Product Development

Under MTP2025, centering on ophthalmic solutions for glaucoma, dry eye and allergies, we will focus on developing our core businesses that will underpin medium-to-long-term growth. At the same time, we will enter new disease areas to achieve new growth that is more than just an extrapolation of existing areas.

Understanding the true needs of patients and their caregivers will lead to ideas and innovations for achieving their Best Vision Experience.

Reza Haque, MD, Ph.D

Head of Ophthalmology Innovation Center

The mission of the Ophthalmology Innovation Center is to listen to the voices of patients and their caregivers to identify their true needs, then to promptly create products and services that address those needs using existing or new technologies or a fusion of the two. Lately, we have been advancing to the clinical trial stage a pipeline of projects that are expected to improve patient convenience, including a new formulation to follow *Alesion LX* and a next-generation treatment for inhibiting myopia progression in children. In addition, we stay on top of information on global trends in ophthalmology research and startup companies and combine Santen's strengths with those of external organizations through open innovation to create a pathway to ophthalmic applications that leverage internally and externally held technologies. We are already collaborating with many external organizations including the Singapore Eye Research Institute and University College London. Unconstrained by preconceptions, we will create new value and contribute to a world where patients can live their happiest lives through the Best Vision Experience.

We are steadily applying for and obtaining approval for projects under development. We will also create new value for products on the market in response to the voices of patients.

Peter Sallstig, MD, MBA

Corporate Officer
Head of Product Development Division

In product development, we consistently emphasize people centricity in our approach and actions. To this end, we will create a method, based on providing all the necessary information on eye diseases and treatments, that enables patients who participate in clinical trials to have immediately greater ownership and feel the value of new pharmaceuticals. We are also conducting clinical trials that allow remote patient participation, thus enabling patients to participate who would otherwise have declined, e.g., if they lived too far away, and trials required too many blood draws that is patient focus. Late-stage development projects in our pipeline target glaucoma, dry eye, allergies and uveitis, and we are enhancing the pipeline in new areas including myopia, ptosis and retinitis pigmentosa. These candidates address needs in each area. Reliably filing applications and obtaining approval for these candidates is a core mission of ours. For product life cycle, we will not only conduct regional rollouts but also secure exclusive global rights as we create products that further enhance patient convenience.

Product Development

Initiatives to Enhance Core Businesses

In addition to the importance of effectiveness and safety, reducing the burden on patients when they use ophthalmic solutions leads to adherence to treatment and ultimately to target therapeutic effects and outcomes. It is known that the greater the frequency of application required, the less likely patients are to apply them. Santen is developing products using technologies to reduce the frequency of application of existing ophthalmic solutions, including changing the formulation while maintaining the effects and creating drugs that combine two agents. We are also developing applicators and containers that are easier to use, as well as changing dosage forms. These initiatives will enhance patient convenience and differentiate Santen products from those of other companies.

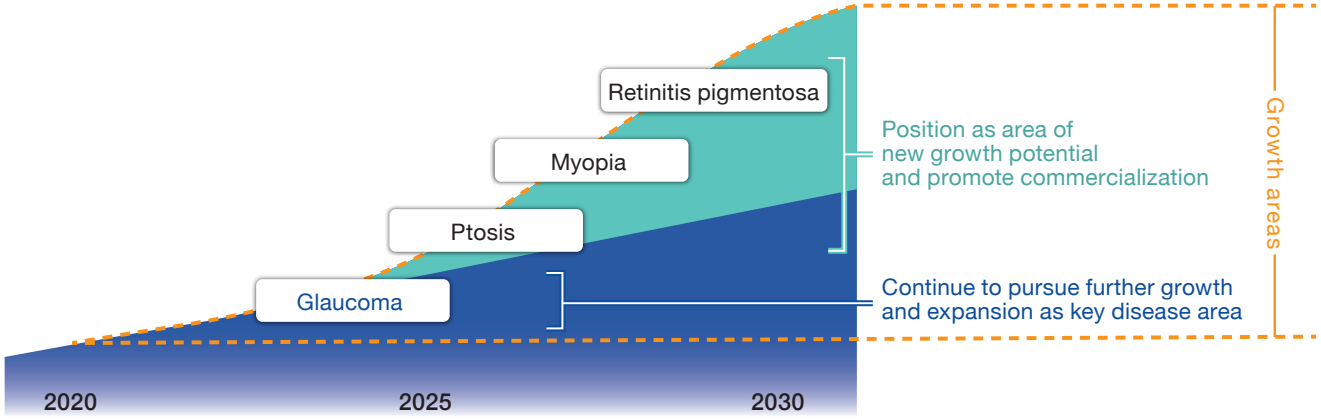
Furthermore, the experience that we gain in our core business of developing ophthalmic solutions is applied for new product development and lifecycle management.

