Santen
Imagine Your Happiness

Santen's Global R&D

2022

Santen's Global R&D Network

Addressing global unmet medical needs by networking around the world

CONTENTS

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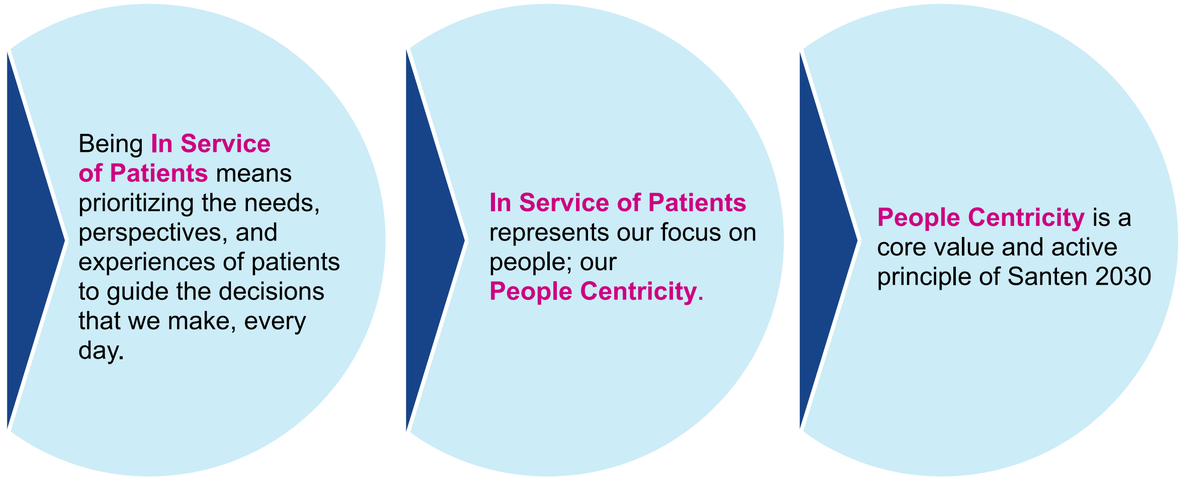
From Product Innovation to Patient Centric Innovation

In Service of Patients (ISOP), originated at R&D, is a global initiative that will enable Santen to work as a trusted partner for people with visual challenges so that together we will co-develop and provide innovative solutions that bring value and more happiness through best vision experience. Santen will improve people's lives and happiness by continuously learning and actively partnering with patients throughout every step of research and development to provide innovative solutions that enable the best vision experience that bring value to our patients.

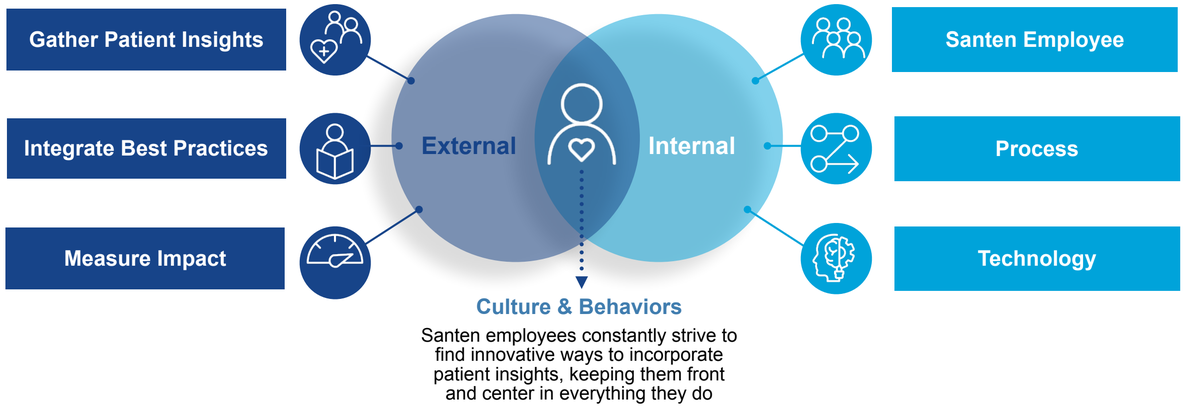
ISOP to Achieve Our Vision



From Product Innovation to Patient Centric Innovation

We have been nurturing the mindset of the entire organization at Santen to be further patient centric. We will continue to listen carefully to what patients need and gather patient's insights. We will look for opportunities to take the information learned from our patients and apply it to our R&D strategy and objectives. Our business policies, processes and practices will also reflect how Santen will operationalize the needs of the patient. Lastly, we are always seeking new technologies e.g., digital apps to engage with patients to learn more about how they are living with their eye disease so that better information, treatments and alternative solutions can be provided. All these efforts to keep patients front and center in everything we do at Santen helps us to further transform not only our organization, but also our behaviors to achieve a true patient centric culture.

Patient Centric Approach at Santen



Message from the Head of Ophthalmology Innovation Center

Santen is working to create products by considering patient needs, scientific understanding, and medical perspectives, while continually being people centric. In order to strategically create new products for target diseases, we, the Ophthalmic Innovation Center, collect patients' real voices and visualize the patient journey to accurately grasp the progression of symptoms, treatment methods, and patients' circumstances. This process enables us to clarify the points that should be addressed in each disease and the product concept, and then establish an appropriate disease strategy. In addition, our pipeline in the early stages of research is mapped on two axes: the number of patients with a given disease and the degree of potential therapeutic contribution to the patients. Through this mapping we identify areas in our pipeline to strengthen and focus on. Based on these strategies and priorities, we engage with universities, research institutes, pharmaceutical companies, and startup companies worldwide to strengthen our networks and collaborations. This approach is one of Santen's strengths, and leads to the development of new drug candidates and therapeutic technologies. We have created a collaborative research and development framework with academic institutions such as the Singapore Eye Research Institute (SERI) and University College of London (UCL). In addition, through our alliances we have been able to find drug candidates for myopia and Fuchs endothelial corneal dystrophy. We are also working toward the objective of increasing the probability of success in product creation, including by increasing the percentage of products that advance to the next stage of clinical trials. For diseases where it is difficult to establish clinical efficacy indicators, we perform biomarker exploration and translational research. In these and other ways, we will contribute to the creation of new products from a scientific standpoint and from the patient's perspective.

Reza Haque, MD, Ph.D.
Head of Ophthalmology Innovation Center

Message from the Head of Product Development Division

The Product Development Division's mission is to develop and deliver products that meet the needs of patients as quickly as possible, without compromising quality. In order to achieve this goal, we maintain the following three deliverables as priorities: 1) develop and implement a development strategy that reflects both patient insights and market needs; 2) continuously maximize product value through life cycle management; and 3) strengthen global scientific and operational excellence, supporting our ability to accomplish the development objectives we set.

