Press Conference
March 9, 2017
Eisai Co., Ltd.
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• The Company discloses its consolidated financial statements according to the International Financial Reporting Standards (IFRS)
The Alzheimer’s Disease Update - Eisai’s Approach -

1. Aricept
2. Demography
3. Drug Discovery
4. Clinical Study
5. Market Potential
6. Access and Solution
7. Our Mission
1. Aricept
**Aricept**

*20 years since its launch as the world’s first Dementia standard treatment*

**Approved in over 90 countries**

Global peak sales\(^*1\)
322.8B yen in FY2009

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<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>Launched 5mg/10mg tablet with mild to moderate AD indication in US</td>
</tr>
<tr>
<td>1997</td>
<td>Launched 5mg/10mg tablet with mild to moderate AD indication in EU</td>
</tr>
<tr>
<td>1999</td>
<td>Launched 3mg/5mg tablet with mild to moderate AD indication in Japan</td>
</tr>
<tr>
<td>2001</td>
<td>Launched granules formulation in Japan</td>
</tr>
<tr>
<td>2004</td>
<td>Launched orally-disintegrating tablet (OD) in US and Japan</td>
</tr>
<tr>
<td>2005</td>
<td>Approved for vascular dementia in South Korea, Philippines and India</td>
</tr>
<tr>
<td>2007</td>
<td>Approved for severe AD in US and Japan</td>
</tr>
<tr>
<td>2009</td>
<td>Launched jelly formulation in Japan</td>
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<tr>
<td>2010</td>
<td>Launched 23mg high-dose formulation in US</td>
</tr>
<tr>
<td>2013</td>
<td>Launched dry syrup formulation in Japan</td>
</tr>
<tr>
<td>2014</td>
<td>Approved for dementia with Lewy bodies in Japan</td>
</tr>
</tbody>
</table>

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**Clinical effects demonstrated in Study 302 in US**

**ADAS-Cog score change over time\(^*2\)**

<table>
<thead>
<tr>
<th>Weeks at evaluation</th>
<th>Mean change from the start of treatment (points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>12</td>
<td>2.0</td>
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<tr>
<td>18</td>
<td>3.0</td>
</tr>
<tr>
<td>24</td>
<td>4.0</td>
</tr>
<tr>
<td>30 (weeks)</td>
<td>5.0</td>
</tr>
</tbody>
</table>

**CIBIC-plus score change over time\(^*2\)**

<table>
<thead>
<tr>
<th>Weeks at evaluation</th>
<th>CIBIC-plus score change over time (points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>-0.5</td>
</tr>
<tr>
<td>12</td>
<td>-1.0</td>
</tr>
<tr>
<td>18</td>
<td>-2.0</td>
</tr>
<tr>
<td>24</td>
<td>-3.0</td>
</tr>
<tr>
<td>30 (weeks)</td>
<td>-4.0</td>
</tr>
</tbody>
</table>

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**Continuously provided innovation for 20 years**

Contributed to patients and their families worldwide by seeking new formulations/indications and expanding disease awareness and diagnosis method

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\(^*1\): Sales booked by Eisai
Challenges We Faced and The Solutions We Provided through Aricept

“Donepezil was a ray of light in the darkness”
Dr. Kazuo Hasegawa, Director Emeritus at Tokyo Dementia Care Research and Training Center

Challenges to deliver Aricept
- Forgetfulness is one of the signs of aging; no need to see a doctors
- Severe forgetfulness of parents, but no idea where to consult for
- Huge burden on caregivers due to lack of know-how in dementia care
- Vascular dementia is a major disease, but AD is minor
- Uncertainty in value of slowing the progress of dementia
- When to start and how long will medical treatment last

Practice that Eisai has implemented globally as a pioneer in the dementia field for 20 years

Awareness for diagnosis
Expansion of simple screening tool, MMSE*
for primary care doctors
Implementation of Dr. to Dr. program to enhance know-how on diagnosis

Disease awareness
Enhance awareness of dementia through the media, websites and civic forums

Community networking
Aiming at a society where patients can live with dementia

Japan Academy for Alzheimer's Disease
Achieved to transform “disease for specialists” to “common disease”

Importance of collaboration between stakeholders surrounding patients

* Mini Mental State Examination
2. Demography
Demography of Dementia

There was 9.9 million new cases of dementia in 2015 worldwide, **one case every 3 seconds**

Higher incidence have been observed in middle income countries, accounting for 56% in 2015 and will rise to 65% in 2050

In terms of region/area, **number of patients is increasing in Asia**, and will increase to 67.2 million in 2050

*High income countries are defined as those with a GNI (Gross National Income) per capita of $12,736 or more, Middle income countries are defined as those with a GNI per capita of more than $1,045 but less than $12,736 and Low income countries are defined as those with a GNI per capita of $1,045 or less*  
High Growth Rate Observed in Number of Patients with Dementia

Increasing trend observed in number of patients with major diseases worldwide

From 2015 to 2025, patients with dementia and MCI will significantly increase

Number of patients with major diseases in worldwide* (million)

- Dyslipidemia
- Hypertension
- Type II diabetes
- Chronic kidney disease
- Irritable bowel syndrome
- COPD
- Age-related macular degeneration

MCI
Dementia

Number of patient with MCI
2015: 84.2 million
2025: 119 million

Number of patient with Dementia
2015: 40.1 million
2025: 55.4 million

Source: Decision Resources Group
* Countries filed to DRG Epidemiology database in Mature Markets, Emerging Markets, Americas, Europe, Middle East & Africa, and Asia Pacific
<Cost estimation on dementia>

- 817.9 billion US dollars in 2015, which has been growing 35% in 5 years from 2010
- Dementia will be a trillion US dollar disease in 2018 and will increase up to 2 trillion US dollars in 2030
- Huge burden on care cost (social care cost and family care cost), compared to medical cost

<table>
<thead>
<tr>
<th>Year</th>
<th>Low income countries</th>
<th>Middle income countries</th>
<th>High income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>604.0</td>
<td>22.6</td>
<td>20.4</td>
</tr>
<tr>
<td>2015</td>
<td>817.9</td>
<td>19.4</td>
<td>10.4</td>
</tr>
</tbody>
</table>

*High income countries are defined as those with a GNI (Gross National Income) per capita of $12,736 or more, Middle income countries are defined as those with a GNI per capita of more than $1,045 but less than $12,736 and Low income countries are defined as those with a GNI per capita of $1,045 or less.

