

## State of New Product Development (as of Oct. 29, 2009)

### 1. Pipeline in Japan

#### (1) New Molecular Entities

Development code (Generic name)	Category (Indications)	Stage	Origin	Remarks
TA-8317 / ACREF (Fentanyl citrate)	Narcotic analgesic (Breakthrough cancer pain: oral transmucosal)	NDA filed (Aug. 2008)	US:Cephalon	
MCC-847 (Masilukast)	Leukotriene D4 antagonist (Asthma) (Allergic rhinitis)	Phase 3 Phase 2	UK: AstraZeneca	
MP-424 (Telaprevir)	NS3-4A protease inhibitor (Chronic hepatitis C)	Phase 3	US:Vertex	
MP-513 (Teneligliptin)	DPP4 Inhibitor (Type 2 Diabetes mellitus)	Phase 3	In-house	
APTA-2217 (Roflumilast)	PDE4 inhibitor (Asthma) (COPD)	Phase 2/3 Phase 2/3	Switzerland: Nycomed	Co-development -Nycomed
CNTO148 (Golimumab)	Anti-TNF $\alpha$ monoclonal antibody (Rheumatoid arthritis)	Phase 2/3	US:Centocor	Co-development -Janssen Pharma
FTY720 (Fingolimod hydrochloride)	Sphingosine-1-phosphate receptor modulator (Multiple Sclerosis*)	Phase 2	In-house	Co-development -Novartis Pharma -Mitsui Sugar
MP-214 (Cariprazine)	D3/D2 antagonist (Schizophrenia)	Phase 2	Hungary: Gedeon- Richter	
MP-435	C5a antagonist (Rheumatoid arthritis)	Phase 1	In-house	
TA-6666	DPP4 inhibitor (Type 2 Diabetes mellitus)	Phase 1	In-house	
TA-7284 (Canagliflozin)	SGLT2 inhibitor (Diabetes mellitus)	Phase 1	In-house	

\*: Orphan drug designated

(2) Additional Indications

Product name (Generic name)	Category (Indications)	Stage	Origin	Remarks
Venoglobulin-IH (Polyethylene glycol treated human normal immunoglobulin)	Human immunoglobulin G (IgG2 deficiency)	sNDA filed (Dec. 1997)	In-house	
	(Polymyositis, Dermatomyositis* )	sNDA filed (May 2003)		
	(Hypo and gammaglobulinemia: additional dose)	sNDA filed (Mar. 2008)		
	(Systemic scleroderma)	Phase 3		
	(Myasthenia gravis*)	Phase 3		
Remicade (Infliximab(recombinant))	Anti-TNF $\alpha$ monoclonal antibody		US:Centocor	
	(Psoriasis)	sNDA filed (Feb. 2008)		
	(Ankylosing spondylitis*)	sNDA filed (Sep. 2008)		
	(Ulcerative colitis)	sNDA filed (June 2009)		
	(Crohn's disease: dose escalation)	Phase 3		
Pazucross (Pazufloxacin mesilate)	New quinolone antibacterial agent (Severe or intractable case: additional dose) (Sepsis, Pneumococcus)	sNDA filed (June 2009)	Japan: Toyama Chemical	Co-development -Toyama Chemical
Omeprazole (Omeprazole)	Proton pump inhibitor (The eradication of <i>Helicobacter pylori</i> in 1. Gastric mucosa-associated lymphoid tissue ("MALT") lymphoma, 2. The stomach after endoscopic resection of early stage gastric cancer, 3. Idiopathic thrombocytopenic purpura ).	sNDA filed (Sep. 2009)	UK; AstraZeneca	Joint application (9 Companies)
Modiodal (Modafinil)	Psychoneurotic agent (Obstructive sleep apnea)	Phase 3	US:Cephalon	Co-development -Alfresa Pharma
Radicut (Edaravone)	Free radical scavenger (Amyotrophic lateral sclerosis*)	Phase 3	In-house	
Maintate (Bisoprolol)	Selective $\beta$ 1 antagonist (Chronic heart failure)	Phase 3	Germany: Merck KGaA	
Cholebine (Colestimide(JAN))	Bile acid signal regulation (Type 2 Diabetes mellitus)	Phase 2	In-house	
	Non-absorbed phosphate binder (Hyperphosphatemia)	Phase 1		

