ALZHEIMER’S DISEASE – GLOBAL DRUG FORECAST AND MARKET ANALYSIS TO 2023
Executive Summary

Table below presents the key metrics for Alzheimer’s disease (AD) in the nine major pharmaceutical markets (US, France, Germany, Italy, Spain, UK, Japan, China, and India) during the forecast period from 2013–2023.

### Alzheimer’s Disease: Key Metrics in Nine Major Pharmaceutical Markets, 2013–2023

<table>
<thead>
<tr>
<th>2013 Epidemiology</th>
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<tr>
<td>AD Prevalent Population</td>
<td>12.9 million</td>
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<tr>
<td>AD Treated Population</td>
<td>3.7 million</td>
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<td>MCI Prevalent Population</td>
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<tr>
<td>MCI Treated Population</td>
<td>5.7 million</td>
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<table>
<thead>
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<th>2013 Market Sales</th>
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<tr>
<td>US</td>
<td>$2.4bn</td>
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<tr>
<td>5EU</td>
<td>$0.6bn</td>
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<td>Japan</td>
<td>$1.2bn</td>
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<tr>
<td>China and India</td>
<td>$0.9bn</td>
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<tr>
<td>Total</td>
<td>$5.0bn</td>
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**Pipeline Assessment**

<table>
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<td>Number of first-in-class drugs</td>
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**Most Promising Pipeline Drugs**

<table>
<thead>
<tr>
<th>Peak-Year Sales</th>
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<tr>
<td>Solanezumab (Eli Lilly)</td>
<td>$2.9bn</td>
</tr>
<tr>
<td>Crenezumab (Roche)</td>
<td>$1.6bn</td>
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<tr>
<td>MK-8931 (Merck)</td>
<td>$1.2bn</td>
</tr>
<tr>
<td>AZD-3293 (AstraZeneca/Eli Lilly)</td>
<td>$0.9bn</td>
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<td>Gantenerumab (Roche)</td>
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<table>
<thead>
<tr>
<th>Key Events (2013–2023)</th>
<th>Level of Impact</th>
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<tr>
<td>Aricept (donepezil hydrochloride) patent expiry in Japan in 2013</td>
<td>↓</td>
</tr>
<tr>
<td>Ebixa (memantine hydrochloride) patent expiry in the 5EU in 2014</td>
<td>↓↓</td>
</tr>
<tr>
<td>Launch of MK-8931 in the US and 5EU in 2018</td>
<td>↑↑↑</td>
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<tr>
<td>Exelon Patch (rivastigmine transdermal system) patent expiry in US and 5EU in 2019</td>
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<tr>
<td>Launch of solanezumab in the US and 5EU in 2019</td>
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### 2023 Market Sales

<p>| | |</p>
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<tr>
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<td>5EU</td>
<td>$1.1 bn</td>
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<tr>
<td>Japan</td>
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<tr>
<td>China and India</td>
<td>$1.3 bn</td>
</tr>
<tr>
<td>Total</td>
<td>$12.1 bn</td>
</tr>
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</table>

Source: GlobalData, Pharma eTrack [Accessed October 25, 2014]

MCI = mild cognitive impairment; NA = not applicable

Sales for AD by Region During the Forecast Period

During 2013–2023, the growth of the AD market will be driven by the entry of disease-modifying therapies (DMTs), including the passive immunotherapies, solanezumab, gantenerumab, and crenezumab, which will have significant uptake in the US, 5EU, and Japan. In addition to DMTs, novel symptomatic therapies with innovative mechanisms of action (MOAs) are anticipated to become routinely used in care over the 10-year forecast period. Lastly, the increasing prevalence of AD and mild cognitive impairment (MCI) across each of the nine major markets (9MM), coupled with advances in diagnostic capability and increased social awareness of the disease, will contribute further to the expansion of this market.
The major drivers of growth in the AD market in the 9MM over the forecast period include:

- Entry of DMTs, including the passive immunotherapies, solanezumab, gantenerumab, and crenezumab; and the beta-secretase (BACE) inhibitors, MK-8931 and AZD-3293
- Entry of novel symptomatic therapies
- Rising prevalence of AD and MCI
- Expanding diagnostic capability
- Growing social awareness of the disease

Conversely, the major barriers to the growth of the AD market include:

- Recent patent losses of the blockbuster brands, including Aricept and Namenda (memantine hydrochloride)
- Remaining diagnostic challenges, despite advances in positron emission tomography (PET) imaging
- Reluctance to seek diagnosis or treatment due to the lack of effective therapies
- Higher costs of therapy associated with novel products

In 2013, GlobalData estimated that the global AD market reached $5.0 billion across the nine major healthcare markets covered in this report: the US, France, Germany, Italy, Spain, the UK, Japan, China, and India. By the end of the forecast period in 2023, sales across these markets will reach $12.1 billion, increasing at a Compound Annual Growth Rate (CAGR) of 9.16% over the 10-year forecast period, which will see the launch of 14 new therapies, including several drug candidates that have potential to modify the underlying cause of the disease.

Figure below illustrates the global AD sales by region during the forecast period.
Executive Summary

Research and Development Strategies

The current AD market consists of four main brands — Eisai/Pfizer’s Aricept (donepezil hydrochloride), Novartis’ Exelon (rivastigmine), Janssen’s Razadyne/Reminyl (galantamine), and Actavis/Lundbeck/Merz’s Namenda/Ebixa/Axura (memantine hydrochloride) — all of which can confer modest symptomatic benefits. However, given that these brands have all reached or are nearing the expiration of their patents, large and small players in the industry are active in the pursuit of more effective medications to satisfy the abundant unmet needs that exist in this market.

AD has proven to be a difficult area for research and development (R&D), as highlighted by multiple late-stage candidates failing to meet primary measures of efficacy. To mitigate the risks associated with failure, several companies have made investments by developing in-house products while also seeking partnerships with specialized firms for access to novel tools like amyloid PET tracers or bioassays. There is a renewed focus on prodromal AD and MCI, as these patients are understood to have the best chance of responding to DMTs, which, in the late-stage pipeline, consist of compounds that act on amyloid beta (Aβ). In addition, several repurposing studies are ongoing to determine if there are preventative effects with medications used in cardiovascular and metabolic disorders (CVMD), as AD has been increasingly associated with mid-life hypertension and diabetes. Lastly, symptomatic pipeline therapies with actions on novel targets within the central nervous system (CNS) are in research as adjunct treatments, as their addition increases patients’ response to the standard therapies and may also provide additional benefit to their cognitive function.

Currently within the late-stage pipeline, 14 medications for AD are being investigated:

- Biopharmaceutical immunotherapies, with drug candidates from Eli Lilly, Roche, and Grifols
- Oral beta-site amyloid precursor protein cleaving enzyme 1 (beta-secretase-1 [BACE1]) inhibitors from Merck & Co. and AstraZeneca/Eli Lilly
- A peroxisome proliferator-activated receptor-gamma (PPAR-gamma) agonist by Takeda
- Archer’s dihydropyridine calcium channel blocker (CCB)
- A tau aggregation inhibitor (TAI) from TauRx
- A tyrosine kinase inhibitor (TKI) from AB Science
- An alpha-7 nicotinic acetylcholine receptor (nAChR) agonist from Forum
- A small-molecule inhibitor of receptors for advanced glycation endpoints (RAGE) by TransTech
- A novel serotonin 5-HT6 receptor antagonist by Lundbeck/Otsuka
Executive Summary

Figure below presents an analysis of the company portfolio gap in AD during the forecast period.

