Become A Social Innovator

Product Development Meeting
Santen Pharmaceutical Co., Ltd.
October 7, 2021

Santen
Imagine Your Happiness

Taniuchi: Ladies and gentlemen, good morning. I am Taniuchi, CEO of Santen. Thank you very much for taking time out of your busy schedules to participate in the webinar. I take this opportunity to express my hearty thanks again for your interest in Santen and our daily business.

Today is R&D day, a debriefing on product development. Before getting into the actual product development discussion, I just would like to give you the overall picture and the overall strategy from Santen's 2030 perspective.

And the leader in each area will succeed me and explain their own field.

CORE PRINCIPLE and WORLD VISION

CORE PRINCIPLE

天機に参与する

Tenki ni sanyo suru

"Exploring the secrets and mechanisms of nature in order to contribute to people's health" *

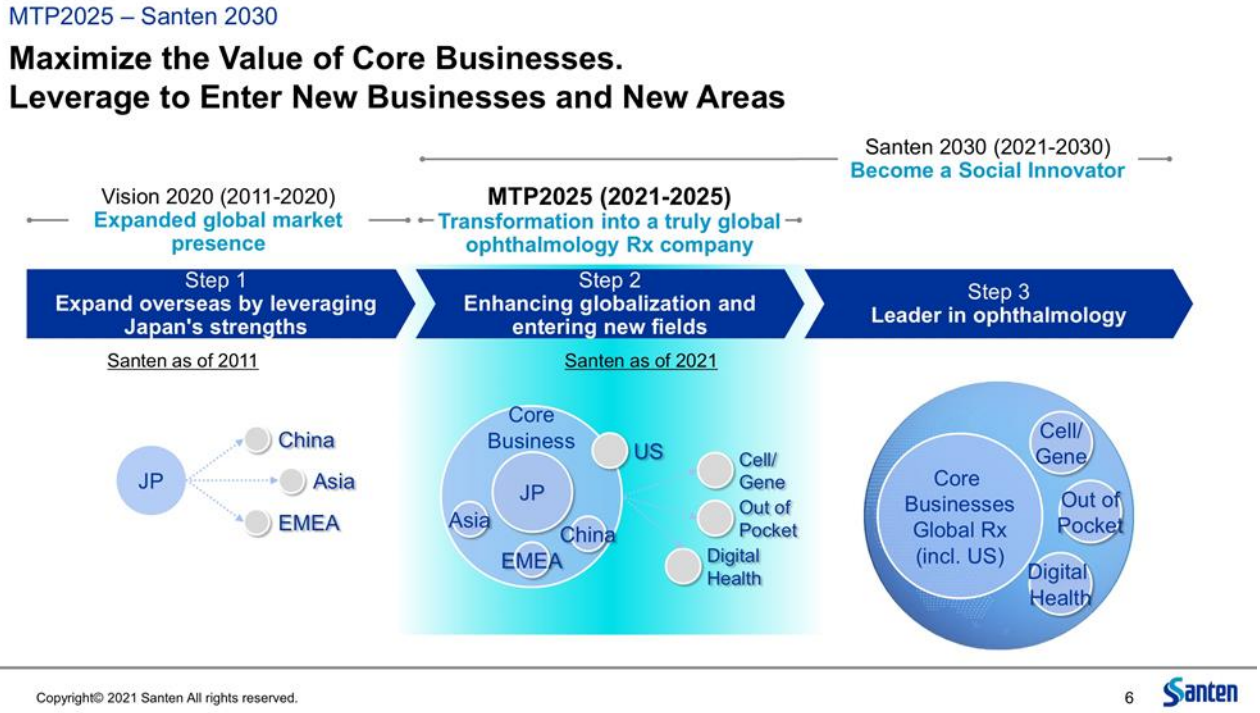
WORLD VISION

Happiness with Vision

The Happiest Life for every individual, through the Best Vision Experience

* Santen's original interpretation of a passage from the Zhongyong (The Doctrine of the Mean) by Confucius.

Please turn to page 5. This is customary, but I will show our basic mission, which is "tenki ni sanyo suru," the ideal world vision—Happiness with Vision. In order to attain this vision through our contribution to the society, we would like to develop ourselves in our daily business. Of course, the product development activity is one of the most important activities in doing so.