Initiatives in New Areas

Entering new areas is a rewarding challenge. However, taking the development of gene or cell therapies as an example, in addition to Santen's experience and technologies, this process will require approaches unconstrained by preconceptions.

Santen acquires expertise for development in new areas by building strong relationships with academia around the world. On a day-to-day basis, we are collaborating with the Singapore Eye Research Institute, University College London and many other universities, specialists and startup companies to generate new ideas by exploring how cutting-edge therapeutic technologies and modalities such as gene therapy and cell therapy can be applied in ophthalmology. We will utilize the know-how we gain from these R&D activities in our product development to increase the probability of success and lead to the creation of reliable products.

Capture new growth in four disease areas, not just extrapolating on existing areas



[1] Hartong DT et al. *Lancet* 2006; 368: 1795–809
https://pubmed.ncbi.nlm.nih.gov/17113430/

Column

Gil Carrasquinho

Vice President
Head of Cell Therapy
Corporate Development
Division

The challenge toward establishing cell therapy

Our mission at Cell Therapy is to innovate at a pace that benefits society and creates a better life and future for patients.

Our immediate focus is accelerating our retinitis pigmentosa (RP) program (STN6000100) for our investigational human retinal progenitor cell therapy asset, while also exploring other indications. RP is a group of rare inherited eye conditions affecting approximately 1 in 3,000-4,000 people.[1] There are currently limited treatment options, making the condition an area of significant unmet medical need. As part of our efforts to provide new treatments, we have been engaging regulatory agencies, KOLs, patient groups, policy influencers and others from an early stage.

Team members at Cell Therapy

Product Development

Development Story of *Alesion LX*: Aiming for a Better Treatment

There are specific needs that Santen is uniquely capable of identifying. We launched anti-allergenic *Alesion LX Ophthalmic Solution 0.1%*, which halves the frequency of application compared with previous products, in November 2019 in Japan.

An Allergic Conjunctivitis Treatment Applied Twice per Day

In Japan, histamine H_1 receptor antagonist ophthalmic solutions used to treat allergic conjunctivitis, including *Alesion*, were applied four times per day. While investigating the issues faced by patients, it was found that many were unable to maintain the proper dosage due to the high frequency of application, leading to a hypothesis that the repeated itching felt throughout the day was lowering their quality of life.[1] We therefore began to develop a product requiring less frequent application, making it easier to comply with the correct dosage.

Promptly Delivering a Product with New Value to Patients

Clinical trial design is key to properly assessing safety and efficacy in humans. Based on findings from the development of *Alesion* and data from non-clinical studies, we considered a plan to appropriately evaluate the safety and efficacy while shortening the development period to the greatest extent possible. After consultation with the relevant authorities and their review, we started clinical trials from Phase 3.

1 Product Planning → **2 Formulation Development** → **3 Non-Clinical Studies Clinical Trials** → **4 Approval/ Launch**

Achieving Both Safety and Effectiveness

In general, increasing the concentration of an active ingredient can be expected to prolong its duration, but it also increases the risk of side effects. In consideration of safety, we decided on a concentration that enables application just twice per day. We also designed a preservative-free formulation in a dimple bottle that we developed in-house with an emphasis on ease of use for patients.

