14. Major R&D Pipeline

(1) Neurology

Development Code: **BAN2401** Generic Name: **lecanemab** Product Name: **Leqembi**	In-license (BioArctic AB)
Indications / Drug class: Treatment for Alzheimer's disease / anti-Aβ protofibril antibody	Injection

Description: An IgG1 antibody that targets amyloid beta (Aβ) protofibrils. Reduces the rate of disease progression and slows cognitive and functional decline in adults with Alzheimer's disease (AD) through the elimination of neurotoxic Aβ protofibrils. In July 2023, lecanemab was granted traditional approval in the United States as a treatment for AD by the U.S. Food and Drug Administration (FDA) after an application supporting the conversion of the accelerated approval to a traditional approval based on the Phase III clinical study Clarity AD. In September 2023, the agent was approved in Japan as a treatment for slowing progression of mild cognitive impairment (MCI) and mild dementia due to AD. In January 2024, the agent was approved in China as a treatment of MCI due to AD and mild AD dementia. Applications have been submitted for use in the treatment of early AD in Europe, Canada, Great Britain, Australia, Switzerland, South Korea, Israel, Taiwan, Singapore, Brazil, Hong Kong, Russia, Saudi Arabia and India. The application has been designated for priority review in Israel. In Great Britain, lecanemab has been designated for the Innovative Licensing and Access Pathway, which aims to reduce the time to market for innovative medicines. In March 2024, a Supplemental Biologics License Application for intravenous (IV) maintenance dosing was submitted in the United States. In April 2024, a subcutaneous injection formulation, which is being developed to enhance convenience for patients, was granted Fast Track Designation in the United States. In May 2024, the rolling submission of a Biologics License Application for maintenance dosing of a subcutaneous injection formulation, which is being developed to enhance convenience for patients, was initiated in the United States under the Fast Track status. The Phase III clinical study AHEAD 3-45 for preclinical (asymptomatic) AD is underway in collaboration with the Alzheimer's Clinical Trials Consortium (ACTC). Joint development with Biogen Inc.

	Early AD	Study 301 (Clarity AD)	US JP CH EU Asia (SK)	○ ○ ◎ ○	Traditional approval (July 2023) Approval (September 2023) Approval (January 2024) Submission (accepted: January 2023)Submission (June 2023)
◎	IV maintenance dosing for early AD (Additional Dosage and Administration)	Study201/301	US		Submission (March 2024)
◎	Maintenance dosing of a subcutaneous injection formulation for early AD (Additional Formulation)	Study301	US		Rolling Submission (initiated: May 2024)
	Preclinical AD	Study 303 (AHEAD 3-45)	JP/US/EU		PIII

Development Code: **E2007** Generic Name: **perampanel** Product Name: **Fycompa**	In-house
Indications / Drug class: Antiepileptic agent / AMPA receptor antagonist	Oral / Injection

Description: Selectively inhibits the AMPA receptor (a glutamate receptor subtype) activation by glutamate. Approved as an adjunctive therapy for partial-onset seizures in over 75 countries including Japan, China and countries in Europe and in Asia. Approved for monotherapy in Japan and China. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in over 75 countries including Japan, China and countries in Europe and in Asia. An oral suspension formulation has been approved in Europe and China. Fine granule and injection formulations have been approved in Japan. In January 2023, the commercial rights in the United States were transferred.

	Injection formulation (Additional Formulation)	—	JP	◎	Approval (January 2024)
	Adjunctive therapy for primary generalized tonic-clonic seizures (Additional Indication)	Study 332	CH	◎	Approval (April 2024)

◎ The development of the agent for Lennox-Gastaut syndrome in Japan, the United States and Europe which was at Phase III stage (Study 338) has finished and therefore was removed from this list.

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 15 countries including Japan, the United States and countries in Asia.

	Insomnia disorder	Study 311	CH	◎	Submission (accepted: January 2024)

○ The development of the agent for irregular sleep-wake rhythm disorder and Alzheimer's disease dementia in Japan and the United States which was at Phase II stage (Study 202) has finished and therefore was removed from this list.

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

◎：Development progress from January 2024 onwards ○：Development progress from April 2023 onwards

Development Code: **E0302** Generic Name: **mecobalamin**					In-house
Indications / Drug class: Treatment for Amyotrophic lateral sclerosis (ALS)					Injection
Description: Ultrahigh-dose of mecobalamin that is 100 times the approved dose used for the treatment of peripheral neuropathy (as a single dose). Based on the results of the investigator-initiated clinical trial JETALS, a new drug application has been submitted for the treatment of ALS in Japan.					
◎	ALS	JETALS	JP		Submission (January 2024)

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 seizures 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: **E2814**					Collaboration (University College London)
Indications / Drug class: anti-MTBR tau antibody					Injection
Description: An 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 are underway.					
	AD	Tau NexGen study Study103	JP/US/EU US/EU		PII/III PI/II

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

Development Code: **E2025**			In-house	Injection
	AD	—	US	PI

Development Code: **E2086**			In-house	Oral
	Narcolepsy	—	US	PI

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

◎ The development of E2027, a phosphodiesterase (PDE) 9 inhibitor, for dementia with Lewy bodies and Parkinson's disease dementia in the United States which was at Phase II stage has finished and therefore was removed from this list.

