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 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, the United States and China. Approved for adjunctive use in the treatment of partial onset seizures (with or without secondarily generalized seizures) in patients 4 years of age and older in Europe. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in over 70 countries including Japan, the United States, and countries in Europe and in Asia. Approved for an adjunctive therapy for primary generalized tonic-clonic seizures in patients 7 years of age and older in Europe, and 12 years of age and older in Japan and United States. An oral suspension formulation has been approved in the United States and Europe. A fine granule formulation has been approved in Japan.

	Pediatric epilepsy (Additional Dosage and Administration)	Study 311	CH	○	Approved (July, 2021)
	Monotherapy for partial-onset seizures (Additional Indication)	Study 335	CH	○	Approved (July, 2021)
	Lennox-Gastaut syndrome (Additional Indication)	Study 338	JP/US/EU		PIII

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 faster onset and maintenance of sleep. It has been approved for the treatment of insomnia in over 10 countries including Japan, the United States and countries in Asia. In addition, development for irregular sleep-wake rhythm disorder and Alzheimer's disease dementia is ongoing.

○	Insomnia disorder	Study 311	CH		PIII
	Irregular sleep-wake rhythm disorder and Alzheimer's disease dementia (Additional Indication)	Study 202	JP/US		PII

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 IgG1 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. 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). The United States Food and Drug Administration (FDA) granted Breakthrough Therapy designation in June 2021, and a rolling submission to the FDA for the Biological License Application for early AD has been initiated under the accelerated approval pathway in September 2021, and completed in May 2022. FDA granted Fast Track designation in December 2021. Submission to the Pharmaceuticals and Medical Devices Agency (PMDA) of application data under the prior assessment consultation system has been initiated in Japan in March 2022 with the aim of obtaining early approval. Joint development with Biogen Inc.

	Early AD	Study 201 Study 301 (Clarity AD)	US JP/US/EU/CH	◎	Completion of rolling submission (May 2022) PIII
	Preclinical AD	Study 303 (AHEAD 3-45)	JP/US/EU		PIII

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

◎：Development progress from January 2022 onwards ○：Development progress from April 2021 onwards

Development Code: **E2023** Generic Name: **Iorcaserin**					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 is underway for this indication. 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 / PDE9 inhibitor					Oral
Description: A selective phosphodiesterase (PDE) 9 inhibitor that reduces the degradation of cyclic GMP, which is critical to signal transduction 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, 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)
Indications / Drug class: anti-MTBR tau antibody					Injection
Description: E2814 is anti-microtubule binding region (MTBR) tau antibody that was discovered as part of the research collaboration between Eisai and University College London. Expected to prevent the spreading of tau seeds within the brain. Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) has selected E2814 as the first investigational medicine among anti-tau drugs for their DIAN-TU tau study, and Phase Ib/II study and Phase II/III study Tau NexGen for dominantly inherited AD have been initiated.					
	Alzheimer's disease	Tau NexGen study Study103	US US/EU	◎ ○	PII/III PI/II

Development Code: **E2511**					In-house
Indications / Drug class: Synapse regenerant					Oral
Description: E2511 is expected to promote recovery and synaptic remodeling of damaged cholinergic neurons, and to suppress cerebral atrophy caused by neurodegeneration.					
	Alzheimer's disease	—	US		PI

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

◎ Aducanumab has been removed from this list due to amendment of collaboration agreement with Biogen Inc.

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

◎：Development progress from January 2022 onwards ○：Development progress from April 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 with a novel binding mode that selectively inhibits 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). Discovered and developed in-house. Approved for use in the treatment of thyroid cancer in over 80 countries including Japan, the United States, China and countries in Europe and in Asia. Approved for use in the treatment of hepatocellular carcinoma (first-line) in over 75 countries including in Japan, the United States, China and countries in Europe and in Asia. Also approved for use in the treatment of thymic carcinoma in Japan. 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 countries in Europe. Approved for use in the treatment of endometrial carcinoma (following prior systemic therapy) in combination with pembrolizumab in over 45 countries including in Japan, the United States, and countries in Europe and in Asia. In addition, approved for use in the treatment of renal cell carcinoma (first-line) in combination with pembrolizumab in over 35 countries including in Japan, the United States, and countries in Europe and in Asia. The agent is marketed under the product name Kisplyx only for this indication in Europe. Joint development with Merck & Co., Inc., Rahway, NJ, USA, through an affiliate.