Offering New Value to More Patients

By offering a proactive treatment that reduces the frequency of itching when applied on a regular basis during periods of allergic reaction (before the onset of symptoms), we aim to improve patient quality of life.[2] In addition, we are conducting joint sales promotion activities with Mitsubishi Tanabe Pharma Corporation, which manufactures and sells oral allergy drugs, to deliver the product to more patients.

Message from an Ophthalmologist

Dr. Atsuki Fukushima

Director, Department of Ophthalmology, Tsukazaki Hospital
Former Chairman, Japanese Society of Ocular Allergology

Alesion had to be applied four times per day. Some patients find it very difficult to continue application four times a day during their busy lives. Consequently, many patients did not adhere to the directions for use though they were instructed to do so by their doctor. On the other hand, *Alesion LX* only needs to be applied twice per day, making it a more attractive prescription choice. Moreover, I am glad to hear that patients are happy with how well *Alesion LX* worked.

I expect Santen, as a company specialized in ophthalmology, to continue creating the superior products and services that patients are eagerly anticipating.

Members involved in the development of *Alesion LX*

[1] Nakagawa, Yayoi (2013). *Progress in Medicine*, 33, 2517 [2] Fukagawa, Kazumi et al. (2019). *The Allergy in Practice*, 39, 825

Development Status: Solving a Wide Range of Eye-Related Issues

In our core business area centered on glaucoma, we are developing many products that address medical needs that are unmet by existing products. We are also working in new disease areas where we expect substantial medium-to-long-term growth.

(Only projects under development for which our partner company has agreed to disclosure are listed.)

Pipeline Development Status (As of May 31, 2021)

		Clinical development plan in preparation[1]	Phase 1	Phase 2	Phase 3	Filed
Core Businesses	Glaucoma	**STN1014000** **STN1008507** *Tapros* with new instillation system **STN1011103** *Tapcom* with new instillation system		**STN1012600** (JP, U.S., EMEA)	**STN1011101** (CN) **STN1013900** (JP) **STN1013001** (EMEA, Asia)	**STN1011700** (U.S.) **STN1011702** (JP; *Eybelis* PFUD) **STN2000100** (JP, U.S., Asia)
	Dry eye		**STN1010905** (JP)		**STN1008903** (JP; *Diquas* new formulation) **STN1013500** (JP)	**STN1000501** (CN; *Cationorm*) **STN1007605/06/07** (EMEA; *Ikervis* PFMD)
	Allergies		**STN1011402** (JP; *Alesion* new formulation)			**STN1007603** (U.S., CN) **STN1007608** (EMEA; *Verkazia* PFMD)
	Uveitis of the posterior segment				**STN1010900** (U.S.)	
New Growth Areas	Myopia	**STN1013300**	**STN1012700** (CN; scheduled to start FY2021) **STN1013400** (JP; scheduled to start FY2021)	**STN1012700** (Asia)	**STN1012700** (P2/3, JP)	
	Presbyopia	**STN1013600**				
	Ptosis	**STN1013800**				
	Retinitis pigmentosa	**STN6000100**				

Joint Research for Drug Discovery	PeptiDream Inc., Tohoku University, Singapore Eye Research Institute, University College London, Massachusetts Eye and Ear, Ulster University
Number of Products Approved in FY 2020	**Glaucoma:** Japan: 1, Asia: 9, EMEA: 34, Americas: 1; **Dry eye:** Asia: 5, EMEA: 1; **Allergies:** Asia: 5, EMEA: 29
Number of Products Launched in FY 2020	**Glaucoma:** Asia: 3, EMEA: 19; **Dry eye:** Asia: 4, EMEA: 4; **Allergies:** Japan: 1, Asia: 5, EMEA: 32

For the latest development status of main projects in the pipeline, please see the Company's website.

https://www.santen.com/en/rd/pdf/pipeline.pdf

[1] Includes projects in the non-clinical stage, projects for which clinical trial protocols are being formulated, and projects for which applications are planned.