

REPORTS FROM THE FRONT LINE: FIRST-YEAR RESULTS OF THE "2003-2005 MEDIUM-TERM MANAGEMENT PLAN"

For any pharmaceuticals firm, success depends on the strength and speed of research and development programs. During the year, we stepped up the pace of clinical trials on compounds for glaucoma treatment and enhanced our in-house development capabilities in high-priority research areas, including retinal disorders. In the clinical trial phase, we are adding to our global presence in the high-growth glaucoma market by advancing development of our prostaglandin (PG) compounds. Tafluprost (development code: DE-085) is expected to show an improved reduction of intraocular pressure, compared to PG products available on the market today.

for the future...

TO LEVERAGE R&D EXPERTISE

SUCCEEDING WITH SHARED COMMITMENT

Thanks to the cooperation both internally and externally at Santen, our group was able to accelerate the clinical trials for tafluprost (DE-085) and move into Phase III at the end of last year. Medical institutions have both begun to deepen their understanding of clinical studies and establish better internal systems, which have allowed us to expedite our process. In addition to the substantially increased number of patients from Phase II to Phase III, we are conducting three different clinical trials concurrently. We added 10 people to our clinical group to conduct the Phase III clinical trials.

Most of the additional clinical manpower has been transferred from our research division. While researchers usually focus on specialized experiments, clinical employees must coordinate the activities of physicians and medical institutions in order to successfully conduct clinical trials. Since clinical development requires different skills and competency from basic research, we offer new clinical employees in-house training for approximately one month after transferring. After the training program, new clinical employees train under the supervision of

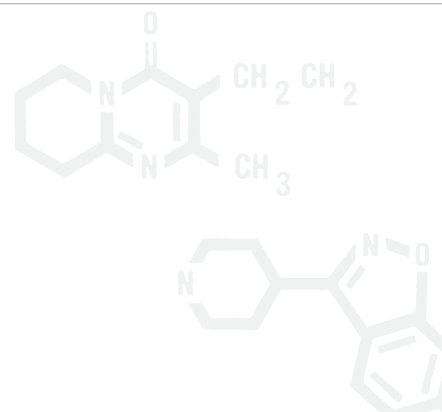


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experienced staff, and are evaluated for their communication skills with the staff of medical institutions. This interpersonal skills training sometimes includes discussions with physicians who call for immediate responses to their questions.

To accelerate our clinical development, we have increased the speed of our decision-making and strengthened internal collaboration with our research centers, production departments, sales departments, academics, regulatory affairs, statistical analysis, quality control and assurance. A high degree of mutual commitment by all those involved allowed us to succeed in this project.

Development of pharmaceuticals is much like a long-distance relay race. Once the medical value and safety of our compounds created by our researchers are confirmed, we then seek to complete clinical trials successfully and on time before moving on to the registration process for the final course of the race. Working towards the same goal, each "runner" is passing the baton of the shared commitment to success.



TAKING UP THE CHALLENGE OF GLOBAL DEVELOPMENT

Because glaucoma treatments, from a global perspective, represent the largest market and are the highest priority for Santen, we have been promoting concurrent clinical development of tafluprost (DE-085) in Japan, the U.S. and Europe. Tafluprost represents our first major global project. To succeed, consistent, detailed collaboration among our project teams in our three geographic regions is extremely important.

In Phase we are conducting multiple clinical trials concurrently in Japan, the U.S. and Europe, making our collaboration more complex. Our global project teams are working very closely to advance clinical trials in



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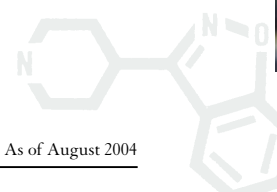
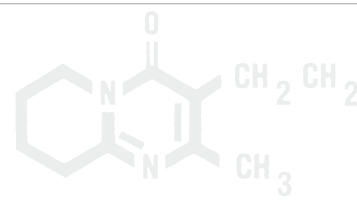
each area, with the goal of utilizing the trial results obtained in one region for registration purposes in other regions of the world as quickly as possible. To complete the trials and file an application in each region in the shortest time, all other related operations such as non-clinical research, regulatory, quality assurance, project management and statistics are also collaborating closely.

From an operational standpoint, when Japanese pharmaceutical companies develop international products, they first get approvals in the U.S. or Europe and use their clinical

trial results for application in Japan. This process – and the success thereof – should become an important asset of the Santen Group.