In combination with anti-PD-1 antibody pembrolizumab, joint development with Merck & Co., Inc., Rahway, NJ, USA, through an affiliate (Additional Indication)					
	Endometrial carcinoma, following prior systemic therapy	Study 309	US EU JP Asia (Taiwan)	○ ○ ○ ◎	Approved (July, 2021) Approved (November, 2021) Approved (December, 2021) Approved (February, 2022)
	Renal cell carcinoma / First-line	Study 307	US EU Asia (Taiwan) JP	○ ○ ◎ ◎	Approved (August, 2021) Approved (November, 2021) Approved (January, 2022) Approved (February, 2022)
	Endometrial carcinoma / First-line	LEAP-001	JP/US/EU/CH		PIII
	Hepatocellular carcinoma / First-line	LEAP-002	JP/US/EU/CH		PIII
	Melanoma / First-line	LEAP-003	US/EU/CH		PIII
	Non-small cell lung cancer (nonsquamous) (in combination with chemotherapy) / First-line	LEAP-006	JP/US/EU/CH		PIII
	Non-small cell lung cancer / Second-line	LEAP-008	JP/US/EU		PIII
	Head and neck cancer / First-line	LEAP-010	JP/US/EU/CH		PIII
	Hepatocellular carcinoma (in combination with transcatheter arterial chemoembolization) / First-line	LEAP-012	JP/US/EU/CH		PIII
○	Esophageal carcinoma (in combination with chemotherapy) / First-line	LEAP-014	JP/US/EU/CH		PIII
	Gastric cancer (in combination with chemotherapy) / First-line	LEAP-015	JP/US/EU/CH		PIII
	Colorectal cancer (non MSI-H / pMMR) / Third-line	LEAP-017	US/EU		PIII
	Melanoma / Second-line	LEAP-004	US/EU		PII
	Selected solid tumors (Gastric cancer, colorectal cancer, glioblastoma, biliary tract cancers and pancreatic cancer)	LEAP-005	US/EU		PII
	Head and neck cancer / Second-line	LEAP-009	US/EU		PII
	Selected solid tumors (Endometrial carcinoma, renal cell carcinoma, head and neck cancer, bladder cancer, non-small cell lung cancer and melanoma)	Study 111 —	US/EU JP		PI/II PI
In combination with anticancer agent everolimus, joint development with Merck & Co., Inc., Rahway, NJ, USA, 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

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◎：Development progress from January 2022 onwards ○：Development progress from April 2021 onwards

○ Based on the external Data Monitoring Committee recommendation, Phase III clinical study of LEAP-007 for Non-small cell lung cancer, PD-L1 positive/First-line has been decided to be discontinued and therefore was removed from this list.

○ Based on the external Data Monitoring Committee recommendation, Phase III clinical study of LEAP-011 for cisplatin-ineligible bladder cancer, First-line has been decided to be discontinued and therefore was 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 80 countries including Japan, the United States, China and countries in Europe and in Asia for use in the treatment of breast cancer. Approved in over 80 countries including Japan, the United States and countries in Europe and in Asia for use in the treatment of liposarcoma (soft tissue sarcoma in Japan).					
Monotherapy (Additional Formulation)					
	Liposomal formulation	—	JP/EU		PI
In combination with anti-PD-1 antibody nivolumab, joint development with Ono Pharmaceutical (Additional Formulation)					
	Liposomal formulation	Study 120	JP		PI/II

Development Code: **E7438** Generic Name: **tazemetostat** Product Name: **Tazverik**					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 histone methyltransferases. Tazverik, a first-in-class, orally administered small molecule inhibitor, was discovered using Epizyme, Inc. proprietary product platform, and is expected to exhibit antitumor effects via inhibition of the epigenetic enzyme EZH2. Eisai holds development and commercialization rights in Japan.					
	Non-Hodgkin B-cell lymphoma	Study 206	JP	○	Approved (June, 2021)

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, FGFR2, FGFR3 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 is ongoing. It has received orphan drug designation with a prospective indication for unresectable biliary tract cancer with *FGFR2* gene fusion by the Ministry of Health, Labour and Welfare (MHLW) in Japan.					
	Cholangiocarcinoma	Study 201	JP/CH		PII
	Breast cancer	—	JP		PI

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

◎：Development progress from January 2022 onwards ○：Development progress from April 2021 onwards

Development Code: **MORAb-202**					In-house
Indications / Drug class: Anticancer agent / farletuzumab- eribulin conjugate					Injection
Description: MORAb-202 is the antibody drug conjugate (ADC) with approved anticancer drug eribulin. Expected to show an antitumor effect against folate receptor α-positive tumors by concentrating eribulin on tumor; inclusive of endometrial, ovarian, lung and breast cancers. In June 2021, Eisai entered into an exclusive global strategic collaboration agreement for the co-development and co-commercialization with Bristol Myers Squibb.					
	Solid tumors	—	US		PI/II
	Solid tumors	—	JP		PI

Development Code: **E7386**			Collaboration (PRISM BioLab)		Oral
○	Solid tumors (in combination with pembrolizumab)	Study 201	JP/US		PI/II
	Solid tumors	—	JP/EU		PI
	Solid tumors (in combination with lenvatinib)	—	JP		PI

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

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

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

○ Phase I/II study of MORAb-009 for mesothelioma in the United States and Europe has been finished and therefore was removed from this list.