\*: Orphan drug designated

## 2. Pipeline Overseas

### (1) New Molecular Entities

Development code (Generic name)	Category (Indications)	Region	Stage	Origin	Region
MCI-196 (Colestilan(INN))	Non-absorbed phosphate binder (Hyperphosphatemia)	US, EU	Phase 3	In-house	
MP-146	Uremic toxin adsorbent (Chronic kidney disease)	US, EU	Phase 3	Japan:Kureha	
TA-6666	DPP4 inhibitor (Type 2 Diabetes mellitus)	US	Phase 2	In-house	
TA-5538	NK-1 receptor antagonist (Overactive bladder)	EU	Phase 2	In-house	
MCC-135 (Caldaret)	Intracellular Ca handling modulator (Myocardial infarction)	US, EU	Phase 2	In-house	
MCC-257	Neurotrophin enhancer (Diabetic neuropathy)	US	Phase 2	In-house	
MT-2832	Vitamin D analog (Secondary hyperparathyroidism)	US, Canada	Phase 2	Canada: Cytochroma	
MCI-186 (Edaravone)	Free radical scavenger (Acute Ischemic Stroke)	EU	Phase 2	In-house	
MP-513 (Teneligliptin)	DPP4 inhibitor (Type 2 Diabetes mellitus)	EU US	Phase 2 Phase 1	In-house	
TA-5493	p38 inhibitor (Rheumatoid arthritis, Psoriasis)	EU	Phase 1	In-house	
GB-1057 (Human serum albumin [recombinant])	Recombinant human serum albumin (Stabilizing agent)	US	Phase 1	In-house	
TA-8995	CETP inhibitor (Dyslipidemia)	EU	Phase 1	In-house	
MP-124	PARP inhibitor (Acute Ischemic Stroke)	US	Phase 1	In-house	
MP-136	PPAR alpha agonist (Dyslipidemia)	EU	Phase 1	In-house	

### (2) Additional Indications

Development code (Generic name)	Category (Indications)	Region	Stage	Origin	Remarks
MCI-9038 (Argatroban)	Thrombin inhibitor (Heparin-induced thrombocytopenia (HIT))	EU	Preparing for MAA	In-house	

### 3. Licensing-out

Development code (Generic name)	Category (Indications)	Region	Stage	Licensee
FTY720 (Fingolimod hydrochloride)	Sphingosine 1-phosphate receptor modulator (Multiple sclerosis)	US, EU	Phase 3	Switzerland:Novartis Pharma
TA-1790 (Avanafil)	PDE5 inhibitor (Erectile dysfunction)	US	Phase 3	US:VIVUS
		Korea	Phase 3	Korea:Choongwae Pharma
TA-7284 (Canagliflozin)	SGLT2 inhibitor (Diabetes mellitus) (Obesity)	US, EU	Phase 3	US: Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
		US, EU	Phase 2	
T-0047 (Firategrast)	Cell adhesion inhibitor [ $\alpha4\beta7/\alpha4\beta1$ inhibitor] (Multiple sclerosis)	EU	Phase 2	UK:GlaxoSmithKline
MKC-242	5-HT1A receptor agonist (Insomnia)	US	Phase 2	US:MediciNova
TA-2005 (Carmoterol)	Long-acting $\beta2$ agonist (Asthma, COPD)	EU	Phase 2	Italy:Chiesi Farmaceutici
MKC-231	Neurogenesis enhancer (Depression/Anxiety)	US	Phase 2	US:BrainCells
Y-39983	ROCK (rho-kinase) inhibitor (Glaucoma)	Japan	Phase 2	Japan: Senju Pharmaceutical
MT-210	5-HT2A/ Sigma 2 antagonist (Schizophrenia)	EU	Phase 2	France: Cyrenaic
T-0128	DNA Topoisomerase I inhibitor [DDS drug camptothecin derivative] (Malignant tumor)	EU	Phase 1	Italy:Menarini
sTU-199 (Tenatoprazole)	Proton pump inhibitor (Gastroesophageal reflux disease)	EU	Phase 1	France:Negma (Sidem)
MP-412	Tyrosine kinase inhibitor (Malignant tumor)	US	Phase 1	US:AVEO Pharmaceuticals
TT-138	$\beta3$ receptor agonist (Pollakiuria, Anischuria)	US	Phase 1	US:MediciNova