In FY2021, we achieved several important pipeline milestones. In Japan, examples include filing for approval of STN1008903, a new formulation of Diquas® that reduces applications needed per day, and obtaining approval for Eybelis® as a single-dose eye drop with improved safety. In the U.S., we obtained approval for Verkazia®. At the same time, we filed for approval of Verkazia® in China as part of our regional expansion. We also refiled STN1011700 in the U.S. in May 2022. These achievements are the result of our efforts to create products that meet the needs of patients by closely communicating with them, as well as with regional health authorities and agencies, and strategically implementing development.

We have been able to minimize delays as well as accelerate the development plans for our late-stage clinical pipeline, despite the COVID-19 pandemic that has been ongoing since 2020. This success can be attributed to our constant efforts to implement new technologies to improve the execution of remote clinical trials, and the close communication between regional clinical development members and study sites. Digitalization is indispensable for the further pursuit of global operational excellence. These technologies are advancing day by day; hence, we are keeping our eyes on the development of new technologies worldwide and will quickly adopt those that are consistent with our clinical trial strategies. We will continue to contribute to Happiness with Vision for our patients by effectively developing a pipeline based on our strategy of continuously delivering products to patients that meet their true needs.

Peter Sallstig, MD, MBA
Chief Medical Officer
Head of Product Development Division

The Medium-Term Plan, ‘MTP2025’

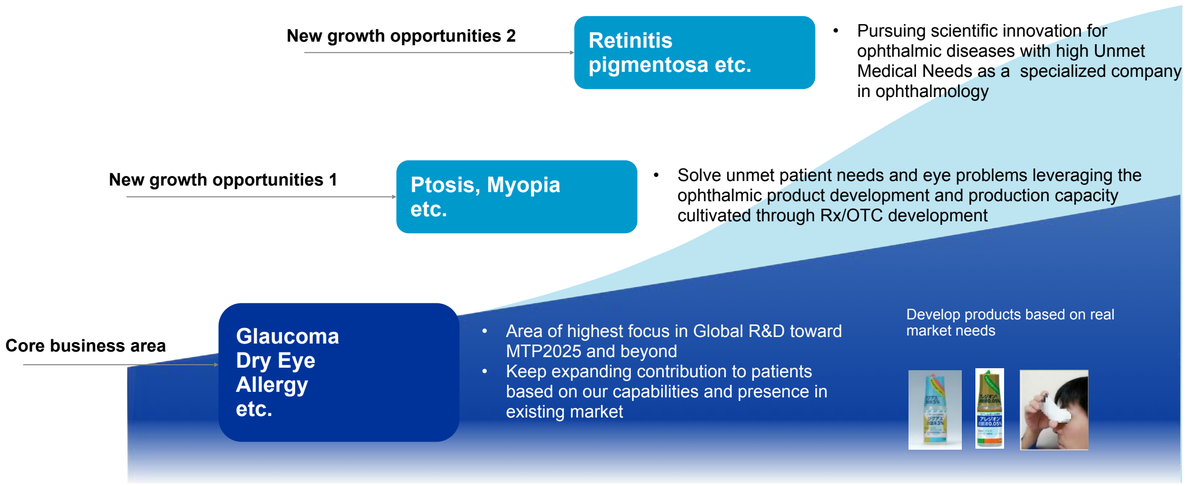
We would like to share our vision for R&D in achieving the MTP2025 as follows. We will use solid science and operational excellence, and these will be managed by a group with extensive experience in the industry. With over 130 years of experience since the founding of Santen, we have unparalleled insight into the needs of our patients. There is no place that understands our patients better than Santen.

We have focused on our core business areas of glaucoma, dry eye, and allergies, but there are several shifts. New treatment options are required due to demographic changes, increasing patient numbers, and an aging population. For example, with new lifestyle changes, Santen's R&D is ready to deliver a patient-oriented pipeline.

Looking at future growth areas such as ptosis and myopia, which affect hundreds of millions of children in China and throughout Asia, we have already begun to prepare for this social challenge and have product pipelines in place. When we look at more complex and challenging disease areas and their modalities such as cell therapy, our collaboration with jCyte demonstrates our commitment to this area. Our prioritized target disease in this area is retinitis pigmentosa, which is a serious disease that causes blindness. We will also consider applying it to other similar diseases in the future. To do so efficiently, we Santen has newly established Cell & Gene Therapy division in addition to the existing OIC and PDD.

We understand that patients are depending on these treatments. In order to most effectively meet patient expectations, we apply an unparalleled level of rigorous planning, analysis, and execution, leveraging technology to deliver virtual and hybrid clinical trials, as well as providing technology to patients. For example, we are experimenting with home care, ePROS (electronic Patient Outcome Reported), and devices to provide newer, better, and smarter products.

Focus Areas of Global R&D Toward MTP2025 and Beyond

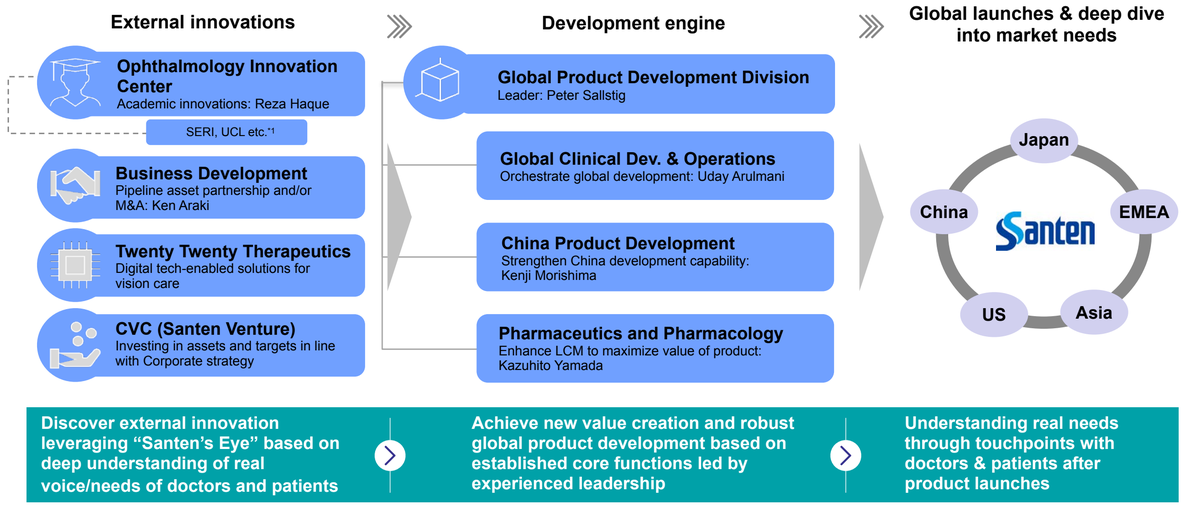


The Medium-Term Plan, ‘MTP2025’

Of course, behind all of this is our strategy. Our strength lies in our patient insights, physician insights, and the integration of these. In addition, we are also gaining insights through external collaboration with academia and business development activities. We have established partnerships with prominent academic hubs, such as Singapore Eye Research Institute and University College London, which have excellent technology and disease insights, especially when considering new treatment options and new disease areas with previously unknown pathological mechanisms. When we combine them with our patient insights, we believe we will have a significant pipeline. With our business development activities, we are also looking at and acquiring external assets that align with our strategic focus.

