Pipeline of Prescription Pharmaceuticals (Clinical Development)

Category: Global product Japan (Asia) product

Corneal and Conjunctival Epithelial Disorders

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
DE-101	Rivoglitazone	Corneal and conjunctival epithelial disorder associated with dry eye, etc.	Daiichi Sankyo	U.S.					
DE-105	Undetermined	Persistent corneal epithelial defects	Original	U.S.					
				Japan					
DE-089	Diquafosol sodium	Dry eye	Inspire	Japan					Launched, December 2010
				Asia (excluding Japan)					December 2011
				China					January 2012

Glaucoma

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
DE-085	Tafluprost	Glaucoma Ocular hypertension	Co-development with Asahi Glass	Japan					Launched, December 2008
				Europe					Launched, June 2008
				U.S.					(License out) Launched, March 2012
				Latin America					(License out) Launched, August 2010
				Asia (excluding Japan)					Launched, March 2010
				China					January 2011
DE-111	Tafluprost/ timolol maleate	Glaucoma Ocular hypertension	Co-development with Asahi Glass	Japan					
			Co-development	Europe					
DE-117	Undetermined	Glaucoma Ocular hypertension	Co-development with Ube Industries	U.S.			Phase 1/2a		
DE-118	Tafluprost	Glaucoma Ocular hypertension	Co-development with Asahi Glass	Japan					February 2012
DE-090	Lomerizine HCl	Glaucoma	MSD[1]	Japan					

1. Formerly Banyu Pharmaceutical

As of August 1, 2012

DE-101 (generic name: rivoglitazone)

A PPARgamma agonist which is thought to improve the condition, quality and volume of tear film. DE-101 is in Phase 2 clinical trials in the U.S.

DE-105 (generic name: undetermined)

A new drug candidate that is expected to provide high levels of safety for persistent corneal epithelial defects compared with existing therapy, DE-105 helps repair corneal epithelial defects by accelerating corneal epithelial migration. Phase 2 clinical trials are being conducted in Japan with preparations being made for Phase 2 clinical trials in the U.S.

DE-085 (generic name: tafluprost)

A prostaglandin derivative for the treatment of glaucoma and ocular hypertension, DE-085 increases uveoscleral outflow of the aqueous humor and shows a potent and stable IOP-lowering effect. DE-085 was launched in Germany in June 2008 and in Japan in December 2008. It is currently directly marketed in 23 countries throughout Europe as well as in Asia—beginning with Hong Kong in March 2010, Korea in May 2010, and Indonesia and Singapore in 2011. An NDA has been filed in China. A licensing agreement with U.S.-based Merck & Co. was concluded in April 2009 that granted sales rights in Western Europe (excluding Germany), North America, South America and Africa. Tafluprost has been marketed by Merck & Co. in a total of 23 countries including the United Kingdom, Spain, Italy and the U.S. since September 2009. Incorporating sales under this licensing agreement, tafluprost is currently sold in a total of 51 countries worldwide.

DE-111 (generic name: tafluprost / timolol maleate)

A combination prostaglandin derivative and beta-adrenergic receptor blocker drug for the treatment of glaucoma and ocular hypertension, DE-111 is in Phase 3 clinical trials in Japan and also in Europe.

DE-089 (generic name: diquafosol sodium)

A treatment for dry eye that stimulates the ocular surface to secrete mucin and tear fluid, DE-089 offers a different mechanism of action from the existing ophthalmic solution *Hyalein* (sodium hyaluronate). It was launched as a dry eye treatment in Japan under the name *Diquas* in December 2010. Manufacturing and marketing approval was received in Korea in December 2011. An NDA has been filed in China.

DE-117 (generic name: undetermined)

A prostaglandin EP2 agonist with a new mechanism of action. DE-117 is in Phase 1 and Phase 2a clinical trials in the U.S.

DE-118 (generic name: tafluprost)

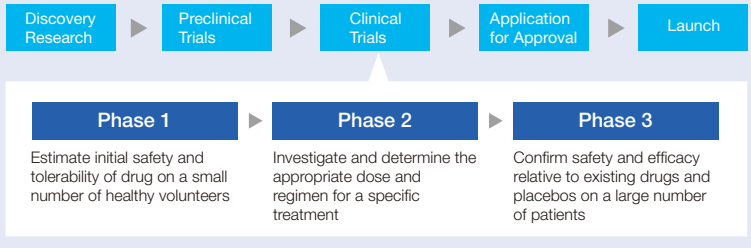
A prostaglandin derivative for the treatment of glaucoma and ocular hypertension, DE-118 is a preservative-free, unit-dose, single-use type product. An application has been filed in Japan for manufacturing and marketing approval.

DE-090 (generic name: lomerizine HCl)

A new type of glaucoma treatment which inhibits the progression of visual field defects, DE-090 is in Phase 2 clinical trials conducted in Japan. It is the only calcium antagonist being developed as an oral glaucoma treatment. Compared to NMDA receptor antagonists, systematic adverse drug reactions are mild, offering an excellent safety profile. The compound is also marketed by MSD K.K. in Japan as a migraine treatment drug.

