13. Major R&D Pipeline

In-House R&D Pipeline List

	Product Name / Development Code	Additional Indication, etc.**	Development Stage***	Therapeutic Area****
New Approval				
◎	Fycompa (Monotherapy for partial-onset seizures)	AI	(US) approved	Neurology
◎	Pariet (Maintenance therapy for proton pump inhibitor-resistant reflux esophagitis)	ADA	(JP) approved	GI
◎	Rectabul (Ulcerative colitis)*		(JP) approved	GI
Submitted / Preparing for Submission				
	Aricept (Severe Alzheimer's disease)	AI	(CN) submitted	Neurology
	AJG533 (Chronic constipation)*		(JP) submitted	GI
◎	Lenvima (Hepatocellular carcinoma: HCC)	AI	(JP/US/EU/CN)submitted	Oncology
○	Halaven (Breast cancer)		(CN) preparing for re-submission	Oncology
Clinical Trial Stage				
	E2006 (Insomnia disorder)		(JP/US/EU) PIII	Neurology
	E2609 (Early Alzheimer's disease)		(JP/US/EU) PIII	Neurology
	BIIB037(Early Alzheimer's disease)		(JP/US/EU) PIII	Neurology
	Lenvima (Thyroid cancer)		(CN) PIII	Oncology
	AJM300 (Ulcerative colitis)*		(JP) PIII	GI
	AJG555 (Chronic constipation)*		(JP) PIII	GI
	Livact (Hypoalbuminemia)		(CN) PIII	GI
	Fycompa (Lennox-Gastaut syndrome)	AI	(JP/US/EU) PIII	Neurology
	Fycompa (Pediatric epilepsy)	AI	(JP/US/EU) PIII	Neurology
○	Fycompa (Monotherapy for partial-onset seizures)	AI	(JP) PIII	Neurology
	Lenvima (Renal cell carcinoma, first-line)	AI	(JP/US/EU) PIII	Oncology
	ME2125 (Parkinson's disease)		(JP) PII/ III	Neurology
	BAN2401 (Alzheimer's disease)		(JP/US/EU) PII	Neurology
	E2006 (Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia)		(JP/US) PII	Neurology
	MORAb-003 (Platinum-sensitive ovarian cancer)		(JP/US/EU) PII	Oncology
	MORAb-004 (Melanoma)		(US/EU) PII	Oncology
	MORAb-009 (Mesothelioma)		(US/EU) PII	Oncology
	E7777 (Peripheral T-cell lymphoma, cutaneous T-cell lymphoma)		(JP) PII	Oncology
	Halaven (Combination therapy with anti-PD1 antibody pembrolizumab in breast cancer)		(US) PI/II	Oncology
	Lenvima (Combination therapy with anti-PD1 antibody pembrolizumab in select solid tumors)		(US) PI/II (JP) PI	Oncology
	E6007 (Ulcerative colitis)*		(JP) PII	GI
	E6011 (Rheumatoid arthritis)		(JP) PII	Other
	E6011 (Primary biliary cholangitis)*		(JP) PII	Other
	Halaven (Bladder cancer)	AI	(US/EU) PI/II	Oncology
	Lenvima (Non-small cell lung cancer, RET translocations)	AI	(JP/US/EU/AS) PII	Oncology
	Lenvima (Biliary tract cancer)	AI	(JP) PII	Oncology
	Halaven (Combination therapy with PEGPH20 in breast cancer)		(US) PI/II	Oncology
	E6011 (Crohn's disease)*		(JP) PI/II	Other
	BELVIQ (Obesity)		(JP) PI	Neurology
	E2027 (Alzheimer's disease)		(US) PI	Neurology
	E2730(Epilepsy)		(US) PI	Neurology
◎	E2082(Epilepsy)		(JP) PI	Neurology
	E7090 (Solid tumors)		(JP) PI	Oncology
	MORAb-066 (Solid tumors)		(US) PI	Oncology
	E7046 (Solid tumors)		(US/EU) PI	Oncology
	H3B-6527 (HCC)		(US/EU) PI	Oncology
	H3B-8800 (Blood cancer)		(US/EU) PI	Oncology
	E7438 (Non-Hodgkin B-cell lymphoma)		(JP) PI	Oncology
	Lenvima (Combination therapy with anti-PD1 antibody pembrolizumab in HCC)		(JP/US) PI	Oncology
◎	E7386 (Solid tumors)		(EU) PI	Oncology
◎	H3B-6545 (Breast cancer)		(US) PI	Oncology
◎	MORAb-202 (Solid tumors)		(JP) PI	Oncology
◎	Lenvima (Combination therapy with anti-PD1 antibody nivolumab in HCC)		(JP) PI	Oncology
	E6130 (Inflammatory bowel disease)*		(JP) PI	GI
	MORAb-022 (Rheumatoid arthritis)		(US) PI	Other
	E6071 (Autoimmune disease)		(EU) PI	Other
○	E6742 (Autoimmune disease)		(US) PI	Other
	Halaven (Liposome formulation)	AF	(JP/EU) PI	Oncology