Today, all of these are brought together under the umbrella of Research and Development, which has a global reach, demonstrating superior execution of clinical trials, and supporting successful launches. As part of MTP2025, the Ophthalmology Innovation Center is working to establish the disease innovation strategy for each indication with the related functions. The Product Development Division is working to build a state-of-the-art development organization that will maximize the value of Santen‘s assets. We focus on further developing capabilities relating to methodology of modern clinical trials, digitalization, data integration, and formulation. This will aid in supporting the value proposition and maximizing the lifecycle of current and future assets.

Mechanism to Drive Value Creation for Patients



*1 SERI: Singapore Eye Research Institute, UCL: University College London, academic collaboration partners

Enrich Pipeline Based on Patient's Needs

Mission for Ophthalmology Innovation Center

There are three pillars at Ophthalmology Innovation Center. First is 'People'. We know all about ophthalmic disease and understand the potential of each disease from patient satisfaction and technical sufficiency. Second is 'Disease Strategy'. We established the disease strategy with a deep understanding of unmet medical needs from patients and caregivers. Third is 'Networking'. We evaluate and introduce the candidates and ophthalmic technology by making full use of external network that we are using it for.

Mission for Ophthalmology Innovation Center

To Respond to Potential Needs, Seek for New Technologies and Product Candidates Beyond the Industries

1) People

2) Disease Strategy

3) Network

Enrich Pipeline Based on Patient’s Needs

People

We collect the interest spectrum of the patient’s voice. We hear what the patients want and what they need. As a company-wide people-centered activity, we mobilized more than 350 employees from all regions and created a community of 100-plus active employees. We mobilized key technologies to capture direct patient insights from over 1,800 survey responses and over 100 patient interviews to enhance the understanding of patients' unmet needs and quality of life. We call it ISOP, which is dedicated to positively impacting patients.

1) People

We Collect >1,000 Patients’ Voices Globally in a Year

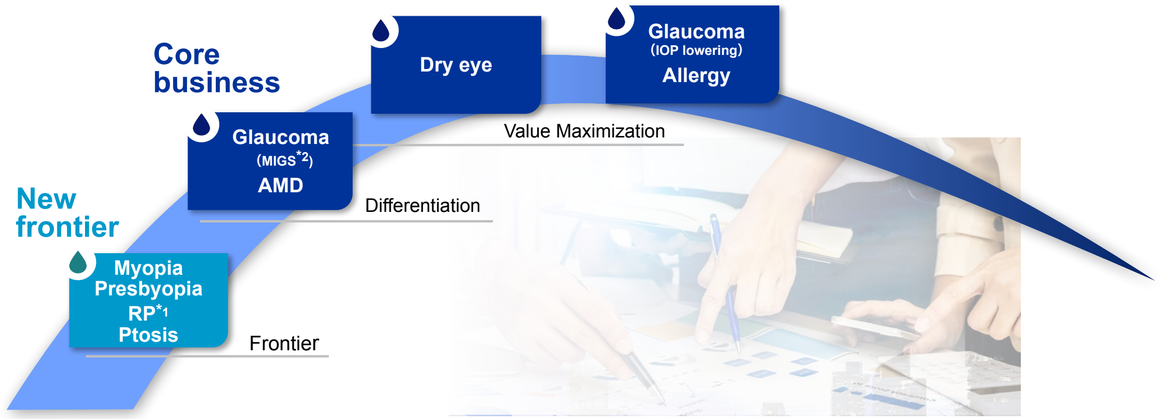
Enrich Pipeline Based on Patient's Needs

Disease Strategy

We identify the disease to be tackled from the disease needs and the maturity of the technologies and build a disease strategy. Our core business is glaucoma, allergy and dry eye and we have supplied some differentiated products to those markets in order to maximize their value. On the other hand, the new frontier is a more important disease group to achieve for Santen 2030. Those are myopia, presbyopia, retinitis pigmentosa (RP), and ptosis.

2) Disease Strategy

Identify Disease to be Tackled from Disease Needs and Levels of Technology and Build Disease Strategy



*1 Retinitis pigmentosa, *2 Micro Invasive Glaucoma Surgery

Enrich Pipeline Based on Patient's Needs

New Frontier, Myopia

Our approach is a comprehensive one by studying the patient journey, how a patient feels from early to late stage, and developing the best-in-class therapeutic options. In our plan for protection of the children from the blindness risk of myopia in conjunction with the low-concentration atropine product, the educate activities in collaboration with key opinion leaders are extremely important. We also need to educate people about how serious myopia will be and the necessity of treatment to avoid further progression of the disease. Our tasks are to accelerate the drug discoveries through collaboration with academia, and in turn to commercialize the low-concentration atropine product under development and a next-generation product.

2) Disease Strategy : New Frontier (Myopia)

Develop for Pre- and Post-"Treatment" Flow and After Launch of Low-does Atropine

Approach to "Protecting Children from Potential Risk of Blindness"

Enlightenment activities in collaboration with KOL	Collaborative study with academia to accelerate **elucidation of pathology** and **drug discovery**
Maximization and **commercialization** of low-dose **atropine**	Overcome the challenges of low-dose atropine with **next-generation drug**

Enrich Pipeline Based on Patient's Needs

New Frontier, Presbyopia

We are planning the new frontier by constructing a new evolution system. It is our approach for freeing the middle-aged and older people in the prime of their lives from the hassle of finding it hard to see. One important milestone is to explore the possible drugs that maintain lens elasticity in their eyes, while a lot of companies are working on the drugs with a pinhole effect. We successfully developed the non-clinical assay system. Now we are aiming for establishment of clinical indicators and early proof-of-concept verification.

2) Disease Strategy: New Frontier (Presbyopia)

Pioneer New Frontier from Construction of Evaluation System

Approach for "Freeing Middle-aged and Older People from Hassle of Being Invisible"

Explore the possible drugs that **maintain lens elasticity**	**Early POC* verification**
Development of non-clinical assay system	**Establishment of clinical indicators**

* Proof of Concept: to demonstrate the development concept. In development of a new drug, it means the efficacy/safety of the candidate is confirmed in humans.