3. Drug Discovery
The patient journey begins 10 to 20 years before diagnosis of dementia.
Symptom is Developed in the Order of Sleep, Behavioral, Cognitive

10 to 20 years before

2 years before

1 year before

Diagnosis of dementia

1 year after

Sleep disorder*1

Hypnagogic disorder, REM Sleep Behavior Disorder (RBD), nocturnal awakening, early morning awakening, nonrestorative sleep, irregular sleep-wake rhythm disorder (ISWRD) and others

Behavioral disorder*2

Depression, suicidal ideation, paranoia, anxiety, irritability dizziness on standing up, constipation, syncope, urinary incontinence, Parkinson’s symptoms, epilepsy*3, delusion, wandering, agitation, hallucination, aggression, social adjustment disorder, and others

Cognitive disorder

Memory impairment, impaired orientation, decline in judgement or problem solving skills and others

The patient journey begins 10 to 20 years before diagnosis of dementia

Relation between Sleep and Beta Amyloid (A-beta)

Deep sleep and A-beta deposition are inversely correlated

A-beta deposition accelerates sleep disorder and potentially induces AD


A-beta clearance from the brain is enhanced by sleep

(ketamine/xylazine)
Symptom of depression and A-beta deposition is correlated

Depression is potentially developed before cognitive impairment due to AD

Relation between Epileptic Seizure and Tau

Total tau protein is inversely correlated with seizure latency


Epileptic seizure is potentially induced before cognitive impairment from tau protein increase


Tau accumulation and cognitive function are inversely correlated

Change of neurofibril density tangles (amount of tau deposition) in postmortem brain
Paradigm Shift in Dementia Treatment
- From aggressive factors to genetic background, environmental factors and protective mechanism -

**Aggressive factors**
(A-beta, Tau, reactive glial cell and others)
- Progress Tau pathology by A-beta accumulation
- Tau protein intracellular accumulation causes neuronal cell death
- Synaptic dysfunction and neuronal cell death are induced by reactive glial cell under pathology

**Protective mechanism**
(astrocyte, microglia, BBB, neural stem cell, glymphatic system and others)
- Neuron functions on the astrocyte etc. that closely stick to blood vessel, as a foundation
- Foundation could be protective mechanism to protect neuron from aggressive factors
- Astrocyte and microglia plays an important role to maintain intracerebral homeostasis

**Environmental factors which affect brain function**
- Exogenous
  - Diet and exercise
  - Medication history
  - Environmental chemicals
  - Microbiome (intestinal and oral)
- Endogenous
  - Age
  - Disease history
  - Metabolites (lipid)
  - Immune-related Substance (cytokine)

**Genetic background (genome)**

**Diagram Elements**
- Blood-brain barrier (BBB)
- Amyloid precursor protein (APP)
- cGMP
- Microglia
- Neuron (cognitive function)
- Neuron (sleep)
- Reactive glial cell
- Glymphatic system
- CSF
New Focus on Dementia Medicine Creation
Aiming to clarify the effect of genetic background and environmental factors against protective mechanism

Genetic background
- Protective gene

Environmental factors
- Positive environmental factors

Protective mechanism
- Maintenance of homeostasis

Examples of inherent protective mechanism for brain maintenance
- Prevents materials from entering the brain: Blood-brain barrier (BBB)
- Clearance of functional waste to cerebrospinal fluid: Glymphatic system
- Phagocytosis and clearance for occurred/entered substance in the brain: Brain immune system including microglia
- Structurally support and enhance neurotransmission and alimentation: Astrocyte
- Restore damaged neuronal cell in the brain: Neural stem cell differentiation

Risk gene
- Negative environmental factors
- Decline of homeostasis
Deep sleep is known to be associated with clearance of wastes in the brain. Therefore, sleep disorder is considered to be one of the risk factors of AD. Orexin pathway is known to be related to the maintenance of sleep-wake rhythm.

Mood disorder, such as depression or anxiety, are known to be caused along with the accumulation of amyloid. Also, mood disorder is thought to cause behavioral disorder, such as social adjustment disorder or social withdrawal, then leads to the acceleration of cognitive impairment.

New Paradigm of Modern Dementia

Three pillars

- **Sleep disorder**
  - Transformation of symptoms over time
  - Deep sleep is known to be associated with clearance of wastes in the brain. Therefore, sleep disorder is considered to be one of the risk factors of AD. Orexin pathway is known to be related to the maintenance of sleep-wake rhythm.

- **Behavioral disorder**
  - Mood disorder, such as depression or anxiety, are known to be caused along with the accumulation of amyloid. Also, mood disorder is thought to cause behavioral disorder, such as social adjustment disorder or social withdrawal, then leads to the acceleration of cognitive impairment.

- **Cognitive disorder**

**Foundation**

- Genetic background
- Environmental factor
- Protective mechanism

**Brain maintenance system**

**Progress of aggressive factors accumulation**

- A-beta
- Tau
- Reactive glial cells
Pipeline Strategy Focusing on Three Pillars in New Paradigm

**Foundation**
- Genetic background
- Environmental factor
- Protective mechanism

**Brain maintenance system**
- Intracerebral clearance enhancer through reinforcing protective mechanism
- Brain homeostasis improving agent targeting astrocyte
- Neural stem cell activation agent

**Progress of aggressive factors accumulation**
- Transformation of symptoms over time

**Sleep disorder**
- Lemborexant
  - ISWRD-associated with AD/dementia
  - Orexin receptor antagonist

**Behavioral disorder**
- E2730
  - Epilepsy
  - New mechanism of action
- E2082
  - Epilepsy
  - Next generation AMPA receptor antagonist

**Cognitive disorder**
- E2027
  - Behavioral/cognitive disorder due to Lewy body disease/dementia
  - PDE9 inhibitor
- EphA4
  - Synapse modulator

**A-beta**
- Aducanumab
  - Early AD
  - Anti-amyloid-beta antibody
- BAN2401
  - Early AD
  - Anti-amyloid-beta protofibrils antibody
- Elenbecestat
  - Early AD
  - BACE inhibitor
- Anti-tau antibody
  - AD/dementia
  - New mechanism of action

**Tau**
- E6011
  - AD/dementia
  - Anti-fractalkine antibody

**Reactive glial cell**

All projects are investigational. *1: Co-development with Purdue Pharma. 2: Irregular Sleep-Wake Rhythm Disorder. 3: Under development by Biogen. Eisai has an option to jointly develop and commercialize. 4: Co-development with Biogen. 5: Generic name for E2609. The generic name is not yet fixed at this time.
10 Candidates Widely Cover New Paradigm

<table>
<thead>
<tr>
<th>Phase III</th>
<th>Aducanumab</th>
<th>Anti-A-beta antibody</th>
<th>Two Phase III studies (ENGAGE and EMERGE) targeting early AD ongoing (Under development by Biogen. Eisai has an option to jointly develop and commercialize)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Elenbecestat</td>
<td>BACE inhibitor</td>
<td>Two Phase III studies (MISSION AD1 and MISSION AD2) ongoing for early AD Topline results for primary endpoint anticipated in FY2020 (Co-development with Biogen)</td>
</tr>
<tr>
<td>Phase II</td>
<td>Lemborexant</td>
<td>Orexin receptor antagonist</td>
<td>Phase II study ongoing for irregular sleep-wake rhythm disorder (ISWRD) due to dementia Phase III studies ongoing for insomnia (Co-development with Purdue Pharma)</td>
</tr>
<tr>
<td></td>
<td>BAN2401</td>
<td>Anti-A-beta protofibrils antibody</td>
<td>Phase II study ongoing for early AD Topline results for primary endpoint anticipated in Q3 FY2017 (Co-development with Biogen)</td>
</tr>
<tr>
<td></td>
<td>E2027</td>
<td>PDE9 inhibitor</td>
<td>Phase II study under preparation Aim to improve behavioral/cognitive disorder due to Lewy body disease/dementia</td>
</tr>
<tr>
<td>Phase I</td>
<td>E2730</td>
<td>New mechanism of action</td>
<td>Phase I study ongoing Aim for neurological disease treatment, such as epilepsy</td>
</tr>
<tr>
<td>Preclinical</td>
<td>E2082</td>
<td>Next generation AMPA receptor antagonist</td>
<td>Preclinical studies ongoing Aim for multiple neurological disease treatment</td>
</tr>
<tr>
<td></td>
<td>Anti-tau antibody</td>
<td>New mechanism of action</td>
<td>Preclinical study ongoing aiming at tauopathy (AD/dementia) treatment Candidate antibody demonstrated reduction of insoluble tau aggregation in neurons in preclinical model</td>
</tr>
<tr>
<td></td>
<td>EphA4 synapse modulator</td>
<td></td>
<td>Preclinical study ongoing targeting EphA4, associated with stabilization of synapse</td>
</tr>
<tr>
<td></td>
<td>E6011</td>
<td>Anti-fractalkine antibody</td>
<td>Preclinical study ongoing targeting AD/dementia treatment by suppressing fractalkine pathway (suppressing reactive glial cell) Phase II study for RA and Phase I/II study for Crohn’s disease (under development by EA Pharma) ongoing</td>
</tr>
</tbody>
</table>

