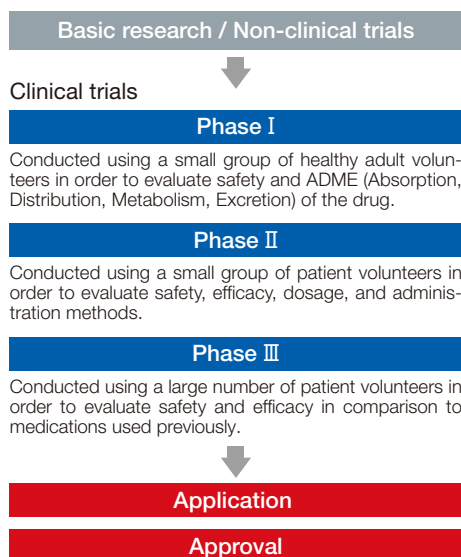


## R&D Pipeline

The R&D pipeline represents ethical drugs under development, from the start of research to approval and launch. Clinical trials are conducted on humans for drugs for which basic research and non-clinical trials have been completed. Newly developed drugs that have undergone efficacy and safety evaluation via three phases of clinical trials are launched onto the market as new drugs after approval by the regulatory authorities.



## Major Pipeline Drugs Offering Potential as Next-Generation Core Products

### [Therapeutic Area I: Lifestyle-Related Diseases]

#### ■ Anti-Diabetic Drug: SYR-322

SYR-322 is a promising pipeline drug for the treatment of diabetes, following our core product *Actos*. SYR-322, which acts as a DPP-4\* inhibitor, was discovered by Takeda San Diego, Inc. (TSD) as a therapeutic agent for Type 2 diabetes. We are also working to develop a product combining SYR-322 with *Actos*.

\* An enzyme that degrades glucagon-like peptide-1 (GLP-1), a hormone that stimulates insulin secretion.

#### ■ Anti-Hypertension Drugs: TAK-491 and TAK-536

TAK-491 and TAK-536 are positioned as successors to our core product *Blopress*. Compared to existing angiotensin II receptor blockers (ARB), they are expected to offer outstanding antihypertensive benefits in addition to improving insulin resistance. As many patients have both hypertension and diabetes, this drug is of particular clinical significance.

## Pipeline

Development Code	Generic Name	Brand Name (Country/Region)
<b>Therapeutic Area I: Lifestyle-Related Diseases</b>		
KAD-1229	Mitiglinide	<i>Glufast</i> (Japan)
AD-4833	Pioglitazone hydrochloride	<i>Actos</i> (Japan, U.S.A., Asia) <i>Actos, Glustin</i> (Europe)
AO-128	Voglibose	<i>Basen</i> (Japan, Asia)
SYR-322	Alogliptin	
SYR-472	Not decided	
TAK-428	Not decided	
TAK-875	Not decided	
TCV-116	Candesartan cilexetil	<i>Blopress</i> (Japan, Europe, Asia) <i>Amias, Kenzen</i> , etc. (Europe)
TAK-491	Azilsartan medoxomil	
TAK-536	Azilsartan	
TAK-085	Omega-3 acid ethyl esters 90	
TAK-442	Not decided	
ATL-962	Cetlistat	
TAK-100	Not decided	
TAK-591	Not decided	

