14. Major R&D Pipeline

In-House R&D Pipeline List

	Product Name / Development Code	Additional Indication, etc.**	Development Stage***	Therapeutic Area****
New Approval				
○	Halaven (Liposarcoma)	AI	(EU) approved	Oncology
○	Fycompa (Oral suspension)	AF	(US/EU) approved	Neurology
○	Lenvima/Kisplyx (Renal cell carcinoma, second-line)	AI	(US/EU/AS) approved	Oncology
○	BELVIQ (Once-daily formulation)	AF	(US) approved	Neurology
○	Humira (Non-infectious uveitis)	AI	(JP) approved	Other
Submitted / Preparing for Submission				
	Aricept (Severe Alzheimer's disease)	AI	(CN) submitted	Neurology
○	Halaven (Breast cancer)		(CN) submitted	Oncology
○	AJG511 (Ulcerative colitis)*		(JP) submitted	GI
○	Pariet (Maintenance therapy for proton pump inhibitor (PPI)-resistant reflux esophagitis)	ADA	(JP) submitted	GI
○	Fycompa (Monotherapy for partial-onset seizures)	AI	(US) submitted	Neurology
◎	AJG533 (Chronic constipation)*		(JP) submitted	GI
Clinical Trial Stage				
○	E2006 (Insomnia disorder)		(JP/US/EU) PIII	Neurology
○	E2609 (Early Alzheimer's disease)		(JP/US/EU) PIII	Neurology
◎	Lenvima (Thyroid cancer)		(CN) PIII	Oncology
	AJM300 (Ulcerative colitis)*		(JP) PIII	GI
	AJG555 (Chronic constipation)*		(JP) PIII	GI
	Livact (Hypoalbuminemia)		(CN) PIII	GI
○	Fycompa (Lennox-Gastaut syndrome)	AI	(JP/US/EU) PIII	Neurology
○	Fycompa (Pediatric epilepsy)	AI	(JP/US/EU) PIII	Neurology
◎	Fycompa (Monotherapy for partial-onset seizures)	AI	(JP) PIII	Neurology
	Lenvima (Hepatocellular carcinoma)	AI	(JP/US/EU/CN/AS) PIII	Oncology
○	Lenvima (Renal cell carcinoma, first-line)	AI	(US/EU) PIII	Oncology
	BAN2401 (Alzheimer's disease)		(JP/US/EU) PII	Neurology
○	E2006 (Irregular sleep-wake rhythm disorder associated with Alzheimer's disease)		(JP/US) PII	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
	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
	Aricept (Regression symptoms in people with Down syndrome)	AI	(JP) PII	Neurology
	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
	E6011 (Crohn's disease)*		(JP) PI/II	Other
	BELVIQ (Obesity)		(JP) PI	Neurology
	E2027 (Alzheimer's disease)		(US) PI	Neurology
◎	E2730(Epilepsy)		(US) PI	Neurology
	E7090 (Solid tumors)		(JP) PI	Oncology
	MORAb-066 (Solid tumors)		(US) PI	Oncology
	E7046 (Solid tumors)		(US/EU) PI	Oncology
○	H3B-6527 (Hepatocellular carcinoma)		(US) PI	Oncology
○	H3B-8800 (Blood cancer)		(US/EU) PI	Oncology
○	E7438 (Non-Hodgkin B-cell lymphoma)		(JP) PI	Oncology
○	E6130 (Inflammatory bowel disease)*		(JP) PI	GI
	MORAb-022 (Rheumatoid arthritis)		(US) PI	Other
	E6071 (Autoimmune disease)		(EU) PI	Other
	Lenvima (Renal cell carcinoma, second-line)	AI	(JP) PI	Oncology
	Halaven (Liposome formulation)	AF	(EU) PI	Oncology

* EA Pharma pipeline product ** AI: Additional Indication, ADA: Additional Dosage and Administration AF: Additional Formulation *** P: Clinical Phase; JP: Japan, US: United States, EU: Europe, CN: China, AS: Asia (excluding Japan and China) ****GI: Gastrointestinal Disorders

○ The transdermal formulation for Aricept has been removed from this list as the developer was changed to Teikoku Pharmaceuticals Co., Ltd.
◎ Development of MORAb-004 for colorectal cancer and soft tissue sarcoma indications have been discontinued at the Phase II stage.
◎ Development of Lenvima for endometrial cancer (monotherapy), melanoma, and non-small cell lung cancer (third-line, monotherapy) indications have been discontinued at the Phase II stage.
◎ Development of Halaven for the non-small cell lung cancer indication has been discontinued at the Phase III stage.
◎ Development of E7820 for the colorectal cancer indication has been discontinued at the Phase II stage.
◎ Development of MORAb-003 for the non-small cell lung cancer indication has been discontinued at the Phase II stage.