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

◎：Development progress from January 2024 onwards ○：Development progress from April 2023 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 available multiple kinase inhibitor that selectively inhibits kinase activities vascular endothelial growth factor receptors (VEGFR): VEGFR1, VEGFR2 and VEGFR3, and fibroblast growth factor receptors (FGFR): FGFR1,FGFR2, FGFR3 and FGFR4, in addition to pathogenic angiogenesis, tumor growth and cancer progression related receptor tyrosine kinases such as the platelet derived growth factor receptor alpha (PDGFRα), KIT, and RET. Discovered and developed in-house. As monotherapy indications, 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 80 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. As a combination therapy with everolimus, approved for use in the treatment of renal cell carcinoma (second-line) in over 65 countries including the United States, countries in Europe and in Asia. As a combination therapy with pembrolizumab, approved for use in the treatment of renal cell carcinoma (first-line) in over 50 countries including in Japan, the United States, and countries in Europe and in Asia, and approved for use in the treatment of endometrial carcinoma (following prior systemic therapy) in over 50 countries including in Japan, the United States, and countries in Europe and in Asia, including conditional approval. The agent is marketed under the product name Kisplyx only for renal cell carcinoma indication in Europe. Joint development with Merck & Co., Inc., Rahway, NJ, USA, through an affiliate.

In combination with anti-PD-1 therapy pembrolizumab, joint development with Merck & Co., Inc., Rahway, NJ, USA, through an affiliate (Additional Indication)					
	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
	Head and neck cancer / Second-line	LEAP-009	US/EU		PII
In combination with anti-PD-1 antibody nivolumab, joint development with Ono Pharmaceutical (Additional Indication)					
	Hepatocellular carcinoma	—	JP		PI

- ○ Based on the independent Data Monitoring Committee recommendation, the Phase III clinical study LEAP-003 for melanoma (first-line, in combination with pembrolizumab) in the United States, Europe and China, was decided to be discontinued, and therefore was removed from this list.
- ○ The Phase III clinical study LEAP-017 for colorectal cancer (third-line, in combination with pembrolizumab) in the United States and Europe, didn't meet its primary endpoint and therefore was removed from this list.
- ○ The Phase III clinical study LEAP-010 for head and neck cancer (first-line, in combination with pembrolizumab) in Japan, the United States, Europe and China, was decided to be discontinued, and therefore was removed from this list.
- ○ Both the Phase III clinical study LEAP-006 for non-small cell lung cancer (first-line, in combination with pembrolizumab) in Japan, the United States, Europe and China, and the Phase III clinical study LEAP-008 for non-small cell lung cancer (second-line, in combination with pembrolizumab) in Japan, the United States and Europe, didn't meet their primary endpoints and therefore were removed from this list.
- ○ The Phase III clinical study LEAP-001 for endometrial carcinoma (first-line, in combination with pembrolizumab) in Japan, the United States, Europe and China, didn't meet its primary endpoint and therefore was removed from this list.
- ◎ The development of the agent for melanoma (second-line, in combination with pembrolizumab) in the United States and Europe which was at Phase II stage (LEAP-004) has finished and therefore was removed from this list.
- ◎ The development of the agent for selected solid tumors (in combination with pembrolizumab) in the United States and Europe which was at Phase II stage (LEAP-005) has finished and therefore was removed from this list.
- ◎ The development of the agent for renal cell carcinoma (first-line, in combination with everolimus) in Japan, the United States and Europe which was at Phase III stage (Study 307) has finished and therefore was removed from this list.

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◎：Development progress from January 2024 onwards ○：Development progress from April 2023 onwards

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 85 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 85 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: **E7090** Generic Name: **tasurgratinib**	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. It has been granted the 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.	

	Biliary tract cancer with *FGFR2* gene fusion	Study 201	JP	○	Submission (December 2023)
	Breast cancer	—	JP		PI

Development Code: **MORAb-202** Generic Name: **farletuzumab ecteribulin (FZEC)**	In-house
Indications / Drug class: Anticancer agent / Folate receptor α targeted antibody drug conjugate (ADC)	Injection
Description: ADC which combines anti-folate receptor α (FRα) antibody with approved anticancer drug eribulin via its linker. Expected to show an antitumor effect against FRα-positive tumors by concentrating eribulin on tumor; inclusive of endometrial, ovarian, lung and breast cancers. Joint development with Bristol Myers Squibb.	