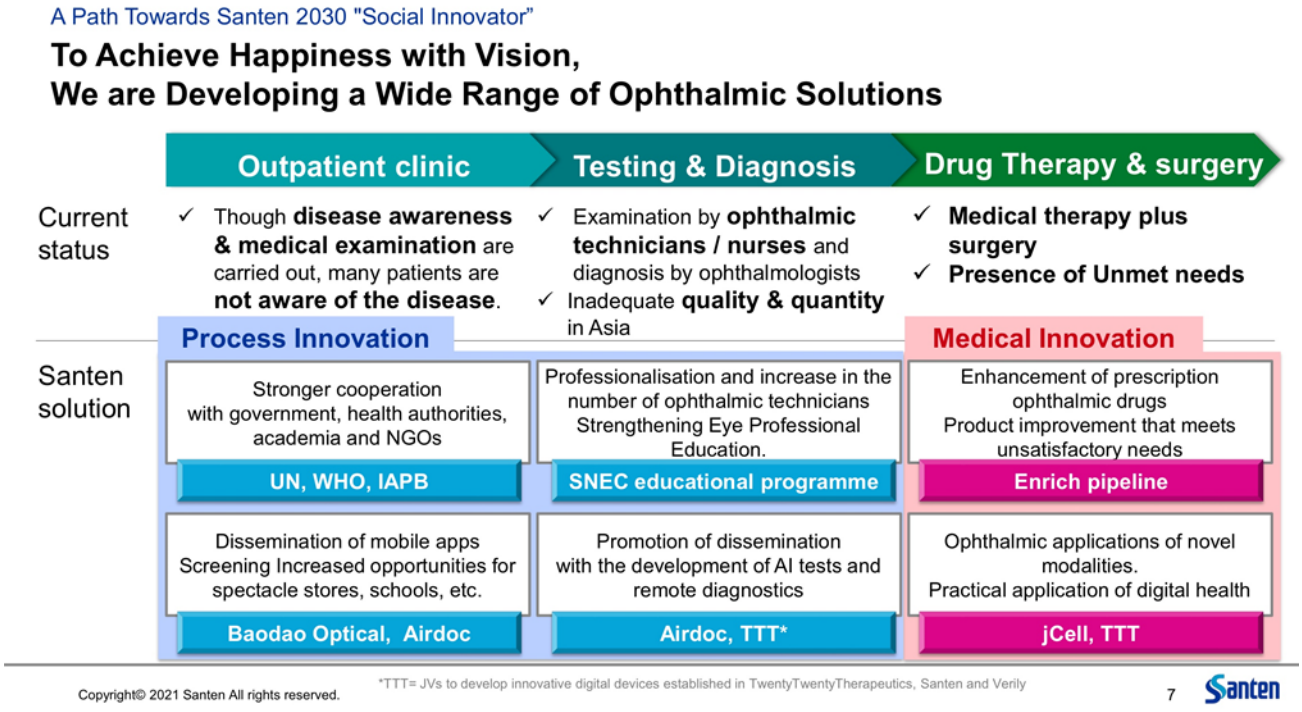


Please turn to page 6. In the period of MTP2025, based on the strengths we have accumulated so far, we would like to further advance and expand the business geographically and in the business area, as well to innovate ourselves to become a truly global ophthalmology Rx company.

To attain the Santen 2030 goal of becoming a Social Innovator, we aim to achieve the reduction of the social and economic loss of the people, which is coming from eye disease and problems. How are we able to achieve that? I would like to share with you the story now.

In Santen, we would like to innovate the experience of the patient and of ophthalmologic medicine as well in our growth. We are facing the challenges of ophthalmologic medicine, listening to the voice of the patient, and providing the solution to the issues.

So, our theme today is product development. Before we get into that, how we are planning to innovate the ophthalmologic as a whole? Let me start off on that point.



On page 7, you see ophthalmology until treatment. There are a number of challenges and issues.

From the left, the outpatient clinic and testing diagnosis. In those stages, there are various issues for treatment as well. There are many unmet medical needs.

So, by unlocking each of them one by one, Santen has tried to become a Social Innovator. We are promoting process innovation as well as medical innovation. I would like to show you some recent developments.