Enrich Pipeline Based on Patient's Needs

Core Business, Glaucoma

We are developing robust new solutions to the challenge of glaucoma through worldwide collaboration, which will reduce our patients' treatment burden. We progressed the collaboration with external research institutions to find solutions other than lowering intraocular pressure (IOP).

IOP lowering is one of the many clinical endpoints for glaucoma. Many patients need two or three kinds of glaucoma eye drops to control their IOP. Some of these patients can hardly instill multi eye drops into their eyes due to burden of instillations, unclear vision with glaucoma, and so on. One of the countermeasures to that issue is a surgical operation and the other is the optic nerve protection, which is a very touch approach. Many researchers in the world have been trying to find a suitable candidate compound with the effective mechanism of action. There are two reasons for the tough approach. One is the difficulty to conduct the clinical trials and the other is difficulty to find the effective candidate with margin of safety. It takes a long time, over 3 years, to finish single clinical study. On the other hand, we have to have the candidate with safety in addition with sufficient efficacy. In order to solve such issues, we proceed to collaborate with external research laboratories.

2) Disease Strategy: Core Business (Glaucoma)

Tackling Solutions other than IOP Lowering Agents through Collaboration with

Approach to "Protecting Lifetime Vision by Minimizing the Burden of Eye Drops"

Correspondence to surgical operation
MIGS

Optic nerve protection
to control visual disturbance

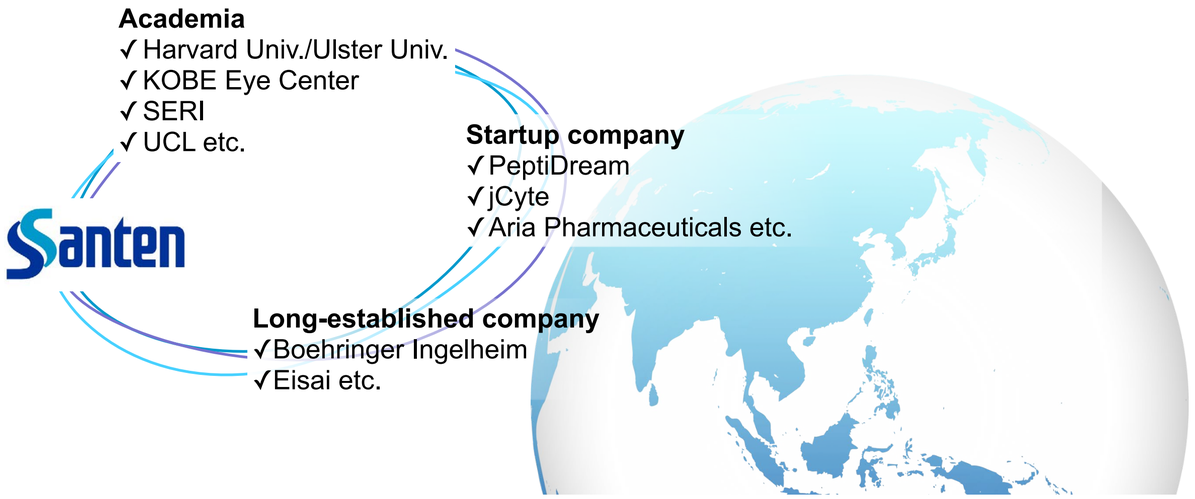
Enrich Pipeline Based on Patient's Needs

Network

We evaluated hundreds of new technologies, therapeutics, and modalities a year. We are confident that we have many opportunities to evaluate because we believe that we have trust. We work with various companies such as start-up companies such as PeptiDream and long-established companies such as Boehringer Ingelheim. As for academia, we partner with the leading ophthalmic centers of excellence and the most prestigious research institutes.

3) Network

Santen Evaluates Approximately 100 of New Technologies and Modalities per Year

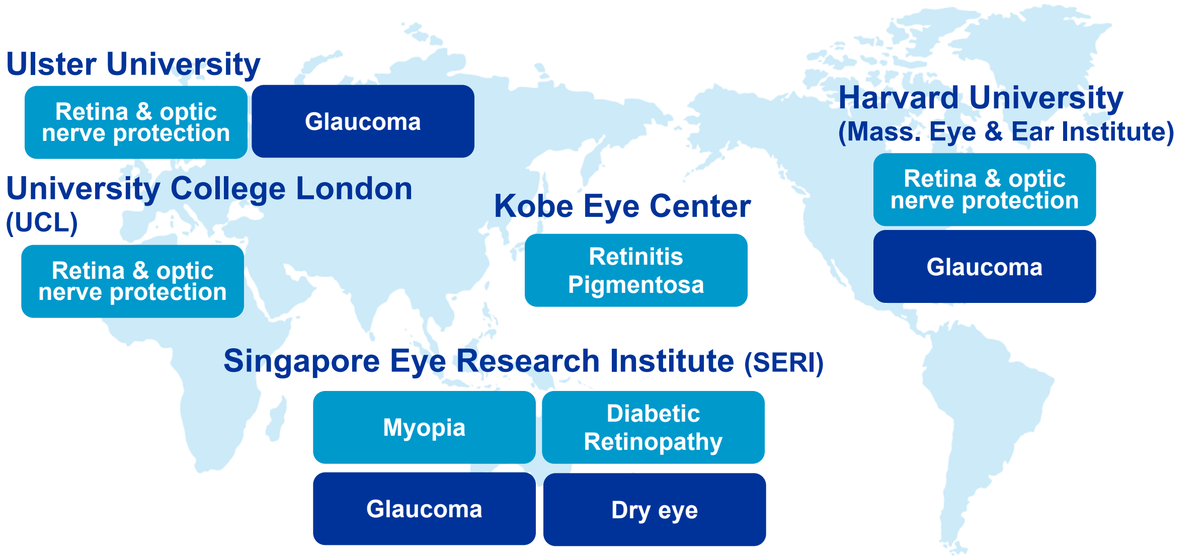


Enrich Pipeline Based on Patient's Needs

We lead ophthalmic medicine with prestigious research institutes around the world. In Japan, we collaborate with Kobe Eye Center with regards to RP. In Asia, we have collaborated with Singapore Eye Research Institute (SERI) since 2017. SERI is not only first ranked in Asia but is very well known in the world. In the US, we collaborated with Harvard University, as we did with Ulster University in the UK to identify, characterize, and develop novel and unique treatments for glaucoma, targeting a component of the immune system for retina and optic nerve restoration. We also collaborated with the University College of London in 2016 and globally focused on ophthalmic research and education. We have adopted a framework to work together in ophthalmic research and to translate the research into therapies that can meet unmet medical needs, such as in retina and optical protection.