	Non-small cell lung cancer	Study 203	US/EU		PII
	Ovarian cancer, peritoneal cancer, fallopian tube cancer	Study 205	JP/US/EU		PII
	Solid tumors	Study 201	US/EU		PI/II

Development Code: **BB-1701**	In-house
Indications / Drug class: Anticancer agent / HER2 targeted ADC	Injection
Description: ADC which combines anti-HER2 antibody with approved anticancer drug eribulin via its linker. Expected to show an antitumor effect against HER2-positive tumors by concentrating eribulin on tumor; inclusive of breast cancer. Joint development agreement with Bliss Biopharmaceutical (Hangzhou) Co., Ltd. with option rights for a strategic collaboration.	

○	Breast cancer	Study 205	JP/US		PII

Development Code: **E7386**	Collaboration (PRISM BioLab)
Indications / Drug class: Anticancer agent / CBP/β-catenin interaction inhibitor	Oral
Description: A CREB-binding protein (CBP) /β-catenin inhibitor that blocks the protein-protein interaction between CBP and β-catenin, and regulates Wnt signaling-dependent gene expression. Expected inhibition of Wnt signaling-dependent tumor growth.	

	Solid tumors (in combination with pembrolizumab)	Study 201	JP/US/EU		PI/II
	Solid tumors	—	JP/US/EU		PI
	Solid tumors (in combination with lenvatinib)	—	JP/US/EU		PI

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◎：Development progress from January 2024 onwards ○：Development progress from April 2023 onwards

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 (in combination with CDK4/6 inhibitor palbociclib)	—	US/EU		PI

◎ A Phase I/II clinical study (Study 101) for breast cancer in the United States and Europe has finished and therefore was removed from this list.

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

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

(3) Global Health

Development Code: **E1224** Generic Name: **fosravuconazole**	In-house
Indications / Drug class: Antifungal agent / ergosterol synthesis inhibitor	Oral
Description: An ongoing collaboration with the Drugs for Neglected Diseases initiative (DNDi) for a new treatment for eumycetoma, a fungal form of mycetoma with a particularly high unmet medical need, and one of the world's most neglected diseases. Eisai is mainly responsible for non-clinical studies and the provision of the investigational drug. A Phase IIb/III clinical study was conducted in Sudan by DNDi and the Mycetoma Research Center of the University of Khartoum, Sudan. Currently, preparation for regulatory filing to the regulatory authorities (National Medicines and Poisons Board) in Sudan is underway. Supported by the Global Health Innovative Technology Fund (GHIT Fund).	

Development Code: **SJ733**	Co-development (University of Kentucky)
Indications / Drug class: Antimalarial agent / ATP4 inhibitor	Oral
Description: Expected to be suitable for treatment in malaria-endemic areas, with rapid efficacy and safety, and providing lasting protection against reinfection. The treatment might potentially solve the problem of increased resistance faced by current antimalarial medicines. In the ongoing collaboration with the University of Kentucky, Eisai is responsible for the provision of drug substance and formulation manufacturing. The Phase II clinical study is being conducted in Peru by the University of Kentucky. Supported by the GHIT Fund.	

Development Code: **AWZ1066S**	Co-development (Liverpool School of Tropical Medicine)
Indications / Drug class: Antifilarial agent / antiwolbachia mechanism	Oral
Description: An ongoing collaboration with the Liverpool School of Tropical Medicine and the University of Liverpool to jointly identify new drugs effective against lymphatic filariasis and onchocerciasis (river blindness), both major types of filariasis. Eisai is responsible for the provision of drug substance and formulation manufacturing. The Phase I clinical study is being conducted in the United Kingdom (UK) by the Liverpool School of Tropical Medicine. Supported by the GHIT Fund and Medical Research Council in the UK.	

(4) Gastrointestinal Disorders

Development Code: **AJG555** Product Name: **MOVICOL**					In-license (Norgine)
Indications / Drug class: Chronic constipation treatment / polyethylene glycol preparation					Oral
Description: An orally available constipation treatment consisting of a polyethylene glycol preparation which facilitates bowel movement by regulating osmolality in the intestines. Approved for chronic constipation treatment for children of 2 years and above and adult patients in Japan. Development conducted by EA Pharma.					
○	Chronic constipation in children under 2 years of age (Additional Dosage and Administration)	Study CT3	JP		PIII

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
	Metabolic dysfunction-associated steatohepatitis (Development conducted by EA Pharma)	—	JP		PI

(5) Other

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, hyperuricemia	—	Asia (Philippines)		Submission (September 2023)
	Gout	Study 301	CH	◎	Submission (accepted: January 2024)

Development Code: **E6742**					In-house
Indications / Drug class: Treatment for Systemic lupus erythematosus / TLR 7/8 inhibitor					Oral
Description: Toll-Like Receptors (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) grant 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, SK: South Korea, P: (Clinical trial) Phase

◎：Development progress from January 2024 onwards ○：Development progress from April 2023 onwards