ASIA-PACIFIC | Biotechnology

Alzheimer's disease

Alzheimer's in China – Largest patient pool in the world

Alzheimer's disease is the most common type of dementia, accounting for 60-80% of dementia cases. It is a progressive disease beginning with mild memory loss and could end up with the loss of conversational ability and unable to respond to happenings in the surroundings.

China has 17mn of dementia patients, accounting for ~30% WW. Its aged 60+ Alzheimer's patients has reached ~10mn and is expected to triple by 2050E. Besides urbanization and pollution, the key driver to the rise is driven by the aging population, where we expect 24% of the vast population will be aged 60+ by 2030E and 28% by 2040E. We estimate the Alzheimer's drug market was ~US$300mn in 2023 and to be more than double reaching over US$650mn by 2030E. In addition to drugs, more investment is needed in improving diagnosis given current under-diagnosis and improving current fragmented senior care. Though China's healthcare system struggles with limited dementia specialists and drug access, initiatives like the National Dementia Prevention and Treatment Plan and AI diagnostics aim to improve screening. Domestic pharma/biotech are actively advancing therapies (such as GV-971), as China's vast patient pool offers unique opportunities for global Alzheimer's developers.

Today, there is a worldwide effort underway to find better ways to treat the disease, delay its onset and prevent it from developing. US FDA has approved three amyloid-targeting therapies for Alzheimer's – aducanumab, lecanemab and donanemab, all demonstrating clinical efficacy in slowing cognitive decline in early-stage patients. Both lecanemab and donanemab have been approved in China, though their high cost of about US$26k each per year and lack of NDRL coverage limit access to patients in China. Local biotech Green Valley's sodium oligomannate (GV-971) was approved in China in 2019 as the world's first Alzheimer's drug targeting the gut-brain axis. Priced at US$1 per capsule (NDRL inclusion in 2022), its annual cost is ~US$2,000 with an annual out-of-pocket expense of ~US$1,000, making it more affordable than imported drugs.

Although existing therapies can modestly slow progression, none have shown disease reversal. Emerging approaches – including GLP-1-based therapies, tau-targeting drugs, therapeutic vaccines, and innovative technologies such as focused ultrasound, deep brain stimulation, stem cell therapy, and gene editing – may offer transformative strategies. In China, Alzheimer's drug pipeline features a mix of amyloid-targeting biologics, tau-based therapies, TCM derivatives, and innovative small molecules. Notable pipelines include biologics such as SHR-1707 (Hengrui, anti-Aβ mAb, Ph II) and CM383 (Keymed, anti-Aβ mAb, Ph I), as well as small molecules such as varoglutamstat (Simcere/Vivoryon, QPCT inhibitor, Ph II), RP-902 (Risen Pharma, anti-Aβ small molecule, Ph II) and flunopirine (Kanion, AChE inhibitor, Ph II) which aim for oral convenience. There are also TCM-inspired candidates, such as KH-110 (Kanghong, Ph III) and Sailuotong (Shineway, Ph III).

See more inside.

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Alzheimer's disease

Alzheimer's disease is the most common type of dementia, accounting for 60-80% of all dementia cases. It is a progressive disease beginning with mild memory loss and overtime, a loss in ability to carry a conversation and ultimately, unable to respond to the environment. Alzheimer's disease involves parts of the brain that control thought, memory, and language. It can seriously affect a person's ability to carry out daily activities.

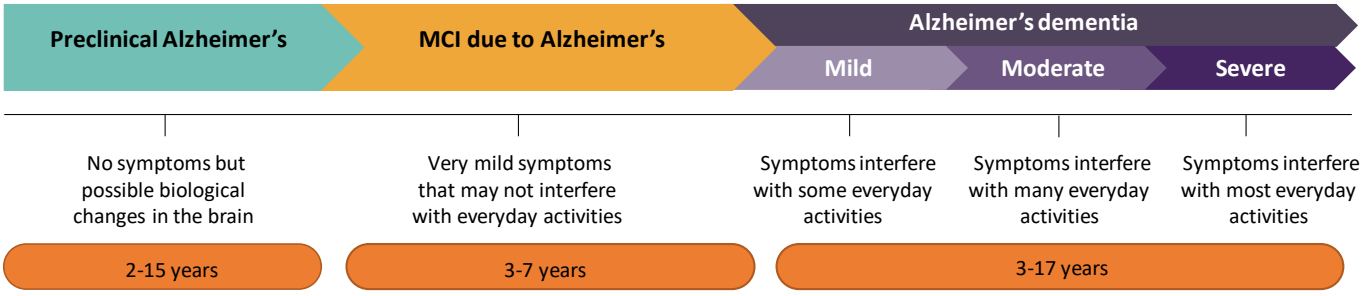
Exhibit 1: Alzheimer – the most common cause of dementia

Cause	Percentage of dementia cases
Alzheimer's disease	**The most common cause of dementia, accounting for an estimated 60% to 80% of cases**
Cerebrovascular disease	About 5% to 10% of individuals with dementia show evidence of vascular dementia alone
Frontotemporal degeneration (FTD)	About 60% of people with FTD are ages 45 to 60. FTD accounted for about 3% of dementia cases in studies that included people 65 and older and about 10% of dementia cases in studies restricted to those younger than 65
Hippocampal sclerosis (HS)	HS is present in about 3% to 13% of people with dementia. An estimated 0.4% to 2% of dementia cases are due to HS alone
Lewy body disease	About 5% of older individuals with dementia show evidence of DLB alone, but most people with DLB also have the brain changes of Alzheimer's disease
Mixed pathologies	More than 50% of people diagnosed with Alzheimer's dementia had mixed dementia. Mixed dementia is most common in people age 85 or older
Parkinson's disease (PD)	3.6% of dementia cases were due to PD and 24.5% of people with PD developed dementia

Source: Alzheimer's Association

Alzheimer's disease starts from unnoticeable brain changes with no symptoms shown. It then progress with the person having problems with memory and thinking, and eventually physical disability. On this continuum, there are three broad phases: preclinical Alzheimer's, MCI (mild cognitive impairment) due to Alzheimer's, and Alzheimer's dementia. The Alzheimer's dementia phase is further divided into mild, moderate and severe dementia.

