

Development pipeline (as of February 3, 2010)

Development code	Indication # Additional indication	Stage (date)	Generic name Product name Dosage form	Origin Overseas name (Collaborator)	Mode of Action
<u>Oncology</u>					
RG340	Colorectal cancer #	Launched Sep. 09	capecitabine Xeloda	Roche Xeloda	Antimetabolite, 5-FU derivative
	Gastric cancer #	Phase III Multinational study	Oral		
RG435	Non-small cell lung cancer #	Launched Nov. 09	bevacizumab Avastin	Roche Avastin	Humanized anti-VEGF(Vascular Endothelial Growth Factor) monoclonal antibody
	Breast cancer #	Filed Oct. 09	Injection		
	Colon cancer (adjuvant) #	Phase III Multinational study			
	Gastric cancer #	Phase III Multinational study			
	Breast cancer (adjuvant) #	Phase III Multinational study			
	Glioblastoma #	Phase III Multinational study			
	Glioblastoma (relapsed) #	Phase II			
RG1415	Pancreatic cancer #	Filed Sep. 09	erlotinib Tarceva Oral	Roche/OSI Tarceva	EGFR tyrosine kinase inhibitor
EPOCH	Chemotherapy-induced anemia #	Filed Nov. 09	epoetin beta Epogin Injection	In-house	Recombinant human erythropoietin
RG597	Gastric cancer #	Phase III Multinational study	trastuzumab Herceptin Injection	Roche Herceptin	Humanized anti-HER2 monoclonal antibody
RG1273	Breast cancer	Phase III Multinational study	pertuzumab Injection	Roche	Humanized HER dimerization inhibitory monoclonal antibody
TP300	Gastric cancer, etc	Phase II Overseas	Injection	In-house	Topoisomerase I inhibitor

Development code	Indication # Additional indication	Stage (date)	Generic name Product name Dosage form	Origin Overseas name (Collaborator)	Mode of Action
MRA	Pancreatic cancer #	Phase I / II	tocilizumab Actemra Injection	In-house (Roche)	Humanized anti-human IL-6 receptor monoclonal antibody
CIF (RG7167)	Solid tumors	Phase I	Oral	In-house (Roche)	MEK inhibitor
		Phase I Overseas			
CKI27 (RG7304)	Solid tumors	Phase I	Oral	In-house (Roche)	-
		Phase I Overseas			
GA101 (RG7159)	Non-Hodgkin's lymphoma	Phase I	Injection	GlycArt	Humanized anti-CD20 monoclonal antibody
RG3502	Breast cancer	Phase I	Injection	Roche	HER2 antibody-drug conjugate
GC33	Liver cancer	Phase I Overseas	Injection	In-house	Humanized anti-Glypican-3 monoclonal antibody
<u>Bone and Joint diseases</u>					
MRA	Rheumatoid arthritis #	Launched Jan. 10 Overseas(US)	tocilizumab Actemra(US) / RoActemra (EU) Injection	In-house (Roche)	Humanized anti-human IL-6 receptor monoclonal antibody
	Systemic onset juvenile idiopathic arthritis (sJIA) #	Phase III Overseas			
	Rheumatoid arthritis (new formulation: subcutaneous injection)	Phase I / II	tocilizumab Actemra Injection		
ED-71	Osteoporosis	Filed Oct. 09	eldecalcitol Oral	In-house (Taisho Pharmaceutical)	Activated Vitamin D ₃ derivative
RG1594	Rheumatoid arthritis	Phase III Multinational study	ocrelizumab Injection	Roche	Humanized anti-CD20 monoclonal antibody