* EA Pharma pipeline product ** AI: Additional Indication, AF: Additional Formulation, ADA: Additional Dosage and Administration *** JP: Japan, US: United States, EU: Europe, CN: China, AS: Asia (excluding Japan and China), P: Clinical Phase ****GI: Gastrointestinal Disorders

◎ Development of Aricept for regression symptoms in people with Down syndrome has been discontinued at the Phase II stage in Japan
- BIIB037 has been added to this list.
- Regarding Lenvima, Japan was also added to the Phase III study for renal cell carcinoma, first-line.

○: Development progress from April 2017 onwards, ◎: Development progress from July 2017 onwards

(1) Neurology

Development Code: **E2020** Generic Name: **donepezil** Product Name: **Aricept**

Indications / Drug class: Treatment for Alzheimer's disease / dementia with Lewy bodies			In-house
Description: Increases levels of the neurotransmitter acetylcholine in the brain by inhibiting the enzyme acetylcholinesterase from breaking down acetylcholine, thereby slowing the overall progression of symptoms associated with Alzheimer's disease (AD). Currently approved in more than 100 countries around the world for the treatment of mild to moderate AD. Also approved as a treatment for patients with severe AD in numerous countries including the United States, Japan, Canada, and several other Asian and Latin American countries. Approved in Japan, the Philippines and Thailand for dementia with Lewy bodies.			
Severe Alzheimer's disease (Additional Indication)	Study 339	CN: submitted (February 2015)	Oral

◎ Development for regression symptoms in people with Down syndrome has been discontinued at the Phase II stage in Japan

Development Code: **E2007** Generic Name: **perampanel** Product Name: **Fycompa**

Indications / Drug class: Antiepileptic agent / AMPA receptor antagonist			In-house
Description: A selective antagonist against the AMPA receptor (a glutamate receptor subtype). Approved as an adjunctive therapy for partial-onset seizures in over 55 countries including Japan, the United States, in Europe and in Asia. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in over 45 countries including Japan, the United States, in Europe and in Asia. In the United States, an oral suspension formulation has been approved and is being marketed.			
Monotherapy for partial-onset seizures (Additional Indication)	— ◎ Study 342 ○	US: approved (July 2017) JP: PIII	Oral
Lennox-Gastaut syndrome (Additional Indication)	338	JP/US/EU: PIII	Oral
Pediatric epilepsy (Additional Indication)	311	JP/US/EU: PIII	Oral

Development Code: **E2006** Generic Name: **lemborexant**

Indications / Drug class: Orexin receptor antagonist			In-house	
Description: By antagonizing the orexin receptors that are involved in the regulation of sleep and wakefulness, it is expected to alleviate wakefulness, thereby facilitating the initiation and maintenance of natural sleep.				
Insomnia disorder	Study 303/304	JP/US/EU: PIII	Joint development with Purdue Pharma L.P.	Oral
Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia	202	JP/US: PII	Joint development with Purdue Pharma L.P.	Oral

Development Code: **E2609** Generic Name: **elenbecestat*** *The generic name is not yet fixed at this time.