Exhibit 2: Stages and symptoms of Alzheimer's

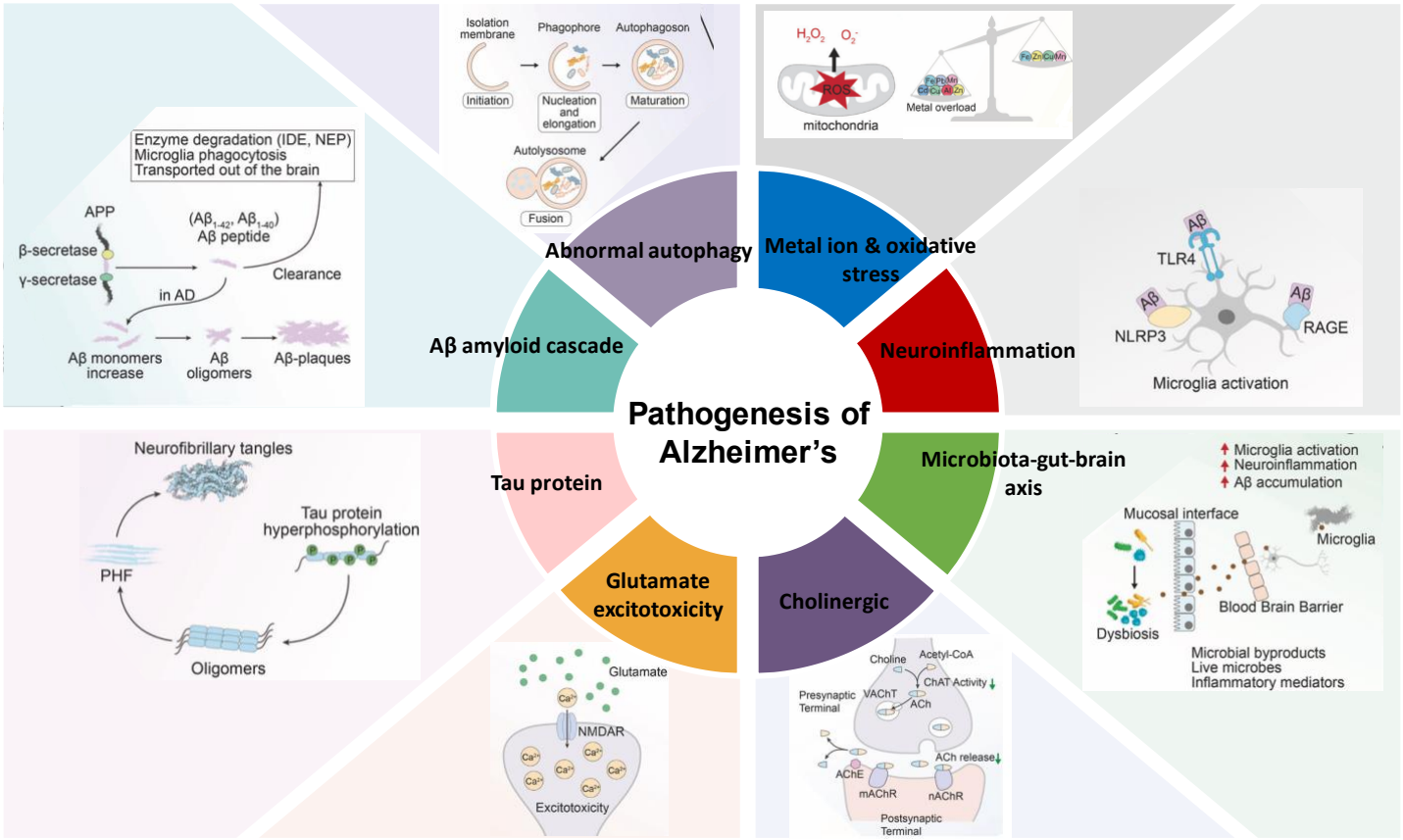


Source: Alzheimer's Association

Scientists have yet to fully understand what causes Alzheimer's disease. There likely is not a single cause but rather several factors which could affect each person differently. Risk factor wise, age is the best known risk factor, while family history/genetics may also play a role. However, there is growing scientific evidence that healthy behaviors, which have been shown to prevent cancer, diabetes, and heart disease, may also reduce risk for subjective cognitive decline.

Over the past decades, several theories have been advanced to explain the etiology of Alzheimer's, which can be divided into two main categories. 1) theories to explain possible causes of Alzheimer's, such as the cholinergic hypothesis, inflammation hypothesis, lymphatic system hypothesis, metal ion hypothesis, and vascular dysfunction hypothesis; 2) theories focus more on the pathological events taking place after Alzheimer's has started, whihch include the amyloid cascade hypothesis, calcium homeostasis hypothesis, mitochondrial cascade hypothesis, and the tau propagation hypothesis.

Exhibit 3: Popular pathogenesis of Alzheimer's

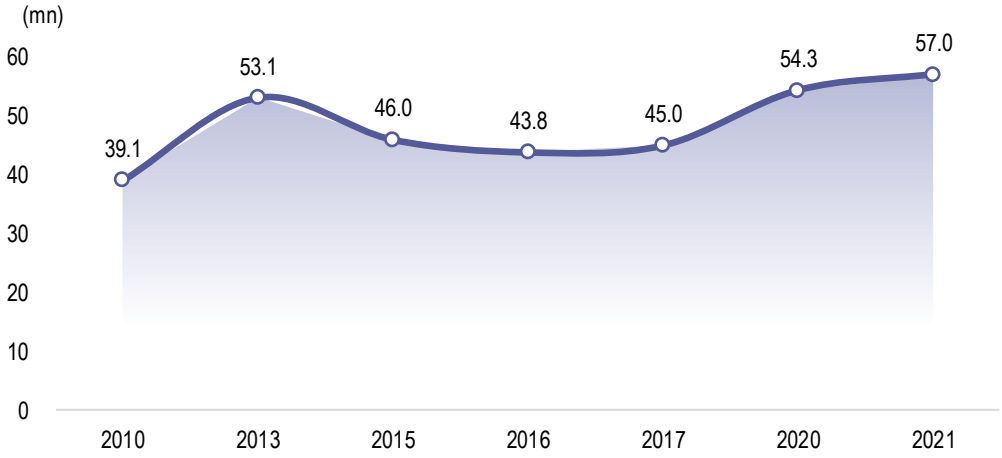


Source: Zhang, J. et al. Recent advances in Alzheimer's disease: mechanisms, clinical trials and new drug development strategies. Sig Transduct Target Ther 9, 211 (2024)

Prevalence and unmet needs

Globally, there were 57mn people living with dementia (including Alzheimer's) in 2021, with China contributing ~17mn cases, representing ~30% of the global number. The age-standardized prevalence rate of dementia in China stood at 900.8/100,000, significantly higher than the global average of 696.0/100,000, highlighting the disproportionate burden of the disease in China.

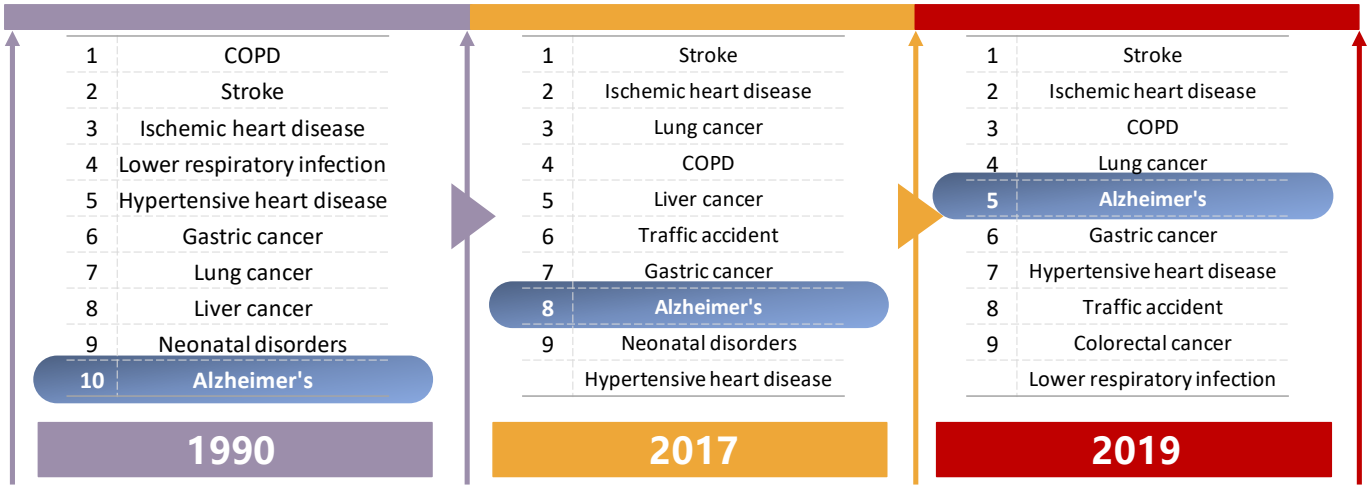
Exhibit 4: Prevalence of Alzheimer's dementia and other dementia worldwide



