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Artificial Intelligence-Enabled New Drugs Discovery for Neurodegenerative Diseases

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Abstract

To assess the usefulness of artificial intelligence (AI) in developing new drugs against neurodegenerative diseases, a synoptic overview of the main currently available drugs employed against such diseases will be reviewed. The AI platforms used to screen thousands of existing FDA-approved drugs to find "hidden" Alzheimer's treatments as well as the newly discovered molecules currently in clinical trials will subsequently be presented. Further, beyond simply screening compounds, AI-led drug discovery and research will also be outlined. While no AI drug candidates for Alzheimer's have completed the full clinical journey yet, it might only be a matter of time until new solutions are brought to patients.

Abbreviations

AAIC: Alzheimer's Association International Conference; AChE: Acetylcholinesterase; AD: Alzheimer's disease; ADD: Alzheimer's disease dementia; AI: Artificial intelligence; ALS: Amyotrophic lateral sclerosis; ARIA: Amyloid-related imaging abnormalities; BBB: Blood-brain barrier; BChE: Butyrylcholinesterase; DDL: Drug discovery laboratory; DLB: Dementia with Lewy bodies DRIAD: Drug repurposing in AD; FDA: (U.S.) Food & Drug Administration; HD: Huntington's disease; JAKI: Janus kinase inhibitors; MAB: Monoclonal antibodies; MCI: Mild cognitive impairment; MG: Myasthenia gravis; ML: Machine language; MRI: Magnetic resonance imaging; NDD: Neurodegenerative disease; NETTAG: Network topology-based to (disease-) associated genes; PHGDH: Phosphoglycerate dehydrogenase; RBC; Red blood cell; PD: Parkinson's disease: PDD: Parkinson's disease dementia; PET: Positron-emission tomography; PTSD: Post-traumatic stress disorder.

Drugs: Aducanumab (Aduhelm); Amantadine; Bumetanide; Carbidopa; D-cycloserine; Dextromethorphan/quinidine; Deutetrabenazine; Diflunisal; Donanemab; Donepezil (Aricept); D-serine; Edaravone (Radicava); Entacapone; Esketamine;

Galantamine (Razadyne): Istradefylline; Janus kinase inhibitors; Kinsula; Lecanemab (Leqembi); Levodopa; Memantine (Namenda); Opicapone; Pramipexole; Rasagiline; Riluzole; Rivastigmine (Exelon); Ropinirole; Rotigotine; Safinamide; Salsalate; Selegiline; Sildenafil (Viagra); Tetrabenazine; Tofersen.

Diseases mentioned: Alzheimer's disease; Alzheimer's disease dementia; Amyotrophic lateral sclerosis; Dementia with Lewy bodies; Huntington's disease; Myasthenia gravis; Parkinson's disease: Parkinson's disease dementia; Post-traumatic stress disorder; Schizophrenia; Stroke.

Keywords

Alzheimer's disease; Amyloid-related imaging abnormalities; Artificial intelligence; Cholinesterase inhibitors; Drugs repurposing; Drug research; Symptoms-targeting drugs; Disease-modifying drugs; Monoclonal antibodies; NMDA receptor antagonists.

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To assess the usefulness of artificial intelligence (AI) in developing new drugs against neurodegenerative diseases (NDDs), it will be of interest to first provide a synoptic overview of the main currently available drugs employed against such diseases. The AI platforms used to screen thousands of existing FDA-approved drugs to find "hidden" Alzheimer's treatments as well as the newly discovered molecules currently in clinical trials will subsequently be presented.

Currently available drugs

The drugs available today against NDDs generally fall into two broad categories: 1/ Symptoms-targeting drugs, which purport to temporarily improve cognition, movement, mood, or function; and 2/ Disease-modifying therapies, still relatively rare, which attempt to slow the underlying degeneration itself. Speaking of therapy (or treatment or cure) implies that we fully understand the etiology of the disease which, unfortunately, is rarely the case.

Symptoms-targeting drugs

There are two such drug types, cholinesterase inhibitors and NMDA-receptor agonists, as elaborated upon below:

Cholinesterase inhibitors

Acetylcholine, a neurotransmitter, is a chemical that carries signals between nerves and muscles. Cholinesterase is the enzyme that breaks down acetylcholine after neurons communicate and helps stop nerve signals once they have performed their function. In this process, after a signal is sent, cholinesterase quickly destroys acetylcholine, preventing the continuous stimulation of muscles or nerves.