All projects are investigational. * Generic name for E2609. The generic name is not yet fixed at this time
4. Clinical Study
Diagnosis Methods of AD

Disease stage

- 10 to 20 years before
- 2 years before
- 1 year before
- Diagnosis of dementia
- 1 year after

Preclinical AD

Prodromal AD

AD

Sleep disorder

Behavioral disorder

Cognitive disorder

Major diagnosis methods

- Genetic marker
- ApoE gene diagnosis
- Lifestyle

Symptoms of sleep disorder
- Symptoms of behavioral disorder
- Blood, CSF A-beta/Tau, and PET imaging
- Functional/structural imaging (vMRI, fMRI and FDG PET)
- Web-based cognitive function assessment
- Diagnosis assessment scales in dementia
- CDR-SB
- ADCOMS

Symptom of cognitive disorder
- Functional/structural imaging (CT, MRI and SPECT)
- Diagnosis assessment scales in dementia
- Hasegawa’s Dementia Scale (HDS)
- MMSE
- ADAS-cog
Diagnosis Methods of Early AD Challenges in Current Situation

ApoE gene diagnosis
- Costs not reimbursed by the insurance in Japan
  (Approx. 20,000 to 40,000 yen at one’s own expense)

Amyloid PET imaging
- Costs not reimbursed by the insurance in Japan (Approx. 450,000 yen at one’s own expense)
- Very limited facilities
  Several synthesis equipment approved as medical device and florbetapir approved as a diagnostic agent in 2016. It will be adopted in the medical field, however, only 4 medical facilities, which obtained manufacturing authentication by Japanese Society of Nuclear medicine could produce with synthesis equipment and utilize it as hospital prepared agent.

Cerebrospinal examination (measure A-beta level in cerebrospinal fluid)
- Costs not reimbursed by the insurance in Japan (Approx. 30,000 yen at one’s own expense)
- Highly invasive: It is reported that headache, nausea, discomfort and other symptoms were observed as CSF hypovolemia a few days after the examination
- Number of hours spent for the examination: Need to rest more than 2 hours in face-up position after paracentesis

Morphological imaging diagnosis (CT, MRI)
- Cost (in case of 30% out of pocket): approx. 4,500 to 6,000 yen for CT and approx. 4,500 to 9,000 yen for MRI
- It is useful to find the level of brain atrophy as a diagnostic aid, but not suitable for early AD diagnosis, which brain atrophy is not clearly observed

* This page shows Japan situation only. It may vary in each country/territory
## Potential of Hemodiagnosis

<table>
<thead>
<tr>
<th>Probability of Success*</th>
<th>Soluble amyloid aggregates</th>
<th>Co-development with Sysmex</th>
<th>Protein derived from neural cell death</th>
<th>Aβ1-40, 1-42</th>
<th>Tau, Total tau Phosphorylated tau</th>
<th>Micro RNA (miRNA)</th>
<th>Autoantibody</th>
<th>Neural-derived exosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>It is considered that very small amount of A-beta aggregates in the blood is brain-derived, so that there is a potential to be able to measure correlation of A-beta amount in brain. Multiple companies reported the data showing that amyloid amount in the blood was correlated to amyloid amount in cerebrospinal fluid (CSF) based on the measurement with utilization of special antibodies and devices. Eisai is also implementing research of reproducibility for those methods with original clinical samples, but it is crucial that they cannot prove scientifically for difficulty in identifying the types of amyloid. For that reason, joint research aiming at innovative method which enable to identify the types of amyloid (aggregates) is ongoing with Sysmex, utilizing super-resolution fluorescence microscope and morphological analysis. If the method was validated with Eisai’s samples, the probability of success for hemodiagnosis from this collaboration research could be high.</td>
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<tr>
<td>Low</td>
<td>It has become possible to measure proteins released along with neural cell death. Possibility for new hemodiagnosis if the measurement system with high sensitivity for certain type protein was developed.</td>
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<tr>
<td>Unknown</td>
<td>It is confirmed that amyloid amount in the blood is not correlated with CSF or strength of amyloid PET signal because most amyloid in the blood is produced by peripheral tissue/component. Therefore, probability of success cannot be higher by simply improve sensitivity to amyloid measurement system. Even though there is a report published in 2014, that AD diagnosis with blood is possible by multiple analysis of amount of A-beta or APP fragments, reproducibility with different cohort has not achieved yet. In addition, this is an inductive method, which considered lower possibility to verify scientific evidence.</td>
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<tr>
<td></td>
<td>If tau amount was measureable, correlation between intracerebral tau amount could be observed. However, tau is consider to be absent in the blood because of Blood-brain barrier (BBB). Consequently, it is considered to be difficult to measure tau in the blood without utilization of unique methods.</td>
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<tr>
<td></td>
<td>It is widely known that miRNA controls gene expression, so that measuring miRNA, which is associated with gene expression in relate to AD, could potentially be utilized as AD diagnosis. However, it is considered that the potential as a diagnosis to identify heterozygous AD is still under investigation, through multiple analysis of either single or numerous miRNA, due to that risk gene for sporadic AD is varied.</td>
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<tr>
<td></td>
<td>The concept to seek potential of AD diagnosis through autoantibody pattern. (There is no scientific evidence at this time)</td>
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<tr>
<td></td>
<td>Intracerebral protein including tau is considered to be released to the blood included in the endoplasmic reticulum called exosome. If exosome derived from the brain could be separated from the blood, increase or decrease of intracerebral protein amount could potentially be estimated through measuring the contents.</td>
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</tbody>
</table>