Source: Alzheimer's Association

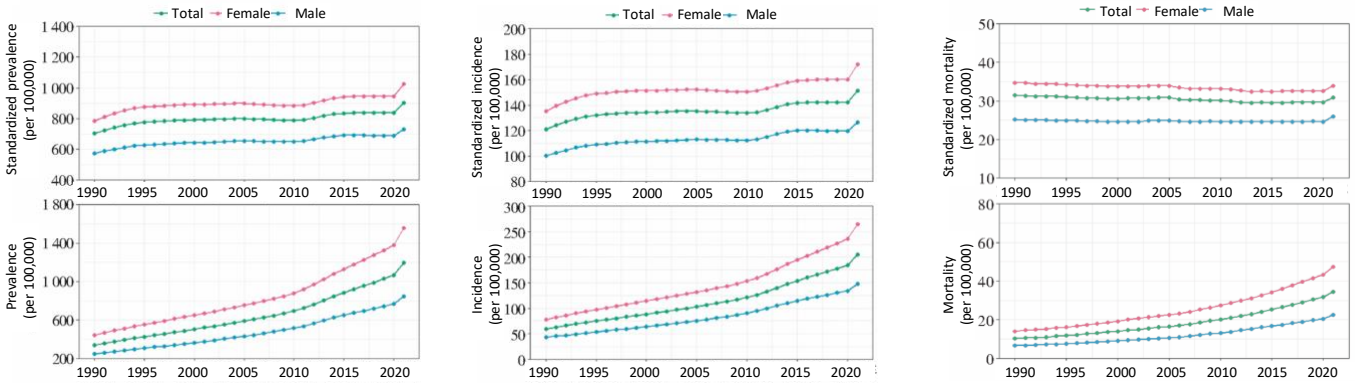
More than 15mn people in China aged 60+ suffer from dementia, of which ~10mn have Alzheimer's disease. China has largest number of Alzheimer's patients in the world. Moreover, the disease is also occurring at a younger age. In China, the highest proportion of people diagnosed with Alzheimer's disease for the first time was in people aged 60 to 79 years, accounting for 60%+ of the total. But people with Alzheimer's disease who are aged below 60 account for ~20%, a proportion higher than patients with Alzheimer's disease in their early stages globally, which is between 5% to 10%.

Exhibit 5: Alzheimer's is now one of the top 10 causes of death in China (1990 vs. 2017 vs. 2019)



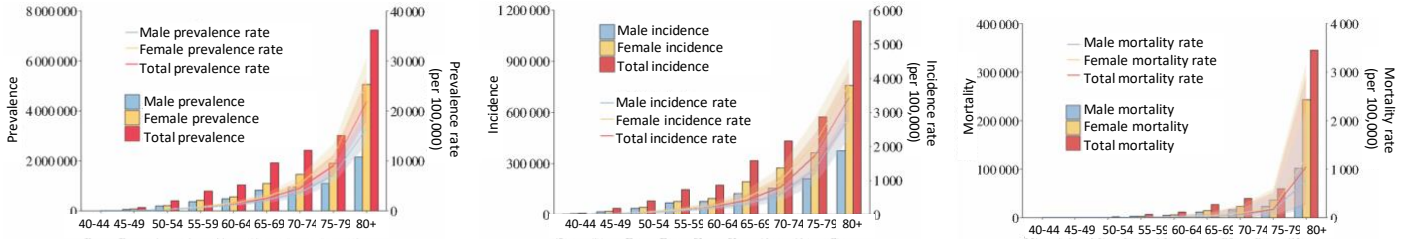
Source: China NHC

Exhibit 6: On the rise – Prevalence, incidence and mortality of Alzheimer's are going up in China (1990-2021)



Source: China Alzheimer's report 2024

Exhibit 7: Onset seen as early as 40's – 2021 prevalence, incidence and mortality of Alzheimer's in China by age group

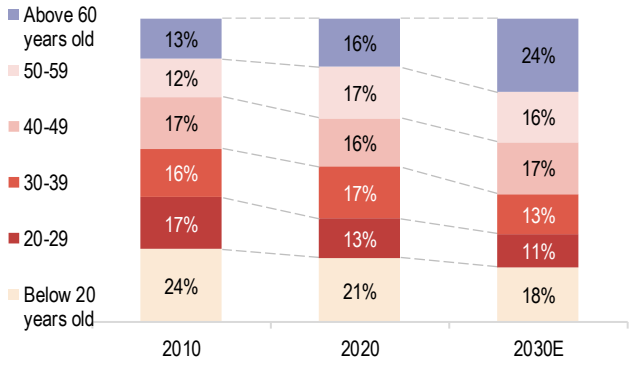


Source: China Alzheimer's report 2024

Note people aged 60+ are projected to reach 24% of China's total population of by 2030E. The rapidly aging population is a key driver to the rising Alzheimer's crisis – namely ~10mn current cases expected to triple to ~30mn by 2050E. In additional to aging population, urbanization and pollution are not helping the disease progression. Besides drugs, more investment is needed in terms of improving diagnosis - (<20% detected early) and improving

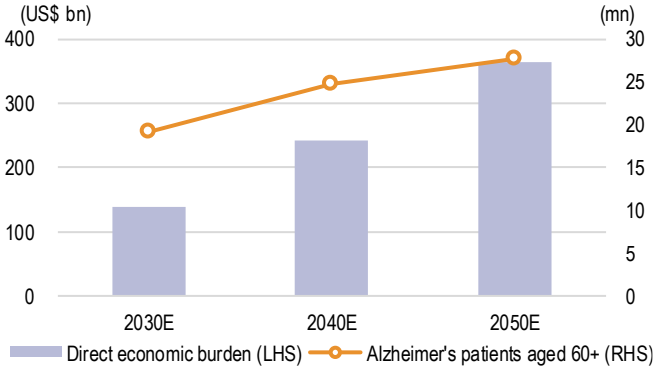
senior care (which is very fragmented), which in turn will alleviate foreseeable upcoming economic burden.

Exhibit 8: Aging population in China – population above 60 years old to reach 24% in 2030



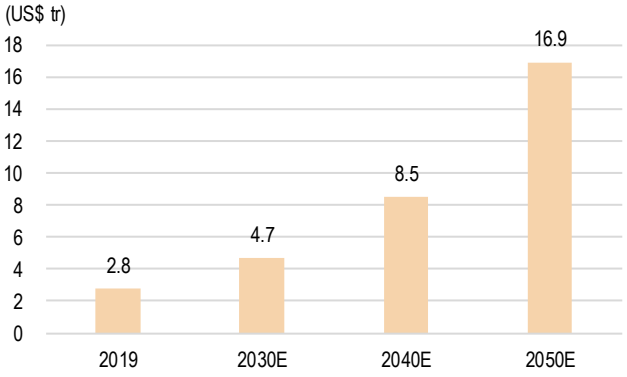
Source: China Statistics Bureau, UN

Exhibit 9: Projected prevalence and economic burden of Alzheimer's in China



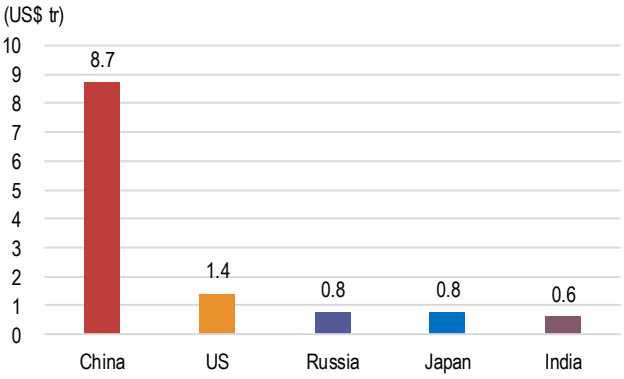
Source: China Alzheimer's data and prevention strategy 2023

Exhibit 10: Projected worldwide economic burden of Alzheimer's and related-dementias, 2019-2050E



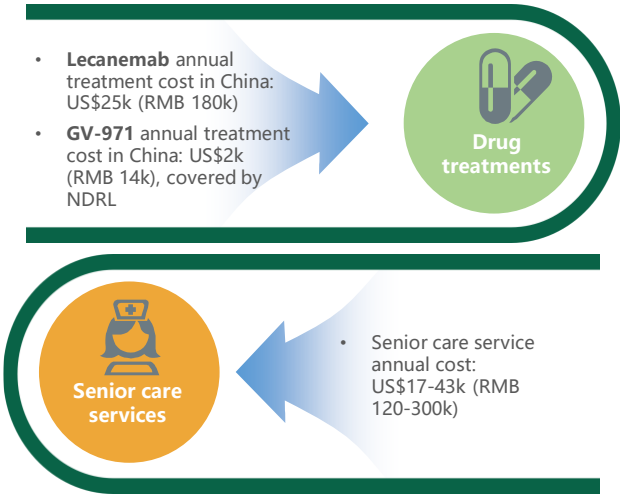
Source: Industry reports, Selesta estimates