Cholinesterase inhibitors block that enzyme, increasing acetylcholine levels in the brain. They work as shown in Figure 1:

Conceptually:

Acetylcholine ⇒ Acetylcholinesterase
⇒ Breakdown products

After blockade (simplified effect):

Less enzyme activity ⇒ Acetylcholine signaling

Figure 1: How cholinesterase inhibitors work

This can temporarily improve: Memory, attention, alertness, and daily functioning. However, they do not cure neurodegeneration or stop neuron loss.

There are two main types of cholinesterase:

1. Acetylcholinesterase (AChE): It is found in nerve endings and in red blood cells (RBCs) where it plays a key role in nerve function.

2. Butyrylcholinesterase (BChE): It is found mainly in blood plasma and in the liver, where it has a broader, less specific role.

Proper cholinesterase activity is essential for normal muscle movement and brain function. (Note: Some toxins - like nerve agents and certain pesticides - also block cholinesterase, but they may cause dangerous overstimulation of nerves.)

Cholinesterase inhibitor drugs

Cholinesterase inhibitors are drugs that block the enzyme that breaks down acetylcholine, a neurotransmitter important for memory, attention, and learning; they increase acetylcholine signaling in the brain. They are employed mainly in cases of mild-to-moderate cognitive symptoms, mainly in Alzheimer's disease (AD) but sometimes also in Parkinson's disease dementia (PDD), dementia with Lewy bodies (DLB) and occasionally, Myasthenia gravis (MG) (a different use case).

The main cholinesterase inhibitors include:

• **Donepezil (Aricept):** It is most prescribed; once daily dosing; and used in mild, moderate, and severe AD;
• **Galantamine (Razadyne):** It is used in mild-to-moderate AD. It also modulates nicotinic receptors; and
• **Rivastigmine (Exelon):** Available as capsule or skin patch. The patch can reduce gastrointestinal side effects. Rivastigmine is often used in PDD and DLB.

Benefits

Benefits are usually measured over months rather than years. They are modest but apparently clinically meaningful for some patients. They lead to:

- Slight improvement in cognition;
- Slower decline in daily functioning;
- Temporary stabilization of symptoms; and
- Reduced caregiver burden in some cases.

Common side effects

Because acetylcholine also affects the gut and heart, gastrointestinal (GI) effects are the most common side effects and include:

• Nausea;
• Vomiting;
• Diarrhea;
• Loss of appetite;
• Weight loss; and
•Dizziness.

Other side effects include:

• Vivid dreams; and
• Slow heart rate (bradycardia).

Important limitations

These drugs:

• Help symptoms more than the underlying disease;
• Work better earlier in the disease;
• Eventually, lose effectiveness as neurons continue degenerating; and
• The response varies widely between patients.

NMDA receptor antagonists

For neurodegenerative diseases (NDDs), the clinically used drugs are mostly NMDA receptor antagonists, not agonists. The main example is:

• **Memantine (Namenda):** It is often used in moderate-to-severe AD to help cognition and daily functioning. Memantine is a low-affinity, uncompetitive, voltage-

dependent NMDA receptor antagonist, which preferentially blocks excessive receptor activation.

• **Combination (Memantine + Donepezil):** Approved mainly for moderate-to-severe AD.

Benefits

Memantine may modestly improve: Cognition, behavior, daily functioning, and agitation in some patients. Effects are usually moderate rather than dramatic.

Side effects

Common side effects are generally better tolerated than cholinesterase inhibitors and may include:

• Dizziness;
• Confusion;
• Headaches;
• Constipation, and
• Sleep disturbances

Why are antagonists used?

The NMDA receptor is a glutamate receptor which is involved in: Learning, memory, and synaptic plasticity. But excessive activation causes excitotoxicity wherein neurons become damaged from too much calcium influx (Figure 2).

Conceptually:

Excess glutamate ⇒↑ Ca^{2+} influx
⇒ neuronal injury

After blockade (simplified effect):

NMDA blockade ⇒↓ excitotoxicity

Figure 2: How glutamates work

This mechanism is implicated in AD, amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), other NDDs, but also stroke.

So, drugs like Memantine partially block pathological NMDA activity while trying to preserve normal signalling.