* Evaluation based on internal assessment
**Overview of BACE Inhibitor Clinical Trial Designs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sponsor</th>
<th>Current status</th>
<th>Study name</th>
<th>Target population</th>
<th>Estimated enrollment</th>
<th>Dose</th>
<th>Inclusion criteria (partial)</th>
<th>Efficacy measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elenbecestat*1,2</td>
<td>Eisai</td>
<td>Phase III</td>
<td>MISSION AD1</td>
<td>Early AD</td>
<td>1330</td>
<td>50mg placebo</td>
<td>MMSE: ≥24 CDR: 0.5 CDR memory box ≥0.5 Amyloid positive</td>
<td>CDR-SB (24 months)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>MISSION AD2</td>
<td>Early AD</td>
<td>1330</td>
<td>50mg placebo</td>
<td>MMSE: ≥24 CDR: 0.5 CDR memory box ≥0.5 Amyloid positive</td>
<td>CDR-SB (24 months)</td>
</tr>
<tr>
<td>Verubecestat MK-8931</td>
<td>Merck</td>
<td>Phase III</td>
<td>APECS</td>
<td>Prodromal AD</td>
<td>1500</td>
<td>12mg 40mg placebo</td>
<td>Diagnosis of prodromal AD (history of subjective memory decline, does not meet criteria for dementia, Amyloid-beta positive)</td>
<td>CDR-SB (104 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EPOCH*3</td>
<td>Mild to moderate AD</td>
<td>2221</td>
<td>12mg 40mg 60mg placebo</td>
<td>Diagnosis of probable AD based on both NINCDS-ADRDA criteria and DSM-IV-TR criteria for AD, AD is of mild to moderate severity</td>
<td>ADAS-cog (78 weeks) ADCS-ADL (78 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase II/III</td>
<td>AMARANTH</td>
<td>Early AD (MCI or mild AD)</td>
<td>2202</td>
<td>20 mg 50 mg placebo</td>
<td>MMSE ≥20 MCI due to AD, Probable AD (NIA-AA)</td>
<td>ADCS-cog13 (104 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DAYBREAK-ALZ</td>
<td>Mild AD</td>
<td>1899</td>
<td>LY3314814 placebo</td>
<td>MMSE: 20-26 CDR: 0.5 or 1 and CDR memory box ≥0.5 Probable AD dementia (NIA-AA)</td>
<td>ADCS-ADL (78 weeks)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>ADCS-iADL, FAQ, iADRS, CDR-SB, NPI, MMSE, CSF A-beta, CSF total tau, Amyloid PET, tau PET</td>
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<td></td>
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<td>CFI, ADCS-ADL (prevention instrument), RBANS, CDR-SB, NABDLTs, fibrillar Amyloid accumulation, neurodegeneration</td>
</tr>
<tr>
<td>Lanabecestat LY3314814/ AZD3293</td>
<td>Eli Lilly</td>
<td>Phase II/III</td>
<td>AMARANTH</td>
<td>Early AD (MCI or mild AD)</td>
<td>2202</td>
<td>20 mg 50 mg placebo</td>
<td>MMSE ≥20 MCI due to AD, Probable AD (NIA-AA)</td>
<td>ADCS-cog13 (104 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase III</td>
<td>DAYBREAK-ALZ</td>
<td>Mild AD</td>
<td>1899</td>
<td>LY3314814 placebo</td>
<td>MMSE: 20-26 CDR: 0.5 or 1 and CDR memory box ≥0.5 Probable AD dementia (NIA-AA)</td>
<td>ADCS-ADL (78 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ADCS-iADL, FAQ, iADRS, CDR-SB, NPI, MMSE, CSF A-beta, CSF total tau, Amyloid PET, tau PET</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CFI, ADCS-ADL (prevention instrument), RBANS, CDR-SB, NABDLTs, fibrillar Amyloid accumulation, neurodegeneration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ADCS-ADL, FAQ, iADRS, CDR-SB, NPI, MMSE, CSF A-beta, CSF total tau, Amyloid PET, tau PET</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CFI, ADCS-ADL (prevention instrument), RBANS, CDR-SB, NABDLTs, fibrillar Amyloid accumulation, neurodegeneration</td>
</tr>
</tbody>
</table>

Study design for Phase II and beyond in the chart above is created by Eisai based on the information on ClinicalTrials.gov as of February 14 2017. All projects are investigational.

*1: Co-development with Biogen  *2: Generic name of E2609. The generic name not yet fixed at this time  *3: Merck announced EPOCH study to stop as of February 14, 2017 on their news release  *4: 60 mg dose is only in Part I of study  *5: Target population for this trial is participants who are asymptomatic at risk for developing AD
## Overview of Anti-A-beta Antibody Clinical Trial Designs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sponsor</th>
<th>Current status</th>
<th>Study name</th>
<th>Target population</th>
<th>Estimated Enrollment</th>
<th>Dose</th>
<th>Inclusion criteria (partial)</th>
<th>Efficacy measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BAN2401</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Eisai</td>
<td>Phase II</td>
<td>Early AD</td>
<td>800</td>
<td>2.5mg/kg biweekly 5.0mg/kg biweekly 10mg/kg biweekly 5.0mg/kg monthly 10mg/kg monthly Placebo</td>
<td>MMSE ≥ 22 MCI due to AD, Probable AD dementia (NIA-AA) CDR: 0.5-1.0 and CDR memory box ≥ 0.5, Amyloid positive</td>
<td>ADCOMS (12 months) Safety ADDCOMS (18 months), total hippocampal volume, brain amyloid levels as measured by PET</td>
<td></td>
</tr>
<tr>
<td><strong>Aducanumab</strong> (BIIB037)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Biogen</td>
<td>Phase III</td>
<td>Early AD</td>
<td>1350</td>
<td>Low dose aducanumab Placebo High dose aducanumab Placebo</td>
<td>MCI due to AD or mild AD CDR-Global Score: 0.5 MMSE ≥ 24 Amyloid positive</td>
<td>CDR-SB (78 weeks) MMSE, ADAS-Cog13, ADCS-ADL-MCI</td>
<td></td>
</tr>
<tr>
<td><strong>Gantenerumab</strong> (RG1450/RO4909832)</td>
<td>Roche</td>
<td>Phase III</td>
<td>SCARLET RoAD&lt;sup&gt;3&lt;/sup&gt; Prodromal AD</td>
<td>799</td>
<td>225mg 105mg Placebo</td>
<td>MMSE ≥ 24 Prodromal AD who are not receiving memantine or cholinesterase inhibitors</td>
<td>CDR-SB (104 weeks)</td>
<td></td>
</tr>
<tr>
<td><strong>Crenezumab</strong></td>
<td>Roche</td>
<td>Phase III</td>
<td>Marguerite RoAD&lt;sup&gt;4&lt;/sup&gt; Mild AD</td>
<td>1000</td>
<td>Gantenerumab Placebo</td>
<td>Clinical diagnosis of probable mild AD (NINCDS/ADRDA), Amyloid-beta positive in CSF ADAS-Cog12, ADAS-Cog13, Amyloid PET, CSF tau, CSF A-beta, hippocampal volume, amyloid PET, MMSE</td>
<td>ADAS-Cog13 (104 weeks) ADCS-ADL (104 weeks)</td>
<td></td>
</tr>
<tr>
<td><strong>Gantenerumab</strong> (RG1450/RO4909832), <strong>Solanezumab</strong> (LY2062430)</td>
<td>Eli Lilly</td>
<td>Phase III</td>
<td>EXPEDITION3&lt;sup&gt;5&lt;/sup&gt; Mild AD</td>
<td>2100</td>
<td>Solanezumab 400mg Placebo</td>
<td>Probable AD (NINCDS/ADRDA) Modified Hachinski Ischemic Scale ≤ 4 MMSE: 20-26 Geriatric Depression Scale ≤ 6 Amyloid-beta positive</td>
<td>ADAS-Cog14 (80 weeks) ADCS-IALD, ADAS-Cog11, ADCS-ADL, FAQ, CDR-SB, NPI, MMSE, RUD-Lite, QoL-AD, Plasma A-beta, CSF A-beta, Amyloid PET, vMRI</td>
<td></td>
</tr>
<tr>
<td><strong>Gantenerumab</strong> (RG1450/RO4909832), <strong>Solanezumab</strong> (LY2062430)</td>
<td>Washington University School of Medicine</td>
<td>Phase II/III</td>
<td>DIAN-TU Preclinical AD&lt;sup&gt;6&lt;/sup&gt;</td>
<td>210</td>
<td>Solanezumab 400mg Placebo</td>
<td>MMSE ≥ 25 CDR: 0 Logical Memory II score 6-18 Amyloid positive</td>
<td>ADCS-PACC (168 weeks) CFI, ADCS-ADL-Prevention Questionnaire, SUVr, CSF Tau, CSF A-beta, vMRI</td>
<td></td>
</tr>
</tbody>
</table>