3) Network

Innovate Ophthalmology with Prestigious Research Institutes Around the World



Pursue Added Value by Steadily Promoting Product Development

Mission for Product Development Division

We are focused on moving projects as quickly as possible from proof of concept to where we have made an initial understanding of the mechanism of action until commercialization. Our understanding of the mechanism then translates itself into a development strategy that takes into consideration, not only the patient voices, but also the market needs. The market needs can be the regulatory environment or the commercial environment, but we believe that all that combined will actually solidify the development strategy. We are also focused on continuing to improve our capabilities with regards to how to maximize the life cycle management of our products. And now, we are looking to further differentiate ourselves. Moving away from just trying to improve the bottle, we also start looking into other disease areas that we have not looked into before. We try to bring out here the maximum for the sake of our patients. None of this is possible unless we have a very strong commitment to operational excellence, where we basically are setting the stage in order for us to be successful from a day-to-day operational perspective, but also from a strategic perspective.

Mission for Product Development Division

Maximize Product Values of POC-acquired Pipelines, Ensure Commercialize Them

1) Development strategy

2) Maximized product value

3) Global operation excellence

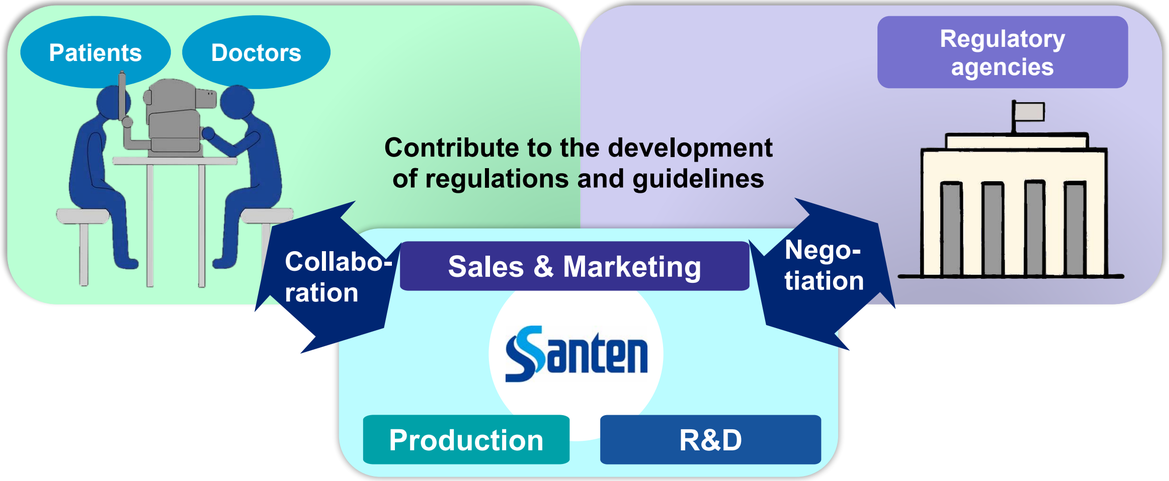
Pursue Added Value by Steadily Promoting Product Development

Development Strategy

We believe that at the forefront of everything has to be the patients. We want to make sure that when the patient actually comes and speaks to the physician, they get what they need, and that the physician is able to deliver on this for them. We take pride in communication. Particularly in our long-term history that we have been collaborating with physicians within and, more recently, outside of Japan, we understand our patients' needs. Through our initiatives ‘ISOP’, we are getting those insights and making sure that we can implement them in better clinical trials. We are also paying a lot of attention to collaborations with health authorities and are making sure that we are able to engage with them, particularly when it comes to new technologies, which is really something at the forefront for us. All of this comes together internally by having a very coherent understanding with our commercial organization and our manufacturing organization so that when we are putting our products out to the market, the patients and the physicians can get the products.

1) Development Strategy

Build an Integrated Development System in Collaboration with Ophthalmology-related Medical Professionals and Regulatory Agencies



Pursue Added Value by Steadily Promoting Product Development

Maximized Product Value

What we have been good at is taking formulations and moving them from their original state to a more optimal, logical, improved ophthalmic drugs. There are several steps that you can go through in trying to improve products when you are trying to get them to the patients.
It is often believed that benzalkonium chloride (BAK), used as a preservative, actually adds to the efficacy. On the other hand, it is considered not to be optimal because it is associated with unexpected responses, allergy and hyperemia. One of the things that we then did, was to reduce the BAK concentration. Now patients and physicians prefer BAK-free ophthalmic solutions. This is one of the capabilities we have. The last step is to give patients a preservative-free ophthalmic solution, which further enhances the safety. This is something that we have become very good at doing and you will see also in our product line.

2) Maximized Product Value

Santen's Unparalleled Formulation – Continuous Product Improvement for Further Safety

Pursue Added Value by Steadily Promoting Product Development

As another example for our capabilities on this is shown in left figure. we can see the improved formulation which are highly convenient for the patients. We understood that patients actually might consider dosing 4 or 6 times a day to be burdensome, at least for some patients. Therefore, what we really wanted to achieve was reducing the frequency per day of the instillation.

2) Maximized Product Value

Santen's Unparalleled Formulation – Improve Medication Adherence

Pursue Added Value by Steadily Promoting Product Development

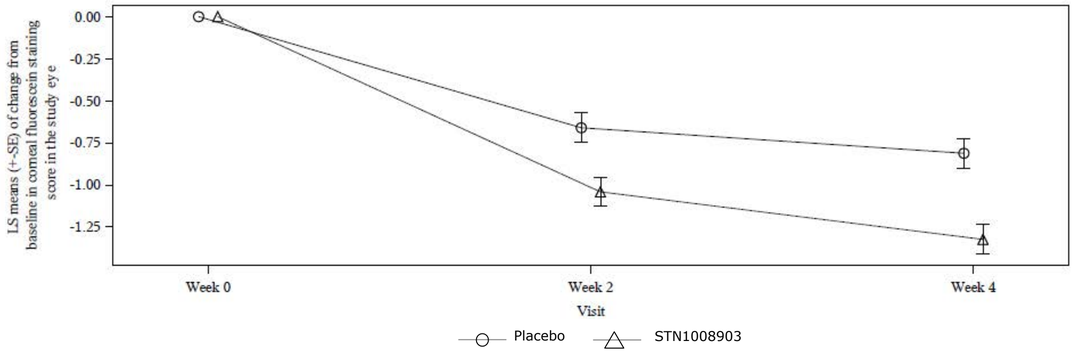
Maximized Product Value, Dry Eye

The figure on the left below is the clinical result of STN1008903, Diquas® new formulation, from the phase 3 study in Japan. The dosing frequency of the current Diquas® eye drop is 6 times a day. As we can see, even though we reduced the dosing of Diquas® new formulation to 3 times a day, we could achieve the primary endpoint, the improvement of corneal epithelial damage. The figure on the right shows the burden of dosing several times a day. As part of our patient-centric philosophy, we could confirm that the dry eye patients feel 6 times of instillation a day is more burdensome than 3 times. We are looking forward to bringing the new, improved Diquas® eye drop to the patients in Japan soon.

