14. Major R&D Pipeline

(1) Neurology

Development Code: **E2007** Generic Name: **perampanel** Product Name: **Fycompa**					In-house
Indications / Drug class: Antiepileptic agent / AMPA receptor antagonist					Oral
Description: A selective antagonist against the AMPA receptor (a glutamate receptor subtype). Approved as an adjunctive therapy for partial-onset seizures in over 70 countries including Japan, the United States, China 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 Japan and the United States. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in over 70 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. A fine granule formulation has been approved in Japan.					
	Pediatric epilepsy (Additional Dosage and Administration)	Study 311	EU CH	○ ○	Approved (November, 2020) Submitted (accepted: October, 2020)
○	Monotherapy for partial-onset seizures (Additional Indication)	Study 335	CH		Submitted (accepted: October, 2020)
	Lennox-Gastaut syndrome (Additional Indication)	Study 338	JP/US/EU		PIII

Development Code: **ME2125** Generic Name: **safinamide** Product Name: **Equfina**					In-license (Meiji Seika Pharma)
Indications / Drug class: Anti-Parkinson's disease agent / MAO-B inhibitor					Oral
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. Eisai took over by transfer the manufacturing and marketing approval of safinamide from Meiji Seika Pharma in Japan , and has the exclusive rights to develop and market safinamide in Asia.					
	Improvement of wearing-off phenomenon in patients with Parkinson's disease	—	South Korea	○	Approved (June, 2020)

Development Code: **E2006** Generic Name: **lemborexant** Product Name: **Dayvigo**					In-house
Indications / Drug class: Insomnia treatment / Orexin receptor antagonist					Oral
Description: An orexin receptor antagonist that blocks the receptors involved in the regulation of sleep and wakefulness. It is expected to alleviate wakefulness, thereby facilitating onset and maintenance of sleep. It has been approved for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance in adults in the United States. It has been approved for the treatment of insomnia in Japan. In addition, development for Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia is ongoing.					
	Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia (Additional Indication)	Study 202	JP/US		PII

Development Code: **BIIB037** Generic Name: **aducanumab**					Co-development (Biogen Inc.)
Indications / Drug class: Treatment for Alzheimer's disease / anti-Aβ monoclonal antibody					Injection
Description: A human recombinant monoclonal antibody (mAb) that is 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, Reverse Translational Medicine (RTM). Biogen Inc. licensed aducanumab from Neurimmune. Aducanumab is thought to target aggregated forms of amyloid beta (Aβ) including soluble oligomers and insoluble fibrils, which can form into amyloid plaque in Alzheimer's disease patients. The United States Food and Drug Administration (FDA) accepted Biologics License Application (BLA) with Priority Review in August 2020. Marketing Authorization Application (MAA) was accepted by the European Medicines Agency (EMA) in October 2020, and in Japan, New Drug Application (NDA) was submitted in December 2020. It was disclosed in April 2021 that submission of MAA has been conducted in Brazil, Canada, Australia and Switzerland. In Canada, Australia and Switzerland, the validation of whether the applications are accepted is underway. Joint development with Biogen Inc.					
	Alzheimer's disease	ENGAGE/ EMERGE Studies	US EU JP	○ ○ ○	Submitted (accepted: August, 2020) Submitted (accepted: October, 2020) Submitted (December, 2020)

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

Development Code: **BAN2401** Generic Name: **lecanemab**					In-license (BioArctic AB)
Indications / Drug class: Disease modifying treatment for Alzheimer's disease / anti-Aβ protofibril antibody					Injection
Description: An lgG1 antibody that targets amyloid beta (Aβ) protofibrils. Expected to be effective in the treatment of Alzheimer's disease (AD) by halting disease progression through the elimination of neurotoxic Aβ protofibrils. Joint development with Biogen Inc. The Phase III clinical study Clarity AD in patients with mild cognitive impairment due to AD or mild AD (collectively known as early AD) is underway. The Phase III clinical study AHEAD 3-45 for preclinical (asymptomatic) AD has been initiated and is underway in collaboration with the Alzheimer's Clinical Trials Consortium (ACTC).					
	Early AD	Study 301 (Clarity AD)	JP/US/ EU/CH		PIII
○	Preclinical AD	Study 303 (AHEAD 3-45)	JP/US/EU		PIII