Study design for Phase II and beyond in the chart above is created by Eisai based on information from ClinicalTrials.gov as of February 14 2017. All projects are investigational *1: Co-development with Biogen *2: Under development by Biogen. Eisai has an option to joint develop and commercialize *3: Roche announced the decision to discontinue the trial as of December 19, 2014 on their press release. FDA in open label extension study 4Q 2015 was announced at Roche Nine Months 2016 Sales Conference Call on October 20, 2016 *4: The ClinicalTrials.gov entry for this study was updated to reflect that this trial has stopped enrolling at 389 participants but is actively continuing, in October 2016, FDA Q1 2016 for open label extension was announced at Roche Nine Months 2016 Sales Conference Call on October 20, 2016 *5: AC Immune SA announced that Genentech, a member of Roche group, has decided to start a second Phase 3 clinical trial CREAD2 as of February 28 2017 on their press release. Not yet updated on ClinicalTrials.gov *6: Eli Lilly announced that solanezumab did not meet the primary endpoint in the EXPEDITION3 clinical trials as of November 23, 2016 on their press release *7: Eli Lilly announced that they made the decision to terminate the EXPEDITION-PRO study as of January 31, 2017 at 2016 4Q earnings call *8: Target population for this trial is older individuals who may be at risk for memory loss *9: Target population for this trial is individuals at risk for or with a type of early onset Alzheimer's disease caused by a genetic mutation
Major A-beta Related AD Projects
Targeting the Progression of the Disease Stage

- **Elenbecestat**\(^*^{,2}\) Phase III (MISSION AD1)
- **Elenbecestat E2609**\(^*^{,2}\) Phase III (MISSION AD2)
- **Verubecestat MK-8931** Phase III (APECS)
- **Verubecestat MK-8931** Phase II/III (EPOCH)\(^*^{3}\)
- **Lanabecestat LY3314814 / AZD3293** Phase II/III (AMARANTH)
- **Lanabecestat LY3314814 / AZD3293** Phase III (DAYBREAK-ALZ)
- **BAN2401** Phase II
- **Aducanumab**\(^*^{5}\) (BIIB037) Phase III (ENGAGE)
- **Aducanumab**\(^*^{5}\) (BIIB037) Phase III (EMERGE)
- **JNJ54861911** Phase II/III\(^*^{4}\)
- **Gantenerumab (RG1450/RO4909832)**, Solanezumab (LY2062430) Phase II/III (DIAN-TU)\(^*^{6}\)
- **Gantenerumab (RG1450/RO4909832)** Phase III (SCarlet RoAD)\(^*^{7}\)
- **Solanezumab (LY2062430)** Phase III (A4)\(^*^{8}\)
- **Gantenerumab (RG1450/RO4909832)** Phase III (Marguerite RoAD)\(^*^{9}\)
- **Crenezumab** Phase III (CREAD2)\(^*^{10}\)
- **Crenezumab** Phase III (CREAD)
- **Solanezumab (LY2062430)** Phase III (EXPEDITION 3)\(^*^{11}\)

Study design for Phase II and beyond in the chart above is created by Eisai based on the information on ClinicalTrials.gov as of February 14 2017. All projects are investigational. "1: Co-development with Biogen. "2: The generic name for E2609 is not yet fixed at this time. "3: Merck announced to stop EPOCH study on February 14, 2017 on their news release. "4: Target population for this trial is participants who are asymptomatic at risk for developing AD. Under development by Biogen. Eisai has an option to jointly develop and commercialize. "6: Target population for this trial is individuals at risk for or with a type of early onset Alzheimer's disease caused by a genetic mutation. "7: Roche announced the decision to discontinue the trial on December 19, 2014 on their press release. FPI in open label extension study Q4 2015 was announced at Roche Nine Months 2016 Sales Conference Call on October 20, 2016. "8: Target population for this trial is older individuals who may be at risk for memory loss. "9: The ClinicalTrials.gov entry for this study was updated to reflect that this trial has stopped enrolling at 389 participants but is actively continuing, in October 2016. Roche announced FPI Q1 2016 for open label extension at Roche Nine Months 2016 Sales Conference Call on October 20, 2016. "10: AC Immune SA announced that Genentech, a member of Roche group, has decided to start a second Phase 3 clinical trial CREAD2 as of February 28, 2017 on their press release. "11: Eli Lilly announced that solanezumab did not meet the primary endpoint in the EXPEDITION3 clinical trials on November 23, 2016 on their press release. "12: Eli Lilly announced that they made the decision to terminate the EXPEDITION-PRO study at 2016 4Q earnings call on January 31, 2017.
<table>
<thead>
<tr>
<th><strong>Dosage and administration setting for Anti-A-beta antibody</strong></th>
<th><strong>Possible failure factors</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>➢ Dose setting without evidence-based consideration especially for antibody; A high degree of difficulty in optimal dose setting from blood concentration for lower brain penetration because of Blood-brain barrier (BBB) and absence of biomarker that capture the type of amyloid target</td>
</tr>
<tr>
<td></td>
<td>➢ Difficulty in higher dose setting for safety risk</td>
</tr>
<tr>
<td><strong>Important factor for success</strong></td>
<td>➢ Consider optimal dosage and administration in clinical studies (Bayesian adoptive design) with various dose and interval</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Patient target</strong></th>
<th><strong>Possible failure factors</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>➢ Targeted patients in later stage against the mechanism of action of the agent</td>
</tr>
<tr>
<td></td>
<td>➢ Absence of diagnosis criteria to enroll right patients (amyloid PET imaging)</td>
</tr>
<tr>
<td><strong>Important factors for success</strong></td>
<td>➢ Enroll patients in right disease stage (need for medical treatment in earlier stage and Patient enrollment ratio in consideration of disease stage. prodromal AD: early mild AD=3:1)</td>
</tr>
<tr>
<td></td>
<td>➢ Enroll A-beta positive patients (Some reports indicated 1/3 of patients diagnosed as AD, did not have A-beta deposition in the brain in past clinical studies)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Endpoint</strong></th>
<th><strong>Possible failure factor</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>➢ Possibility for erroneously selected endpoint (Problems with sensitivity for selected endpoint)</td>
</tr>
<tr>
<td><strong>Important factor for success</strong></td>
<td>➢ Select/include evaluation index (endpoint) with high sensitivity for target patients, such as ADCOMS and CDR-SB</td>
</tr>
<tr>
<td></td>
<td>➢ Cooperate with medical facilities aiming at improving the quality of endpoint evaluation</td>
</tr>
</tbody>
</table>
**Keys for Clinical Studies of Elenbecestat\(^1,2\) and BAN2401\(^1\)**

**Biomarker magnitude**
- Normal
- Abnormal

**Clinical disease stage**
- Cognitively normal
- Preclinical AD
- Prodromal AD
- Mild AD
- Moderate AD
- Severe AD

**Optimal dose setting**
- Optimal single dose of 50mg based on human genetic evidence and PK/PD data of Phase I and II studies
- Adopt Bayesian adaptive design aiming at enabling to find out optimal dose and administration from 6 different dose/administration arms including placebo

**Optimal endpoint setting**
- Primary endpoint CDR-SB
- Primary endpoint ADCOMS

**Right patient target**
- Patients in right disease stage (Patients with early AD, MMSE ≥ 24\(^3\))
- A-beta positive patients