Drugs	Diseases	Benefit(s)	Limitation	Side effects	Notes
Cholinesterase inhibitors	AD, PDD, DLB, MG	o Temporary improvement in cognition, memory, attention, alertness o Slower decline in daily functioning o Temporary stabilization of symptoms o Reduction of caregiver burden in some cases	o Help symptoms more than underlying disease o Work better earlier in disease	o Nausea, vomiting, diarrhea, loss of appetite, weight loss; and dizziness. o Other side effects include vivid dreams and slow heart rate (bradycardia).	o Do not cure neurodegeneration or stop neuron loss o Lose effectiveness as neurons continue to degenerate. o Response varies widely between patients
Donepezil	Mild, moderate and severe AD				
Rivastigmine	PDD, LBD				
Galantamine	Mild-to-moderate AD				
NMDA-					

receptor antagonists					
Memantine	Moderate-to-severe AD	Helps cognition and daily functioning			o Involved in learning, memory, and synaptic plasticity o Excessive activation causes excito-toxicity

Table 1: Symptoms-targeting drugs for NDDs

(*Abbreviations*: AD: Alzheimer's disease; LBD: Lewy body dementia; MG: Myasthenia gravis; PDD: Parkinson's disease dementia.)

Ketamine note: Ketamine is also an NMDA antagonist, but it is used primarily for:

• Anesthesia;
• Treatment-resistant depression; and
• Pain management.

NMDA receptor agonists

NMDA agonists (direct or partial) are usually not used in NDDs because excessive NMDA activation can damage neurons. Experimental contexts may involve: Cognitive enhancement research, psychiatric research, and synaptic plasticity studies. Examples include:

• **D-cycloserine (partial agonist/modulator):** Originally an antibiotic, at low doses it acts as a partial agonist at the glycine site of the NMDA receptor. It is studied for: PTSD therapy augmentation, anxiety disorders, exposure therapy enhancement, and cognitive modulation.

• **Glycine-site modulators;** lt also activates the glycine site on NMDA receptors. It is studied for schizophrenia negative symptoms and cognitive dysfunction. The problem is that it has a poor brain penetration; and

• **D-serine:** It acts at the glycine co-agonist site of the NMDA receptor, but these are not standard neurodegenerative therapies.

Mechanism

"NMDA activation requires glutamate + coagonist (glycine/D-serine).

Key concept:

NMDA modulation ⇒↑ synaptic plasticity

Figure 3: How NMDA modulation works

Limitations

• Possible kidney toxicity at high doses; and
• Inconsistent clinical efficacy.

Research areas

• Schizophrenia;
• Cognition enhancement;
• Neuroplasticity; and
• Depression: Use of Esketamine (a derivative of ketamine). Despite being an antagonist rather than agonist, it indirectly increases synaptic plasticity and rapid antidepressant signaling.

Disease-modifying anti-amyloid therapies

Disease-modifying anti-amyloid therapies are a newer class of drugs for AD designed to slow the underlying

disease process rather than only improve symptoms. They mainly target beta-amyloid plaques (those abnormal protein aggregates that accumulate in the brain). They use MABs to bind amyloid and help remove it from the brain (Figure 4).

In the amyloid hypothesis:

β-amyloid accumulation
⇒ synaptic dysfunction
⇒ neurodegeneration

Figure 4: How the amyloid hypothesis works

Earlier controversial example

• **Aducanumab (Aduhelm):** It was the first accelerated FDA approval in this class. It was highly controversial because clinical benefit data were debated. While it demonstrated amyloid removal clearly, whether that translated into meaningful clinical improvement was disputed.

Currently approved major therapies

• **Lecanemab (Leqembi):** It targets soluble amyloid protofibrils. It shows cognitive decline mostly in early AD. It is usually employed in mild cognitive impairment (MCI) due to AD and mild Alzheimer's disease dementia (ADD).
• **Donanemab:** It targets deposited amyloid plaques. Clinical trials have showed clinical reduction in deposited amyloid plaque burden with a slowing of disease progression in selected patients.

Mechanism

These antibodies bind amyloid (Figure 5):

Key concept:

Antibody + β-amyloid

⇒ immune-mediated plaque clearance

Figure 5: How the antibody- beta amyloid works

The microglia (brain immune cells) then help clear the tagged plaques.

Important limitation

These drugs are not cures. They generally slow decline modestly and work best early in the disease but do not restore lost neurons. The benefit is measured statistically over months to years.