○: Development progress from April 2016 onwards ◎: Development progress from January 2017 onwards

(1) Neurology

Development Code: **E2020** Generic Name: **donepezil** Product Name: **Aricept**

Indications / Drug class: Treatment for Alzheimer's disease / dementia with Lewy bodies			In-house	
Description: Increases levels of the neurotransmitter acetylcholine in the brain by inhibiting the enzyme acetylcholinesterase from breaking down acetylcholine, thereby slowing the overall progression of symptoms associated with Alzheimer's disease (AD). Currently approved in more than 90 countries around the world for the treatment of mild to moderate AD. Also approved as a treatment for patients with severe AD in numerous countries including the United States, Japan, Canada, and several other Asian and Latin American countries. Approved in Japan and the Philippines for dementia with Lewy bodies.				
	Severe Alzheimer's disease (Additional Indication)	Study 339	CN: Submitted (February 2015)	Oral
	Regression symptoms in people with Down syndrome (Additional Indication)	345	JP: PII	Oral

○ The transdermal formulation has been removed from this list as the developer was changed to Teikoku Pharmaceuticals Co., Ltd.

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, in Europe, the United States, and Asia. Also approved as an adjunctive therapy for primary generalized tonic-clonic seizures in countries such as Japan, the United States and in Europe.				
	Oral suspension (Additional Formulation)		○ US: approved (April 2016) ○ EU: approved (September 2016)	Oral
	Monotherapy for partial-onset seizures (Additional Indication)	— Study 342	○ US: submitted (September 2016) ◎ JP: PIII	Oral
○	Lennox-Gastaut syndrome (Additional Indication)	338	JP/US/EU: PIII	Oral
○	Pediatric epilepsy (Additional Indication)	311	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 304	JP/US/EU: PIII	Joint development with Purdue Pharma L.P.	Oral
○	Irregular sleep-wake rhythm disorder associated with Alzheimer's disease	202	JP/US: PII	Joint development with Purdue Pharma L.P.	Oral

Development Code: **E2609**

Indications / Drug class: Anti-Alzheimer's agent / 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: PIII	Joint development with Biogen Inc.	Oral

Development Code: **BAN2401**

Indications / Drug class: Anti-Alzheimer's agent / anti-Aβ protofibril monoclonal antibody				In-license (BioArctic Neuroscience)	
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.					
	Alzheimer's disease	Study 201	JP/US/EU: PII	Joint development with Biogen Inc.	Inj.

○ Development progress from April 2016 onwards ◎ Development progress from January 2017 onwards

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 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.			
○	Obesity once-daily formulation (Additional Formulation)	US: approved (July 2016)	Oral
	Obesity	JP: PI	Oral

Development Code: **E2027**

	Alzheimer's disease	US: PI	In-house	Oral

Development Code: **E2730**

◎	Epilepsy	US: PI	In-house	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 60 countries including in the United States, in Europe, Japan and Asia for use in chemotherapy for breast cancer. Approved in countries including the United States, Japan and in Europe for use in the treatment of soft tissue sarcoma.					
○	Breast cancer	Study304	CN: submitted (July 2016)		Inj.
○	Advanced soft tissue sarcoma (Additional Indication)	309	EU: approved (May 2016, for liposarcoma)		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	Co-development with Merck & Co., Inc., Kenilworth, NJ, USA	Inj.
○	HER2-negative breast cancer (in combination with PEGPH20)	219	US: PI/II	Co-development with Halozyme Therapeutics, Inc.	Inj.
	Liposome formulation (Additional Formulation)	112	EU: PI		Inj.

◎ Development for the non-small cell lung cancer indication has been discontinued at the Phase III stage.

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. Confirmed through X-ray crystal structural analysis to be the first compound to demonstrate a new binding mode (Type V) to VEGFR2, exhibiting rapid and potent inhibition of kinase activity, according to kinetic analysis. Approved as a treatment for refractory thyroid cancer in over 50 countries including the United States, Japan, in Europe and Asia. Also approved as a treatment for renal cell carcinoma in countries including the United States and Europe. The agent is marketed under the product name Kisplyx only for this indication in Europe.				
◎	Thyroid cancer	Study 308	CN: PIII	Oral
	Renal cell carcinoma/Second-line (Additional Indication)	205	○ US: approved (May 2016) ○ EU: approved (August 2016) ○ Asia (Philippines) approved (December 2016)	Oral
		—	JP: PI	
○	Renal cell carcinoma/First-line (Additional Indication)	307	US/EU: PIII	Oral
	Hepatocellular carcinoma (Additional Indication)	304	JP/US/EU/CN/AS: PIII	Submission Target: FY2017	Oral
	Non-small cell lung cancer (RET translocations) (Additional Indication)	209	JP/US/EU/AS: PII	Oral
	Biliary tract cancer (Additional Indication)	215	JP: PII	Oral
	Select solid tumors (Endometrial cancer, Renal cell carcinoma, head and neck cancer, urothelial cancer, non-small cell lung cancer, melanoma)	111	US: PI/II	Co-development with Merck & Co., Inc., Kenilworth, NJ, USA	Oral /Inj.
	Select solid tumors (Hepatocellular carcinoma, Endometrial cancer etc.) (in combination with anti-PD1 antibody pembrolizumab)	—	◎ JP: PI	

＊ The submission timeline for hepatocellular carcinoma has been reviewed and subsequently changed from FY2016 to FY2017.
◎ Development for endometrial cancer (monotherapy), melanoma, and non-small cell lung cancer (third-line, monotherapy) indications have been discontinued at the Phase II stage.