Exhibit 11: Top 5 countries with the highest economic burden of Alzheimer's and related-dementias, 2050E



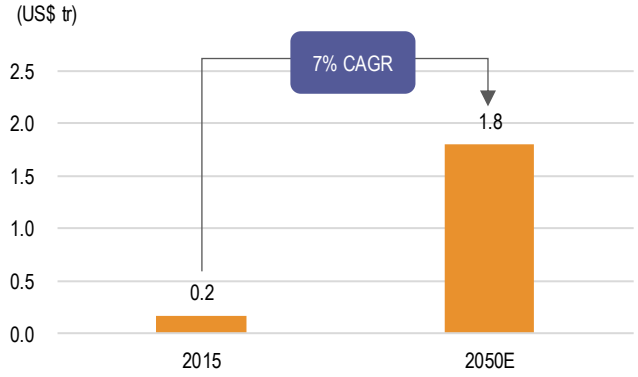
Source: Industry reports, Selesta estimates

Exhibit 12: Annual treatment and healthcare costs for Alzheimer's patients in China



Source: China NHSA, industry data

Exhibit 13: Total annual treatment cost for Alzheimer's in China

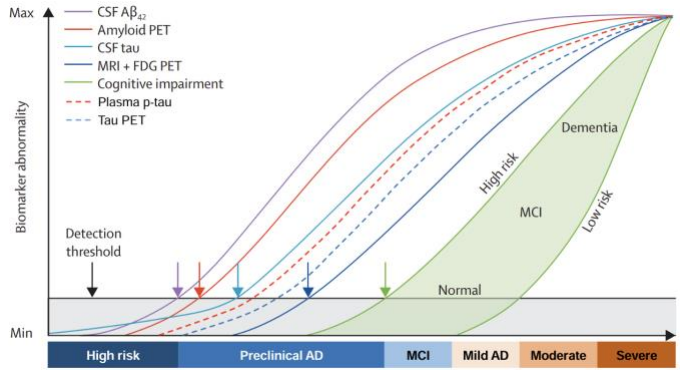


Source: China Alzheimer's report 2022

Diagnostics and standard of care

The diagnosis of Alzheimer's is being revolutionized by next-generation tools that enable earlier and more accurate detection. Amyloid-PET and Tau-PET scans now visualize brain pathology in vivo, while CSF biomarkers (Aβ42, p-tau181/217) and ultra-sensitive plasma tests offer minimally invasive alternatives with 90%+ accuracy. Challenges remain in cost (PET scans: ~US$1.4k in China), and access (only available in large hospitals).

Exhibit 14: Biomarkers in different stages of Alzheimer's



Source: Lancet Neurology, doi:10.1016/S1474-4422(12)70291-0

Exhibit 15: Pathological changes and dynamic biomarkers of Alzheimer's

Change in pathological state	Biomarker		
	Image diagnosis	CSF	Plasma
Amyloid accumulation	Amyloid PET	Aβ42/40 comparison	Aβ42/40 comparison, etc.
Tau accumulation	Tau PET	p-Tau	p-Tau181,p-Tau217, etc.
Neuro-degenerative	FDG PET, MRI	Tau	Tau, etc.

Source: Alzheimer's Association

Exhibit 16: Comparison of three mainstream Alzheimer's diagnostics methods

	Image diagnosis	CSF	Plasma	
			Antibody	Exosomes
Sensitivity	High	High	Low	High
Specificity	Low	High	Medium	High
Invasive	Low	High (lumbar puncture)	Low	Low
Early diagnosis accuracy	Poor	Medium	Good	Good
Requirement for equipment	High (PET-CT/MRI)	Medium	High (MS, ELISA)	Low (qPCR)
Price	High (PET US$1.4k, MRI US$140)	Medium (US$140-430)	Low	Low
Technology	Mature	Mature	Early-stage	Early-stage
Clinical application	High	High	Low	Low

Source: Alzheimer's Association, China NHSA, industry data

Though China's healthcare system struggles with limited dementia specialists and drug access (only limited therapies such as donepezil and memantine are widely covered by NDRL), initiatives like the National Dementia Prevention and Treatment Plan and AI diagnostics aim to improve screening. Domestic pharma/biotech are actively advancing therapies (such as GV-971), as China's vast patient pool offers unique opportunities for global Alzheimer's developers.

Exhibit 17: Diagnostic guidelines for Alzheimer's disease in China

Method		Method/Biomarker	Recommendation	Evidence grade
Image diagnosis	Structural Imaging	MTA-MRI	Moderate performance in defining Alzheimer's dementia; acceptable accuracy for distinguishing Alzheimer's dementia from MCI, but poor for differentiating early Alzheimer's from FTD	2B
		MRI	Structural MRI helps differentiate Alzheimer's from non-Alzheimer's etiologies	3C
	Functional Imaging	Aβ-PET	High performance in defining Alzheimer's dementia but low specificity for MCI	2B
		FDG-PET	High performance in defining Alzheimer's dementia and distinguishing Alzheimer's from DLB	2B
		Tau-PET	High performance in defining Alzheimer's dementia but low sensitivity for MCI	2B
CSF		Aβ42	CSF Aβ42 reduction shows high performance in defining Alzheimer's dementia and differentiating Alzheimer's dementia from non-Alzheimer's dementia	2B
		Aβ42/Aβ40	Moderate performance in defining Alzheimer's dementia and differentiating Alzheimer's dementia from non-Alzheimer's dementia	2B
		Tau or P-tau181	Elevated Tau/P-tau181 levels show moderate performance in defining Alzheimer's; P-tau181/T-tau ratio reduction has high performance	2B

Source: China Alzheimer's and Dementia Diagnostic Guidelines (2020)

Exhibit 18: Treatment guidelines for Alzheimer's disease

Category	Drug class	Drug	Indication	Efficacy and Safety
Cognitive symptom management	Cholinesterase Inhibitors	Donepezil Rivastigmine Galantamine	All stages	GI effects: Nausea, vomiting, diarrhea; Cardiovascular: Bradycardia, heart block; Neurological: Dizziness, headache, insomnia, drowsiness; Other: Skin irritation, rhabdomyolysis, malignant syndrome, hypersensitivity.
	NMDA Receptor Antagonist	Memantine, Memantine + Cholinesterase Inhibitor	Moderate-to-severe	Generally well-tolerated; occasional dizziness, headache, constipation, diarrhea, drowsiness, blood pressure fluctuations.
Behavioral/Psychiatric symptom management	Atypical Antipsychotics	Olanzapine Risperidone Quetiapine Aripiprazole		May worsen cognitive decline; Olanzapine shows relatively better efficacy for behavioral symptoms, followed by Risperidone and Quetiapine.
	Selective 5-HT Receptor Agonists	Pimavanserin Buspirone Tandospirone		Pimavanserin offers short-term benefits for psychiatric symptoms in Alzheimer's.
	SSRIs	Citalopram		May exacerbate cognitive impairment.
Sequential TCM therapy	Kidney-tonifying		All stages	Sequential TCM therapy combined with conventional Western drugs shows synergistic benefits for cognition and behavior.
	Phlegm-resolving		Moderate	
	Blood-activating		Moderate	
	Fire-purging		Moderate	
	Detoxification		Severe	