Company Portfolio Gap Analysis in AD, 2013–2023

Strength of Pipeline

<table>
<thead>
<tr>
<th>Current Players</th>
<th>Current and Future Players</th>
<th>Future Players</th>
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</thead>
<tbody>
<tr>
<td>High</td>
<td>Takeda</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Janssen</td>
<td>Actavis</td>
</tr>
<tr>
<td>Novartis</td>
<td>Pfizer</td>
<td></td>
</tr>
<tr>
<td>Eli Lilly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Unmet Needs in the AD Market

The AD market is unique in its level of unmet clinical and environmental need, as there are no curative therapies, and the rates of diagnosis and treatment are low across all stages of the disease. As there is a rising prevalence of AD and MCI in the 9MM included in this analysis, a more unified global coalition of neurology specialists is needed to address MCI and AD as a public health concern, as several factors suggest an impending budgetary crisis for the governments of the 9MM due to the costs associated with healthcare for populations with dementia caused by AD.

The clinical unmet needs for AD include the lack of a curative or DMT; accurate diagnostic tests that can be applied with relative ease; biomarkers for assessing the treatment response; patient classification and determination of risk; and improved control of the primary cognitive symptoms of the disease. The lack of effective therapies has affected the environmental landscape of the AD market, as KOLs interviewed by GlobalData indicated that there is a widespread tendency for patients to diverge from the recommended pathways for treatment, either due to the failure of physicians to establish a diagnosis on behalf of the patient or their family, or primary care physicians’ (PCPs’) delaying referral to a neurologist in order to provide earlier access to treatment and the option to participate in clinical trials.

“One of the challenges is that we haven’t really got great early diagnostic markers for early Alzheimer’s disease, as [of] yet.”

OUS KOL

“The absence of really good ideas is always a limitation. [Even] if we had better mechanisms to test, once we get to the stage of testing, patient recruitment is a well-known problem in the Alzheimer’s field.”

US KOL
Executive Summary

Remaining Opportunity for New Market Entrants

As mentioned by several KOLs interviewed by GlobalData, there is no available AD treatment on the market that is capable of modifying the disease course. Consequently, all the drug treatments that are currently used have limited symptomatic benefit due to the ongoing pathology of the disease. The AD drug market in its current form is marked by an overwhelming need for DMTs and a more diverse set of treatment options for patients who are experiencing cognitive symptoms related to dementia. Any medication that can stop, slow, or prevent AD will satisfy one of the greatest unmet needs in healthcare today. Nonetheless, KOLs remained hopeful that agents that act on Aβ will prove effective, although many urged that other targets should continue to be explored.

“The reality is that amyloid and cognition do not interact or correlate well.”

US KOL

“A tau approach is probably going to be more effective than [the] amyloid approach.”

OUS KOL

Leading Pipeline Agents and the Future Market Outlook

Following the anticipated approval and launch of the first-in-class BACE1 inhibitors and passive immunotherapies in 2018 and 2019, respectively, both of which are drug classes with disease-modifying potential, the AD market will undergo rapid expansion, as several blockbuster therapies are expected to come from these two therapeutic classes. The experimental monoclonal antibodies (mAbs), solanezumab (Eli Lilly), gantenerumab (Roche), and crenezumab (Roche), will compete with the BACE1 inhibitors, MK-8931 (Merck & Co.) and AZD-3293 (AstraZeneca/Eli Lilly), as both treatment approaches are designed to prevent the formation of senile amyloid plaques. The symptomatic therapies in the pipeline, such as LuAE-58054, a serotonin 5-HT6 receptor antagonist from Lundbeck; and EVP-6124, an alpha-7 nAChR agonist from Forum, will also gain market share as the prevalence of symptomatic AD increases throughout the 9MM during the forecast period.
Executive Summary

Figure below provides a competitive assessment of the late-stage pipeline agents in AD during the forecast period.

<table>
<thead>
<tr>
<th>Clinical Attributes</th>
<th>Commercial Attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

Note: Bubble size represents approximate peak-year sales of pipeline drug.

Source: GlobalData

What Do Physicians Think?

The physicians interviewed by GlobalData expressed the importance of a DMT for AD.