#### 4. Changes Since Previous Announcement on July 30, 2009

Product name Development code (Generic name)	Category (Indications)	As of July 30, 2009	As of Oct. 29, 2009
MCI-9038 (Argatroban)	Thrombin inhibitor  (HIT Patients undergoing percutaneous coronary intervention(PCI): Type II Variation)	Type II Variation filed (May 2009)	Approved in EU (Sep. 2009)
	(Multiple dose vial: additional formulation)	None	Approved in EU (Sep. 2009)
MP-513 (Teneligliptin)	DPP4 Inhibitor  (Type 2 Diabetes mellitus)	Phase 2 in Japan  Phase 1 in EU	Phase 3 in Japan  Phase 2 in EU
Omeprazole (Omeprazole)	Proton pump inhibitor  (The eradication of <i>Helicobacter pylori</i> in 1. Gastric mucosa-associated lymphoid tissue ("MALT") lymphoma, 2. The stomach after endoscopic resection of early stage gastric cancer, 3. Idiopathic thrombocytopenic purpura ).	None	sNDA (joint-application) filed (Sep. 2009)
TA-7284 (Canagliflozin)	SGLT2 inhibitor  (Diabetes mellitus)	Phase 2 in US, EU	Phase 3 in US, EU

## 5. Additional Information for State of New Product Development (as of Oct. 29, 2009)

### (1) Japan New Molecular Entities

TA-8317 / ACREF (Fentanyl citrate)	TA-8317 is an oral transmucosal fentanyl citrate product for the management of breakthrough pain in cancer patients, licensed from Cephalon (U.S.). This product is marketed in the United States and Europe. NDA was filed in August, 2008.
MCC-847 (Masilukast)	MCC-847 is a leukotriene D4 antagonist and an orally available product to treat respiratory diseases. Clinical stages in patients with asthma is Phase 3, and allergic rhinitis is Phase 2.
MP-424 (Telaprevir)	MP-424 is an orally-available product for treatment of chronic liver diseases due to hepatitis C virus infection, licensed from Vertex (US). This compound inhibits protease NS3/4 in hepatitis C virus. Clinical stage in Japan is Phase 3.
MP-513 (Teneligliptin)	MP-513 is developed for the treatment of type-2 diabetes mellitus. It selectively inhibits dipeptidyl peptidase 4 (DPP4), thus accelerates the insulin secretion after meal intake. Clinical stage in Japan is Phase 3.
APTA-2217 (Roflumilast)	APTA-2217 is a potent, highly selective and orally available product for the treatment of respiratory diseases, and licensed from Nycomed (Switzerland). An efficacy was obtained both in asthma and COPD. Phase 2/3 trials for asthma and COPD are underway in Japan.
CNTO148 (Golimumab)	CNTO148 is an anti-TNF $\alpha$ monoclonal antibody, licensed from Centocor. Clinical stage in Japan is Phase 2/3 for rheumatoid arthritis with subcutaneous injections as co-development with Janssen Pharma K.K.
FTY720 (Fingolimod hydrochloride)	FTY720 is a sphingosine-1-phosphate receptor modulator. Overseas clinical trial in patients with multiple sclerosis is in Phase 3, and is being conducted by Novartis Pharma AG. In Japan, Phase 2 clinical trial in patients with multiple sclerosis is currently under co-development with Novartis Pharma K.K. and Mitsui Sugar Co., Ltd.
MP-214 (Cariprazine)	MP-214 is a dopamine D3/D2 antagonist, licensed from Gedeon-Richter (Hungary). Clinical stage in Japan is Phase 2 for schizophrenia.
MP-435	MP-435 is a C5a (complement factor) receptor antagonist which modulates the immune system. Clinical stage in Japan is Phase 1 for oral antirheumatoid drug.
TA-6666	TA-6666 is developed for the treatment of type-2 diabetes mellitus. It selectively inhibits dipeptidyl peptidase 4 (DPP4), thus accelerates the insulin secretion after meal intake. Clinical stage in Japan is Phase 1.
TA-7284 (Canagliflozin)	As a selective SGLT2 inhibitor, TA-7284 decreases blood glucose levels by inhibiting reabsorption of glucose in the kidney. Clinical stage in Japan is Phase 1 for diabetes mellitus.