2) Product Value Maximization (Dry Eye)

STN1008903, *Diquas* New Formulation, maintained the Improved effect on Corneal epithelial damages. Submitted NDA on Aug 30th 2021 in Japan

Phase 3 (Japan)



2) Product Value Maximization (Dry Eye)

Reduced Patient's Burden due to the Reduced Dosing Frequency. Improved Markedly Adherence of Instillation.

Phase 3b (Japan)

Survey after study completion

Which was more burdensome?

3 times daily STN1008903	7/59 (**11.9%**)
6 times daily *Diquas*	52/59 (**88.1%**)

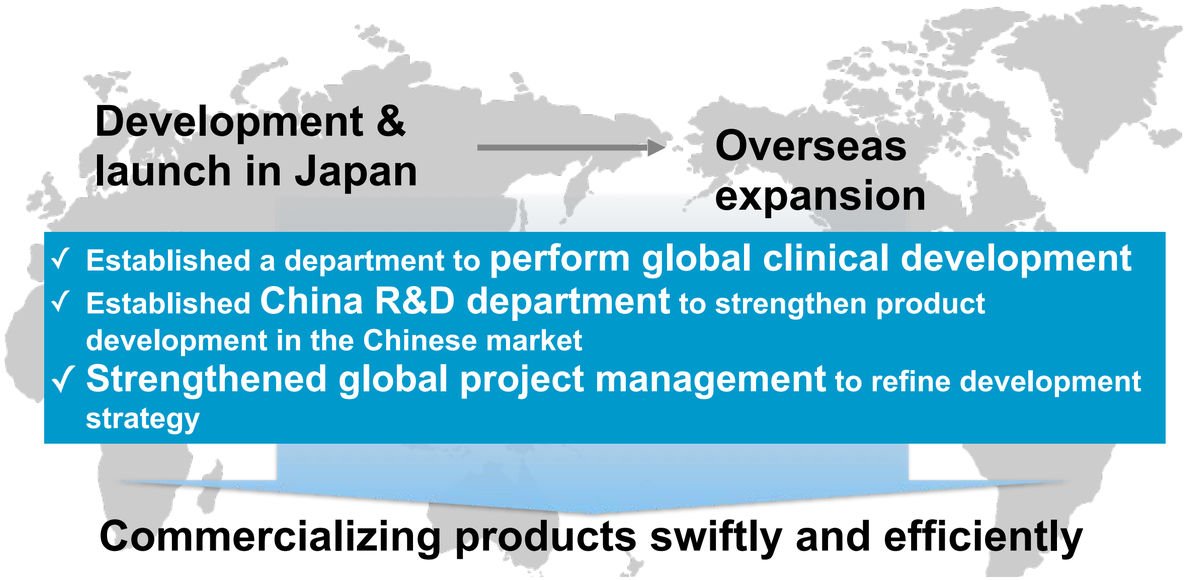
Pursue Added Value by Steadily Promoting Product Development

Global Operation Excellence

There are three areas that we have been able to create in the last two years and that we believe are actually going to be able to move us forward. First, as part of our strategy, we are moving away from just focusing on development and launching in Japan and expanding overseas, by establishing the Global Clinical Development & Operations Department, that is skilled in everything and can bring us to that next stage. Second, the China R&D Department was also established. In order for us to be able to deliver on our promises to become a global organization, these are the right steps for us to take. We recognize that the US and China are at the forefront of everything we need to achieve in the next decade. Therefore, we need to make sure that we have talents that actually can deliver on these promises. Third, overseeing all of this, we have to have a global project management function, who are ready to drive the development and the strategy of the development from early research all the way to commercialization. We believe that all of the factors mentioned will actually get us to a much faster and much more efficient product development.

3) Global Operation Excellence

Organization that can Execute Global Development from Early Research to Commercialization of a Project



Column

Cell & Gene Therapy

Santen Cell & Gene was established in 2022 as an independent global business segment. We aspire to change the lives of patients with ophthalmology diseases around the globe by delivering transformative solutions and redefining the healthcare delivery ecosystem. In doing this, we want to support the transformation of the company by building new capabilities and creating a sustainable and scalable platform for future therapies. The Cell & Gene team exhibits significant diversity, with numerous years of experience spanning across ophthalmology, retina and rare disease in key regions. Our platform covers the entire value chain from development to commercialization. While focused on the execution of existing opportunities, we also aim to become a partner of choice by leveraging Santen's existing footprint and infrastructure and combining this with our dedicated focus on ophthalmic cell and gene therapies. In 2020, we in-licensed the rights for development and commercialization of our first asset, an investigational human retinal progenitor cell therapy with the potential to address a considerable unmet need in retinitis pigmentosa (RP), an inherited retinal disease that often leads to blindness by the age of 40. Cell and gene therapies have the potential to address high unmet medical needs in ophthalmology and can ultimately bring us closer to achieving our Santen 2030 of reducing the loss of social and economic opportunities for people living with eye conditions.

Marianthi Psaha, MBA
Global Head, Cell & Gene Business Segment

Pipeline Update: Current Status of Pipelines, as of May 2022

	Code	Indication	Region	status
Omidenepag isopropyl **EYBELIS**	**STN1011700**	Glaucoma / ocular hypertension	US	Received CRL from FDA in November 2021 Plan: May 2022, re-filing
			Japan	Launched
			Asia	Launched
Sepetaprost	**STN1012600**	Glaucoma / ocular hypertension	US	P2 (met primary endpoint)
			Japan	P2b (dose finding study completed) Plan: FY2022 P3 start
			Europe	P2 (exploratory study) Plan: FY2022 P2 completion
Glaucoma implant device **PRESERFLO MicroShunt**	**STN2000100**	Glaucoma	Japan	Approved in February 2022 Plan: FY2022 soft launch
			Europe	Launched
			Asia	Approved Plan: FY2022 launch
Netarsudil dimesylate **Rhopressa**	**STN1013900** AR-13324	Glaucoma / ocular hypertension	Japan	P3 Plan: FY2023 P3 completion
			Asia	Filed in March 2022 Plan: FY2023 approval
Netarsudil mesylate /latanoprost (combination) **Rocklatan/Roclanda**	**STN1014000** PG324	Glaucoma / ocular hypertension	Japan	Plan: FY2022 filing