I'll start with the outpatient clinic. As you know, at the UN and WHO, there has been a resolution arrived at and issued regarding the health of the eye. That is the latest development.

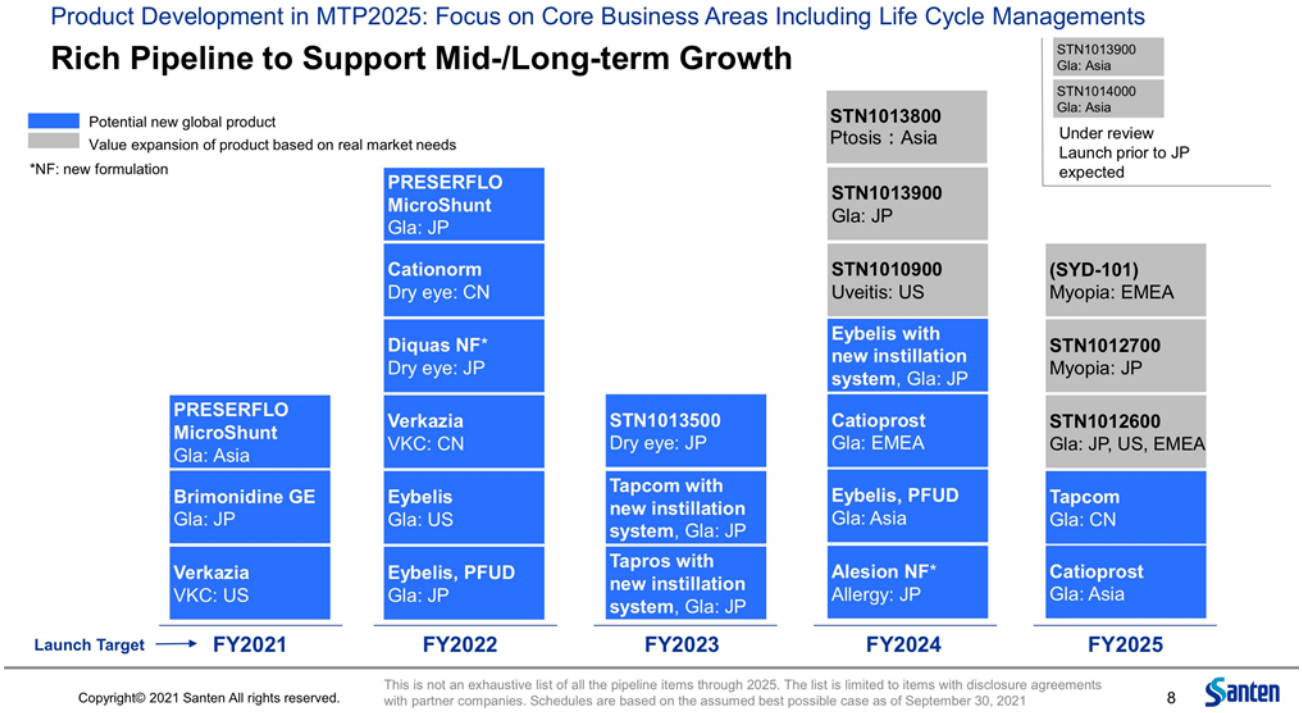
On the basis of this, we have joined with the government and the companies of the world to promote an enlightenment activity. For example, in China, together with Baodao Optical, the largest spectacle store in China, we promote screening. The others include also the alliance with Plano to promote its application designed for children with myopia, which are already integrated in Southeast Asia.

Now, coming to the testing and diagnosis, this has been released last week. We joined with the Singapore National Eye Center. Mainly in Southeast Asia, we increased the number of ophthalmic technicians. That's the new effort.

As we have informed you already, for testing and diagnosis, we need lots of the ophthalmic staff technicians to go for an eyesight test and visual field test. However, looking at China and Asia, they are insufficient qualitatively and quantitatively. So in our program, we established the ophthalmic technician as a new medical professional qualification to increase the capacity of the medicine and increase the throughput of the treatment, and a similar effort is considered in China as well.

From a DX perspective, for example, through the Airdoc AI diagnosis equipment and Twenty Twenty Therapeutics, the joint venture with Verily in the States, we will provide the digital products to promote process innovation.