Major risk: ARIA

The biggest safety issue is: Amyloid-related imaging abnormalities (ARIA). This includes brain swelling (ARIA-E) and small brain bleeds (ARIA-H). Risk factors include: ApoE ε4 genotype, higher amyloid burden, and anticoagulant use. Patients usually require: MRI monitoring, careful selection, and specialist supervision.

Key trends in the field

The major shift over the last few years has been from purely symptomatic treatment toward: monoclonal antibodies; RNA-targeting drugs; gene therapies; and precision medicine approaches.

Examples include amyloid antibodies in Alzheimer's; antisense oligonucleotides like Tofersen in ALS; and emerging gene-silencing approaches for HD and PD.

These treatments generally slow progression modestly rather than cure the disease, but they represent the first generation of truly mechanism-targeted neurodegenerative therapies.

Monoclonal antibodies

Disease-modifying anti-amyloid therapies are monoclonal antibodies (MABs) that remove beta-amyloid plaques from the brain. It is here implied that these plaques are the root cause of the disease. While this implication has long permeated the field of research and clinical practice, it is now generally believed that it is not correct. In fact, as early as 2017, this author has opined that AD is but a runaway autoimmune disease and that the beta plaques as well as the neurofibrillary tangles (NFTs) - the main hallmarks of AD - are but symptoms or consequences of the disease not its root cause.

As of March 2026, in the U.S., there are only 2 FDA-approved drugs. They are similar and prescribed solely for those patients in the early stages of AD and early stages of dementia. They are not cures but rather treatments for slowing down the symptoms of the disease, essentially to reduce the infamous amyloid-beta plaques in the neuronal cells of the brain.

• **Leqembi (approved in 2023):** It is administered every other week by intravenous or skin injection during approximately 1 hour for a total of 7 infusions (or 14 weeks). The approximate cost of the treatment is (U.S.) $ 35,613 (generally not insurance covered, whether private or governmental insurance). Depending on the results obtained, the treatment may be renewed for indefinite periods.

• **Kinsula (approved in July 2024):** It is administered once every 4 weeks. Treatment duration depends on the results obtained as determined by a positron emission tomography (PET) scan. Treatment is stopped after 6-18 months. The mean annual cost of the treatment is (U.S.) $ 32.000 (cost is less if treatment is stopped earlier) and may purportedly be reimbursed, at least in part by Medicare (this is to be ascertained). Clinical trials have apparently showed an important reduction in cognitive decline.

The risks associated with the above two drugs are similar. They can be serious and are referred to by the acronym ARIA (amyloid-related imaging abnormalities). They consist in temporary oedemas and bleedings of the brain, which can lead to serious and potentially fatal symptoms. This would be in addition to other common risks (headaches, confusion, vertigo, vision troubles, nausea, weakness, loss of speech, tremors).

Before any treatment is contemplated by either Leqembi or Kinsula, it would be important to seriously consider the treatment benefits (apparently minimal) and the potential risks (serious), in addition to the excessive cost of the intervention.

It is a sad (even scandalous) situation for, after more than 125 years since Dr. Alois Alzheimer described the disease associated with his name, the expenditure of tens of billions of dollars worldwide, the conduct of numerous clinical trials, and the publication of thousands of scientific articles … we still do not fully comprehend the pathobiology of the human brain and still have not identified the root cause of the disease and are still timidly treating its symptoms.

Benefits

Clinical trials have showed modest slowing of cognitive decline in early-stage disease.

Important limitation

These drugs require monitoring for brain swelling or bleeding known as ARIA (see below), especially in some genetic risk groups.

AI-led drug discovery and research

AI's capabilities in drug discovery extend beyond simply screening compounds. In fact, AI-based platforms can quickly simulate molecular interactions, assess blood-brain barrier (BBB) permeability, and predict adverse effects, significantly reducing the time and cost traditionally required. While no AI drug candidates for Alzheimer's have completed the full clinical journey yet, it might only be a matter of time until new solutions are brought to patients.

As of 2026, AI-driven drug discovery for AD has moved from the laboratory to human trials, focusing on both repurposed existing drugs or entirely new molecules, thus drastically reducing the time and cost required to find new treatments.

AI-led drug repurposing

AI platforms like DRIAD (Drug repurposing in AD) and NETTAG (Network topology-based to (disease-) associated genes) use machine language (ML) to screen thousands of existing FDA-approved drugs to find "hidden" Alzheimer's treatments, significantly shortening development timelines. Examples include:

• **Janus kinase inhibitors (JAKI):** The DRIAD platform has prioritized these anti-inflammatory drugs as high-potential candidates for modifying AD pathology.