**Elenbecestat\(^1,2\)**
- Phase III studies MISSION AD1
- MISSION AD2

**BAN2401\(^1\)**
- Phase II study

---

\(^1\): Co-development with Biogen  
\(^2\): Generic name for E2609. The generic name is not yet fixed at this time.  
\(^3\): Inclusion criteria for MISSION AD (Phase III study for E2609)
Phase III studies for Elenbecestat*1,2
Evaluation Items in MISSION AD

MISSION AD

Cognition & Clinical function
- CDR-SB

Primary endpoint
(General clinical symptoms)

Profiling of disease modifier based on multiple evaluation

Disease modifying effect (changes in disease)

Disease modifying effect

Clinical benefit

Brain structure
- Volumetric MRI

A-beta accumulation
- CSF A-beta
- Amyloid PET

Neuronal injury
- CSF t-Tau/p-Tau

Synaptic dysfunction
- Functional MRI

Disease progression
- Time to AD conversion
- CDR-SB slope

Cognition
- CDR-SB
- MMSE
- ADAS-cog14

ADL/QOL
- FAQ
- EQ-5D, QOL-AD

Psychological symptom
- NPI-10

Caregiver burden
- Zarit’s Burden Interview

Adopt multiple secondary endpoints to support efficacy confirmed in primary endpoint and evaluation of correlation between biomarker

*1: Co-development with Biogen  
*2: Generic name for E2609. The generic name is not yet fixed at this time
Key Factors for Clinical Development Success of Disease Modifier for AD

- Select appropriate patient target group (early AD) and implement precise screening to confirm amyloid deposition
- Concerns on dose setting
  Minimize arm setting as possible to confirm efficacy with utilization of biomarker for small molecule candidates
  (MISSION AD1,2 for Elenbecestat*1,2)
  Prudently consider dose setting in Phase II study for antibody candidates
- Select/include endpoint for clinical effect evaluation with high sensitivity in early AD patients
  MISSION AD1,2 for Elenbecestat: CDR-SB
  Phase II study for BAN2401*1: ADCOMS
- Implement two pivotal studies with the same study design simultaneously aiming at fulfilling regulatory requirements
- Seek FDA Fast-track designation/Priority review

*1: Co-development with Biogen  *2: Generic name for E2609. The generic name is not yet fixed at this time
### Seek Potential of Various Combination Therapy with Pipeline Covering New Paradigm

#### Example of combination therapy candidates

<table>
<thead>
<tr>
<th>Traditional Combination</th>
<th>Potential impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>BACE inhibitor + Anti-A-beta antibody</td>
<td>Aiming at realization of enhanced efficacy to slower the disease progression through inhibition of aggressive factors by two different approaches</td>
</tr>
<tr>
<td>Anti-A-beta treatment (BACE inhibitor/Anti-A-beta antibody) + Sleep disorder treatment /Behavioral disorder treatment /Cognitive disorder treatment</td>
<td>Aiming at achieving multidisciplinary care for patients in various early disease stage</td>
</tr>
<tr>
<td>Anti-A-beta antibody(BACE inhibitor/Anti-A-beta antibody) + Anti-tau antibody</td>
<td>Aiming at realization of multidisciplinary therapy for multiple aggressive factors with stronger disease modifier for patients in broad disease stage</td>
</tr>
<tr>
<td>Anti-A-beta treatment (BACE inhibitor/Anti-A-beta antibody) + Anti-tau antibody + Intracerebral protective mechanism enhancer</td>
<td>Potential for preemptive medicine and expectation as an ultimate disease modifying multidisciplinary cure by inhibition of aggressive factors and enhancement of protective mechanism</td>
</tr>
</tbody>
</table>
5. Market Potential
### Potential Market Size for Next Generation AD treatments

**Number of patients with early AD (prodromal AD and mild AD)**

<table>
<thead>
<tr>
<th>Approximate number of Prodromal AD patients</th>
<th>US</th>
<th>Europe*¹</th>
<th>Japan</th>
<th>Emerging*²</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of Prodromal AD</td>
<td>3.0 million</td>
<td>3.6 million</td>
<td>1.8 million</td>
<td>6.8 million</td>
<td>15.2 million</td>
</tr>
<tr>
<td>% Diagnosed</td>
<td>60%</td>
<td>50%</td>
<td>60%</td>
<td>15%</td>
<td>5.7 million</td>
</tr>
<tr>
<td>Diagnosed</td>
<td>1.8 million</td>
<td>1.8 million</td>
<td>1.1 million</td>
<td>1.0 million</td>
<td>3.7 million</td>
</tr>
<tr>
<td>% Drug Treated</td>
<td>80%</td>
<td>60%</td>
<td>80%</td>
<td>35%</td>
<td>2.2 million</td>
</tr>
<tr>
<td>Drug Treated</td>
<td>1.4 million</td>
<td>1.1 million</td>
<td>0.8 million</td>
<td>0.4 million</td>
<td>(100%)</td>
</tr>
<tr>
<td>% Amyloid Positive*³</td>
<td>60%</td>
<td>60%</td>
<td>60%</td>
<td>60%</td>
<td>(100%)</td>
</tr>
<tr>
<td>Amyloid Positive</td>
<td>0.9 million</td>
<td>0.6 million</td>
<td>0.5 million</td>
<td>0.2 million</td>
<td>(100%)</td>
</tr>
<tr>
<td>(% of share)</td>
<td>(39%)</td>
<td>(29%)</td>
<td>(23%)</td>
<td>(10%)</td>
<td>(100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Approximate number of Mild AD patients</th>
<th>US</th>
<th>Europe*¹</th>
<th>Japan</th>
<th>Emerging*²</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of Mild AD</td>
<td>3.0 million</td>
<td>4.3 million</td>
<td>2.4 million</td>
<td>6.8 million</td>
<td>16.5 million</td>
</tr>
<tr>
<td>% Diagnosed</td>
<td>75%</td>
<td>55%</td>
<td>75%</td>
<td>30%</td>
<td>8.4 million</td>
</tr>
<tr>
<td>Diagnosed</td>
<td>2.2 million</td>
<td>2.4 million</td>
<td>1.8 million</td>
<td>2.0 million</td>
<td>5.6 million</td>
</tr>
<tr>
<td>% Drug Treated</td>
<td>80%</td>
<td>70%</td>
<td>80%</td>
<td>35%</td>
<td>3.9 million</td>
</tr>
<tr>
<td>Drug Treated</td>
<td>1.8 million</td>
<td>1.7 million</td>
<td>1.4 million</td>
<td>0.7 million</td>
<td>(100%)</td>
</tr>
<tr>
<td>% Amyloid Positive*³</td>
<td>70%</td>
<td>70%</td>
<td>70%</td>
<td>70%</td>
<td>(100%)</td>
</tr>
<tr>
<td>Amyloid Positive</td>
<td>1.2 million</td>
<td>1.2 million</td>
<td>1.0 million</td>
<td>0.5 million</td>
<td>(100%)</td>
</tr>
<tr>
<td>(% of share)</td>
<td>(32%)</td>
<td>(30%)</td>
<td>(26%)</td>
<td>(13%)</td>
<td>(100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total number of A-beta positive patient target</th>
<th>US</th>
<th>Europe*¹</th>
<th>Japan</th>
<th>Emerging*²</th>
<th>Total</th>
</tr>
</thead>
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<tr>
<td>(% of share)</td>
<td>(34%)</td>
<td>(29%)</td>
<td>(25%)</td>
<td>(12%)</td>
<td>(100%)</td>
</tr>
</tbody>
</table>

Source: Internal estimates at 2028, based on Decision Resources. Figures are approximate.