○ H3B-8800 was licensed to a subsidiary of Roivant Sciences Ltd. and therefore has been removed from this list.

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

◎：Development progress from January 2022 onwards ○：Development progress from April 2021 onwards

(3) Gastrointestinal Disorders

Development Code: **AJM300** Generic Name: **carotegrast methyl** Product Name: **Carogra**					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. In March 2022, EA Pharma obtained manufacturing and marketing approval in Japan as the first orally-available α4 integrin antagonist in the world to be effective in ulcerative colitis. Joint development by EA Pharma and Kissei Pharmaceutical.					
	Ulcerative colitis	—	JP	◎	Approved (March, 2022)

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	

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

Development Code: **EA3571**					In-house	Oral
◎	Nonalcoholic steatohepatitis (Development conducted by EA Pharma)	—	JP		PI	

○ Due to business priorities, EA Pharma is no longer progressing the development at Phase I/II study in Japan of EA4000 as bowel cleansing agent and therefore EA4000 was removed from this list.

○ Due to business priorities, EA Pharma is no longer progressing the development at Phase I study in Japan of EA3355 as an agent for liver disease and therefore EA3355 was removed from this list.

◎ Due to business priorities, EA Pharma is no longer progressing the development at Phase II study in Japan of E6007 as an agent for ulcerative colitis treatment and therefore E6007 was removed from this list.

◎ Due to business priorities, EA Pharma has decided to discontinue Phase II study in Japan and Europe of E6011 as an agent for Crohn's disease and therefore E6011 was removed from this list.

(4) Other

Development Code: **D2E7** Generic Name: **adalimumab** Product Name: **Humira**					In-license (AbbVie GK)
Indications / Drug class: Fully human anti-TNFα monoclonal antibody					Injection
Description: A fully human anti-TNFα monoclonal antibody, which neutralizes tumor necrosis factor alpha (TNFα), a type of cytokine that plays a central role in inflammatory reactions in patients with autoimmune diseases. Approved in Japan for the treatment of rheumatoid arthritis (including inhibition of the progression of structural damage), psoriasis, Crohn's disease, ankylosing spondylitis, polyarticular juvenile idiopathic arthritis, intestinal Behçet's disease, ulcerative colitis, non-infectious uveitis, hidradenitis suppurativa, and pyoderma gangrenosum.					
○	Ulcerative Colitis (High-Dosage in Adult, and Pediatric)	—	JP		Approved (September, 2021)

Development Code: **E5564** Generic Name: **eritoran**					In-house
Indications / Drug class: Suppression for increasing of severity of COVID-19/ TLR 4 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. Joint development with GCAR (Global Coalition for Adaptive Research).					
	Suppression for increasing of severity of COVID-19	REMAP-COVID	JP/US		PIII

Development Code: **FYU-981** Generic Name: **dotinurad**					In-license (FUJI YAKUHIN)
Indications / Drug class: Treatment for Hyperuricemia and Gout / selective URAT1 inhibitor					Oral
Description: Dotinurad selectively inhibits URAT1, one of the uric acid transporters, thus preventing reabsorption of uric acid by kidneys and promoting uric acid excretion in urine. In addition, it has a small effect on other transporters affecting uric acid secretion, so it reduces serum uric acid levels at lower doses. Therefore, dotinurad is expected to have a low risk of side effects and drug interaction. In Japan, FUJI YAKUHIN obtained manufacturing and marketing approval for dotinurad in January 2020. Eisai entered into a license agreement concerning the development and distribution in China in February 2020, and in five ASEAN countries in August 2021 with FUJI YAKUHIN.					
○	Gout	Study 301	CH		PIII

Development Code: **E6742**					In-house
Indications / Drug class: Treatment for Systemic lupus erythematosus / TLR 7/8 inhibitor					Oral
Description: TLRs are receptors of the innate immune system, and activated TLRs initiate an inflammatory reaction or an antiviral response. E6742 is the inhibitor of oral and selective TLR7/8 which is associated with the pathogenesis of systemic lupus erythematosus. This project has been selected by the Japan Agency for Medical Research and Development (AMED) for its Cyclic Innovation for Clinical Empowerment (CiCLE) grand program.					
◎	Systemic lupus erythematosus	Study 101	JP		PI/II

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 January 2022 onwards ○：Development progress from April 2021 onwards