• **Sildenafil (Viagra):** A significant association was identified between Sildenafil usage and a reduced likelihood of AD, which has since been validated in laboratory models.

• **P300/CBP inhibitors (Salsalate and Diflunisal):** Identified via AI analysis of insurance claims from 7.2 million patients, these drugs are associated with decreased AD incidence and have shown neuroprotective effects in mice.

• **Bumetanide:** AI modeling suggests this common diuretic may offer a specific treatment path for patients carrying the ApoE4 risk gene.

New AI-discovered molecules in clinical trials

AI's capabilities in drug discovery extend beyond simply screening compounds. AI-driven drug discovery for AD has moved from the laboratory to human trials, focusing on both repurposed existing drugs and discovering entirely new molecules, thus drastically reducing the time and cost required to find new treatments.

Several novel compounds designed or optimized by AI are currently in active clinical testing or late-stage preclinical development (Table 2):

• **DDL-920 & DDL-218:** Identified by the Drug Discovery Laboratory of the University of California, Los Angeles (UCLA), these molecules target memory circuitry and protective proteins like sirtuin 1. DDL-920 specifically aims to restore "gamma oscillations" that are responsible for cognitive processing.

• **DSP-0038:** Developed using Exscientia Centaur's platform, this AI-designed candidate targets serotonin receptors to treat AD-related psychosis and is currently in clinical testing.

• **FJMU1887:** A brain-penetrant small-molecule (Galectin-3 inhibitor) was identified through AI-based screening. Recent research highlights its potential to reduce neuroinflammation and improve cognitive function by disrupting the Gal-3/TREM2 interaction.

• **ONC-841 (phase1/2 clinical trial NCT06509659):** On April 9, 2026, OncoC4 announced a significant milestone in which it begun dosing the first participant after various stages ranging from early Phase 1 trials to

promising preclinical animal data in a Phase 2 trial. This anti-SIGLEC 10 antibody, originally developed for oncology, was identified for its ability to normalize microglial function and clear pathogenic protein aggregates in the brain. Its expression may contribute directly to the pathogenesis of late-onset AD. The trial's primary objective was to evaluate the safety, tolerability, and preliminary efficacy of ONC-841 in early-stage AD. Preclinical data presented at the Alzheimer's Association International Conference (AAIC) showed that ONC-841 successfully restored the function of microglia (brain immune cells) to clear amyloid plaques and reduce levels of phosphorylated tau in mouse models.

Candidate molecule	AI platform/ lead	Action mechanism	Current stage (early 2026)
Bumetanide	Multiple AI studies	ApoE4-specific diuretic	Repurposing validation
DDL-920	UCLA Drug Discovery Laboratory	Memory circuit restorer	Preclinical
DSP-0038	Exscientia (Centaur Chemist)	Serotonin receptor modulator	Clinical testing for Alzheimer psychosis
FJMU-1887	Llama-Gram model	Galectin-inhibitor	Preclinical/lead compound
ONC-841	OncoC4	o Normalization of microglia (the brain's resident immune cells) normalization o Targets SIGLEC 10, an immune regulation protein	Phase 1/2 clinical trial

Table 2: New AI-discovered molecules in clinical trials

AI-inspired research

• **Protein folding:** Tools like Google's DeepMind's AlphaFold have identified the 3D structures of nearly all human proteins, allowing researchers to design drugs that fit specifically into targets related to AD's pathology.

• **Clinical trials optimization:** AI identifies the best candidates for clinical trials by predicting who is most likely to progress or respond to a treatment, making trials faster and more likely to succeed.

AI-identified next generation biological targets

Researchers are also using AI to find the "next generation" of biological targets beyond traditional amyloid and tau:

***In silico* medicine targets**

Using its PandaOmics model, *In silico* identified targets like MARCKS and CAMKK2 proteins that form abnormal aggregates and represent new pathways for therapeutic intervention.

PHGDH inhibitors for spontaneous AD

About one in nine people aged 65 and older has AD, the most common cause of dementia. While some mutated genes can lead to AD, that connection only accounts for a small percentage of all Alzheimer's patients. Most patients do not have a mutation in a known disease-causing gene; instead, they have "spontaneous" Alzheimer's, and the causes for that are unclear. Discovering those causes could ultimately improve medical care.