“If there are better treatment[s], and, above all, if there are treatment[s] that can slow the progression of the disease…, at the very beginning of the disease in the MCI level or in the asymptomatic treatment level, clearly it will be something very important, and we will use them more earlier than the cholinesterase inhibitors.”

OUS KOL

The physicians also described the potential impact of a DMT for AD on healthcare systems.

“If [we] have a disease-modifying drug, and [we] start to slow the rate of [AD] progression by 50%, in 10 years, you’ll see a significant reduction in nursing home placement.”

US KOL

In addition, some KOLs expressed optimism about the preventative therapies in the late-stage pipeline.

“I’m still hopeful that we will see Alzheimer’s go from a terminal disease to a chronically managed disease, like diabetes.”

US KOL

The physicians also revealed the need for therapies that effectively treat the symptoms related to AD.

“The best [therapy] is the disease-modifying drug, but it[’s efficacy] depends on the symptomatic effect. If the symptomatic effect is very mild, it’s difficult to convince the patient and the family [of the benefit of the drug].”

OUS KOL
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Cardiovascular risk factors in midlife significantly increase the risk of developing AD in later life.

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### 4.2.4 The incidence and prevalence of AD double every five years after age 65 years

The incidence and prevalence of AD double every five years after age 65 years.

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### 4.2.5 Diabetes doubles the risk of AD in men, but only marginally affects the risk in women

Diabetes doubles the risk of AD in men, but only marginally affects the risk in women.

50

### 4.2.6 Women are 1.5 times more likely to develop AD than men

Women are 1.5 times more likely to develop AD than men.

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### 4.2.7 Depression triples the risk for AD, and is the most common comorbidity

Depression triples the risk for AD, and is the most common comorbidity.

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### 4.2.8 Up to 70% of AD patients also suffer from anxiety

Up to 70% of AD patients also suffer from anxiety.

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### 4.2.9 Psychosis and agitation are common comorbidities in Alzheimer’s patients

Psychosis and agitation are common comorbidities in Alzheimer’s patients.

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Global Trends

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Epidemiology Forecast (2013–2023)

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Total Prevalent Cases of AD

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Age-Specific Total Prevalent Cases of AD

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Sex-Specific Total Prevalent Cases of AD

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Age-Standardized Total Prevalence of AD

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Introduction

2 Introduction

2.1 Catalyst

Alzheimer's disease (AD) is a looming endangerment to global health, and a threat to the world economy. One in every three seniors in the US dies with AD or another form of dementia. It is the sixth leading overall cause of death in the US, and ranks as the fifth leading cause of death among those age 65 years old or older. The overall costs of AD were estimated to reach upwards of $200 billion in 2013 in the US alone, $143 billion of which was paid for by Medicaid or Medicare. By 2050, the total cost of AD will reach $1.2 trillion in the US, with government spending on the disease set to increase five fold during this time. Caregivers of dementia patients contribute more than 17.5 billion hours of unpaid care each year, and these working conditions lead to poor health outcomes among those providing care. Due to the high levels of stress encountered when providing care for a person with AD, more than one third of caretakers report symptoms of depression. Along with the physical demands associated with caregiving, AD and dementia caregivers contributed an additional $9.1 billion in health care costs of their own in 2012. To make the problem worse, nearly 80% of all caregiving services are unpaid (AA, 2013).

Amidst several failures, the AD pipeline is large and consists of many novel mechanisms. The market landscape is set to undergo rapid changes in the next decade, driven by advancing diagnostic capabilities and growing social awareness of the disease. Disease-modifying mechanisms are on the horizon, which will bring about a new era in the treatment of this devastating neurodegenerative condition. As a global push is made for early diagnosis and treatment, there will be a surge in the number of AD patients, who will require effective therapies.

2.2 Related Reports


## Introduction

### 2.3 Upcoming Related Reports

Appendix

11.8 About GlobalData

GlobalData is a leading global provider of business intelligence in the healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports, and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

GlobalData has offices in New York, San Francisco, Boston, London, India, Korea, Japan, Singapore, and Australia.

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