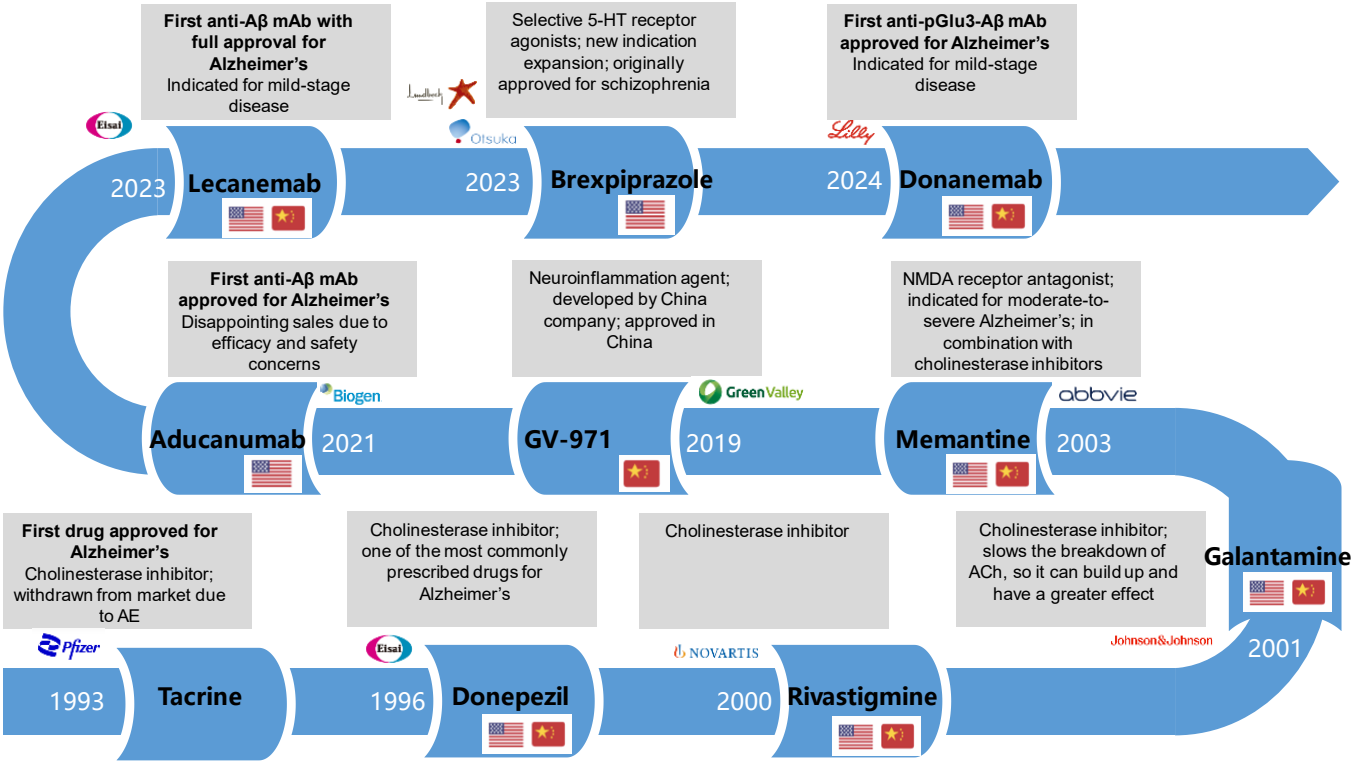
Source: China Alzheimer's and Dementia Diagnostic Guidelines (2020)

Approved and next-generation therapeutics in China

Alzheimer's has no cure, but emerging anti-Aβ drugs demonstrate that removing beta-amyloid, one of the hallmarks of Alzheimer's, from the brain reduces cognitive and functional decline in people living with early Alzheimer's. Other treatments can temporarily slow the worsening of dementia symptoms and improve quality of life for those with Alzheimer's and their caregivers. Today, there is a worldwide effort underway to find better ways to treat the disease, delay its onset and prevent it from developing.

US FDA has approved 9 drugs for Alzheimer's, including 6 symptomatic treatments and 3 DMTs (disease-modifying therapies). The cholinesterase inhibitors – donepezil (1996, for all stages), rivastigmine (2000, oral/patch), and galantamine (2001) – boost acetylcholine to temporarily improve cognition, while memantine (2003, for moderate-severe Alzheimer's) blocks NMDA receptors to slow decline. The combination drug memantine/donepezil (2014) offers dual mechanisms. In 2021, aducanumab became the first amyloid-targeting DMT, approved controversially under accelerated approval, followed by lecanemab (2023) and donanemab (2024), which showed clearer efficacy in slowing early Alzheimer's progression, but require IV infusions and MRI monitoring for ARIA side effects. These drugs highlight the shift from symptom management to targeting amyloid plaques, though access remains limited by cost, eligibility, and infrastructure challenges. Besides, Shanghai Green Valley Pharma's sodium oligomannate (GV-971), approved in China in 2019, is the world's first Alzheimer's drug targeting the gut-brain axis.

Exhibit 19: Alzheimer's drugs on the market



Source: US FDA, China NMPA

Amyloid-based therapies

Currently, US FDA has approved three amyloid-targeting therapies for Alzheimer's, all demonstrating clinical efficacy in slowing cognitive decline in early-stage patients. The first approved drug, Aduhelm (aducanumab, 2021) selectively binds amyloid plaques, though its accelerated approval remains controversial due to mixed trial results and safety concerns about ARIA (amyloid-related imaging abnormalities). Leqembi (lecanemab, 2023), the second amyloid-targeting therapy, gained full US FDA approval after showing a statistically significant 27% reduction in cognitive decline over 18mo in Ph III trials, albeit with manageable ARIA risks. Most recently, Kisunla (donanemab, 2024) was approved based on its Ph III data demonstrating up to 35% slowing of progression and the unique feature of treatment discontinuation upon amyloid clearance. While these therapies represent a breakthrough in disease modification, challenges like restricted eligibility (early symptomatic Alzheimer's), high costs, and infusion requirements limit broad accessibility, underscoring the need for safer, more convenient alternatives.

Both lecanemab and donanemab have been approved in China, though the high cost for each drug (US$26k per year) and lack of NDRL coverage limit access to patients in the country.

Exhibit 20: Comparison of three amyloid-based therapies with market approvals

Generic name	Aducanumab		Lecanemab		Donanemab	
Company	Biogen		Eisai		Eli Lilly	
Target	Aggregated Aβ		Aggregated Aβ		pGlu3-Aβ	
Dosing	10mg/kg q4W		10mg/kg q2W		700mg q4Wx3 +1400mg q4W	
Treatment duration	78w		18mo (~78w)		18mo (~78w)	
Patient population	MCI (~80%), mild-AD (~20%)		MCI (~60%), mild-AD (~40%)		MCI (~80%), mild-AD (~20%)	
Treatment arm	Aducanumab	Placebo	Lecanemab	Placebo	Donanemab	Placebo
CDR-SB baseline	2.5±1.1/2.4±1.0	2.5±1.0/2.4±1.0	3.2±1.3	3.2±1.3	4.0±2.1	3.9±2.1
CDR-SB change	+1.1/+1.6	+1.7/+1.6	+1.2	+1.7	+1.7	+2.3
ARIA-E	35%/36%	2%/3%	12.6%	1.7%	24.0%	1.9%
ARIA-H	-	-	17.3%	9.0%	19.7%	7.4%

Source: Company data

The pipeline for amyloid-based Alzheimer's therapies spans mAbs, vaccines, and small molecules. Next-generation antibodies like remternetug (e.g., Eli Lilly, Ph III) aim for improved safety and subcutaneous dosing. Anti-Aβ vaccines (e.g., UB-311, Ph II) and gamma-secretase modulators (e.g., ALZ-801, Ph III) offer alternative approaches to reduce plaques. Meanwhile, dual-target therapies (Aβ + tau or inflammation) and BBB-penetrating small molecules (e.g., CT1812, Ph II) are advancing to address limitations of current drugs. Challenges include patient stratification, biomarker validation, and cost/access barriers, but the pipeline reflects a robust shift toward disease modification and combination strategies.