Indications / Drug class: Treatment for Alzheimer's disease / beta secretase cleaving enzyme (BACE) inhibitor			In-house	
Description: By inhibiting beta-site amyloid precursor protein cleaving enzymes (BACE), the agent reduces the amount of amyloid beta in the brain, potentially slowing the progression of Alzheimer's disease.				
Early Alzheimer's disease	Study 301/302 (MISSION AD1/2)	JP/US/EU: PIII	Joint development with Biogen Inc.	Oral

Development Code: **BIIB037** Generic Name: **aducanumab**

Indications / Drug class: Treatment for Alzheimer's disease / anti-Aβ monoclonal antibody			In-license (Biogen Inc.)	
Description: Aducanumab is a human recombinant monoclonal antibody (mAb) derived from a de-identified library of B cells collected from healthy elderly subjects with no signs of cognitive impairment or cognitively impaired elderly subjects with unusually slow cognitive decline using Neurimmune's technology platform called Reverse Translational Medicine (RTM). Biogen licensed aducanumab from Neurimmune. Aducanumab is thought to target aggregated forms of beta amyloid including soluble oligomers and insoluble fibrils which can form into amyloid plaque in the brain of AD patients.				
Early Alzheimer's disease	ENGAGE/EMERGE Study	JP/US/EU: PIII	Joint development with Biogen Inc.	Inj.

○ Development progress from April 2017 onwards, ◎ Development progress from July 2017 onwards

Development Code: **BAN2401**

Indications / Drug class: Treatment for Alzheimer's disease / anti-Aβ protofibril monoclonal antibody			In-license (BioArctic AB)	
Description: An lgG1 monoclonal antibody that targets amyloid beta (Aβ) protofibrils. Expected to be effective in the treatment of Alzheimer's disease by halting disease progression through the elimination of neurotoxic Aβ protofibrils.				
Alzheimer's disease	Study 201	JP/US/EU: PII	Joint development with Biogen Inc.	Inj.

Development Code: **ME2125** Generic Name: **safinamide**

Indications / Drug class: Anti-Parkinson's disease agent / MAO-B inhibitor		In-license (Meiji Seika Pharma)
Description: A selective monoamine oxidase B (MAO-B) inhibitor, which reduces the degradation of secreted dopamine, helping to maintain the density of dopamine in the brain. Additionally, it blocks sodium ion channels and inhibits glutamate release, and as such, has potential as a new Parkinson's disease treatment which possesses both dopaminergic and non-dopaminergic mechanisms.		
Parkinson's disease	JP: PII/III	Oral

Development Code: **APD356** Generic Name: **lorcaserin** Product Name: **BELVIQ**

Indications / Drug class: Anti-obesity agent / serotonin 2C receptor agonist		In-license (Arena Pharmaceuticals)
Description: Anti-obesity agent with novel mechanism of action. By selectively activating serotonin 2C receptors in the brain, it is believed to decrease food consumption and promote satiety. Approved in the United States by the U.S. Food and Drug Administration in June 2012 as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m^2 or greater (obese) or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition. Launched in the United States in June 2013 after receiving a final scheduling designation from the U.S. Drug Enforcement Administration (DEA). Approved in Mexico in July 2016 and Brazil in December 2016. Additionally, in the United States, a once-daily formulation has been approved and is being marketed.		
Obesity	JP: PI	Oral