Development code	Indication # Additional indication	Stage (date)	Generic name Product name Dosage form	Origin Overseas name (Collaborator)	Mode of Action
RG484	Osteoporosis	Phase II / III	ibandronate sodium hydrate Injection	Roche Boniva (US) / Bonviva (EU) (Taisho Pharmaceutical)	Bisphosphonate
		Phase II	ibandronate sodium hydrate Oral		
Renal diseases					
RG744	Renal anemia	Filed Jul. 09	Injection	Roche Mircera	Continuous erythropoietin receptor activator
Transplant, Immunology and Infectious diseases					
RG964	Compensated liver cirrhosis caused by hepatitis C virus	Phase II / III	ribavirin Copegus Oral	Roche Copegus	Anti-viral agent, in combination with Pegasys
RG442	# Chronic hepatitis B		Phase II / III	peginterferon alfa-2a Pegasys Injection	Roche Pegasys
NA808	Chronic hepatitis C	Phase I	Injection	In-house	Serine palmitoyl transferase inhibitor
		Phase I Overseas			
NTZ	Chronic hepatitis C	Phase I	nitazoxanide Oral	Romark Laboratories Alinia	Thiazolide compound
Other diseases					
EPOCH	Predeposit of autologous blood transfusion #	Filed Jun. 94	epoetin beta Epogin Injection	In-house	Recombinant human erythropoietin
RG1678	Schizophrenia	Phase II Multinational study	Oral	Roche	GLYT1 inhibitor
CSG452 (RG7201)	Type II diabetes	Phase II Multinational study	Oral	In-house (Roche)	SGLT2 inhibitor
RG1583 (ITM-077)	Type II diabetes	Phase II	tasoglutide Injection	Roche/Ipsen (Teijin)	GLP-1 analogue

Development code	Indication # Additional indication	Stage (date)	Generic name Product name Dosage form	Origin Overseas name (Collaborator)	Mode of Action
RG1450	Alzheimer's disease	Phase I	gantenerumab Injection	Roche/Morphosys	Human anti-amyloid-beta monoclonal antibody

Changes from the last announcement on October 27, 2009

Oncology

- RG435 Filed → Launched (non-small cell lung cancer)
- EPOCH Phase III → Filed (chemotherapy induced-anemia)
- RG1507 Phase I → Development suspended(solid tumors)
- CIF(RG7167) Phase I (solid tumors/Japan)
- CKI27(RG7304) Phase I (solid tumors/Japan)

Bone and Joint diseases

- MRA Filed → Launched (Rheumatoid Arthritis/US)

R&D Activities (Jan. 1, 2009 – Feb. 3, 2010)

As for clinical development activities in Japan, the Company saw progress as described below:

Oncology

- In September 2009, we obtained approval for an additional indication of RG340 (product name: Xeloda), a 5-FU derivative, for colorectal cancer, as a combination therapy with oxaliplatin.
- In August 2009, we participated in a multinational Phase III study (expected indication: glioblastoma) conducted by Roche and started a domestic Phase II trial (expected indication: glioblastoma [relapsed]) for a humanized anti-VEGF monoclonal antibody RG435 (product name: Avastin). Also for RG435, we filed an application for an additional indication (expected indication: breast cancer) in October and obtained approval for an additional indication (expected indication: non-small cell lung cancer).
- In September 2009, we filed an application for an EGFR tyrosine kinase inhibitor, RG1415 (product name: Tarceva, expected indication: pancreatic cancer).
- In November 2009, we filed an application for a recombinant human erythropoietin EPOCH (product name: Epogin, expected indication: treatment of chemotherapy-induced anemia).
- In July 2009, we participated in a multinational Phase III study (expected indication: breast cancer) conducted by Roche for RG1273, a humanized HER dimerization inhibitory monoclonal antibody.
- In September 2009, we started a Phase I/II trial (expected indication: pancreatic cancer) for a humanized anti-human IL-6 receptor monoclonal antibody, MRA (product name: Actemra).
- In November 2009, we started a Phase I trial (expected indication: solid tumors) for a MEK inhibitor, CIF (RG7167).
- In January 2010, we started a Phase I trial (expected indication: solid tumors) for CKI27 (RG7304).
- In October 2009, we started a Phase I trial (expected indication: breast cancer) for a HER2 antibody-drug conjugate, RG3502.
- We decided to terminate development of RG744 for chemotherapy-induced anemia after reviewing priorities of our projects.
- We decided to terminate development for a human anti-IGF-1R monoclonal antibody RG1507 (expected indication: solid tumors) following the fact that results from overseas Phase II clinical trials conducted by Roche (target indication: non-small cell lung cancer, sarcoma) did not meet the efficacy criteria to proceed. No safety or tolerability signals were observed.