Development Code: **E2023** Generic Name: **lorcaserin**					In-license (Arena Pharmaceuticals)
Indications / Drug class: Treatment for Dravet syndrome / serotonin 2C receptor agonist					Oral
Description: By selectively activating serotonin 2C receptors in the brain, through the activation GABAergic inhibitory interneuron, expected to suppress seizure of Dravet syndrome by increasing synaptic suppression from GABAergic. Although approval for the obesity indication has been voluntarily withdrawn, due to the request from Dravet syndrome patient groups, the extended access program has been continued in the United States, and the Phase III clinical study has been initiated and is underway for this indication. The FDA has designated it as an orphan drug for Dravet syndrome.					
○	Dravet syndrome	Study 304	US		PIII

Development Code: **E2027**					In-house
Indications / Drug class: Treatment for dementia with Lewy bodies, Parkinson's disease dementia / PDE 9 inhibitor					Oral
Description: A selective phosphodiesterase (PDE) 9 inhibitor that reduces the degradation of cyclic GMP, which is critical to signal transmission among cells. Expected to be a new treatment for dementia with Lewy bodies and Parkinson's disease dementia by helping to maintain the concentration of cyclic GMP in the brain.					
	Dementia with Lewy bodies	Study 201 (DELPHIA)	JP/US/EU		PII/III
◎	Dementia with Lewy bodies, Parkinson's disease dementia	Study 203	US		PII

Development Code: **E2730**					In-house
Indications / Drug class: Antiepileptic agent, treatment for neurological diseases / synapse function modulator					Oral
Description: A compound with a novel mechanism of action that selectively regulates the function of activated synapses. Expected to be a new treatment for neurological diseases such as epilepsy, including orphan epilepsy and epileptogenesis.					
	Epilepsy	Study 201	US		PII

Development Code: **E2814**			Collaboration (University College London)		Injection
	Alzheimer's disease	—	US		PI

Development Code: **E2511**			In-house		Oral
○	Alzheimer's disease	—	US		PI

Development Code: **EA4017**			In-house		Oral
○	Chemotherapy-induced peripheral neuropathy (Development conducted by EA Pharma)	—	JP		PI

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

(2) Oncology

Development Code: **E7080** Generic Name: **lenvatinib** Product Name: **Lenvima**					In-house
Indications / Drug class: Anticancer agent / kinase inhibitor					Oral
Description: 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. Discovered and developed in-house. Approved for use in the treatment of thyroid cancer in over 70 countries including Japan, the United States, China and other countries in Europe and in Asia. Also approved in combination with everolimus for use in the treatment of renal cell carcinoma (second-line) in over 60 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 70 countries including in Japan, the United States, China and other countries in Europe and in Asia. Approved for use in the treatment of endometrial cancer in combination with pembrolizumab in over 10 countries, including the United States, Canada and Australia. Joint development with Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate.					
Monotherapy, joint development with Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate (Additional Indication)					
	Thyroid cancer	Study 303/308	CH	○	Approved (November, 2020)
	Thymic cancer	NCCH1508	JP	◎	Approved (March, 2021)
In combination with anti-PD-1 antibody pembrolizumab, joint development with Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate (Additional Indication)					
	Renal cell carcinoma/First-line	Study 307	EU JP US	◎ ◎ ◎	Submitted (accepted: March, 2021) Submitted (March, 2021) Submitted (accepted: April, 2021)
	Endometrial cancer/Second-line	Study 309	EU JP US	◎ ◎ ◎	Submitted (accepted: March, 2021) Submitted (April, 2021) Submitted (accepted: April, 2021)
	Hepatocellular carcinoma/First-line	LEAP-002	JP/US/EU/CH		PIII
	Melanoma/First-line	LEAP-003	US/EU/CH		PIII
	Nonsquamous non-small cell lung cancer/First-line	LEAP-006	JP/US/EU/CH		PIII
	Non-small cell lung cancer, PD-L1 positive/First-line	LEAP-007	JP/US/EU/CH		PIII
	Endometrial carcinoma/First-line	LEAP-001	JP/US/EU/CH		PIII
	Non-small cell lung cancer/Second-line	LEAP-008	JP/US/EU		PIII
	Bladder cancer, cisplatin-ineligible/First-line	LEAP-011	JP/US/EU/CH		PIII
	Head and neck cancer/First-line	LEAP-010	JP/US/EU/CH		PIII
○	Gastric cancer/First-line	LEAP-015	JP/US/EU/CH		PIII
◎	Colorectal cancer/Third-line	LEAP-017	US/EU		PIII
	Selected solid tumors (Endometrial cancer, renal cell carcinoma, head and neck cancer, urothelial cancer, non-small cell lung cancer and melanoma)	Study 111 —	US/EU JP		PI/II PI
	Melanoma/Second-line	LEAP-004	US/EU		PII
	Selected solid tumors (Triple negative breast cancer, ovarian cancer, gastric cancer, colorectal cancer, glioblastoma, biliary tract cancers and pancreatic cancer)	LEAP-005	US/EU		PII