Development Code: **E2027**

Alzheimer's disease	US: PI	In-house	Oral

Development Code: **E2730**

Epilepsy	US: PI	In-house	Oral

Development Code: **E2082**

◎ Epilepsy	JP: PI	In-house	Oral

(2) Oncology

Development Code: **E7389** Generic Name: **eribulin** Product Name: **Halaven**

Indications / Drug class: Anticancer agent / microtubule dynamics inhibitor				In-house
Description: A synthetic analog of halichondrin B derived from the marine sponge, *Halichondria okadai*. Shows an antitumor effect by arresting the cell cycle through inhibition of the growth of microtubules. Approved in over 60 countries including Japan, the United States, in Europe and in Asia for use in chemotherapy for breast cancer. Approved in over 45 countries including Japan, the United States, in Europe and in Asia for use in the treatment of soft tissue sarcoma.				
○	Breast cancer	Study304	CN: preparing for re-submission	Inj.
	Bladder cancer (Additional Indication)	702	US/EU: PI/II	Inj.
	Triple negative breast cancer (in combination with anti-PD1 antibody pembrolizumab)	218	US: PI/II Joint development with Merck & Co., Inc., Kenilworth, NJ, USA	Inj.
	HER2-negative breast cancer (in combination with PEGPH20)	219	US: PI/II Joint development with Halozyme Therapeutics, Inc.	Inj.
	Liposome formulation (Additional Formulation)	—	JP/EU: PI	Inj.

Development Code: **E7080** Generic Name: **lenvatinib** Product Name: **Lenvima/Kisplyx**

Indications / Drug class: Anticancer agent / molecular targeted drug				In-house
Description: Discovered and developed in-house, the agent is an orally administered multiple receptor tyrosine kinase (RTK) inhibitor that selectively inhibits the kinase activities of vascular endothelial growth factor receptors (VEGFR) and fibroblast growth factor receptors (FGFR) in addition to other proangiogenic and oncogenic pathway related RTKs (including the platelet-derived growth factor receptor (PDGFR), KIT and RET) involved in angiogenesis and tumor proliferation. Confirmed through X-ray crystal structural analysis to be the first compound to demonstrate a new binding mode (Type V) to VEGFR2, exhibiting rapid and potent inhibition of kinase activity, according to kinetic analysis. Approved as a treatment for refractory thyroid cancer in over 50 countries including Japan, the United States, in Europe and in Asia. Also approved as a second-line treatment for renal cell carcinoma in over 40 countries including the United States and in Europe. The agent is marketed under the product name Kisplyx only for this indication in Europe.				
	Thyroid cancer	Study 308	CN: PIII	Oral
	Renal cell carcinoma/First-line (Additional Indication)	307	JP/US/EU: PIII	Oral
	Hepatocellular carcinoma (Additional Indication)	304	○ JP: submitted (June 2017) ◎ US: submitted (July 2017) ◎ EU: submitted (July 2017) ◎ CN: submitted (October 2017)	Oral
	Non-small cell lung cancer (RET translocations) (Additional Indication)	209	JP/US/EU/AS: PII	Oral
	Biliary tract cancer (Additional Indication)	215	JP: PII	Oral
	Select solid tumors (Endometrial cancer, renal cell carcinoma, head and neck cancer, urothelial cancer, non-small cell lung cancer, melanoma) (in combination with anti-PD1 antibody pembrolizumab)	111 —	US: PI/II JP: PI Joint development with Merck & Co., Inc., Kenilworth, NJ, USA	Oral /Inj.
	Hepatocellular carcinoma (in combination with anti-PD1 antibody pembrolizumab)	—	JP/US: PI Joint development with Merck & Co., Inc., Kenilworth, NJ, USA	Oral /Inj.
◎	Hepatocellular carcinoma (in combination with anti-PD1 antibody nivolumab)	—	JP: PI Joint development with Ono Pharmaceutical	Oral /Inj.

・Japan was also added to the study 307 for renal cell carcinoma/first-line.

Development Code: **MORAb-003** Generic Name: **farletuzumab**

Indications / Drug class: Anticancer agent / humanized anti-FRA monoclonal antibody				In-house
Description: A humanized IgG1 monoclonal antibody that targets folate receptor alpha (FRA). Expected to show an antitumor effect against cancers that over-express FRA.				
	Platinum-sensitive ovarian cancer	Study 011	JP/US/EU: PII	Inj.