Exhibit 21: Pipeline for amyloid-based therapies globally

Category	Generic name	Company	Target/MoA	Global stage	China stage
Antibody	Remternetug	Eli Lilly	N3pG-Aβ	Ph III	Ph III
	Sabirnetug/ACU-193	Acumen	Soluble Aβ oligomers	Ph II/III	
	ABBV-916	AbbVie	N3pG-Aβ	Ph II	
	Troninemab	Roche	Aβ	Ph I/II	
	SHR-1707	**Hengrui**	**Aβ**		**Ph II**
	PRX012	Prothena	Aβ	Ph I	
	PMN 310	ProMIS	Aβ (oligomer)	Ph I	
	CM383	**Keymed**	**Aβ**		**Ph I**
	ALIA-1758	Alida	N3pG-Aβ	Ph I	
Vaccine	ABvac40	Araclon	$Aβ_{33-40}$	Ph II	
	ACI-24.060	AC Immune/Takeda	$Aβ_{1-15}$	Ph II	
	UB-311	Vaxxinity	$Aβ_{1-14}$	Ph II	
	ALZ-101	Alzinova	Soluble oligomeric Aβ	Ph I	
	AV-1959D	Nuravax	$Aβ_{1-11}$	Ph I	
Small molecule	ALZ-801	Alzheon	Prodrug of homotaurine	Ph III	
	CT1812	Cognition	Sigma2-RA	Ph II	
	Varoglutamstat/SIM0408	**Vivoryon/Simcere**	**QPCTL/QPCT**	**Ph II**	**Ph I**
	ALX-001	Allyx/BMS	mGluR5	Ph I	
	RP902	**Risen Pharma**	**Aβ aggregation inhibitor**		**Ph II**
	CS6253	Artery	ABCA1 (affects Aβ clearance via ApoE)	Ph I	
	PRI-002	Priavoid	Aβ stabilizer	Ph I	
	PK501	PharmaKure	APP inhibitor	IND	

Source: Pharmcube

Hengrui's SHR-1707 – the first China domestic Aβ mAb entering Ph II

Hengrui's SHR-1707 injection is a novel humanized mAb (IgG1 subtype) targeting Aβ. The investigational drug demonstrates dual mechanisms: disrupting Aβ plaque formation and activating microglia to clear toxic protein aggregates, offering new hope to slow cognitive decline in Alzheimer's patients. Preclinical data show reduced Aβ burden and improved cognitive metrics, positioning SHR-1707 as a potential best-in-class candidate.

In March 2021, SHR-1707 received IND approval from China NMPA for Alzheimer's. By 2022, the company completed two Ph I studies in healthy volunteers in China and Australia, demonstrating favorable safety and tolerability at doses ranging from 2mg/kg to 60mg/kg. Following these results, Hengrui initiated Ph Ib study with the first patient dosed in March 2023. SHR-1707 has progressed to Ph II trials in China while continuing Ph I studies in Australia.

In Feb 2024, the Ph II study was kicked off in patients with mild cognitive impairment or mild dementia due to Alzheimer's. At one site in China, the study plans to enroll 45 patients in four cohorts at 5, 10, 20, or 40 mg/kg SHR-1707, or placebo, every two weeks for six months, followed by a one-year open-label extension. The primary endpoint is safety, and secondary endpoints include change in amyloid PET at six months, and after the long-term extension. Other secondary and exploratory endpoints span serum and CSF pharmacokinetics, antidrug antibodies, biomarkers, and measures of cognition. Trial completion is expected in Jun 2026.

Risen Pharma's PR902 – the first China domestic Aβ small molecule entering Ph II

RP902 is a potential first-in-class stable isotope-substituted small molecule drug independently developed by Risen Pharma, target Aβ for Alzheimer's treatment by uniquely inhibiting soluble amyloid oligomer formation – a key driver of cognitive decline. Preclinical data demonstrate RP902's triple action: reducing neurotoxic Aβ aggregates, protecting blood-brain barrier integrity, and restoring synaptic plasticity in Alzheimer's mouse models, with marked improvements in spatial/long-term memory and hippocampal neuron repair. Currently in Ph II trials in China, RP902's ability to lower both soluble and insoluble Aβ1-40/1-42 levels – coupled with a favorable safety profile – positions it as a potential oral alternative to current infusion therapies.

Cognitive symptom management agents

Current cognitive symptom management agents for Alzheimer's primarily target neurotransmitter systems to temporarily alleviate symptoms, with 4 drugs approved both in the US and China dominating clinical use: cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) boost acetylcholine to improve memory and attention in mild-to-moderate Alzheimer's, while memantine, an NMDA receptor antagonist, helps regulate glutamate in moderate-to-severe Alzheimer's. These drugs offer modest symptomatic relief (e.g., 1-3-point improvement on ADAS-Cog over 6-12mo) but do not alter disease progression.

Exhibit 22: Comparison of major cognitive symptom management agents

Generic name	Donepezil	Rivastigmine	Galantamine	Memantine	Donepezil + Memantine
Originator	Eisai	Novartis	J&J	Forest Labs	Allergan/Adamas
Target/MoA	AChE	AChE	AChE	NMDA	AChE + NMDA
Indication	Alzheimer's	Mild-to-moderate Alzheimer's/Parkinson's	Mild-to-moderate Alzheimer's	Moderate-to-severe Alzheimer's	Moderate-to-severe Alzheimer's
Approval year	US (1996), JP (1999), CN (1999)	US (2000), EU (1998), JP (2011), CN (2018)	US (2001), JP (2011), CN (2020)	US (2003), EU (2009), CN (2010), JP (2011)	US (2014)
Dosing	● 5mg qd for at least 1mo, , may increase to 10mg after clinical evaluation. ● For moderate-to-severe patients, max dose can be raised to 23mg after 3 months.	● Oral: Start at 1.5mg qd, max 6mg (titrate slowly). ● Patch: Start at 4.6mg/24h, may increase to 9.5mg after 4 weeks, max 13.3mg.	Start at 4mg qd, adjust after 4 weeks, max 32mg.	Max dose 20mg qd, recommended 10mg (start at 5mg qd, titrate weekly to 20mg by week 4).	For memantine-naïve patients: Start at 7mg/10mg qd, max 28mg/10mg. For stable memantine users: Directly switch to 28mg/10mg qd.
Efficacy	10mg qd for mild-to-moderate Alzheimer's over 24 weeks vs placebo: ● Significant cognitive improvement (ADAS-Cog: MD=2.67, MMSE: MD=1.28) ● Functional ability (ADCS-ADL: MD=0.35) and global impression (CIBIC-Plus: MD=0.44) improved. ● Effects sustained for 8-9 months.	Mild-to-moderate Alzheimer's over 24 weeks vs placebo: ● Cognitive (ADAS-Cog: MD=1.65), functional (ADCS-ADL: MD=1.93), and global impression (ADCS-CGIC: MD=0.29) improvements.	2.4mg qd for mild-to-moderate AD over 21-28 weeks: ● Cognitive benefit vs placebo (ADAS-Cog: MD=2.23). ● Functional (ADCS-ADL: MD=2.13), global impression (CIBIC-Plus: OR=1.63), and mild behavioral symptom relief (NPI: MD=-1.75).	20mg qd for moderate-to-severe AD over 24-28 weeks vs placebo: ● Mild cognitive and global improvement (ADAS-Cog: MD=1.33, CIBIC-Plus: MD=0.16). ● Ineffective for mild Alzheimer's cognition, function, or behavior.	Memantine 20mg/d + donepezil for moderate-to-severe AD over 24-28 weeks: ● Small synergistic effects vs donepezil monotherapy in cognition, global function, and behavior. ● Duration of efficacy: ~5 months.
Safety	● Very common AE (≥10%): diarrhea, nausea, headache. ● Common AE (1%-10%): cold, anorexia, vomiting, etc.	● GI AE: nausea, and vomiting	● AE: nausea, vomiting, diarrhea, headache. ● SAE: cardiovascular, pulmonary, and gastrointestinal disorders.	● AE incidence <2%: hallucinations, confusion, dizziness, headache, fatigue. ● Rare AE (0.1%): anxiety, hypertonia, vomiting, cystitis.	● Good tolerability with AEs of nausea, vomiting, diarrhea, etc.