▲ Laboratory of Santen Oy



Prescription Pharmaceuticals in Development

As of August 2004

Generic name	Brand Name/ Development Code	Indication	Region	Pre-clinical	Phase I	Phase II	Phase III	NDA Filed	Approved	Characteristics
Levofloxacin 1.5%	<i>Iquix</i>	Bacterial corneal ulcer	USA							Antibacterial ophthalmic solution containing the active ingredient fluoroquinolone three times higher than current product (<i>Quixin</i>). Exhibits potent antibacterial action. Approved in March 2004.
Ciclosporin	DE-076	Vernal keratoconjunctivitis	Japan							An orphan drug ^{*2} . Expected to treat advanced vernal keratoconjunctivitis for which existing anti-allergy agents are not effective. NDA filed in August 2003.
Tafluprost	DE-085	Glaucoma and ocular hypertension	Japan USA/Europe							Prostaglandin glaucoma treatment that is expected to have greater efficacy in reducing intraocular pressure than other prostaglandin glaucoma treatments. Can be stored at room temperature.
Olmesartan	DE-092	Glaucoma and ocular hypertension	Japan USA/Europe			*				The only angiotensin receptor antagonist in full-fledged development as a glaucoma treatment. Comparable to prostaglandin products in reducing intraocular pressure.
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.
Diquafosol tetrasodium	DE-089	Dry eye	Japan							A dry eye treatment that stimulates corneal and conjunctival epithelial secretion of tear fluid and moisture.
Levofloxacin and prednisolone A	DE-094	Infectious keratitis	USA							Combination of levofloxacin and steroid.
Sodium hyaluronate	<i>Hyalain</i>	Dry eye	USA			*				Ophthalmic solution containing sodium hyaluronate for dry eye.
(Undetermined)	DE-096	Rheumatoid arthritis	Japan							An oral TNF inhibitor. Anti-rheumatic effect comparable to injectable biological agents has been observed in basic research.
Gefarnate	DE-099	Corneal and conjunctival epithelial disorder associated with dry eye, etc.	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 ointment that can be used in combination with existing drugs.
(Undetermined)	DE-098	Rheumatoid arthritis	Japan							Anti-APO-1 antibody. Joint injection that induces apoptosis in diseased joints of rheumatoid arthritis patients. Bulk pharmaceutical manufacturing process for actual production scale has been established, and drug development is being studied.
Bucillamine	<i>Rimatil</i>	Osteoarthritis (additional indication)	Japan							Shown to be effective on joint inflammation caused by osteoarthritis.

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

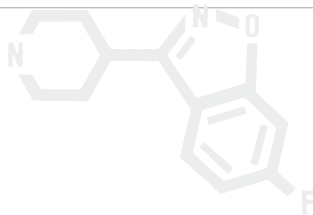
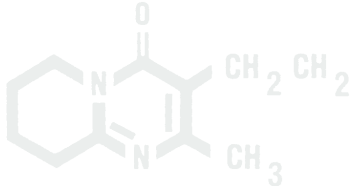
Phase : Tests to check drug safety with a small number of healthy volunteers.

Phase : Tests to determine dosage and administration method with a small number of patients.

Phase : Tests to confirm safety and efficacy by comparing to existing drugs and placebo with a large number of patients.

*1 In preparation

*2 Orphan drug: A drug with an indication for treating a relatively small number of patients. Orphan drug R&D expenses are eligible for government subsidies in Japan.



UPDATING PROGRESS IN DISCOVERY RESEARCH

Over the past several years, unmet medical needs in ophthalmologic diseases have shifted focus for research from the anterior segment (cornea and conjunctiva) to the posterior segment (retina and optic nerve). Rheumatoid arthritis shares common etiological and pathological symptoms, such as angiogenesis, cell growth, edema and inflammation with retinal and other diseases in the posterior segment of the eye. By deploying our accumulated knowledge gained in rheumatism research over the years, we are working to establish efficient, unique drug-discovery techniques to develop breakthrough ophthalmic pharmaceuticals.

During the year, we advanced our drug discovery efforts in the priority fields of retinal disorder and osteoarthritis. In the ophthalmic field, we placed special emphasis on reinforcing our in-house drug discovery capabilities.

Today, the mainstream glaucoma treatments are prostaglandin products that lower intraocular pressure by promoting the outflow of aqueous humor through the uveal and scleral channels. At Santen, we are currently making steady progress in the preclinical development of a protein kinase inhibitor, as a new mechanism of action that promotes the outflow of aqueous humor through the trabecular channel. This channel is responsible for 80% of the outflow of aqueous humor. We have positioned this pharmaceutical agent as a treatment possibility to replace surgery. Another approach to glaucoma treatment is protection of the optic nerve. There are two ways to protect the optic nerve: improvement of retinal circulation and direct action on the optic nerve. We have already embarked on discovery research and preclinical experiments in both methods.

In the field of retinal disorders, we have been advancing preclinical studies of candidate compounds designed to treat age-related macular degeneration (AMD) and other retinal disorders, diseases with which the number of patients increases as the population ages.

In the osteoarthritis field, we have discovered an oral tumor necrosis factor (TNF) inhibitor (DE-096) and have initiated Phase I clinical trials in Japan.



REINFORCING INTELLECTUAL PROPERTY STRATEGIES

The importance of intellectual property strategies has been growing in the prescription pharmaceuticals market today. From candidate compounds under development to basic research results, we are developing and implementing our intellectual property strategies on a global scale in order to maximize the value of our products and technologies.



▲ The ninth worldwide intellectual property committee meeting was held in Osaka in February 2004.