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

○	Head and neck cancer/Second-line	LEAP-009	US/EU		PII
In combination with anti-PD-1 antibody pembrolizumab and transcatheter arterial chemoembolization, joint development with Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate (Additional Indication)					
○	Hepatocellular carcinoma/First-line	LEAP-012	JP/US/EU/ CH		PIII
In combination with anticancer agent everolimus, joint development with Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate (Additional Indication)					
	Renal cell carcinoma/First-line	Study 307	JP/US/EU		PIII
In combination with anti-PD-1 antibody nivolumab, joint development with Ono Pharmaceutical (Additional Indication)					
	Hepatocellular carcinoma	—	JP		PI

○In July 2020, regarding applications seeking accelerated approval of the combination therapy with pembrolizumab for the first-line treatment of patients with unresectable hepatocellular carcinoma in the United States based on the Study 116 results, a Complete Response Letter (CRL) was received from the FDA and therefore were removed from this list.

Development Code: **E7389** Generic Name: **eribulin** Product Name: **Halaven**					In-house
Indications / Drug class: Anticancer agent / microtubule dynamics inhibitor					Injection
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 75 countries including Japan, the United States, China and other countries in Europe and in Asia for use in the treatment of breast cancer. Approved in over 75 countries including Japan, the United States and other countries in Europe and in Asia for use in the treatment of liposarcoma (soft tissue sarcoma in Japan).					
Monotherapy (Additional Formulation)					
	Liposome formulation	—	JP/EU		PI
In combination with anti-PD-1 antibody nivolumab, Joint development with Ono Pharmaceutical (Additional Formulation)					
	Liposome formulation	Study 120	JP		PI/II

○The development of the agent in combination with PEGPH20 by Halozyme Therapeutics, Inc. for HER2-negative breast cancer which was in Phase I/II stage in the United States has been finished.

○The development of the agent in combination with anti-PD-1 antibody pembrolizumab for triple negative breast cancer which was in Phase I/II stage in the United States has been finished.

Development Code: **E7777** Generic Name: **denileukin diftitox (genetic recombinant)** Product Name: **Remitoro**					In-house
Indications / Drug class: Anticancer agent / a fusion protein that combines the interleukin-2 receptor binding domain with diphtheria toxins					Injection
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 of tumoral lymphocyte, causing diphtheria toxins that have entered cells to inhibit protein synthesis and induce cell death.					
	Peripheral T-cell lymphoma and cutaneous T-cell lymphoma	Study 205	JP	◎	Approved (March, 2021)

Development Code: **E7438** Generic Name: **tazemetostat**					In-license (Epizyme, Inc.)
Indications / Drug class: Anticancer agent / EZH2 inhibitor					Oral
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, Inc. 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 holds development and commercialization rights within Japan.					
	Non-Hodgkin B-cell lymphoma	Study 206	JP	○	Submitted (June, 2020)

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

Development Code: **MORAb-009** Generic Name: **amatuximab**					In-house
Indications / Drug class: Anticancer agent / chimeric anti-mesothelin monoclonal antibody					Injection
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		PI/II

Development Code: **H3B-6545**					In-house
Indications / Drug class: Anticancer agent / ERα inhibitor					Oral
Description: An orally administered selective estrogen receptor (ER) α 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
	Breast cancer (in combination with CDK4/6 inhibitor palbociclib)	—	US/EU		PI

Development Code: **E7090**					In-house
Indications / Drug class: Anticancer agent / FGFR1,2,3 inhibitor					Oral
Description: An orally administered fibroblast growth factor receptors (FGFR1, FGFR2, FGFR3) selective tyrosine kinase inhibitor. Phase II clinical study for unresectable cholangiocarcinoma (one of biliary tract cancers) with FGFR2 gene fusion ongoing. It has been granted the SAKIGAKE designation by Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of unresectable biliary tract cancer with FGFR2 gene fusion, and it has received orphan drug designation with a prospective indication for unresectable biliary tract cancer with FGFR2 gene fusion by the MHLW.					
	Cholangiocarcinoma	Study 201	JP/CH		PII
○	Breast cancer	—	JP		PI