Source: Company data

Exhibit 23: Major manufacturers of cognitive symptom management agents in China

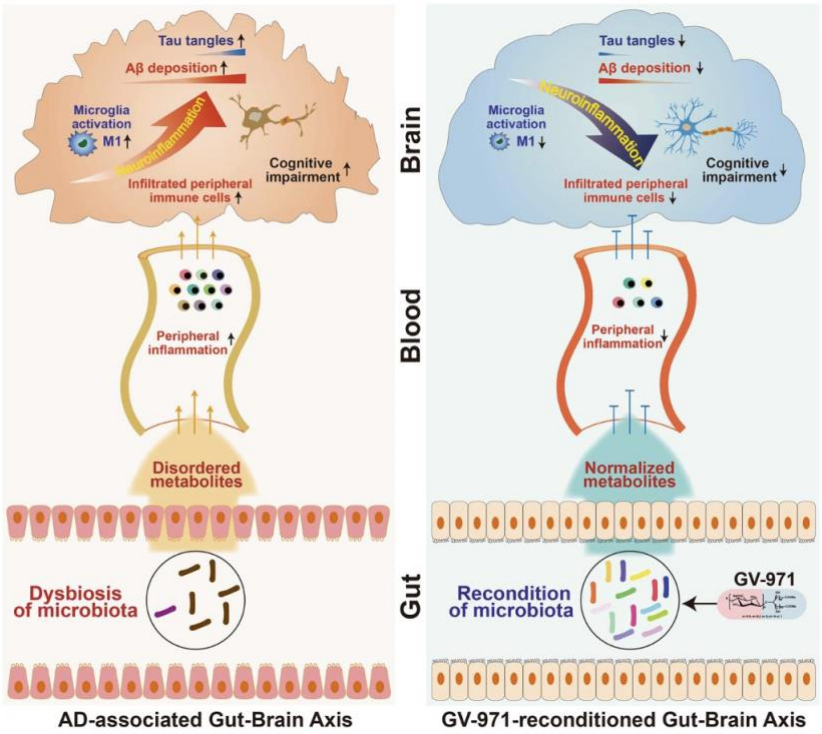
Generic name	VBP	Manufacturers	Annual treatment costs
Galantamine	-	Hubei Minkang, Xudong Haipu, Conba, Zhejiang Yixin, etc.	US$470-600
Donepezil	2nd batch	Eisai, Huahai Pharma, Zhien Biotech	US$120-1420
Memantine	3rd & 7th batch	Lundbeck, United Labs, Hunan Dongting, Anhui Huachen, Baiyunshan, Easton, Jingxin Pharma, etc.	US$115-940
Huperzine A	-	Hainan Likang, Wanbangde, Fudan Forward, Chenxin Pharma, etc.	US$150-300
Rivastigmine (oral)	-	Novartis, Jingxin Pharma, Sun Pharma	US$950
Rivastigmine (patch)	-	Novartis, Luye Pharma	US$510

Source: Company data

Neuroinflammation-based therapies

GV-971 (sodium oligomannate), developed by Shanghai Green Valley Pharma, was approved in China (but not in other countries) in 2019 as the world's first Alzheimer's drug targeting the gut-brain axis. It addresses Alzheimer's progression by modulating gut microbiota, which are disrupted in Alzheimer's, leading to metabolic dysfunction and the accumulation of abnormal metabolites (e.g., Aβ deposits and hyperphosphorylated tau). These metabolites trigger peripheral inflammation, promoting immune cell infiltration into the brain, where they interact with M1 microglia, exacerbating neuroinflammation and cognitive decline. GV-971 restores gut microbial balance, normalizes metabolic byproducts, reduces neuroinflammation, and mitigates Aβ/tau pathology, ultimately improving cognitive function.

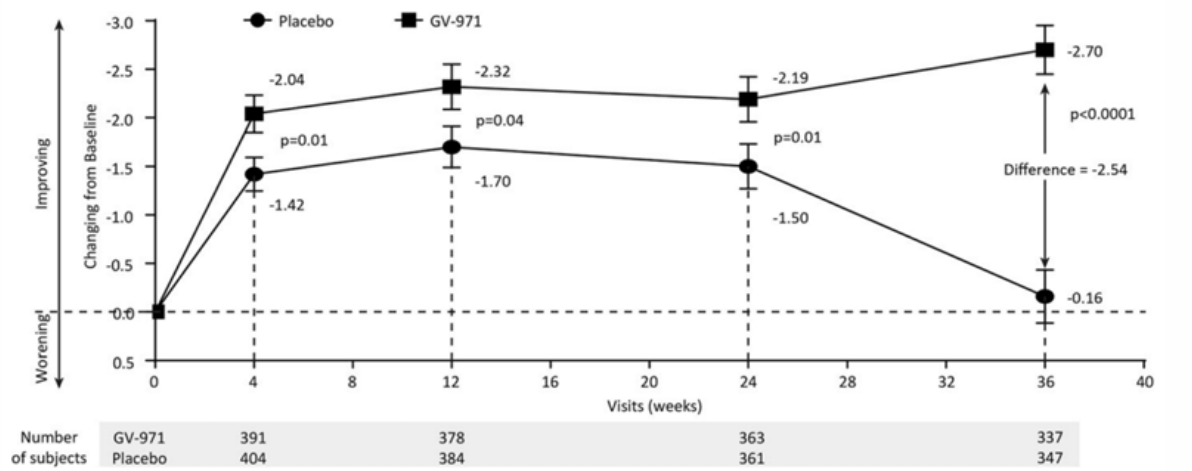
Exhibit 24: MoA of GV-971



Source: Company data

In Ph III trials, GV-971 demonstrated a 2.54-point improvement in ADAS-Cog12 scores vs. placebo during 36-week treatment. Priced at US$1 per capsule (NDRL inclusion in 2022), its annual cost is ~US$2,000 with annual out-of-pocket expense of ~US$1,000, making it more affordable than imported drugs such as lecanemab and donanemab which cost ~US$26k per year and lack of NDRL coverage. Despite its 2022 discontinuation in global Ph III trials, GV-971 achieved US$47mn sales in 2022, reflecting strong demand.

Exhibit 25: Ph III: significant difference in cognitive functions measured by ADAS-Cog12 favoring GV-971 at all time-points after 4 weeks and continuing to 36 weeks

