13. Major R&D Pipeline

In-House R&D Pipeline List

	Product Name / Development Code	Additional Indication, etc.**	Development Stage***	Therapeutic Area****
Approved				
◎	Lenvima (Hepatocellular carcinoma: HCC)	AI	(US/EU/CN/AS) approved	Oncology
◎	Fycompa (Pediatric epilepsy)	AI	(US) approved	Neurology
◎	Movicol (Chronic constipation)*		(JP) approved	GI
Submitted / Preparing for Submission				
	Halaven (Breast cancer)		(CN) submitted	Oncology
◎	Fycompa (Adjunctive therapy for partial-onset seizures)		(CN) submitted	Neurology
◎	ME2125 (Parkinson's disease)		(JP) submitted	Neurology
Clinical Trial Stage				
	E2006 (Insomnia disorder)		(JP/US/EU) PIII	Neurology
	E2609 (Early Alzheimer's disease)		(JP/US/EU/CN) PIII	Neurology
	BIIB037 (Early Alzheimer's disease)		(JP/US/EU) PIII	Neurology
○	Lenvima (Endometrial carcinoma, second-line, combination therapy with anti-PD1 antibody pembrolizumab)		(JP/US/EU) PIII	Oncology
	AJM300 (Ulcerative colitis)*		(JP) PIII	GI
	Livact (Hypoalbuminemia)		(CN) PIII	GI
	Fycompa (Lennox-Gastaut syndrome)	AI	(JP/US/EU) PIII	Neurology
	Fycompa (Pediatric epilepsy)	AI	(JP/EU) PIII	Neurology
	Fycompa (Monotherapy for partial-onset seizures)	AI	(JP) PIII	Neurology
	Lenvima (Thyroid cancer)	AI	(CN) PIII	Oncology
	Lenvima (Renal cell carcinoma, first-line, combination therapy with everolimus or anti-PD1 antibody pembrolizumab)	AI	(JP/US/EU) PIII	Oncology
	BAN2401 (Early Alzheimer's disease)		(JP/US/EU) PII	Neurology
	E2006 (Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia)		(JP/US) PII	Neurology
	E2027 (Dementia with Lewy bodies)		(JP/US/EU) PII/III	Neurology
◎	E2730 (Epilepsy)		(US) PII	Neurology
◎	E2082 (Epilepsy)		(US) PII (JP) PI	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
	E7438 (Non-Hodgkin B-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
◎	E6011 (Crohn's disease)*		(JP/EU) 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
	H3B-6545 (Breast cancer)		(US) PI/II	Oncology
	BELVIQ (Obesity)		(JP) PI	Neurology
	E7090 (Solid tumors)		(JP) PI	Oncology
	H3B-6527 (HCC)		(US/EU) PI	Oncology
	H3B-8800 (Blood cancer)		(US/EU) PI	Oncology
	Lenvima (Combination therapy with anti-PD1 antibody pembrolizumab in HCC)		(JP/US) PI	Oncology
	E7386 (Solid tumors)		(EU) PI	Oncology
	MORAb-202 (Solid tumors)		(JP) PI	Oncology
	Lenvima (Combination therapy with anti-PD1 antibody nivolumab in HCC)		(JP) PI	Oncology
	E7130 (Solid tumors)		(JP) PI	Oncology
	MORAb-022 (Rheumatoid arthritis)		(US) 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
*** JP: Japan, US: United States, EU: Europe, CN: China, AS: Asia (excluding Japan and China), P: Clinical Phase ****GI: Gastrointestinal Disorders

○ Development of E6130 for inflammatory bowel disease has been discontinued at the Phase I stage in Japan and was therefore removed from this list.
○ Development of MORAb-066 for solid tumors has been discontinued at the Phase I stage in the United States and was therefore removed from this list.

○: Development progress from April 2018 onwards ◎: Development progress from July 2018 onwards

(1) Neurology

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. Approved for use as monotherapy for the treatment of partial onset seizures (with or without secondarily generalized seizures) in patients 4 years of age and older in the United States. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in over 50 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	JP: PIII Submission Target: FY2018	Oral
	Lennox-Gastaut syndrome (Additional Indication)	338	JP/US/EU: PIII	Oral
	Pediatric epilepsy (Additional Indication)	311	◎ US: approved (September 2018) JP/ EU: PIII Submission Target: FY2018	Oral
◎	Adjunctive therapy for partial-onset seizures	335	CN: submitted (accepted October 2018)	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	Submission Target: FY2018 Joint development with Purdue Pharma	Oral
	Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia	202	JP/US: PII	Joint development with Purdue Pharma	Oral

Development Code: **E2609** Generic Name: **elenbecestat**

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/CN: 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 amyloid beta including soluble oligomers and insoluble fibrils which can form into amyloid plaque in Alzheimer's disease patients.				
	Early Alzheimer's disease	ENGAGE/EMERGE Study	JP/US/EU: PIII	Joint development with Biogen Inc.	Injection (Inj.)