Development Code: **H3B-6527**					In-house	Oral
	Hepatocellular carcinoma	—	US/EU		PI	

Development Code: **H3B-8800**					In-house	Oral
	Blood cancer	—	US/EU		PI	

Development Code: **E7386**					Collaboration (PRISM BioLab)	Oral
	Solid tumors	—	JP/EU		PI	
	Solid tumors (in combination with lenvatinib)	—	JP		PI	

Development Code: **MORAb-202**					In-house	Injection
	Solid tumors	—	JP		PI	
○	Solid tumors	—	US		PI/II	

Development Code: **E7130**					Collaboration (Harvard University)	Injection
	Solid tumors	—	JP		PI	

Development Code: **E7766**					In-house	Liquid
	Solid tumors	—	US/EU		PI	

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

(3) Gastrointestinal Disorders

Development Code: **EAM007** Product Name: **Eleview**					In-license (Cosmo Technologies)
Indications / Drug class: Submucosal injectable composition/ medical device					Submucosal injectable composition
Description: A submucosal injectable composition that provides a submucosal cushion of optimal height and duration, achieving an easier and safer resection procedure in endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in the esophagus, the stomach, the intestine and the rectum. This is the EA Pharma's first medical device to be approved marketing authorization. Development conducted by EA Pharma.					
○	Submucosal injectable composition for endoscopic mucosal resection and submucosal dissection	—	JP		Approved (November, 2020)

Development Code: **AJM300** Generic Name: **carotegrast methyl**					In-house
Indications / Drug class: Ulcerative colitis treatment / α4 integrin antagonist					Oral
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. In January 2021, EA Pharma and Kissei Pharmaceutical disclosed that the Phase III clincal study in Japan met the primary endpoint. Joint development by EA Pharma and Kissei Pharmaceutical.					
	Ulcerative colitis	—	JP	◎	Preparation of submission

Development Code: **E6007** Generic Name: **milategrast**					In-house
Indications / Drug class: Ulcerative colitis treatment / integrin activation inhibitor					Oral
Description: A compound with a novel mechanism of action that is believed to suppress the adhesion and infiltration of 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. Development conducted by EA Pharma.					
	Ulcerative colitis	Study 201	JP		PII

Development Code: **E6011** Generic Name: **quetmolimab**					In-house
Indications / Drug class: Crohn's disease / Anti-humanized monoclonal fractalkine antibody					Injection
Description: The world's first humanized anti-fractalkine monoclonal antibody discovered by the Eisai Group subsidiary KAN Research Institute Inc. Expected 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 inflammatory bowel disease. Development conducted by EA Pharma.					
	Crohn's disease	Study ET2	JP/EU		PII

Development Code: **EA4000**			In-license (Norgine)		Oral
○	Bowel cleansing agent (Development conducted by EA Pharma)	—	JP		PI/II

Development Code: **E3112**			In-house		Injection
	Liver disease (Development conducted by EA Pharma)	—	JP		PI

Development Code: **AJM347**			In-house		Oral
○	Inflammatory bowel disease (Development conducted by EA Pharma)	—	EU		PI

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards

Development Code: **EA1080**			In-house		Oral
○	Inflammatory bowel disease (Development conducted by EA Pharma)	—	EU		PI

Development Code: **EA3355**			In-license (Dr. Falk Pharma)		Oral
○	Liver disease (Development conducted by EA Pharma)	—	JP		PI

(4) Other

Development Code: **E5564** Generic Name: **eritoran**			In-house		
Indications / Drug class: Suppression for increasing of severity of COVID-19/ TLR4 antagonist			Injection		
Description: Eritoran is a TLR (Toll-Like Receptor) 4 antagonist created with natural product organic synthesis technology. It is a structural analogue of Lipid A which is an activator of endotoxins of bacteria. It is expected to suppress inflammation and increasing in severity caused by COVID-19 by inhibiting the activation of TLR4, which is found in the most upstream position of various cytokine gene expression signaling that causes the cytokine-storm. Development is in collaboration with GCAR (Global Coalition for Adaptive Research).					
○	Suppression for increasing of severity of COVID-19	REMAP-COVID	US		PIII

Development Code: **E6742**			In-house		Oral
	Autoimmune disease	—	JP/US		PI

Development Code: **E8001**			In-house		Injection
○	Rejection reaction associated with organ transplantation	—	JP		PI

JP: Japan, US: the United States, EU: Europe, CH: China, P: (Clinical trial) Phase

○：Development progress from April 2020 onwards, ◎：Development progress from January 2021 onwards