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 for the non-small cell lung cancer indication has been discontinued at the Phase II stage.

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 has been discontinued for colorectal cancer and soft tissue sarcoma indications at the Phase II stage.

Development Code: **MORAb-009** Generic Name: **amatuximab**

Indications / Drug class: Anticancer agent / chimeric anti-mesothelin monoclonal antibody			In-house
Description: A chimeric IgG1 monoclonal 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: **E7090**

	Solid tumors	JP: PI	In-house	Oral

Development Code: **MORAb-066**

	Solid tumors	US: PI	In-license (Janssen Biotech)	Inj.

Development Code: **E7046**

	Solid tumors	US/EU: PI	In-house	Oral

Development Code: **H3B-6527**

○	Hepatocellular carcinoma	US: PI	In-house	Oral

Development Code: **H3B-8800**

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

Development Code: **E7438**

○	Non-Hodgkin B-cell lymphoma	JP: PI	In-license (Epizyme, Inc.)	Oral

◎ Development of E7820 for the colorectal cancer indication has been discontinued at the Phase II stage in the U.S. and Europe.

(3) Gastrointestinal Disorders

Development Code: **E3810** Generic Name: **rabeprazole** Product Name: **Pariet/AcipHex**

Indications / Drug class: Proton pump inhibitor				In-house
Description: A proton pump inhibitor approved for the treatment of gastric and duodenal ulcers, reflux esophagitis, eradication of *Helicobacter pylori* infections and triple formulation packs (combination packs) for *H. pylori* eradication that include rabeprazole. Approved for the prevention of recurrent gastric or duodenal ulcer caused by low-dose aspirin therapy as well as 5 mg tablet formulation in December 2014.				
○	Maintenance therapy for proton pump inhibitor (PPI)-resistant reflux esophagitis10 mg twice daily (Additional Dosage and Administration)	Study 311	JP: submitted (October 2016) Joint development with EA Pharma	Oral

Development Code: **AJG511** Generic Name: **budesonide**

Indications / Drug class: Ulcerative colitis treatment / locally-active steroid				In-license (Dr. Falk Pharma)
Description: The first rectal foam product in Japan containing budesonide as active ingredient. Budesonide is a locally-active steroid and, thus, is expected to reduce systemic side effects. In addition, AJG511 is a foam type product that can reach the inflamed sites of rectum and sigmoid colon by rectal administration, and has a characteristic feature of preventing leakage after administration. Budesonide rectal foam is already available on the market in Europe.				
○	Ulcerative colitis	Study CT1	JP: submitted (October 2016) Joint development by EA Pharma and Kissei Pharmaceutical	Foam

Development Code: **AJG533** Generic Name: **elobixibat**

Indications / Drug class: Chronic constipation treatment / bile acid transporter inhibitor				In-license (Albireo)
Description: An orally available constipation treatment having a novel action mechanism. AJG533 inhibits the bile acid transporter that regulates reabsorption of bile acids and thereby increases spontaneous colonic motility				
◎	Chronic constipation	Study CT1	JP: submitted (February 2017) Joint development by EA Pharma and Mochida Pharmaceutical	Oral

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**

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 suppressing osmotic pressure in the intestines.				
	Chronic constipation	Study CT1/CT2	JP: PIII	Development conducted by EA Pharma	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: FY2017 Joint development with EA Pharma	Oral

○ Development progress from April 2016 onwards ◎ Development progress from January 2017 onwards

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 Code: **E6130**

○	Inflammatory bowel disease	JP: PI	In-house (development conducted by EA Pharma)	Oral

(4) Other

Development Code: **D2E7** Generic name: **adalimumab** Product name: **Humira**

Indications / Drug class: Fully human anti-TNF-α monoclonal antibody formulation			In-license (Abbvie)
Description: The world's first fully human anti-TNF-α monoclonal antibody that exerts its effects by neutralizing TNF-α, a cytokine that plays a central role in inflammatory responses. Approved in Japan as a treatment for rheumatoid arthritis (including inhibition of the progression of structural damage), psoriasis, Crohn's disease, ankylosing spondylitis, juvenile idiopathic arthritis, intestinal Behcet's disease, ulcerative colitis and non-infectious uveitis.			
○	Non-infectious uveitis (Additional Indication)	JP: approved (September 2016) Joint development with Abbvie	Inj.

Development Code: **E6011**

Indications / Drug class: Anti-Fractalkine antibody				In-house	
Description: The world's first humanized anti-fractalkine monoclonal antibody discovered by Eisai Group subsidiary KAN Research Institute Inc. Believed to exert an anti-inflammatory effect by neutralizing fractalkine which 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	101	JP: PI/II	Development conducted by EA Pharma	Inj.

Development Code: **MORAb-022**

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

Development Code: **E6071(GSK3050002)**

Autoimmune disorder (antibody)	EU: PI	In-house (joint development with GlaxoSmithKline)	Inj.