*¹ Europe: UK, France, Germany, Italy, Spain, Austria, Greece, Netherlands, Norway, Poland, Portugal, Sweden, Switzerland, Belgium, Czech Republic, Denmark, Finland

*² Emerging Countries: Brazil, China, India, Mexico, Russia, South Korea, Turkey. *³ The percentage of Amyloid positive patients who receives drug therapy
Pricing of next generation AD treatments based on the benefit they offer patients

Next generation AD treatments are expected to alter disease progression from earlier stages and for longer periods of time, unlike today's AD treatments. Pricing for next generation AD treatments is expected to reflect their enhanced patient value.

Pricing of medicine reflects the value it contributes to patients, not its drug structure*1

<table>
<thead>
<tr>
<th>Drug treatment</th>
<th>Drug structure</th>
<th>Unit</th>
<th>Price² (yen)</th>
<th>Price/day³ (yen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>Small molecule</td>
<td>0.5 mg</td>
<td>8,172</td>
<td>8,172</td>
</tr>
<tr>
<td>Gilenya®/Imusera®</td>
<td>Antibody</td>
<td>300 mg</td>
<td>228,164</td>
<td>8,149</td>
</tr>
<tr>
<td>Tysabri®</td>
<td>Antibody</td>
<td>300 mg</td>
<td>228,164</td>
<td>8,149</td>
</tr>
<tr>
<td>Tecfidera®</td>
<td>Small molecule</td>
<td>120 mg</td>
<td>2,037</td>
<td>8,149</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug treatment</th>
<th>Drug structure</th>
<th>Unit</th>
<th>Price² (yen)</th>
<th>Price/day³ (yen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>Antibody</td>
<td>100 mg</td>
<td>113,190</td>
<td>4,042</td>
</tr>
<tr>
<td>Treatment</td>
<td>Antibody</td>
<td>40 mg</td>
<td>71,097</td>
<td>5,078</td>
</tr>
<tr>
<td>Remicade®</td>
<td>Antibody</td>
<td>100 mg</td>
<td>113,190</td>
<td>4,042</td>
</tr>
<tr>
<td>(Generic name: infliximab)</td>
<td>Antibody</td>
<td>40 mg</td>
<td>71,097</td>
<td>5,078</td>
</tr>
<tr>
<td>Humira®</td>
<td>Antibody</td>
<td>40 mg</td>
<td>71,097</td>
<td>5,078</td>
</tr>
<tr>
<td>(Generic name: adalimumab)</td>
<td>Antibody</td>
<td>40 mg</td>
<td>71,097</td>
<td>5,078</td>
</tr>
<tr>
<td>Xeljanz®</td>
<td>Antibody</td>
<td>5 mg</td>
<td>2,539</td>
<td>5,078</td>
</tr>
<tr>
<td>(Generic name: tofacitinib)</td>
<td>Antibody</td>
<td>5 mg</td>
<td>2,539</td>
<td>5,078</td>
</tr>
<tr>
<td>Multiple myeloma treatment</td>
<td>Antibody</td>
<td>300 mg</td>
<td>160,696</td>
<td>19,131</td>
</tr>
<tr>
<td>Kyprolis®</td>
<td>Antibody</td>
<td>300 mg</td>
<td>160,696</td>
<td>19,131</td>
</tr>
<tr>
<td>(Generic name: carfilzomib)</td>
<td>Antibody</td>
<td>300 mg</td>
<td>160,696</td>
<td>19,131</td>
</tr>
<tr>
<td>Empliciti®</td>
<td>Antibody</td>
<td>300 mg</td>
<td>160,696</td>
<td>19,131</td>
</tr>
<tr>
<td>(Generic name: elotuzumab)</td>
<td>Antibody</td>
<td>300 mg</td>
<td>160,696</td>
<td>19,131</td>
</tr>
</tbody>
</table>

*1: Eisai view based on internal research  
*2: Price in Japan  
*3: Source: MHLW (Ministry of Health, Labour and Welfare) List of Approved Products for new drugs  
*4: Daily prices are calculated as follows: Remicade®: 2 vials every 8 weeks, Humira®: 1 syringe every 2 weeks, Xeljanz®: 2 tablets daily
6. Access and Solution
Establish comprehensive public-private partnership (PPP) to support establishing a base (capacity building) of prevention/diagnosis/treatment/care of dementia

Prioritize dementia care, and establish strategies including funding, by leveraging WHO’s Global Action Plan

Current situation

- More than 50% of dementia patients live in developing countries where social security system is not well established
- While more countries are willing to introduce Universal Healthcare Coverage (UHC), priority for dementia care is still low in each country
- WHO’s goal is for 75% of its member states to have policies or strategies for dementia in place by 2025

Important aspects for the future

- Improve patient access though Affordable Pricing Policy
  - Provision of next generation AD treatments depending on the payment capability and medical infrastructure of each county
### Initiatives for Dementia and Cancer in Japan

<table>
<thead>
<tr>
<th>Dementia</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of specialized facilities</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Designated cancer hospitals: 427</td>
</tr>
<tr>
<td>Dementia-related Disease Medical Centers: 339</td>
<td>2 National Cancer Center Research Institutes, 49 Designated cancer hospitals in each prefecture, 347 Local designated cancer hospitals, 1 Designated cancer hospital specializing in the treatment of specific types and 28 local cancer hospitals</td>
</tr>
<tr>
<td>10 National and 30 Prefectural</td>
<td></td>
</tr>
<tr>
<td>299 hospitals and clinics that meet the criteria for Dementia-related Disease Medical Centers in each prefecture</td>
<td></td>
</tr>
<tr>
<td><strong>Government initiatives</strong></td>
<td>Comprehensive 10-year Strategy for Cancer Control (1984)</td>
</tr>
<tr>
<td>Emergency Project for Improvement of Medical Care and Quality of Life for People with Dementia (2008)</td>
<td>Basic Plan to Promote Cancer Control Programs (2007)</td>
</tr>
<tr>
<td><strong>Related laws</strong></td>
<td>Cancer Control Act (2006)</td>
</tr>
<tr>
<td>Long-Term Care Insurance Act (1997)</td>
<td>Law Concerning the Promotion of Cancer Registration(2013)</td>
</tr>
<tr>
<td>Law to Promote The Use of Adult Guardianship (2016)</td>
<td></td>
</tr>
<tr>
<td><strong>Screening initiated by law&lt;sup&gt;3&lt;/sup&gt; or based on government guideline&lt;sup&gt;4&lt;/sup&gt;</strong></td>
<td>Initiation of gastric/womb cancer screening (1983)</td>
</tr>
<tr>
<td>None</td>
<td>Initiation of uterine/lung/breast cancer screening (1987)</td>
</tr>
<tr>
<td>(Partially implemented by local government decision)</td>
<td>Initiation of colorectal cancer screening (1992)</td>
</tr>
</tbody>
</table>

- There is no law for dementia that includes comprehensive guidelines, like the Cancer Control Act
- Further expansion of public funding on development of dementia treatment is expected
- Screening for dementia is expected to be implemented with public budget, like screening for cancer

**Countermeasures for dementia have a relatively short history, compared to cancer.**

Prompt action to establish countermeasures for dementia is expected along with the rapid aging of the population.