About Research and Development

After passing preclinical trials for safety and efficacy, new drug candidates are put through the clinical trial phases outlined on the right. Upon receiving manufacturing and marketing approval, they can be sold as prescription pharmaceuticals.



Pipeline of Prescription Pharmaceuticals (Clinical Development)

Category: Global product Japan (Asia) product

Retinal and Uveal Disorders

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
DE-102	Betamethasone	Macular edema secondary to diabetes and BRVO[1]	Co-development with Oakwood	Japan			Phase 2/3		
DE-109	Sirolimus	Uveitis	Original	U.S.					
				Europe					
				Japan					

1. BRVO: branch retinal vein occlusion

Ocular Infections/Allergy

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
DE-108	Levofloxacin (1.5%)	Bacterial conjunctivitis	Daiichi Sankyo	Japan					Launched, June 2011
				Asia					October 2011
DE-114	Epinastine HCl	Allergic conjunctivitis	Nippon Boehringer Ingelheim	Japan					

Novagali's Pipeline of Prescription Pharmaceuticals

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
Cyclokat	Ciclosporin	Severe dry eye	Original	Europe					
				U.S.					
Vekacia	Ciclosporin	Vernal keratoconjunctivitis	Original	Europe					
Catioprost	Latanoprost	Glaucoma Ocular hypertension	Original	Europe					
Cortiject	Dexamethasone palmitate	Diabetic macular edema	Original	U.S.			Phase 1/2		

*Catioprost and Cortiject are under project evaluation

Rheumatoid Arthritis

Dev. Code	Generic Name	Indication	Original / Licensor	Region	Phase 1	Phase 2	Phase 3	NDA Filed	Approved
DE-098	Undetermined	Rheumatoid arthritis	Janssen Biotech	Japan					

As of August 1, 2012

DE-102 (generic name: betamethasone)

A steroid microsphere product for sustained release injection, DE-102 is in Phase 2 and Phase 3 clinical trials in Japan as a treatment for macular edema secondary to diabetes and BRVO[1]. Animal studies demonstrated sustained efficacy when injected around the affected area. Santen is collaborating with Oakwood Laboratories of the U.S. in the development of the microsphere delivery platform for this product.

1. BRVO: branch retinal vein occlusion

DE-108 (generic name: levofloxacin (1.5%))

A fluoroquinolone antibacterial agent with higher concentration, DE-108 was launched in Japan in June 2011 as an indication for bacterial conjunctivitis under the name *Cravit Ophthalmic Solution 1.5%*. An application has been filed in Korea for manufacturing and marketing approval.

DE-114 (generic name: epinastine HCl)

An H_1 receptor antagonist with membrane-stabilizing function as a treatment for allergic conjunctivitis, DE-114 was licensed from Nippon Boehringer Ingelheim Co., Ltd. and is currently in Phase 3 clinical trials in Japan.

Responding to Unmet Medical Needs

Development of Therapy for Orphan Disease Uveitis

The uvea is the vascular middle layer of the eye that connects the iris at the front to the ciliary body and choroid toward the back of the eye. Uveitis covers a range of conditions. The development indication for DE-109 of "non-infectious posterior uveitis" is an orphan disease for which there are currently few therapeutic options.

DE-109 (generic name: sirolimus)

An intravitreal injection with immunosuppressive effect, anti-angiogenic effect, etc. In June 2010, Santen acquired global rights from U.S.-based MacuSight, Inc. for the development, manufacturing, and marketing of sirolimus. Phase 3 clinical trials have now begun in Europe; Phase 3 clinical trials were already underway for uveitis in the U.S. and Japan.

Cyclokat (generic name: ciclosporin)

This is a topical ophthalmic emulsion which improves symptoms and signs of severe dry eye by immunosuppressive effect. Cationic emulsion technology has enhanced ocular tissue absorption. It is currently in Phase 3 clinical trials in Europe and Phase 2 clinical trials have been completed in the U.S.

Vekacia (generic name: ciclosporin)

This is a topical ophthalmic emulsion which improves vernal keratoconjunctivitis symptoms by immunosuppressive effect. Cationic emulsion technology has enhanced ocular tissue absorption. It is in Phase 3 in Europe.

DE-098 (generic name: undetermined)

A joint injection that induces apoptosis in diseased joints of rheumatoid arthritis patients, DE-098 is an anti-APO-1 antibody in-licensed from Janssen Biotech, Inc. for the treatment of rheumatoid arthritis. We are currently considering the next development plan based on the results of Phase 2 clinical trials in Japan.

Catioprost (generic name: latanoprost)

This is a topical ophthalmic emulsion of a prostaglandin $F_{2\alpha}$ derivative, for the treatment of glaucoma and ocular hypertension. It is currently under project evaluation.

Cortiject (generic name: dexamethasone palmitate)

An intravitreal injection with anti-inflammatory effect. It is currently under project evaluation.