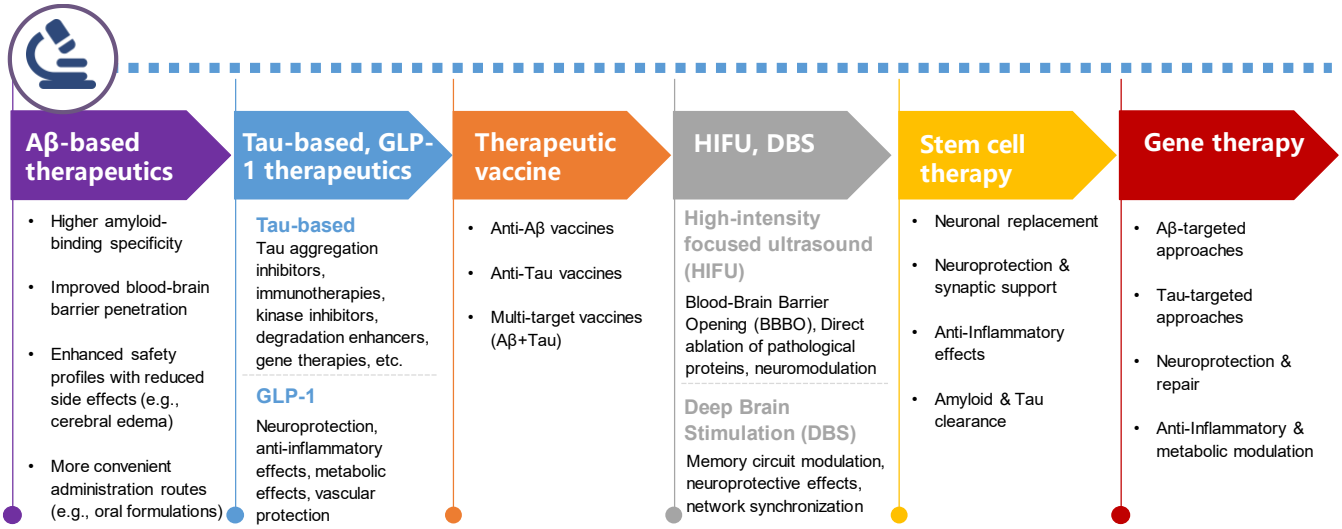


Source: Company data

Next generation therapies under development

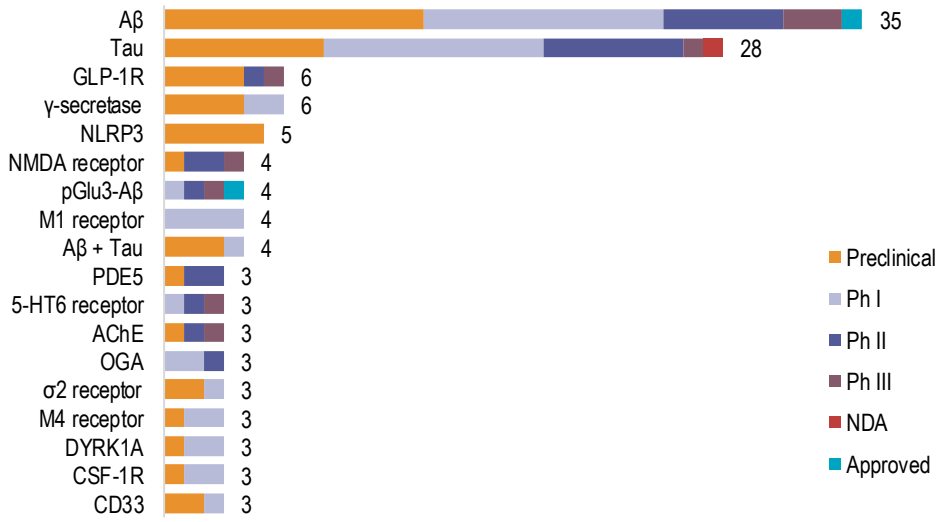
Alzheimer's drug development presents both challenges and opportunities. Current anti-amyloid therapies (e.g., donanemab, lecanemab), while demonstrating clinical benefits, still require improved efficacy and better safety profiles due to side effects such as ARIA (amyloid-related imaging abnormalities). Most mAbs require I.V. infusion, highlighting the need for more convenient delivery methods (e.g., S.C. or oral formulations) to enhance long-term adherence in this chronic condition. Although existing therapies can modestly slow progression, none have shown disease reversal. Emerging approaches – including GLP-1-based therapies, tau-targeting drugs, therapeutic vaccines, and innovative technologies such as focused ultrasound, deep brain stimulation, stem cell therapy, and gene editing – may offer transformative strategies. The future of Alzheimer's treatment may also lie in multi-target combinations, early intervention, and novel delivery systems to address unmet needs.

Exhibit 26: Major categories of next-generation therapies under development for Alzheimer's



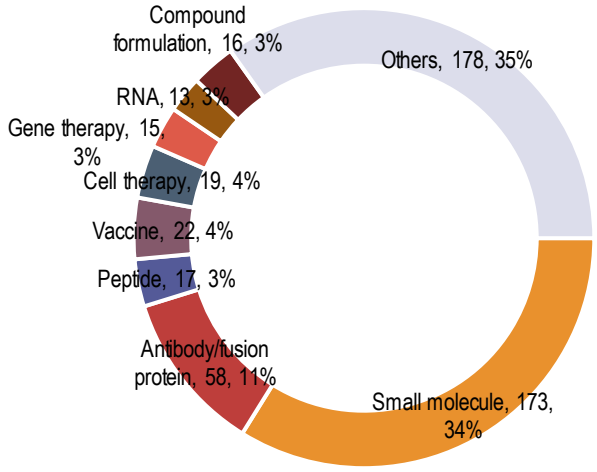
Source: Literature review

Exhibit 27: Pipeline drugs under development for Alzheimer's, by target



Source: Pharmcube. Note: as of Jul 2024

Exhibit 28: Pipeline drugs under development for Alzheimer's, by modality



Source: Pharmcube. Note: as of Jul 2024

In China, Alzheimer's drug pipeline features a mix of amyloid-targeting biologics, tau-based therapies, TCM (traditional Chinese medicine) derivatives, and innovative small molecules. Notable pipelines include biologics such as SHR-1707 (Hengrui, anti-Aβ mAb, Ph II) and CM383 (Keymed, anti-Aβ mAb, Ph I), and small molecules such as varoglutamstat (Simcere/Vivoryon, QPCT inhibitor, Ph II), RP-902 (Risen Pharma, anti-Aβ small molecule, Ph II) and flunopirine (Kanion, AChE inhibitor, Ph II) which aim for oral convenience. There are also TCM-inspired candidates, such as KH-110 (Kanghong, Ph III) and Sailuotong (Shineway, Ph III).

Exhibit 29: Pipeline drugs under development in China for Alzheimer's

Pipeline	Company	Target	Modality	China status
Rivastigmine	Novartis	AChE; BuChE	Small molecule	Approved
Galantamine	Johnson & Johnson	AChE; nAChR	Small molecule	Approved
Huperzine A	Biscayne	AChE	Small molecule	Approved
Memantine	Merz Pharma; Eli Lilly; Lundbeck; Daiichi Sankyo; Forest Labs (AbbVie)	NMDAR; 5-HT3R; nAChR; D2R	Small molecule	Approved
Lecanemab	Biogen; BioArctic; Eisai	Aβ	mAb	Approved
Donanemab	Eli Lilly	pGlu3-Aβ	mAb	Approved
Donepezil+Memantine	Forest Labs (AbbVie)	NMDAR; 5-HT3R; nAChR; D2R; AChE	Small molecule	NDA
Octahydroaminoacridine succinate	Tonghua Golden-Horse (000766 CH)	AChE	Small molecule	NDA
Aducanumab	Biogen; University of Zurich; Eisai; Neurimmune	Aβ	mAb	Ph III
Remternetug	Eli Lilly	pGlu3-Aβ	mAb	Ph III
Crenezumab	Roche; AC Immune	Aβ	mAb	Ph III
Semaglutide	Novo Nordisk	GLP-1R	Peptide	Ph III
Rybelsus	Novo Nordisk	GLP-1R	Peptide	Ph III
Stilbene	Beijing SL Pharma (002038 CH)	/	Small molecule	Ph III
KH-110	Kanghong (002773 CH)	/	TCM	Ph III
Sailuotong	Shineway (2877 HK)	/	TCM	Ph III
KarXT	Zai Lab (ZLB US)/BMS	M1/M4 muscarinic cetylcholine receptor activator	Small molecule	Ph III
Varoglutamstat	Simcere (2096 HK); Vivoryon	Amyloid, QPCT	Small molecule	Ph II
SHR-1707	Hengrui (600276 CH)	Aβ	mAb	Ph II
RP-902	Risen Pharma	Aβ	Small molecule	Ph II
MN-08	Magpie Pharma	NMDAR	Small molecule	Ph II
Benfotiamine	Raising Pharma	Aβ, GSK3A, GSK3B	Small molecule	Ph II
50561	Joekai	/	Small molecule	Ph II
Flunopirine	Kanion (600557 CH)	AChE	Small molecule	Ph II
Yangxue Qingnao	Tasly (600535 CH)	/	TCM	Ph II
Gossypium Flavones	Uyghur Pharma; Xinjiang Technical Institute of Physics & Chemistry	Flavonoid Compounds	TCM	Ph II
Posdinemab	Johnson & Johnson	Tau	mAb	Ph I
BrAD-R13	Braegen	TrkB	Small molecule	Ph I
HEC30654	HEC Pharma (1558 HK)	5-HT6R	Small molecule	Ph I
OAB-14	Xinhua Pharma (719 HK)	RXR	Small molecule	Ph I
Mecopylin	Simovay; Simcere (2096 HK); Neurodawn; Innostar	TRPML1, AChE	Small molecule	Ph I
CM383	Keymed	Aβ	mAb	Ph I
LY03020	Luye Pharma (2186 HK)	TAAR1/5-HT2CR	Small molecule	Ph I
QD202	Quietdbio	Synaptic signaling	Small molecule	Ph I
Anemarrhena Saponin BII	Institute of Radiation Medicine (AMS); Wellso	Natural Product	TCM	Ph I

Source: Pharmcube

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