Development Code: **BAN2401**

Indications / Drug class: Treatment for Alzheimer's disease / anti-Aβ protofibril monoclonal antibody				In-license (BioArctic AB)
Description: An IgG1 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.				
	Early 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 inhibits glutamate release by blocking sodium ion channels, and as such, has potential to be a new Parkinson's disease treatment which possesses both dopaminergic and non-dopaminergic mechanisms.			
◎ Parkinson's disease		JP: submitted (October 2018)	Oral

Development Code: **E2027**

Indications / Drug class: Treatment for dementia with Lewy bodies / phosphodiesterase (PDE) 9 inhibitor			In-house
Description: A selective phosphodiesterase (PDE) 9 inhibitor, which reduces the degradation of cyclic GMP which is critical to signal transmission among cells. By helping maintain the concentration of cyclic GMP in the brain, E2027 has the potential to be a new treatment for dementia with Lewy bodies.			
Dementia with Lewy bodies	Study 201 (DELPHIA)	JP/US/EU: PII/III	Oral

Development Code: **E2730**

Indications / Drug class: Antiepileptic agent, treatment for neurological diseases / Synapse function modulator			In-house
Description: A compound with a novel mechanism of action that selectively regulates the function of activated synapses. Has potential to be a new treatment for neurological diseases such as epilepsy, including orphan epilepsy, and epileptogenesis.			
◎ Epilepsy	Study 201	US: PII	Oral

Development Code: **E2082**

Indications / Drug class: Antiepileptic agent, treatment for neurological diseases / AMPA receptor antagonist			In-house
Description: Next-generation AMPA receptor antagonist that inhibits glutamate activity of AMPA receptors, a subtype of glutamate receptor. Has potential to be a new treatment for neurological diseases such as epilepsy, in particular as a treatment for epileptogenesis and others.			
Epilepsy	Study 201	◎ US: PII JP: PI	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 (FDA) 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

(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 65 countries including Japan, the United States, and other countries in Europe and Asia for use in the treatment of breast cancer. Approved in over 50 countries including Japan, the United States and other countries in Europe and Asia for use in the treatment of liposarcoma (soft tissue sarcoma in Japan).				
	Breast cancer	Study 304	CN: submitted (accepted November 2017)	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, through an affiliate	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. Approved for use in the treatment of thyroid cancer in over 50 countries including Japan, the United States and other countries in Europe and Asia. Also approved in combination with everolimus for use in the treatment of renal cell carcinoma (second-line) in over 45 countries including the United States and other countries in Europe. The agent is marketed under the product name Kisplyx only for this indication in Europe. Approved for use in the treatment of hepatocellular carcinoma in over 35 countries including Japan, the United States, Europe, China and Asia.				
	Thyroid cancer (Additional Indication)	Study 308	CN: PIII Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Renal cell carcinoma/First-line (Additional Indication) (in combination with anticancer agent everolimus or anti-PD1 antibody pembrolizumab)	307	JP/US/EU: PIII Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
○	Endometrial carcinoma/Second-line (in combination with anti-PD1 antibody pembrolizumab)	309	JP/US/EU: PIII Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Hepatocellular carcinoma (Additional Indication)	304	◎ US: approved (August 2018) ◎ EU: approved (August 2018) ◎ CN: approved (September 2018) ◎ AS: approved (August 2018 • South Korea) Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Non-small cell lung cancer (RET translocations) (Additional Indication)	209	JP/US/EU/AS: PII Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Biliary tract cancer (Additional Indication)	215	JP: PII Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	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, through an affiliate	Oral
	Hepatocellular carcinoma (in combination with anti-PD1 antibody pembrolizumab)	—	JP/US: PI Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Hepatocellular carcinoma (in combination with anti-PD1 antibody nivolumab)	—	JP: PI Joint development with Ono Pharmaceutical	Oral

○ Development progress from April 2018 onwards ◎ Development progress from July 2018 onwards

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 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 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: **E7438** Generic Name: **tazemetostat**

Indications / Drug class: Anticancer agent / EZH2 inhibitor			In-license (Epizyme, Inc.)
Description: Believed to have an important role in carcinogenesis, the epigenetic enzyme EZH2 is one of the proteins that constitute the histone methyltransferases. Discovered by Epizyme through its proprietary product platform, E7438 is a first-in-class, orally administered small molecule inhibitor, and is expected to exhibit antitumor effects via inhibition of the epigenetic enzyme EZH2. Eisai is responsible for development and commercialization within Japan and has the right of first negotiation for licensing rights in Asia.			
Non-Hodgkin B-cell lymphoma	Study 206	JP: PII	Oral

Development Code: **H3B-6545**

Breast cancer	US: PI/II	In-house	Oral

Development Code: **E7090**

Solid tumors	JP: 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: **E7386**

Solid tumors	EU: PI	Collaboration (PRISM Pharma)	Oral

○ Development progress from April 2018 onwards ◎ Development progress from July 2018 onwards

Development Code: **MORAb-202**

Solid tumors	JP: PI	In-house	Inj.

Development Code: **E7130**

Solid tumors	JP: PI	Collaboration (Harvard University)	Inj.

○ Development of MORAb-066 for solid tumors has been discontinued at the Phase I stage in the United States and was therefore removed from this list.

(3) Gastrointestinal Disorders

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** Generic Name: **macrogol 4000, sodium chloride, sodium bicarbonate, potassium chloride** Product Name: **MOVICOL**

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 regulating osmolality in the intestines.				
◎	Chronic constipation	Study CT1/CT2	JP: approved (September 2018) 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: FY2018 Joint development with EA Pharma	Oral

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 of E6130 for inflammatory bowel disease has been discontinued at the Phase I stage in Japan and was therefore removed from this list.

(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 the 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	ET2	JP/EU: PII	Development conducted by EA Pharma	Inj.

Development Code: **MORAb-022**

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

Development Code: **E6742**

	Autoimmune disease	US: PI	In-house	Oral