	Code	Indication	Region	Status
Atropine sulfate	**STN1012700**	Myopia	Japan	P2/3 Plan: FY2023 P2/3 completion
			China	P1 (confirmed safety and tolerability) Plan: FY2022 P3 start
			Asia	P2 (met primary endpoint)
	STN1012701 SYD-101	Myopia	Europe	P3 (conducted by Sydnexis Inc.) Plan: FY2024 P3 completion
AFDX0250BS	**STN1013400**	Myopia	Japan	P1 (confirmed safety and tolerability)
Ursodeoxycholic acid	**STN1013600**	Presbyopia	US	Plan: FY2022 P2a start
			Japan	P1 (confirmed safety and tolerability)
Oxymetazoline hydrochloride	**STN1013800** RVL-1201	Ptosis	Japan	Plan: FY2022 P3 start
			Asia	Plan: FY2022 Filing
jCell	**STN6000100**	Retinitis pigmentosa	-	P2 safety study (US, conducted by jCyte, Plan to complete in FY2022). Considering P3 plan

Pipeline Update: Current Status of Pipelines, as of May 2022

	Code	Indication	Region	Status
Epinastine HCl (Ophthalmic Cream)	**STN1011402**	Allergic conjunctivitis	Japan	Started P3 in February 2022 Plan: FY2022 P3 completion
Ciclosporin **Verkazia**	**STN1007603**	Vernal Keratoconjunc-tivitis	US	Launched in May 2022
			China	Approved in April 2022 Plan: FY2022 launch
Diquafosol sodium (long-lasting) **Diquas**	**STN1008903**	Dry eye	Japan	Filed Plan: FY2022 Approval
Sirolimus (eye drop)	**STN1010904**	Fuchs endothelial corneal dystrophy	US France India	P1 completion (Japan) Plan: FY2022 P2a start
Sirolimus (eye drop)	**STN1010905**	Meibomian gland dysfunction	US	P2a Plan: FY2022 P2a completion
Tafluprost / timolol maleate (combination) **TAPCOM/TAPTIQOM**	**STN1011101**	Glaucoma / ocular hypertension	China	P3 Plan: FY2023 P3 completion
STN1013001 DE-130A **Catioprost**	**STN1013001**	Glaucoma / ocular hypertension	Europe	P3 (met primary endpoint) Plan: FY2022 filing
			Asia	P3 (met primary endpoint)

Link: the latest information of pipeline (Japanese)
Link: the latest information of pipeline (English)

Pipeline Update: Clinical Study Results of Main Projects

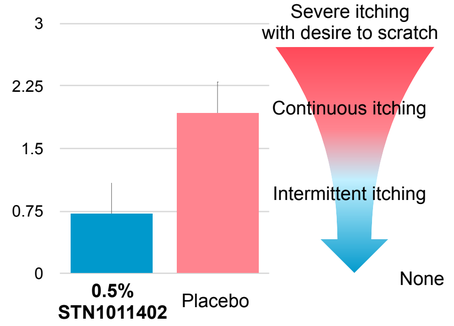
STN1011402

The figure to the right shows the results of the POC study for STN1011402 in Japan, which will be the basis for the Phase 3 study to be conducted. The same subject received the study drug epinastine to one eye and placebo to the other, and 25 hours after administration, an antigen was administered to induce allergy. We compared and observed the inhibitory effects in both eyes. This slide shows graph and table on the important endpoints of itching and conjunctival hyperemia. There was a statistically significant reduction in itching and conjunctival hyperemia compared to placebo. The improvement in this score is from itchy to not itchy, and the degree of hyperemia has improved from many blood vessels being hyperemic to few or none. In a different study, compared to previous data, we expect it to be as effective as the existing Alesion® ophthalmic solution even after 24 hours of administration.

STN1011402: Initiation of Phase 3 Study Preparation of Epinastine HCl New Formulation

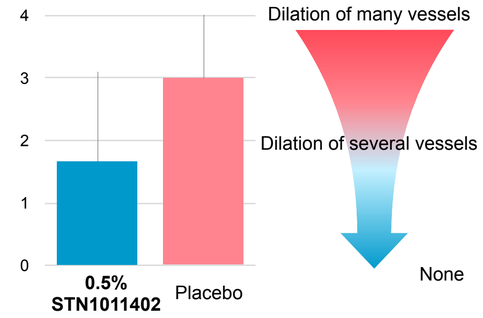
POC study showed statistically significant difference between once a day STN1011402 and placebo

Efficacy on ocular itching after 25 hours



Treatment group (n)	Mean (SD)	Diff (STN1011402 VS placebo)	P value
0.5% STN1011402 (n=8)	0.71 (0.375)	-1.21 (0.396)	P=0.0001
Placebo (n=8)	1.92 (0.154)		

Efficacy on conjunctival hyperemia after 25 hours



Treatment group (n)	Mean (SD)	Diff (STN1011402 VS placebo)	P value
0.5% STN1011402 (n=8)	1.67 (1.425)	-1.33 (1.234)	P=0.0185
Placebo (n=8)	3.00 (0.713)		

Pipeline Update: Clinical Study Results of Main Projects

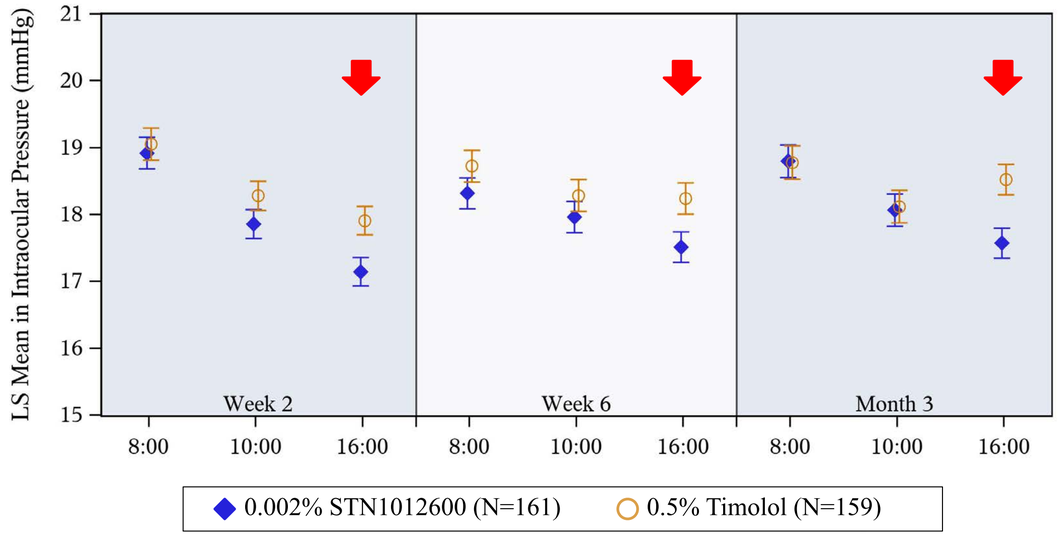
STN1012600

The figure to the left shows the result of the US Phase 2 study for STN1012600, which is being developed as an intraocular pressure lowering agent. The primary endpoint of the study was non-inferiority of STN1012600 once-daily ophthalmic solution to timolol twice-daily ophthalmic solution, and STN1012600 has been proven to be statistically non-inferior to timolol at all time points. Especially at the 16:00 point on the measurement day, there was a statistically significant difference, with the value lower than that of timolol (shown in arrows). This indicates the stable intraocular pressure lowering effect of the drug over a long period of time. Based on these results, we will consider the plan for Phase 3 studies.

