

Medium-term Policy 1: Enhance Global Strategic Pipeline

Santen's consistent R&D strategy is to focus efforts on areas where there are significant unmet medical needs, where our strengths can be fully utilized and where there is significant growth potential. Specifically, such fields include glaucoma, retinal disorders and corneal disorders (dry eye). Developing new products in these fields represents the underlying foundation of our growth strategies.

The global strategic products currently under development are as follows:

● DE-101 (Generic name: Rivoglitazone)

【Corneal and conjunctival epithelial disorders associated with dry eye】

DE-101 is an eye drop that effectively improves conditions caused by corneal and conjunctival epithelial disorders including dry eye. With a novel mechanism of action that differs from any drugs currently on the market or under development, DE-101 works directly on the corneal and conjunctival epithelial cells. Santen and DAIICHI SANKYO COMPANY, LIMITED, entered into a contract for exclusive global development and manufacturing. Currently, the Phase II clinical trial for this drug is underway in the United States.

● DE-104 (ROCK inhibitor)

【Glaucoma and ocular hypertension】

DE-104 has a mechanism of action which differs from that of existing drugs and works directly on trabecular cells to facilitate the outflow of the aqueous humor and powerfully reduce ocular pressure. This drug is being developed through a collaboration between Santen and UBE INDUSTRIES, LTD. Currently, the Phase I clinical trial is underway in the United States.

During the period of this Medium-term Management Plan, we plan to file applications for or launch the following new drug candidates mainly in Japan.

● DE-085 (Generic name: Tafluprost)

【Glaucoma and ocular hypertension】

DE-085, which facilitates the outflow of the aqueous humor from the uveal and scleral channels, exhibits a powerful and stable effect for alleviating ocular hypertension. In July 2006, we filed for manufacturing approval in Japan and, in April 2007, we filed for marketing approval in Europe. In the United States, we will decide whether to apply for approval based on discussions of future operations.

● DE-089 (Generic name: Diquafosol tetrasodium)

【Corneal and conjunctival epithelial disorders associated with dry eye】

DE-089 is a drug to treat corneal and conjunctival epithelial disorders mainly caused by dry eye by facilitating the secretion of components of lacrimal fluid and water out of the corneal and

conjunctival epithelia. The use of DE-089 with existing drugs is also possible. Currently, the Phase III clinical trial for this drug is underway in Japan.

● MD-14 (Intraocular lenses)

【Foldable intraocular lens using acrylic materials with a high refractive index】

MD-14 is an intraocular lens developed by Advanced Vision Science, Inc., one of Santen's U.S. subsidiaries. We obtained the manufacturing and marketing approval in Japan in October 2006. In the United States, preparation for application is underway.

In this way, Santen is gradually developing and commercializing various new drug candidates. To expedite R&D and enhance the probability of commercialization, Santen adopts the following three methods for drug development.

The first method is to identify chemical compounds through in-house drug discovery. The second method, called "network-based drug discovery," is a collaborative research method that links Santen's accumulated knowledge and expertise with advanced external technologies. The third method is strategic licensing and introducing chemical compounds owned by other companies.

For each development candidate, Santen prepares backup compounds to strengthen our global portfolio and to maximize the chances of success for commercialization.



Research workers at the Nara Research Center and Development Center and Santen Oy

Clinical Trials

When safety and efficacy of candidate compounds are determined in preclinical studies, they undergo the following clinical trials. After completing the Phase III clinical trials, a new drug application (NDA) is filed for marketing approval.

- **Phase I**
Tests to check drug safety with a small number of healthy volunteers.
- **Phase II**
Tests to determine dosage and administration method with a small number of patients.
- **Phase III**
Tests to confirm safety and efficacy by comparing to existing drugs and placebo with a large number of patients.

Pipeline of prescription pharmaceuticals (Clinical studies)

As of July 31, 2007

Generic name	Brand name/ dev. code	Indication	Region	Phase I	Phase II	Phase III	NDA Filed	Approved	Launched	Characteristics
Levofloxacin (0.5%)	Cravit	Bacterial conjunctivitis	Japan	April-2000						Fluoroquinolone antibacterial agent. Levofloxacin + prednisolone A is a combination treatment with steroids.
	Quixin		USA	November-2000						
	Oftaquix		Europe	May-2002						
Levofloxacin + prednisolone A	DE-094	Infectious keratitis	USA							
Tafluprost	DE-085	Glaucoma/ Ocular hypertension	Japan	July-2006						Please see Page 10.
			Europe	April-2007						
			USA							
Diquafosol tetrasodium	DE-089	Corneal and conjunctival epithelial disorder associated with dry eye	Japan							Please see Page 10.
Olmesartan	DE-092	Glaucoma/ Ocular hypertension	Japan	Pilot study						The angiotensin II receptor antagonist. In Japan, Europe and the USA, the Phase II studies did not demonstrate clear dose-response relationship, and therefore we decided to suspend clinical studies. We are now conducting the Phase II pilot study with different formulation.
			USA/ Europe	Pilot study						
Lomerizine HCL	DE-090	Glaucoma	Japan							A new type of oral glaucoma treatment studied for inhibiting the progression of visual field defects. The only calcium antagonist in full-fledged development as a glaucoma treatment. Compared with NMDA receptor antagonists, fewer generalized side effects are expected, thus having excellent safety. Marketed by Nippon Organon as a migraine drug.
(Undetermined)	DE-096	Rheumatoid arthritis	Japan							An oral TNF inhibitor. Anti-rheumatic effect comparable to injectable biological agents. In addition to RA, the effect on DME was also observed in basic research, and the Phase II studies are being conducted with both diseases.
		Diabetes macular edema	Japan							
Gefarnate	DE-099	Corneal and conjunctival epithelial disorder associated with dry eye	Japan							Treats corneal and conjunctival epithelial disorder mostly associated with dry eye, by stimulating the secretion of mucin and promoting the corneal epithelial migration. Preservative-free eye ointment that can be used in combination with existing drugs.
Rivoglitazone	DE-101	Corneal and conjunctival epithelial disorder associated with dry eye	USA							Please see Page 10.
(Undetermined)	DE-102	Diabetes macular edema	Japan	(Phase I / IIa)						A steroid microsphere product for a sustained release injectable drug delivery. Demonstrated sustained efficacy when injected around the affected area. In order to produce sterile microsphere in commercial scale, we collaborate with Oakwood Laboratories (USA).
(Undetermined)	DE-104	Glaucoma/ Ocular hypertension	USA							Please see Page 10.
(Undetermined)	DE-103	Allergic conjunctivitis	Japan							A PDE4 (Phosphodiesterase type 4) inhibitor for allergic conjunctivitis which has a different action mechanism from the existing drugs. Expected to be effective for allergic conjunctivitis through its inhibitory effect against PDE4.