter Receptors | Selective 5-HT6 receptor antagonist | Symptomatic | Completed | CT.gov, ICTPR, EudraCT | NCT02669433  2015-005495-19 | January 2016 | December 2017 |
| Nelotanserin | Neurotransmitter Receptors | Selective antagonist of the 5-HT2A serotonin receptor | Symptomatic | Completed | CT.gov and ICTPR | NCT02640729 | December 2015 | November 2017 |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Completed | ICTPR | JapicCTI-122040 | March 2013 | April 2014 |
| Zonisamide | Neurotransmitter Receptors | Sulfonamide, antiseizure. Inhibitor of sodium and T-type calcium channels. Potentiates dopaminergic and serotonergic neurotransmission | Symptomatic | Completed | ICTPR | UMIN000010631 | September 2012 | May 2013 |
| Ferulic acid | Oxidative Stress | Suppresses free radicals, chronic inflammation and aggregation of amyloid-β protein in the brain | Symptomatic | Completed | ICTPR | UMIN000003683 | June 2010 | May 2013 |
| Armodafinil | Unknown target | Unknown/Eugeroics: stimulants that provide long-lasting mental arousal | Symptomatic | Withdrawn | CT.gov and ICTPR | NCT01256905 | January 2011 | August 2011 |
| Youkukansan | Multi-target | Prevents neurotoxicity induced by amyloid-associated oxidative stress. Improves glutamate uptake and inhibits glutamate-induced neuronal death. Partial agonistic effect on serotonin 5-HT1A receptors | Symptomatic | Missing data | ICTPR | UMIN000001832 | April 2009 | Missing data |
| Ramelteon | Neurotransmitter Receptors | Agonist of MT1 and MT2 melatonin receptors | Symptomatic | Withdrawn | CT.gov and ICTPR | NCT00907595 | May 2009 | July 2010 |
| Ramelteon | Neurotransmitter Receptors | Agonist of MT1 and MT2 melatonin receptors | Symptomatic | Terminated | CT.gov | NCT00745030 | June 2008 | December 2009 |
| Donepezil | Neurotransmitter Receptors | Acetylcholinesterase inhibitor | Symptomatic | Completed | CT.gov and ICTPR | NCT00543855 | November 2007 | February 2010 |
| Memantine | Neurotransmitter Receptors | Antagonist of NMDA glutamate receptors | Symptomatic | Completed | EudraCT and ICTPR | 2005-004109-27  ISRCTN89624516 | March 2006 | September 2008 |
| Memantine | Neurotransmitter Receptors | Antagonist of NMDA glutamate receptors | Symptomatic | Completed | CT.gov and ICTPR | NCT00630500 | February 2006 | March 2009 |

\*End date: actual end date or study completion date

DMT: disease-modifying treatment

**Table 5: Agents in ongoing phase 1 clinical trials for dementia with Lewy bodies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Agent | CADRO | Mechanism of action | Therapeutic purpose | Status | Registry source | Registry number | Start date | End date\* |
| Terazosin | Metabolism and Bioenergetics | α-1 adrenergic receptor blockers | DMT | Not yet recruiting | CT.gov and ICTPR | NCT04760860 | October 2021 | October 2022 |
| Ambroxol | Proteostasis/Proteinopathies | Increases lysosomal fraction and the enzymatic activity of glucocerebrosidase | DMT | Not yet recruiting | CT.gov and ICTPR | NCT04405596 | November 2023 | November 2025 |

\*End date: actual end date or study completion date

DMT: disease-modifying treatment

**Table 6: Global distribution of clinical trials**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Number of continents | Total  N (%) | Recruitment status | | | Therapeutic purpose | |
| Active  N (%) | Completed  N (%) | Other\*  N (%) | Symptomatic  N (%) | DMTs  N (%) |
| 1 continent | 33 (82.5%) | 7 (77.8%) | 16 (76.2%) | 10 (100%) | 24 (80%) | 9 (90%) |
| *Asia* | *13 (32.5%)* | *0* | *8 (38.1%)* | *5 (50%)* | *12* | *1 (10%)* |
| *Europe* | *4 (10%)* | *2 (22.2%)* | *2 (9.5%)* | *0* | *3* | *1 (10%)* |
| *North America* | *16 (40%)* | *5 (55.6)* | *6 (28.6%)* | *5 (50%)* | *9* | *7 (70%)* |
| 2 continents | 5 (12.5%) | 2 (22.2%) | 3 (14.3%) | 0 | 4 (13.3%) | 1 (10%) |
| *Europe and North America* | *2* | *0* | *2* |  | *1* | *1* |
| *Europe and Oceania* | *2* | *2* | *1* |  | *2* |  |
| *North America and Latin America* | *1* | *0* | *0* |  | *1* |  |
| 3 continents | 2 (5%) | 0 | 2 (9.5%) | 0 | 2 (6.7%) | 0 |
| *Asia, Europe and North America* | *1 (2.5%)* |  | *1 (4.75%)* |  | *1 (3.4%)* |  |
| *Europe, North America and Latin America* | *1 (2.5%)* |  | *1 (4.75%)* |  | *1 (3.3%)* |  |

\*Other: Withdrawn: 3 phase 2, Not yet recruiting: 2 phase 1, Not recruiting: 2 phase 2, Missing data: 2 phase 2, Terminated 1 phase 2.

**Table 7: Sponsorship of clinical trials**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Number of continents | Total  N (%) | Recruitment status | | | Therapeutic purpose | | Repurposed  N (%) |
| Active  N (%) | Completed  N (%) | Other\*  N (%) | Symptomatic  N (%) | DMTs  N (%) |
| Academic centers | 21 (52.5%) | 5 (55.6%) | 8 (38.1%) | 8 (80%) | 14 (46.7%) | 7 (70%) | 19 (76%) |
| Biopharma industry | 17 (42.5%) | 3 (33.3%) | 13 (61.9%) | 1 (10%) | 15 (50%) | 2 (20%) | 5 (20%) |
| Public-private partnership | 2 (5%) | 1 (11.1%) | 0 | 1 (10%) | 1 (3.3%) | 1 (10%) | 1 (4%) |