○ Development progress from April 2017 onwards, ◎ Development progress from July 2017 onwards

Development Code: **MORAb-004**

Indications / Drug class: Anticancer agent / humanized anti-endosialin monoclonal antibody			In-house
Description: A humanized IgG1 monoclonal antibody that targets Tumor Endothelial Marker 1 (TEM-1) / endosialin. Expected to show an antitumor effect against cancers that express endosialin.			
Melanoma	Study 201	US/EU: PII	Inj.

Development Code: **MORAb-009** Generic Name: **amatuximab**

Indications / Drug class: Anticancer agent / chimeric anti-mesothelin monoclonal antibody			In-house
Description: A chimeric IgG1 monoclonal antibody that targets mesothelin. Expected to show an antitumor effect against cancers that express mesothelin.			
Mesothelioma	Study 003/201	US/EU: PII	Inj.

Development Code: **E7777**

Indications / Drug class: Anticancer agent / interleukin-2 diphtheria toxin fusion protein			In-house
Description: A fusion protein that combines the interleukin-2 (IL-2) receptor binding domain with diphtheria toxins. Specifically binds to IL-2 receptors on the cell surface, causing diphtheria toxins that have entered cells to inhibit protein synthesis.			
Peripheral T-cell lymphoma and cutaneous T-cell lymphoma	Study 205	JP: PII	Inj.

Development Code: **E7090**

	Solid tumors	JP: PI	In-house	Oral

Development Code: **MORAb-066**

	Solid tumors	US: PI	In-license (Janssen Biotech)	Inj.

Development Code: **E7046**

	Solid tumors	US/EU: PI	In-house	Oral

Development Code: **H3B-6527**

	Hepatocellular carcinoma	US/EU: PI	In-house	Oral

Development Code: **H3B-8800**

	Blood cancer	US/EU: PI	In-house	Oral

Development Code: **E7438**

	Non-Hodgkin B-cell lymphoma	JP: PI	In-license (Epizyme, Inc.)	Oral

Development Code: **E7386**

◎	Solid tumors	EU: PI	Collaboration (PRISM Pharma)	Oral

Development Code: **H3B-6545**

◎	Breast cancer	US: PI	In-house	Oral

Development Code: **MORAb-202**

◎	Solid tumors	JP: PI	In-house	Inj.

○ Development progress from April 2017 onwards, ◎ Development progress from July 2017 onwards

(3) Gastrointestinal Disorders

Development Code: **E3810** Generic Name: **rabeprazole** Product Name: **Pariet/AcipHex**

Indications / Drug class: Proton pump inhibitor				In-house
Description: A proton pump inhibitor approved for the treatment of gastric and duodenal ulcers, reflux esophagitis, eradication of *Helicobacter pylori* infections and triple formulation packs (combination packs) for *H. pylori* eradication that include rabeprazole. Approved for the prevention of recurrent gastric or duodenal ulcer caused by low-dose aspirin therapy as well as 5 mg tablet formulation in December 2014.				
◎	Maintenance therapy for proton pump inhibitor (PPI)-resistant reflux esophagitis10 mg twice daily (Additional Dosage and Administration)	Study 311	JP: approved (September 2017) Joint development with EA Pharma	Oral

Development Code: **AJG511** Generic Name: **budesonide** Product Name: **Rectabul**

Indications / Drug class: Ulcerative colitis treatment / locally-active steroid			In-license (Dr. Falk Pharma)
Description: The first rectal foam product in Japan containing budesonide as active ingredient. Budesonide is a locally-active steroid and, thus, is expected to reduce systemic side effects. In addition, budesonide is a foam type product that can reach the inflamed sites of rectum and sigmoid colon by rectal administration, and has a characteristic feature of preventing leakage after administration. Budesonide rectal foam is already available on the market in Europe.			
◎	Ulcerative colitis	Study CT1	JP: approved (September 2017) Joint development by EA Pharma and Kissei Pharmaceutical	Foam