## (2) Japan Additional Indication

Venoglobulin-IH (Polyethylene glycol treated human normal immunoglobulin)	(IgG2 deficiency) sNDA has been filed.  (Polymyositis and/or Dermatomyositis [orphan drug designated]) sNDA has been filed. Based on the instructions from the authorities, an additional clinical trial is in progress to confirm efficacy of Venoglobulin in patients with polymyositis or dermatomyositis who do not respond to steroid therapy.  (Hypo and agammaglobulinemia: additional dose ) sNDA was filed in March 2008, after Japanese Society for Pediatric Infectious Diseases submitted a letter to the MHLW.  (Diffuse systemic scleroderma) Clinical research in Japan demonstrated IV-IG was effective in improvement of skin manifestation, a primary endpoint of systemic scleroderma. Efficacy of IV-IG was also reported in overseas studies. Clinical stage is Phase 3. It was designated as an orphan drug at September in 2009.  (Myasthenia gravis (Orphan drug designated in September, 2009)) Clinical stage in Japan is Phase 3 in which is compared with blood purification therapy.
Remicade (Infliximab (recombinant))	(Psoriasis) Good effectivity and safety for plaque psoriasis and psoriatic arthritis were reported in validation trials and the indications were approved in the US and EU. sNDA was filed in February 2008.  (Ankylosing spondylitis) Good efficacy and safety for ankylosing spondylitis were reported and the indication was approved in the US and EU. It was designated as an orphan drug in June 2008. sNDA was filed in September 2008.  (Ulcerative colitis) Good effectivity and safety for ulcerative colitis was reported and the indication was approved in the US and EU. sNDA was filed in June 2009.  (Crohn's disease) In order to verify the effectiveness of Remicade when administered in higher doses, Phase 3 trial is on going for patients showing an insufficient response to maintenance therapy.
Pazucross (Pazufloxacin mesilate)	(Severe and intractable case: additional dosage/Sepsis and Streptococcus pneumoniae: additional indication ) New quinolone antibacterial agents for infection. sNDA was filed in June 2009.
Omeprazole (Omeprazole)	(The eradication of <i>Helicobacter pylori</i> in 1. Gastric MALT* Lymphoma, 2. The stomach after endoscopic resection of early stage gastric cancer 3. Idiopathic Thrombocytopenic Purpura) sNDA was jointly filed by 9 companies**, was filed in September 2009 consisting of the said published evidences.
Modiodal (Modafinil)	(Obstructive sleep apnea) Modiodal has been approved for narcolepsy in Japan. It has been also approved in the U.S. and certain major European countries as an agent for the patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, and shift-work sleep disorder. sNDA was filed by Alfresa Pharma Corp. in May 2008. As a result of the consultation with PMDA, additional data has been required. An additional clinical study for sNDA is on going
Radicut (Edaravone)	(Amyotrophic lateral sclerosis (Orphan drug designated)) Clinical stage is Phase 3.
Maintate (Bisoprolol)	(Chronic heart failure) In Europe, the result of the large-scale CIBIS-II trials demonstrated that bisoprolol significantly decreased mortality in patients with chronic heart failure (NYHA III-IV). In Japan, sNDA for an additional indication of chronic heart failure was submitted in April 2006. As a result of the consultation with PMDA, an additional clinical study (Phase 3) for sNDA is now under discussion.

Cholebine (Colestimide (JAN))	(Type 2 diabetes mellitus) Clinical stage is Phase 2.  (Hyperphosphatemia) Clinical stage is Phase 1.
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\*MALT: Mucosal Associated Lymphoid Tissue

Takeda Pharmaceutical Company Limited, AstraZeneca K.K., Mitsubishi Tanabe Pharma Corporation, Eisai Co., Ltd.,

\*\*9 Companies: Kyowa Hakko Kirin Co., Astellas Pharma Inc., ABBOTT JAPAN Co., LTD., Shionogi & Co., Ltd., and Taisho Pharmaceutical Co., Ltd.

