11. Major R&D Pipeline

(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 60 countries including Japan, the United States, and other countries in Europe and in Asia. Approved for monotherapy and adjunctive use in 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 55 countries including Japan, the United States, and other countries in Europe and in Asia. In the United States and other countries in Europe, an oral suspension formulation has been approved and is being marketed.			
Pediatric epilepsy (Additional Dosage and Administration)	Study 311	JP: submitted (January 2019) EU: submitted (February 2019)	Oral
Adjunctive therapy for partial-onset seizures	Study 335	CN: submitted (accepted October 2018)	Oral
Monotherapy for partial-onset seizures (Additional Indication)	Study 342	JP: submitted (January 2019)	Oral
Fine granule formulation (Additional Formulation)	—	JP: submitted (January 2019)	Oral
Lennox-Gastaut syndrome (Additional Indication)	Study 338	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	US: submitted (December 2018) JP: submitted (March 2019)	Oral
Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia	Study 202	JP/US: PII	Oral

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

Indications / Drug class: Disease modifying treatment for Alzheimer's disease / beta-site amyloid precursor protein cleaving enzyme (BACE) inhibitor			In-house	
Description: By inhibiting beta-site amyloid precursor protein cleaving enzymes (BACE), the agent reduces the total amount of amyloid beta (Aβ), 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: **BAN2401**

Indications / Drug class: Disease modifying treatment for Alzheimer's disease / anti-Aβ protofibril antibody			In-license (BioArctic AB)	
Description: An IgG1 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 301 (Clarity AD)	JP/US/EU/CN: PIII	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) ◎ South Korea: submitted (July 2019)		Oral

- submitted: under regulatory submission

◎ Development progress from April 2019 onwards

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

* All clinical studies of E2082 in Japan and the United States have been suspended.

◎ Development progress from April 2019 onwards

(2) Oncology

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

Indications / Drug class: Anticancer agent / kinase inhibitor			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 55 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 50 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 (first-line) in over 50 countries including in Japan, the United States, China, other countries in Europe 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)	Study 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)	Study 309	JP/US/EU: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Hepatocellular carcinoma/First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-002	JP/US/EU/CN: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Melanoma/First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-003	US/EU/CN: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Nonsquamous non-small cell lung cancer/First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-006	JP/US/EU/CN: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Non-small cell lung cancer, PD-L1 positive, /First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-007	JP/US/EU/CN: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
◎	Endometrial carcinoma/First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-001	JP/US/EU/CN: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
◎	Non-small cell lung cancer/Second-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-008	JP/US/EU: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
◎	Bladder cancer, cisplatin-ineligible /First-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-011	JP/US/EU: PIII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Non-small cell lung cancer (RET translocations) (Additional Indication)	Study 209	JP/US/EU/AS: PII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Biliary tract cancer (Additional Indication)	Study 215	JP: PII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Selected solid tumors (Endometrial cancer, renal cell carcinoma, head and neck cancer, urothelial cancer, non-small cell lung cancer and melanoma) (in combination with anti-PD1 antibody pembrolizumab)	Study 111 —	US/EU: PI/II JP: PI	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral
	Melanoma/Second-line (in combination with anti-PD1 antibody pembrolizumab)	LEAP-004	US/EU : PII	Joint development with Merck & Co., Inc., Kenilworth, NJ, USA, through an affiliate	Oral

◎ Development progress from April 2019 onwards

	Selected solid tumors (Triple negative breast cancer, ovarian cancer, gastric cancer, colorectal cancer, glioblastoma and biliary tract cancer) (in combination with anti-PD1 antibody pembrolizumab)	LEAP-005	US/EU: PII	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 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 70 countries including Japan, the United States, and other countries in Europe and Asia for use in the treatment of breast cancer. Approved in over 60 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: approved (July 2019)		Inj.
	Bladder cancer (Additional Indication)	Study 702	US/EU: PI/II		Inj.
	Triple negative breast cancer (in combination with anti-PD1 antibody pembrolizumab)	Study 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)	Study 219	US: PI/II	Joint development with Halozyme Therapeutics, Inc.	Inj.
	Liposome formulation (Additional Formulation)	—	JP/EU: PI		Inj.
◎	Liposome formulation (Additional Formulation) (in combination with anti-PD1 antibody nivolumab)	—	JP: PI/II	Joint development with Ono Pharmaceutical	Inj.

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 lgG1 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 progress from April 2019 onwards

Development Code: **E7777**

Indications / Drug class: Anticancer agent / a fusion protein that combines the interleukin-2 receptor binding domain with diphtheria toxin fragments			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**

Indications / Drug class: Anticancer agent / ERα inhibitor			In-house
Description: An orally administered selective estrogen receptor alpha (ERα) covalent antagonist that inhibits ERα wild type / ERα mutant. Expected to show an antitumor effect against ER positive / HER2 negative breast cancers.			
Breast cancer	Study 101	US/EU: PI/II	Oral

Development Code: **E7090**

			In-house
Solid tumors	—	JP: PI	Oral

Development Code: **H3B-6527**

			In-house
Hepatocellular carcinoma	—	US/EU: PI	Oral

Development Code: **H3B-8800**

			In-house
Blood cancer	—	US/EU: PI	Oral

Development Code: **E7386**

				Collaboration (PRISM Pharma)
	Solid tumors	—	JP/EU: PI	Oral
◎	Solid tumors (in combination with Lenvima)	—	JP: PI	Oral

Development Code: **MORAb-202**

			In-house
Solid tumors	—	JP: PI	Inj.

Development Code: **E7130**

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

◎ Development progress from April 2019 onwards

(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: **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. EA Pharma aims for commercialization 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: **E3112**

			In-house	
Liver disease	—	JP: PI	Development conducted by EA Pharma	Inj.

(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.
Crohn's disease	Study ET2	JP/EU: PII	Development conducted by EA Pharma	Inj.

Development Code: **E6742**

			In-house	
Autoimmune disease	—	US: PI		Oral

◎ Development progress from April 2019 onwards