Development Code: **AJG533** Generic Name: **elobixibat**

Indications / Drug class: Chronic constipation treatment / bile acid transporter inhibitor			In-license (Albireo)
Description: An orally available constipation treatment having a novel action mechanism. AJG533 inhibits the bile acid transporter that regulates reabsorption of bile acids and thereby increases spontaneous colonic motility			
	Chronic constipation	Study CT1	JP: submitted (February 2017) Joint development by EA Pharma and Mochida Pharmaceutical	Oral

Development Code: **AJM300** Generic Name: **carotegrast methyl**

Indications / Drug class: Ulcerative colitis treatment / α4 integrin antagonist			In-house
Description: α4 integrin antagonist with a novel mechanism of action believed to suppress adhesion and infiltration of lymphocytes. Aiming to be marketed as the first orally-available α4 integrin antagonist in the world to be effective in ulcerative colitis.			
	Ulcerative colitis	JP: PIII	Joint development by EA Pharma and Kissei Pharmaceutical	Oral

Development Code: **AJG555**

Indications / Drug class: Chronic constipation treatment / polyethylene glycol preparation			In-license (Norgine)
Description: An orally available constipation treatment consisting of a polyethylene glycol preparation which facilitates bowel movement by suppressing osmotic pressure in the intestines.			
	Chronic constipation	Study CT1/CT2	JP: PIII	Joint development by EA Pharma and Mochida Pharmaceutical	Oral

Generic Name: **isoleucine, leucine and valine granules** Product Name: **Livact Granules**

Indications / Drug class: Branched-chain amino acid formula			In-house
Description: A branched-chain amino acid formula developed by Ajinomoto that increases serum albumin levels in patients with decompensated hepatic cirrhosis. Approved in Japan for “improvement of hypoalbuminemia in patients with decompensated hepatic cirrhosis that have hypoalbuminemia despite adequate dietary intake”, and marketed by EA Pharma.			
	Hypoalbuminemia	CN: PIII	Submission Target: FY2017 Joint development with EA Pharma	Oral

○ Development progress from April 2017 onwards, ◎ Development progress from July 2017 onwards

Development Code: **E6007**

Indications / Drug class: Ulcerative colitis treatment / integrin activation inhibitor				In-house
Description: A compound with a novel mechanism of action that is believed to suppress the adhesion and infiltration by multiple leukocyte types by inhibiting integrin activation. Development is conducted jointly with the University of Tsukuba as an industry-academia practical application project under the Japan Science and Technology Agency.				
Ulcerative colitis	Study 201	JP: PII	Development conducted by EA Pharma	Oral

Development Code: **E6130**

Inflammatory bowel disease	JP: PI	In-house (development conducted by EA Pharma)	Oral

(4) Other

Development Code: **E6011**

Indications / Drug class: Anti-Fractalkine antibody				In-house
Description: The world's first humanized anti-fractalkine monoclonal antibody discovered by Eisai Group subsidiary KAN Research Institute Inc. Believed to exert an anti-inflammatory effect by neutralizing fractalkine. Fractalkine is found in vascular endothelial cells and induces an inflammatory response associated with diseases such as rheumatoid arthritis and inflammatory bowel disease.				
Rheumatoid arthritis	Study 201/202	JP: PII		Inj.
Primary biliary cholangitis	ET1	JP: PII	Development conducted by EA Pharma	Inj.
Crohn's disease	101	JP: PI/II	Development conducted by EA Pharma	Inj.

Development Code: **MORAb-022**

Rheumatoid arthritis (antibody)	US: PI	In-house	Inj.

Development Code: **E6071(GSK3050002)**

Autoimmune disorder (antibody)	EU: PI	In-house (joint development with GlaxoSmithKline)	Inj.

Development Code: **E6742**

○	Autoimmune disorder	US: PI	In-house	Oral