### (3) Overseas New Molecular Entities

MCI-196 (Colestilan(INN))	MCI-196 is anion-exchange resin, and has been developed to obtain indication for the treatment of hyperphosphatemia in patients on dialysis in EU and the US. Clinical stage is Phase 3. It is marketed in Japan for the treatment of hypercholesterolemia, under the brand name of CHOLEBINE®.
MP-146	MP-146 is spherical carbon adsorbent, licensed from Kureha Corporation (Japan) in November, 2006. Clinical stage is Phase 3 for Chronic Kidney Disease patients in EU, North America and South America. It is marketed by other companies in Japan under the brand name, KREMEZIN®.
TA-6666	TA-6666 is developed for the treatment of type-2 diabetes mellitus. It selectively inhibits dipeptidyl peptidase 4 (DPP4), thus accelerates the insulin secretion after meal intake. Clinical stage is Phase 2 in the US.
TA-5538	TA-5538 selectively blocks binding of substance P to the receptor (NK-1 receptor), is under development for the treatment of overactive bladder. Clinical stage is Phase 2 for overactive bladder in Europe.
MCC-135 (Caldaret)	MCC-135 improves cardiac function and clinical outcome in patients with acute myocardial infarction, by improving calcium mobilization in ischemic-reperfused myocardium. Clinical stage is Phase 2 in EU and the US.
MCC-257	MCC-257 is a product to treat diabetic neuropathy by facilitating secretion of neurotropic factors and potentiating their actions. Clinical stage is Phase 2 in the US.
MT-2832	MT-2832 was licensed from Cytochroma Inc. (Canada) in July 2008. Cytochroma development code is CTA018. MT-2832 is a strong activator of the vitamin D signaling pathway and a potent inhibitor of CYP24, intracellular enzyme responsible for catabolism of Vitamin D hormones. Clinical stage is Phase 2 for secondary hyperparathyroidism in patients with chronic kidney disease in Canada.
MCI-186 (Edaravone)	MCI-186 is the world's first cerebral neuroprotectant (free radical scavenger). Clinical stage in EU is Phase 2 for the acute cerebral infarction. It is marketed in Japan under the brand name, Raducut®.
MP-513 (Teneligliptin)	MP-513 is developed for the treatment of type-2 diabetes. It selectively inhibits dipeptidyl peptidase 4 (DPP4), thus accelerates the insulin secretion after meal intake. Clinical stages in the US is Phase 1 and EU is Phase 2.
TA-5493	TA-5493, a p38 MAP kinase inhibitor, suppresses the cytokine production including TNF $\alpha$ and consequently expresses anti-inflammatory effects. Clinical stage is Phase 1 for rheumatoid arthritis and psoriasis in Europe.
GB-1057 (Human serum albumin [recombinant])	GB-1057 is a recombinant human serum albumin. Clinical stage is Phase 1 as a stabilizing agent in the US.
TA-8995	TA-8995 is a CETP inhibitor that has raising the HDL-C and lowering the LDL-C effects. Clinical stage is Phase 1 in Europe.
MP-124	MP-124 is a PARP inhibitor that has neuroprotective effect. Clinical stages in the US and Canada are phase 1 for the acute ischemic stroke.
MP-136	MP-136 is a PPAR alpha agonist. Clinical stage is Phase 1 in E.U. for the dyslipidemia.

### (4) Overseas Additional Indications

MCI-9038 (Argatroban)	(Heparin-induced thrombocytopenia (HIT)) Eight EU countries (Germany, Austria, Sweden, the Netherlands, Denmark, Norway, Iceland and Italy) have given the marketing authorization. We now consider the submission of MAA to other EU countries.
	(Percutaneous coronary intervention in patients with HIT) Type II variation was approved in September 2009 in EU.
	Multi dose vial was approved in September in 2009 EU.