STN1012600: Result of Additional Phase 2 Study in US

Achieved primary endpoint in the timolol-controlled study

Intraocular Pressure: Least Square Mean (+/- Standard Error) by Analysis Visit and Timepoint (Study Eye)



- Statistical non-inferiority of STN1012600 to timolol was confirmed at all points observed
- Intraocular pressure with STN1012600 at 16:00 of each observed day was statistically lower than that with timolol

Pipeline Update: Clinical Study Results of Main Projects

STN1013001

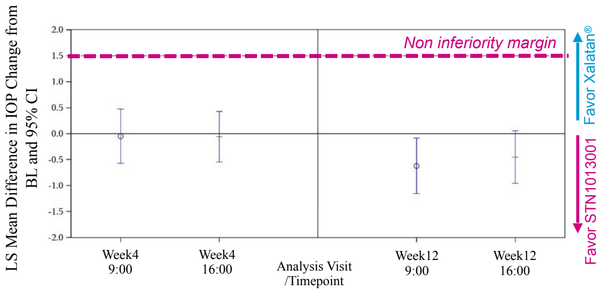
We has applied the formulation technology of emulsified eye drops used in Cationorm®, Ikervis®, and Verkazia® products to develop this product, STN1013001, with the goal of reducing intraocular pressure and improving ocular surface disease. These are the results of the Phase 3 study in EU and Asian country. In terms of intraocular pressure, the compound has been proven to be statistically non-inferior to the control drug Xalatan® at all time points. On the other hand, the key secondary endpoint of corneal fluorescein staining showed superiority over the control drug Xalatan® at the 12-week point (shown in arrows). This reflects one of the useful characteristics of this drug. Corneal fluorescein staining is used to stain the cornea to determine the degree of damage and is also used in dry eye testing to determine the degree of damage to the corneal epithelium. These results are in line with our expectations. We will proceed with the European application for STN1013001 in 2022 fiscal year.

STN1013001: Top line results of P3 study in Europe and Asia

Achieved primary endpoint on IOP (non-inferiority vs *Xalatan*®) , Superiority vs *Xalatan*® on key secondary endpoint (CFS)

Primary endpoint

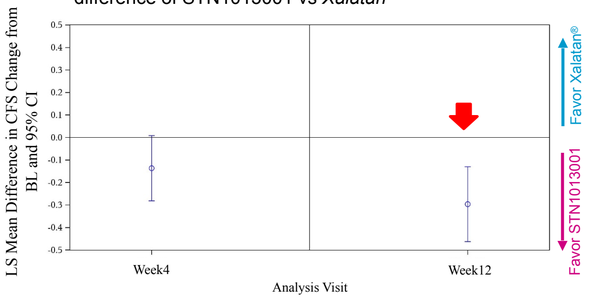
IOP LS mean treatment difference of STN1013001 vs *Xalatan*®



- **STN1013001 statistically non-inferior to *Xalatan*® at all time points**
- Superiority of STN1013001 showed at 9am (peak) at Week12 vs *Xalatan*®

Key efficacy secondary endpoint

CFS (corneal fluorescein staining) LS Mean treatment difference of STN1013001 vs *Xalatan*®



- **Superiority of STN1013001 was demonstrated vs *Xalatan*® at Week12 with a 0.3 CFS difference on modified Oxford Scale**

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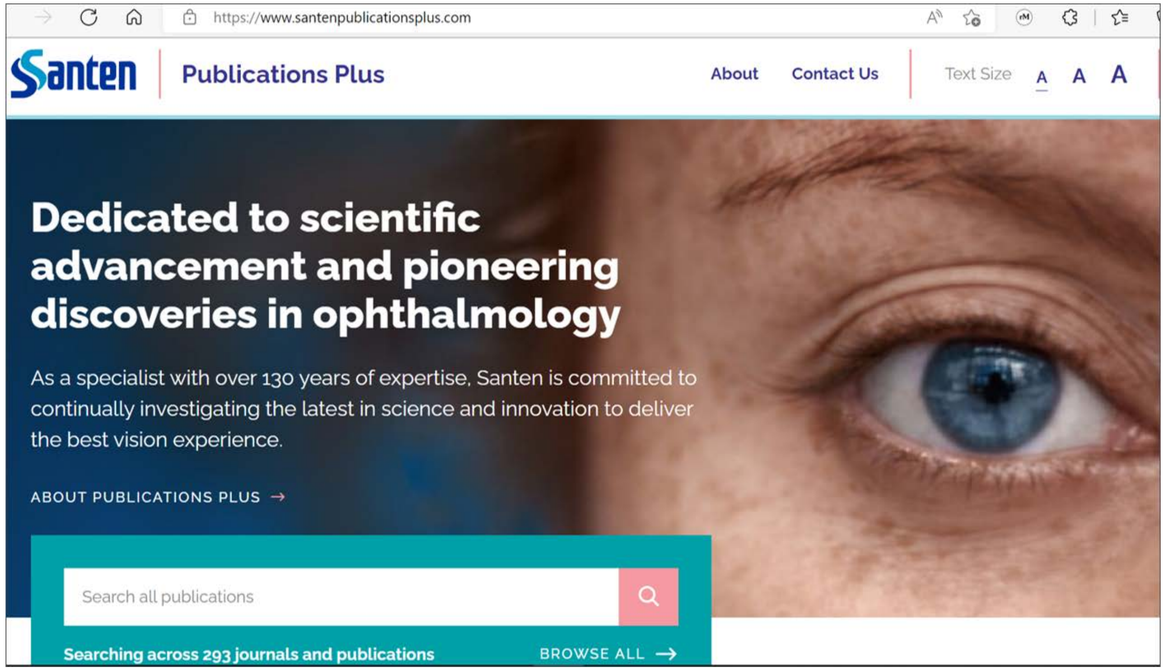
Collaboration is key
Santen's unwavering commitment to ophthalmology has endured for over 130 years. Our mission is to deliver the best vision experience and we understand that collaboration is key to achieving this goal. Santen strives to combine our ophthalmic expertise with external partners' excellence in technology and academia to provide quality products and services that deliver the best vision experience. Visit our Grants Portal to find out how you could collaborate with us!

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