In a new (April 23, 2026) AI-aided study, researchers at the University of California, San Diego (UCSD) found that a gene recently recognized as a biomarker for spontaneous AD may be one mechanism of it, due to its previously unknown secondary function. It may lead to a potential treatment against proteins' buildup that obstructs the gene's moonlighting role. This gene found in cells (phosphoglycerate dehydrogenase, PHGDH) had previously been discovered as a potential blood biomarker for early detection of AD. Expression levels of the PHGDH gene directly correlate with changes in the brain in AD in that the higher the levels of protein and RNA produced by the PHGDH gene, the more advanced the disease. That correlation has since been verified in multiple cohorts from different medical centers. It catalyzes the first step in the biosynthesis of the amino acid serine. Specifically, it converts a glycolysis intermediate (3-phosphoglycerate) into 3-phosphohydroxypyruvate.

Using mice and human brain organoids, the researchers found that altering the amounts of PHGDH expression had consequential effects on AD. Lower levels corresponded to less disease progression, whereas increasing the levels led to more disease advancement, triggering a pathway that disrupts how cells in the brain turn genes on and off. In other words, PHGDH has a previously unknown role, independent of its enzymatic function, that through a novel pathway leads to spontaneous AD, i.e. PHGDH is indeed a causal gene of spontaneous AD. While everyone has the PHGDH gene, the difference comes down to the expression level of the gene, or how many proteins are made by it.

It should be emphasized that while many current treatments focus on treating the abnormal buildup of the sticky protein called beta-amyloid in the brain, some studies suggest that treating those plaques may be ineffective: essentially, by that stage of accumulation, treatment is too late. (Alternatively, as opined by this author, those plaques may only be symptoms of AD, not its root cause which was suggested to be a brain autoimmune disease having gone rogue.) By contrast, the PGHDH pathway is upstream, so preventing this pathway can reduce amyloid plaque formation in the first place. The researchers identified NCT-503 as a candidate that can penetrate the BBB to inhibit the regulatory role of the PHGDH enzyme, which may drive disease progression.

What comes next

Current research is expanding toward: anti-tau therapies; combination amyloid + tau approaches; neuroinflammation modulation; gene therapy; and synaptic repair strategies. Many researchers now think Alzheimer's likely requires multi-target treatment, like cancer or HIV therapy.

Conclusions and take-aways

- To assess the usefulness of AI in developing new drugs against neurodegenerative diseases (NDDs), a synoptic overview of the main currently available drugs employed against such diseases has been provided.

- The drugs available today against NDDs generally fall into two broad categories: symptoms-targeting drugs that purport to temporarily improve cognition, movement, mood, or function; and the still relatively rare disease-modifying therapies that attempt to slow the underlying degeneration itself.

- There are two types of symptoms-targeting drugs: cholinesterase inhibitors and NMDA-receptor agonists. The main cholinesterase inhibitors include Donepezil (Aricept), Rivastigmine (Exelon): and Galantamine (Razadyne). Their benefits are modest but apparently clinically meaningful for some patients. Gastrointestinal effects are the most

common side effects. Response varies widely between patients. NMDA receptor antagonists include Memantine (Namenda) and the combination (Memantine + Donepezil). Effects are usually moderate rather than dramatic. Common side effects are generally better tolerated than cholinesterase inhibitors.

- Disease-modifying anti-amyloid therapies mainly target beta-amyloid plaques using monoclonal antibodies to bind amyloid and help remove it from the brain. Currently approved major therapies include Lecanemab (Leqembi) to target soluble amyloid protofibrils in cases of mild cognitive impairment and Donanemab to target deposited amyloid plaques. Clinical trials have showed clinical reduction in deposited amyloid plaque burden with a slowing of disease progression in selected patients.

- As of March 2026, in the U.S., there are only 2 FDA-approved drugs: Leqembi (approved in 2023) and Kinsula (approved in July 2024). They are prescribed solely for those patients in the early stages of AD. They slow down symptoms to reduce the amyloid-beta plaques. The associated risks are similar and can be serious, consisting in temporary oedemas and bleedings of the brain, which can lead to serious and potentially fatal symptoms. This would be in addition to other common risks (headaches, confusion, vertigo, vision troubles, nausea, weakness, loss of speech, tremors).