## (5) Licensing-Out

FTY720 (Fingolimod hydrochloride)	FTY720 prevents regression of lymphocytes from the lymphoid tissues by acting on sphingosine-1-phosphate receptors. Novartis Pharma A.G. is conducting a Phase 3 clinical trials in patients with multiple sclerosis, primarily in the US and EU.
TA-1790 Avanafil	TA-1790 is developed for the treatment of erectile dysfunction by Mitsubishi Tanabe Pharma, which is expected to have a quick onset and fewer side effects. Clinical trial stage is Phase 3 in the US and Phase 3 in Korea.
TA-7284 (Canagliflozin)	As a selective SGLT2 inhibitor, TA-7284 decreases blood glucose levels by inhibiting reabsorption of glucose in the kidney. Phase 3 clinical trials in diabetes mellitus in EU and the US are underway. Phase2 clinical trials in obesity in EU and US are underway.
T-0047 (Firategrast)	T-0047 inhibits the cell adhesion and cell migration processes of white blood cells in inflammatory region. Although US Food and Drug Administration has taken the precautionary measure of placing a clinical hold on investigational new drugs in the $\alpha 4$ integrin antagonist class being tested on human subjects, including this product. The reason for the clinical hold as cited by the FDA is the uncertainty surrounding the cause of the reports of progressive multifocal leukoencephalopathy (PML) in patients who had been taking Tysabri (natalizumab), a multiple sclerosis biological agent marketed by Biogen Idec and Elan Pharmaceuticals. FDA has approved to relaunch Tysabri in 2006. The resuming clinical Phase 2 trial is conducted by GSK in Europe, Canada, Australia, and New Zealand.
MKC-242	MKC-242 is a serotonin 5-HT1A receptor agonist, used to treat psychiatric disorders such as anxiety and depression. This compound is expected to reveal rapid onset with low possibility of dependency. Medici Nova Inc.(US) is conducting Phase 2 clinical trials in patients with generalized anxiety disorder or insomnia.
TA-2005 (Carmoterol)	TA-2005 is a selective, potent and long acting $\beta 2$ agonist for the treatment of asthma and COPD. Clinical trial stage is Phase 2 in Europe.
MKC-231	MKC-231 is a neurogenesis enhancer. Phase 2 study in major depression is underway by BrainCells Inc.(US).
Y-39983	Y-39983 is a ROCK (Rho-kinase) inhibitor, which relaxes vascular smooth muscle. Clinical trial stage in Japan is Phase 2 by Senju Pharmaceutical Co. Ltd..
MT-210	MP-210 is a 5-HT2A/ Sigma 2 antagonist. Clinical trial stage is Phase 2 in Europe by Cyrenaic (France).
T-0128	T-0128 is a prodrug with its drug-delivery system, which is composed of a novel camptothecin analog covalently linked to a macromolecular carrier via a short peptide chain, and reaches the tumor tissue effectively. Clinical trial stage is Phase 1 in Europe by Menarini (Italy).
sTU-199 (Tenatoprazole)	sTU-199 is an isomer of TU-199, developed in Japan, and licensed to Negma (France). Pharmacokinetic/pharmacodynamic results from phase 1 clinical trials in EU and the US demonstrated that sTU-199 controlled gastric acid secretion at nighttime in patients receiving this compound once-daily, with the long terminal half-life. It is expected that this compound will reveal rapid improvement for non-erosive reflux disease. Sidem Pharma, a subsidiary of Negma, is conducting phase 1 trial for gastroesophageal reflux disease in EU.
MP-412	MP-412 is expected to have superior efficacy for solid tumors to other anticancer agents that belong to the same class. Phase 1 study is conducted by AVEO Pharmaceuticals Inc. in the US.
TT-138	TT-138 is a $\beta 3$ receptor agonist used to treat pollakiuria and anischuria. Phase 1 study id conducted by Medici Nova Inc. in the US.