# R&D Pipeline

Drug Class	Indication/Formulation	Country/ Region	Stage of Development				
			Phase I	Phase II	Phase III	NDA Submission	NDA Approval
Short-acting insulin secretagogue	Diabetes Concomitant therapy with thiazolidinediones	Japan					2009.02
Insulin sensitizer	Diabetes Concomitant therapy with insulin	Japan					2009.03
	Diabetes Concomitant therapy with biguanides	Japan					2008.12
	Diabetes Fixed dose combination with extended-release metformin	U.S.A.					2009.05
		Europe					2008.10
	Diabetes Fixed dose combination with metformin	Japan					2008.10
	Diabetes Fixed dose combination with glimepiride	Japan					2009.07
	Diabetes Orally disintegrating tablet	Japan					2008.09
Delay in progression of atherosclerosis	U.S.A.					2008.08	
	Europe					2009.03	
Alpha-glucosidase inhibitor	Prevention of onset of Type 2 Diabetes with impaired glucose tolerance (IGT)	Japan					2007.12
DPP-4 inhibitor	Diabetes	U.S.A.					2007.12*
		Europe					
		Japan					2008.09
	Diabetes Fixed dose combination with Actos	U.S.A.					2008.09
		Europe					
Japan					2009.06		
Diabetes Concomitant therapy with thiazolidinediones	Japan					2009.06	
Diabetes Fixed dose combination with metformin	—						
DPP-4 inhibitor	Diabetes	U.S.A.					
		Europe					
		Japan					
Neurotrophic factor production accelerator	Diabetic neuropathy	U.S.A.					
		Europe					
Glucose-dependent insulin secretagogue	Diabetes	Japan					
		U.S.A.					
		Europe					
Angiotensin II receptor blocker	Hypertension Fixed dose combination with hydrochlorothiazide (high dose)	Europe (Austria, Portugal)					2009.05
		Europe (Germany, Spain)					2009.06
	Hypertension Fixed dose combination with hydrochlorothiazide	Japan					2009.01
	Hypertension Fixed dose combination with amlodipine besylate	Japan					2009.03
	Hypertension High dose	Japan					
Hypertension accompanying Type 2 diabetes Fixed dose combination with Actos	Japan						
Angiotensin II receptor blocker	Hypertension	U.S.A.					
		Europe					
Hypertension Fixed dose combination with chlorthalidone	U.S.A.						
Angiotensin II receptor blocker	Hypertension	U.S.A.					
		Europe					
		Japan					
EPA/DHA agent	Hypertriglyceridemia	Japan					
Factor Xa (FXa) inhibitor	Venous/arterial thromboembolism	U.S.A.					
		Europe					
		Japan					
Lipase inhibitor	Obesity	Japan					
DPP-4 inhibitor	Diabetes	—					
Angiotensin II receptor blocker	Hypertension	—					

\* FDA complete response letter (June 2009) As of July 31, 2009

## Major Pipeline Drugs Offering Potential as Next-Generation Core Products

[Therapeutic Area II:  
Oncology and Urological Diseases]

### Colonic & Rectal Cancer Drug: Vectibix

In-licensed from Amgen Inc., Vectibix is a fully human monoclonal antibody that inhibits epidermal growth factor receptors (EGFR) and inhibits cell proliferation for a variety of cancers. The drug was approved in the U.S. as the first human antibody for EGFR, and promises to offer outstanding safety compared to earlier products such as chimeric antibodies or the humanized antibodies which are currently under development.

### Non-Small Cell Lung Cancer Drug: AMG 706

AMG 706 is an anti-angiogenic agent, targeting vascular endothelial growth factor receptor 1-3 (VEGFR1-3) and in-licensed from Amgen Inc. for the entire global market. Three anti-angiogenic agents have already been approved and their effectiveness verified for many types of cancers, including colon cancer and kidney cancer.

[Therapeutic Area III:  
Central Nervous System Diseases, Bone /  
Joint Diseases]

### Therapeutic Drug for Mood and Anxiety Disorders: Lu AA21004

Lu AA21004 is a drug used to treat mood and anxiety disorders which Takeda in-licensed from H. Lundbeck A/S. It is currently being jointly developed by Lundbeck and Takeda. Lu AA21004 offers great potential as it belongs to a new chemical class, with a mode of action differing from anti-depressants currently marketed.

[Therapeutic Area IV:  
Gastroenterological Diseases]

### Therapeutic Drug for Inflammatory Bowel Disease: MLN0002

MLN0002 (vedolizumab) was created by re-engineering a human monoclonal antibody. The binding domains of a human antibody were substituted with those from a mouse monoclonal antibody that bound to the human  $\alpha 4 \beta 7$  integrin\*. Hence, vedolizumab is a humanized monoclonal antibody that antagonizes the human  $\alpha 4 \beta 7$  integrin. MLN0002 exerts effects selectively in the digestive tract and is expected to have fewer adverse reactions than other anti-integrin antibodies and the anti-TNF antibodies.

\*  $\alpha 4 \beta 7$  integrin is a protein present on the surface of lymphocytes and is involved in immunological reaction at the intestinal tract.

## Pipeline

Development Code	Generic Name	Brand Name (Country/Region)
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### Therapeutic Area II: Oncology and Urological Diseases

MEPACT	Mifamurtide	
Vectibix	Panitumumab	
VELCADE	Bortezomib	VELCADE (U.S.A.)
Hematide	Not decided	Hematide (U.S.A.)
AMG 706	Motesanib diphosphate	
MLN0518	Tandutinib	
MLN8237	Not decided	
CBP501	Not decided	
TAK-700	Not decided	
TAK-683	Not decided	
TAK-448	Not decided	
TAK-285	Not decided	
TAK-385	Not decided	
TAK-593	Not decided	
TAK-701	Not decided	
TAK-901	Not decided	
MLN4924	Not decided	
MLN9708	Not decided	
AMG 655	Conatumumab	
AMG 386	Not decided	
AMG 479	Not decided	