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<sup>1</sup>: Based on internal research  
<sup>2</sup>: Facilities which met the criteria, established by MHLW  
<sup>3</sup>: Law of Health and Medical Services for the Elderly  
<sup>4</sup>: Plan for Education for Prevention of Cancer and Implementation of Cancer Screening
Aim to establish a social system which enables dementia patients to live safely and with peace of mind in their community through solving their problems by providing solutions in real world in the field of dementia for clinical questions found based on True Needs of patients and their families.

Find clinical questions

Verify in real world

Provide solution
<table>
<thead>
<tr>
<th>Clinical Question</th>
<th>Solution</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Decline in activities of daily living caused by dehydration</td>
<td>Multidisciplinary collaboration to ensure patients to drink 800ml of water per day</td>
<td>Care level was improved from 5 to 3</td>
</tr>
<tr>
<td>2. Management of BPSD*</td>
<td>Analyzing causes of symptoms and sharing countermeasures among multidisciplinary team</td>
<td>Extension of treatment duration at home</td>
</tr>
<tr>
<td>3. Terminal care</td>
<td>Optimizing devices by nurses dedicated in continence care</td>
<td>Enhancement of terminal care through well-managed continence care</td>
</tr>
<tr>
<td>4. Uncontrolled bowel movement</td>
<td>Replacing medicines of possible cause of constipation aiming at manageable bowel movement</td>
<td>Improvement in the quality of life of elderly people living alone through maintenance of continence</td>
</tr>
<tr>
<td>5. Uncontrolled medication</td>
<td>Promotion of drug administration at right interval through utilizing ICT and sharing information among multidisciplinary team</td>
<td>Timely administration contributed to health maintenance</td>
</tr>
<tr>
<td>6. Prevention for fall</td>
<td>Intervention by multidisciplinary team and caregivers Reducing frequency for restroom by excretion care</td>
<td>Reduction in frequency of falling (from 8 to 4 times a month) and fall prevention</td>
</tr>
<tr>
<td>7. Aspiration pneumonia</td>
<td>Infection prevention through improving living environment (room temperature management and switching to a suitable formulation by pharmacists)</td>
<td>Extension of treatment duration at home through aspiration pneumonia prevention</td>
</tr>
<tr>
<td>8. Uncontrolled nighttime blood pressure</td>
<td>Stabilization of blood pressure by improving adherence</td>
<td>Reduction in emergency request (Reduction in the frequency of calling an ambulance etc.)</td>
</tr>
<tr>
<td>9. Medication failure cased by reduced willingness</td>
<td>Medication counseling intervention by pharmacists</td>
<td>Motivated and satisfied for self management in medication and achieved daily rhythm</td>
</tr>
<tr>
<td>10. Frequent bad physical condition</td>
<td>Timely care for the change in physical condition (cold symptoms, vital signs and management of body temperature)</td>
<td>Reduction of health care cost and burden of family by avoiding hospitalization</td>
</tr>
</tbody>
</table>

*B* Behavioral and Psychological Symptoms of Dementia, including impatience, agitation, aggression, psychological symptoms
A Case of Improvement in Care Level of a Bedridden Patient through Rehydration Management

Clinical question

How can we prevent decline in activities of daily living caused by dehydration for bedridden patients?

Solution

Aiming at appropriate rehydration through daily monitoring with information sharing among multidisciplinary team

Tool

Adopted multidisciplinary Collaboration support service “Hikari One Team SP”*

Outcome

Physical condition was improved by appropriate rehydration
Care level improved from 5 to 3

Daily water intake and weight change

- Maximum quantity of water intake within the week
- Average quantity of water intake within the week
- Minimum quantity of water intake within the week

- Initiated to use the system on June 18
- Certification review on August 16
- Physical strength was significantly improved
- The care level improved from 5 to 3 on October 6

The content was presented at International Modern Hospital Show 2015, by Dr. Toshihiro Yoshizawa, Department of Neurology, NTT East NTT Medical Center Tokyo

* Launched by NTT IT
How can we improve adherence and family burden for dementia patients living alone, who are not able to manage medicine administration?

Aiming at informing appropriate timing of administration to improve adherence

Introduction of administration support device, “e-OKUSURI-SAN”

Enabled patient to take medicine at the scheduled time everyday
Reduced burden on family and solved their anxiety about dementia care

Medication administration history (image)

Blank: No administration
Bumps and dents: Irregularity in the time of administration
Tools to Provide Aiming at Solution

Multidisciplinary collaboration service  Hikari One Team SP

Cloud service to support multidisciplinary collaboration in community
1. “One Team Support Function”
   - to share and remind most important “One team policy” (ex. achieving a goal of appropriate rehydration) for each patient
2. “Monitoring function”
   - to visualize items, such as vital signs, cognitive function and status of medication administration continuously and conveniently

Service commenced in July 2016 (Launched by NTT IT)

Olfactory test  UPSIT

Smell screening test to encourage behavior change for health promotion
1. An individual’s olfactory ability can be discriminated easily
2. It triggers an awareness of a fact that the olfactory sense plays an important role in our daily lives
3. Seeing the change of olfactory with objective indicator, improve their own health management consciousness

Launch anticipated in April 2017

Administration support device  e-OKUSURI-SAN

Administration support device to realize continued medical treatment at home
1. Prevent from adherence failure or overdose medication and ensure right dose/timing
2. Support coordination among patients, family, physician and caregiver by sharing adherence data
3. Potential to spend time longer in their way at either nursing home or at one’s home

Launch in January 2017

Tracking tool to support elderly people going out  Me-MAMORIO

Tag type IoT device to support elderly people going out
1. When patients with dementia who carry the tag come and go from home, caregivers can be notified it with their smartphone.
2. “Passing positional data” by “tracking supporters” who have the application installed on their smartphone enable them to search

Under development

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Under development
Realization of “Community Networking” aiming at a society where patients with dementia can live safely and with peace of mind

Partnership agreement for dementia with 84 towns/cities in Japan (as of end of February 2017)

- Promote well-being projects at communities through collaboration between local government, local medical association, local pharmacist’s association and Eisai with sharing know-hows
- Find out clinical questions through socialization with local people
- Create outcome by providing evidence-based solution for issues that patients and local communities are facing

Evidence creation and solution development through Living Lab and limited liability company (LLC)

- Living Lab: Aiming at evidence creation and early solution development through examination/development/evaluation in collaboration of stakeholders, such as “Local people”, “company”, “local government”, “academia” and “medical facility”
- LLC: Aim to solve patients/local issues through providing solution for clinical questions through establishing LLC in collaboration with “company”, “local government”, “academia” and “medical facility”

Aim to realize “community networking” to allow patients with dementia to live safely and with peace of mind through providing solution for patients’/local issues based on clinical questions found at towns/cities where we have partnership agreement.
7. Our Mission
Potential to inhibit the disease progression of dementia to an achievable level, just like the cure of cancer has become realizable.

The paradigm of medicine creation of dementia is further expanding starting from A-beta or tau.

It is essential to establish countermeasures to address the social costs and the burden on families out of cost structure of dementia by both public and private entities.

Eisai is taking charge of the mission to lead the world in dementia care through providing solution for every aspect of the dementia field.
Company Objectives of EWAY
- MEDICO SOCIETAL INNOVATOR -

Domain I.

Prevention — Cure — Care

Aiming to provide product package to support all disease stage and symptom in dementia

Domain II.

Regional medicine that provides peace of mind and safety

“Community networking” through dementia solution based on evidence demonstrated in real world