<Ref.> Major Ethical Drugs 1

Product Name	Launch	Category	Notes
	Product Profile		
Remicade (Infliximab)	May 2002	Anti-TNF $\alpha$ monoclonal antibody (Treatment of rheumatoid arthritis (RA), active Crohn's disease and Behcet's disease with refractory uveoretinitis )	Origin: Centocor, Inc.
	Remicade is an anti-TNF $\alpha$ antibody, which targets TNF $\alpha$ , an important inflammatory cytokine. It is very fast-acting and its efficacy is sustained for two months with a single administration. It was approved in Japan for the treatment of Behcet's disease with refractory uveoretinitis in January 2007 and for the maintenance treatment of Crohn's disease in November 2007. Increase of the dosage/shortage of administration interval and the effect on prevention of structural joint damage for the treatment of rheumatoid arthritis were approved in July 2009.		
Radicut (Edaravone)	June, 2001	Cerebral neuroprotectant (Free radical scavenger)	
	Radicut developed in Japan is the world's first brain protecting agent (free radical scavenger) shown to improve neurological symptoms, interference with activities of daily living, and disability (at hospital discharge) in patients at acute stage of cerebral infarction. Specific indications include the treatment of various types of infarction (Cerebral lacunar, Atherothrombotic and Cardiogenic infarction) It is initiated administration within 24 hours after onset, and is not administrated for more than 14 days.		
Anplag (Sarpogrelate)	Oct. 1993	Anti-platelet (5-HT <sub>2</sub> blocker)	
	Anplag, an oral anti-platelet, is used to patients with arteriosclerosis obliterans (ASO) to improve ischemic symptoms like as ulcer, pain and coldness of limbs associated with chronic arterial occlusion. Anplag especially improves the bloodstream of collateral circulation and inhibits platelet aggregation, vascular contraction and growth of vascular smooth muscle cell by antagonistic action to serotonin receptor in platelets and vessels. The downsized tablet which is convenient for elderly patients was approved in August 2007.		
Ceredist (Taltirelin)	Sep. 2000	Agent for treating spinocerebellar degeneration	
	Thyrotropin releasing hormone (TRH) was known to be effective against ataxia caused by spinocerebellar degeneration, but it was previously administered only through injection. Ceredist, developed by Tanabe, is the world's first oral TRH derivative drug. In June 2009, approval was received for an additional formulation, orally disintegrating tablets, and it was launched in October.		
Urso (Ursodeoxycholic Acid)	Jul. 1962	Agent for improving hepatic, biliary and digestive functions	
	Ursodeoxycholic acid (UDCA), principal ingredient of Urso, had been extracted from blackbear's gallbladder in the past and has been used in the treatment of various digestive diseases. It is one of the bile acids existing in human body. Urso has effects of hepatic protection and indications of improvement of liver function in chronic liver disease and hepatitis C, and dissolution of gallstones.		
Depas (Etizolam)	Mar. 1984	Antianxiety agent	
	Depas is the most widely used anxiolytic agent in Japan. Due to its broad pharmacological properties, Depas shows reasonable effectiveness for psychosomatic disease, neurosis, low back pain, neck pain and muscle-contraction headache, depression and sleep disorder.		
Tanatril (Imidapril)	Dec. 1993	ACE Inhibitor (Treatment of hypertension)	
	Tanatril shows excellent blood pressure control with effective organ protection as well as minimal incidence of dry cough, a common side effect of ACE inhibitors. With the approval of an additional indication in 2002, it became the first drug in Japan approved for diabetic nephropathy with type I diabetes.		
Herbesser (Diltiazem)	Feb. 1974	Calcium antagonist (Treatment of angina pectoris and hypertension)	
	Herbesser is a representative calcium antagonist that is used in more than 110 countries around the world. In addition to a blood pressure lowering effect, it has a cardioprotective action in patients with hypertension or angina pectoris by reducing the cardiac load through a heart rate lowering effect and by increasing the oxygen supply through a coronary vasodilating effect.		