Bone and Joint Diseases

- In January 2009, we started Phase I/II clinical trials for a new formulation (subcutaneous injection) of a humanized anti-human IL-6 receptor monoclonal antibody, MRA (product name: Actemra).
- In October 2009, we filed an application for an activated Vitamin D₃ derivative, ED-71 (expected indication: osteoporosis).

Renal Diseases

- In April 2009, we obtained approval for the partial change of the API manufacturing method and the pharmaceutical formulation of a recombinant human erythropoietin (product name: Epogin).
- In July 2009, we filed an application for a continuous erythropoietin receptor activator, RG744 (expected indication: renal anemia).

Transplant, Immunology and Infectious Diseases

- In August 2009, we started a Phase I trial (expected indication: chronic hepatitis C) for a thiazolidine compound, NTZ.

Other Diseases

- In February 2009, we started a multinational Phase II study (expected indication: type II diabetes) for an SGLT2 inhibitor, CSG452 (RG7201).

- In July 2009, we started a Phase II trial (expected indication: type II diabetes) for a GLP-1 analogue, RG1583 (ITM-077).
- In July 2009, we started a Phase I trial (expected indication: Alzheimer's disease) for a human anti-amyloid-beta monoclonal antibody, RG1450.

At present, we are awaiting the approval of applications (new molecular entities or additions of indications) filed for 6 development themes, including RG435 (expected indication: breast cancer).

Also, as for development activities overseas, the Company saw progress as described below.

- In October 2009, we started a Phase II trial (expected indication: gastric cancer, etc) for a topoisomerase I inhibitor, TP300.
- In March 2009, we concluded a license agreement with ChoongWae Pharma Corporation to grant rights to develop and market a humanized anti-human IL-6 receptor monoclonal antibody, MRA (planned product name: Actemra), in South Korea for the indication of rheumatoid arthritis.
- In January 2010, Roche obtained approval for a humanized anti-human IL-6 receptor monoclonal antibody, MRA (product name: Actemra), for rheumatoid arthritis from the U.S. Food & Drug Administration (FDA).

We deleted the following projects from our development pipeline with due consideration for priorities: a humanized anti-human IL-6 receptor monoclonal antibody, MRA (expected indication: multiple myeloma, Crohn's disease, Castleman's disease [overseas], Systemic lupus erythematosus (SLE)), a motilin agonist GM-611 (expected indication: diabetic gastroparesis, irritable bowel syndrome (IBS)), a DPP-IV inhibitor RG1579 (expected indication: type II diabetes).

Major clinical trials in oncology field currently running in Japan

Theme	Expected Indication	Regimen	Stage	Planned Filing Date
RG435 (bevacizumab) Avastin	Breast	paclitaxel + RG435	Filed (Oct. 09)	-
	Breast (adjuvant)	standard chemotherapy ± RG435	BEATRICE study Phase III Multinational study	2013 2015
	Glioblastoma	temozolomide ± RG435	Phase III Multinational study	2013 2015
	Glioblastoma [relapsed]	RG435	Phase II	2013 2015
RG435 (bevacizumab) Avastin	Colon (adjuvant)	FOLFOX4 ± RG435 XELOX + RG435	AVANT study : Phase III Multinational study	2011
RG340 (capecitabine) Xeloda	Gastric	RG340(5FU) + CDDP ± RG435	AVAGAST study : Phase III Multinational study	2011
RG1415 (erlotinib) Tarceva	Pancreatic	gemcitabine + RG1415	Filed (Sep. 09)	-
RG597 (trastuzumab) Herceptin RG340 (capecitabine) Xeloda	Gastric	RG340/5FU + CDDP ± RG597	ToGA study : Phase III Multinational study	2010
RG1273 (pertuzumab)	Breast	RG597 + docetaxel ± RG1273	CLEOPATRA study Phase III Multinational study	2013 2015