- Before any treatment is contemplated by either Leqembi or Kinsula, it would be important to seriously consider the treatment benefits (apparently minimal) and the potential risks (serious), in addition to the excessive cost of the intervention. The biggest safety issue (amyloid-related imaging abnormalities or ARIA) consists of brain swelling and small brain bleeds. Risk factors include ApoE ε4 genotype, higher amyloid burden, and anticoagulant use.

- While Leqembi and Kisunla are the first FDA-approved drugs to directly attack the underlying mechanism of Alzheimer′s disease (AD), more treatments like them are in the pipeline, and pill-based therapies are on the horizon. Research continues into non-pharmacological treatments for AD, including non-invasive therapies like brain stimulation and focused ultrasound.

- AI platforms are used to screen thousands of existing FDA-approved drugs to find "hidden" Alzheimer's treatments as well as new molecules such as DDL-920 & DDL-218, DSP-0038, FJMU1887, and ONC-841. Beyond simply screening compounds, these platforms can quickly simulate molecular interactions, assess blood-brain barrier permeability, and predict adverse effects, significantly reducing the time and cost traditionally required. While no AI drug candidates for AD have completed the full clinical journey yet, it might only be a matter of time until new solutions are brought to patients.

- As of 2026, AI-driven drug discovery for AD has moved from the laboratory to human trials, focusing on both repurposed existing drugs or entirely new molecules, AI platforms (DRIAD, NETTAG) use machine language to screen thousands of existing FDA-approved drugs to find "hidden" AD treatments, significantly shortening development timelines. Examples include Janus kinase inhibitors, Sildenafil (Viagra), P300/CBP inhibitors (Salsalate and

Diflunisal), and the common diuretic Bumetanide.

- Researchers are also using AI to find the "next generation" of biological targets beyond traditional amyloid and tau such as in silico medicine targets like MARCKS and CAMKK2 proteins and PHGDH inhibitors for spontaneous AD.

- It should be emphasized that while many current treatments focus on treating the abnormal buildup of the beta-amyloid in the brain, some studies suggest that treating those plaques may be ineffective essentially because, by that stage of accumulation, treatment is too late. As early as 2017, this author has opined that the beta plaques may only be symptoms of AD, not its root cause which was suggested to be a brain autoimmune disease having gone rogue.

- Current research is expanding toward anti-tau therapies, combined (amyloid + tau approaches), neuroinflammation modulation, gene therapy, and synaptic repair strategies. Many researchers now think AD likely requires multi-target treatment, like cancer or HIV therapy.

Sidebar 1 - Cases of other neurodegenerative diseases

Parkinson's disease

The major goal here is dopamine replacement and enhancement.

Mainstay therapy

• Levodopa / carbidopa-levodopa

Most effective treatment for motor symptoms like rigidity and tremor.

Dopamine agonists

• Pramipexole;
• Ropinirole; and
• Rotigotine.

MAO-B inhibitors

• Selegiline;
• Rasagiline; and
• Safinamide.

COMT inhibitors

• Entacapone; and
• Opicapone.

Other therapies

• Amantadine; and
• Istradefylline.

At present, Parkinson's therapies are mostly symptomatic. No universally accepted disease-modifying drug has yet been approved.

Amyotrophic lateral sclerosis

Currently approved ALS drugs include:

• Riluzole;
• Edaravone (Radicava);
• Tofersen; and
• Dextromethorphan/quinidine (symptom management)

Tofersen is notable because it targets a specific genetic form of ALS caused by SOD1 mutations, making it one of the first precision genetic therapies in neurodegeneration.

Multiple sclerosis

MS is partly autoimmune and partly neurodegenerative.

It has the largest number of disease-modifying drugs among these conditions. Major approved categories include:

Interferons

• Interferon beta-1a; and
• Interferon beta-1b.

Oral therapies

• Fingolimod;
• Dimethylfumarate;
• Teriflunomide; and
• Ozanimod.

Monoclonal antibodies

• Ocrelizumab;
• Natalizumab;
• Alemtuzumab; and
• Ofatumumab.

These can substantially reduce relapses and MRI lesion activity.

Huntington's disease

No approved disease-modifying therapy exists yet. Current drugs mainly manage symptoms:

• Tetrabenazine; and
• Deutetrabenazine.

These reduce chorea (involuntary movements). Experimental therapies such as antisense oligonucleotides and monoclonal antibodies are still under study.

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