<Ref.> Major Ethical Drugs 2

Product Name	Launch	Category	Notes
<b>Product Profile</b>			
Maintate (Bisoprolol)	Nov. 1990	Selective $\beta_1$ Antagonist (Treatment of angina pectoris hypertension, and arrhythmias)	Origin: Merck KGaA
	Maintate is a representative $\beta$ -blocker used in more than 85 countries around the world. It exhibits high selectivity for $\beta_1$ receptor and excellent pharmacokinetics profiles. It has high efficacy and safety, and there is evidence for its cardioprotective action. An application has been filed in Japan for an additional indication for chronic heart failure.		
Venoglobulin-IH (Human immunoglobulin)	Jan. 1992	Plasma derivatives	
	Venoglobulin-IH is intravenous human immunoglobulin derived from donated plasma in Japan. It shows high efficacy on serious infectious diseases in combined administration with anti-bacterial agent due to its opsonic, immuno-bacteriolytic and antibody-dependent cytotoxic effects and neutralizing effects on toxics and viruses.		
Talion (Bepotastine)	Oct. 2000	Agent for treatment of allergic disorders (Treatment for allergic rhinitis and urticaria)	Origin: Ube Industries, Ltd. Co-development
	Talion has rapid onset of anti-histamine(H1) effects and has been demonstrated to be effective for allergic rhinitis, urticaria, and pruritus accompanying dermatitis. It has minimal incidence of sedation. In March 2007, approval was received for an additional formulation, orally disintegrating tablets, and it was launched in July.		
Liple (ArprostadiI)	Nov. 1988	Chronic arterial occlusion / Circulatory disturbance (PGE1)	Co-developed with Taisho Pharmaceutical Co., Ltd.
	Liple, the world's first DDS (Drug Delivery System) agent of intravenous PGE1, improves the peripheral circulatory disturbance and skin ulcer in chronic arterial occlusive disease and diabetes by its direct vasodilating effects. DDS maximizes the therapeutic effects and simultaneously minimizes the adverse effects of PGE1.		
Sermion (Nicergoline)	June 1988	Cerebral circulation and metabolism ameliorator	Origin: Pfizer Inc.
	Sermion ameliorates blood flow and metabolism in the brain. It is used to treat sequela of cerebral infarction. In 1998, in a reevaluation by the Ministry of Health and Welfare in Japan, its effectiveness was confirmed. In "the treatment guidelines for strokes in 2004," Sermion was recommended as a treatment drug for chronic cerebral infarction.		
Neuart (Anti-thrombin III)	Jun. 1987	Plasma derivatives (Anticoagulant agent)	
	Neuart is highly purified human anti-thrombin III derived from donated plasma in Japan. It shows strong anticoagulant effects in the treatment of DIC patients by inhibiting various kinds of activated serine protease including thrombin.		
Omeprazon (Omeprazole)	Apr. 1991	Antiulcerogenic agent (Proton pump inhibitor)	Origin: AstraZeneca Co-developed with AstraZeneca
	Omeprazon is the world's first proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H <sup>+</sup> /K <sup>+</sup> -ATPase enzyme in the gastric parietal cell. It strongly and sustainably blocks the final step in gastric acid production results in reducing gastric acidity. Omeprazon has excellent efficacy for gastric ulcer, duodenal ulcer and reflux esophagitis. Additional indications for non-erosive reflux disease (NERD) and secondary eradication of Helicobacter pylori were approved in May and August 2007, respectively.		

<Ref.> Major Ethical Drugs 3

Product Name	Launch	Category	Notes
Product Profile			
Novastan  (Argatroban)	June. 1990	Selective Antithrombin Agents	Co-developed with Daiichi-Sankyo  Novastan is a fully synthesized, selective thrombin inhibitor. In Japan, it was launched in June, 1990 and has been approved for the treatment of limb ulcers, rest pain and a sensation of cold in chronic arterial occlusive disease, the acute treatment of neurological symptoms and activities of daily living for patients with acute-phase cerebral thrombosis, and the prevention of blood clotting in the circuit during hemodialysis in the patients with congenitally decreased antithrombin III levels. In July 2008, it was also approved for the prophylaxis of thrombosis in the patients with type 2 heparin-induced thrombocytopenia (HIT). In overseas market, it was approved by the FDA in 2000 for the prophylaxis or treatment of thrombosis in patient with HIT and has since been approved in nine countries for the same indications.
Mearubik  (Measels and Rubella Vaccine Live Attenuated)	Dec. 2005	Measels and rubella immunization	Manufacturer: *BIKEN  Mearubik is the combination vaccine for Measels and Rubella, and children are able to receive both Measels and Rubella shot at a time with Mearubik. It is expected to contribute enhancement of immunization rate for Measels and Rubella in Japan.

\*BIKEN: The Research Foundation for Microbial Diseases of Osaka University