### Therapeutic Area III: Central Nervous System Diseases, Bone / Joint Diseases

TAK-375	Ramelteon	Rozerem (U.S.A.)
SNT-MC17	Idebenon	
Lu AA21004	Not decided	
Lu AA24530	Not decided	
TAK-065	Not decided	
TAK-937	Not decided	

### Therapeutic Area IV: Gastroenterological Diseases

TAK-390MR	Dexlansoprazole	KAPIDEX (U.S.A.)
TMX-67	Febuxostat	ULORIC (U.S.A.)
AG-1749	Lansoprazole	Takepron (Japan, Asia) Prevacid (U.S.A., Asia) Ogast, Agopton, Lansox, etc. (Europe)
SPI-0211	Lubiprostone	Amitiza (U.S.A.)
MLN0002	Vedolizumab	
TAK-438	Not decided	
MLN0415	Not decided	

# R&D Pipeline

Drug Class	Indication/Formulation	Country/Region	Stage of Development				
			Phase I	Phase II	Phase III	NDA Submission	NDA Approval
Immunostimulant	non-metastatic osteosarcoma	Europe					2009.03
Fully human monoclonal antibody (MAB) against the human EGFR	Progressive and relapsing cancer of the colon and rectum	Japan					2008.06
	Head and neck cancer	Japan					
Proteasome inhibitor	Follicular NHL	U.S.A.					
	First line MCL	U.S.A.					
Synthetic, peptide-based erythropoiesis-stimulating agent	Chronic kidney disease related anemia	U.S.A. Europe Japan					
	Chemotherapy-induced anemia	—					* Development suspended
VEGFR1-3 inhibitor	Progressive non-small cell lung cancer	U.S.A. Europe Japan					
	Breast cancer	U.S.A.					
Inhibitor of receptor kinases (FLT-3, PDGF-R, c-KIT)	Glioblastoma	U.S.A.					
Aurora A kinase inhibitor	Aggressive NHL, Acute myelogenous leukemia(AML), High-risk myelodysplastic syndrome (MDS); Ovarian cancer	U.S.A.					
		Europe					
Cell cycle dysregulator	Malignant pleural mesothelioma	U.S.A.					
	Non-small cell lung cancer	U.S.A.					
Sex Hormone synthesis inhibitor	Prostate cancer	—					
GnRH modulator	Prostate cancer	—					
GnRH modulator	Prostate cancer	—					
HER2 inhibitor	Solid tumors	—					
LH-RH receptor antagonist	Endometriosis, Uterus myoma	—					
VEGFR, PDGFR inhibitor	Solid tumors	—					
Anti-HGF antibody	Advanced malignancies	—					
Aurora B kinase inhibitor	Advanced malignancies	—					
Nedd8 activating enzyme inhibitor	Advanced malignancies	—					
Proteasome inhibitor	Advanced malignancies	—					
Fully human monoclonal antibody agonist directed against DR5 (TRAIL-2)	Progressive cancer	Japan					
Anti-angiopoietin peptibody	Progressive cancer	Japan					
Fully human monoclonal antibody against human type 1 Insulin-like Growth Factor Receptor (IGF-1R)	Progressive cancer	Japan					
MT1/MT2 receptor agonist	Insomnia	Europe					*
		Japan					2008.02
Mitochondria targeted anti-oxidant	Friedreich's ataxia	Europe					*
	Duchenne muscular dystrophy	Europe					
Serotonin modulator & stimulator	Mood and anxiety disorders	U.S.A.					
		Europe					
		Japan					
Monoamine modulator	Mood and anxiety disorders	Europe					
		Japan					
Neuroregeneration enhancer	Alzheimer's disease, Parkinson's disease	—					
Cerebroprotective agent	Acute stroke	—					
Proton pump inhibitor	Erosive esophagitis (healing and maintenance) and non-erosive gastro-esophageal reflux disease	U.S.A.					2009.01
		Japan					
Non-purine, selective xanthine oxidase inhibitor	Hyperuricemia in patients with chronic gout	U.S.A.					2009.02
Proton pump inhibitor	Prevention of onset of low dose aspirin related gastric ulcer	Japan					2009.03
	Secondary eradication of Helicobacter pylori (single pack of three drugs)	Japan					2009.03
	Risk reduction of NSAID-associated gastric ulcer	Japan					
Chloride channel opener	Opioid-induced bowel dysfunction (OBD)	U.S.A.					
α4 β7 integrin inhibitor	Ulcerative colitis, Crohn's disease	U.S.A.					
		Europe					
Potassium-competitive acid blocker	Acid-related diseases (GERD, Peptic ulcer disease, etc.)	—					
IKK2 inhibitor	Inflammatory diseases	—					

\* Re-submission of MAA is under consideration As of July 31, 2009