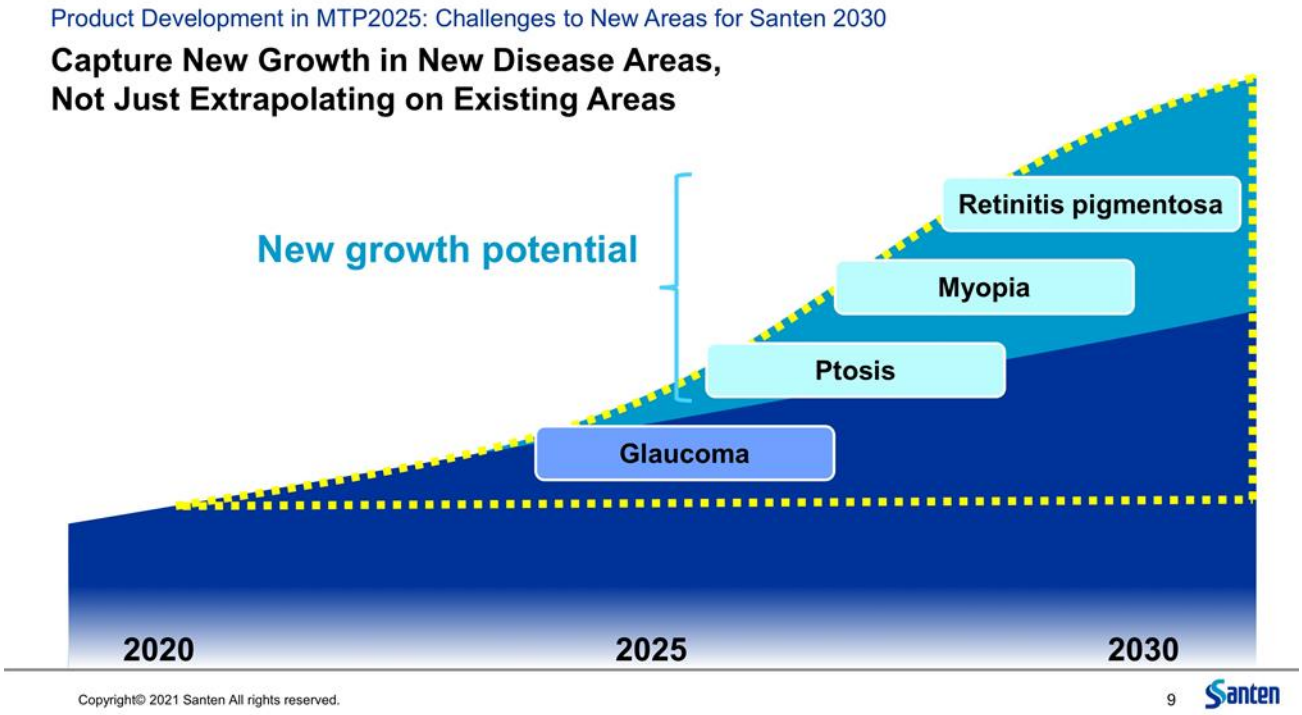
The last theme today is medical innovation in the treatment stage. How will we see the ophthalmic medical future trend and try to capture unmet needs? What solution are we offering? How should the demand from the expanding market of the process innovation be taken in? Those are the areas we are going to discuss today.



This is not an exhaustive list of all the pipeline items through 2025. The list is limited to items with disclosure agreements with partner companies. Schedules are based on the assumed best possible case as of September 30, 2021

Now please refer to page 8. So, this is looking at the pipeline, which will be driving the growth in the mid- to long term.

Now from looking at this from a product development point of view, in the mid- term plan period, we will be working to further reinforce the core business toward MTP2025. At the same time, we plan to treat in the new area, which will be the main growth base into the future.



Please go to slide number 9. This is the growth driver and time access. As I said, we will be ensuring there is continued revenue stream from the core business, and we will also be nurturing growth drivers for the next 5 years as well.

These are the 3 disease areas, which we believe will be the focus. We will continue to attempt to grow in new disease areas by leaps and bounds.

R&D Productivity Formula

Implement Strategic Product Development Based on Productivity

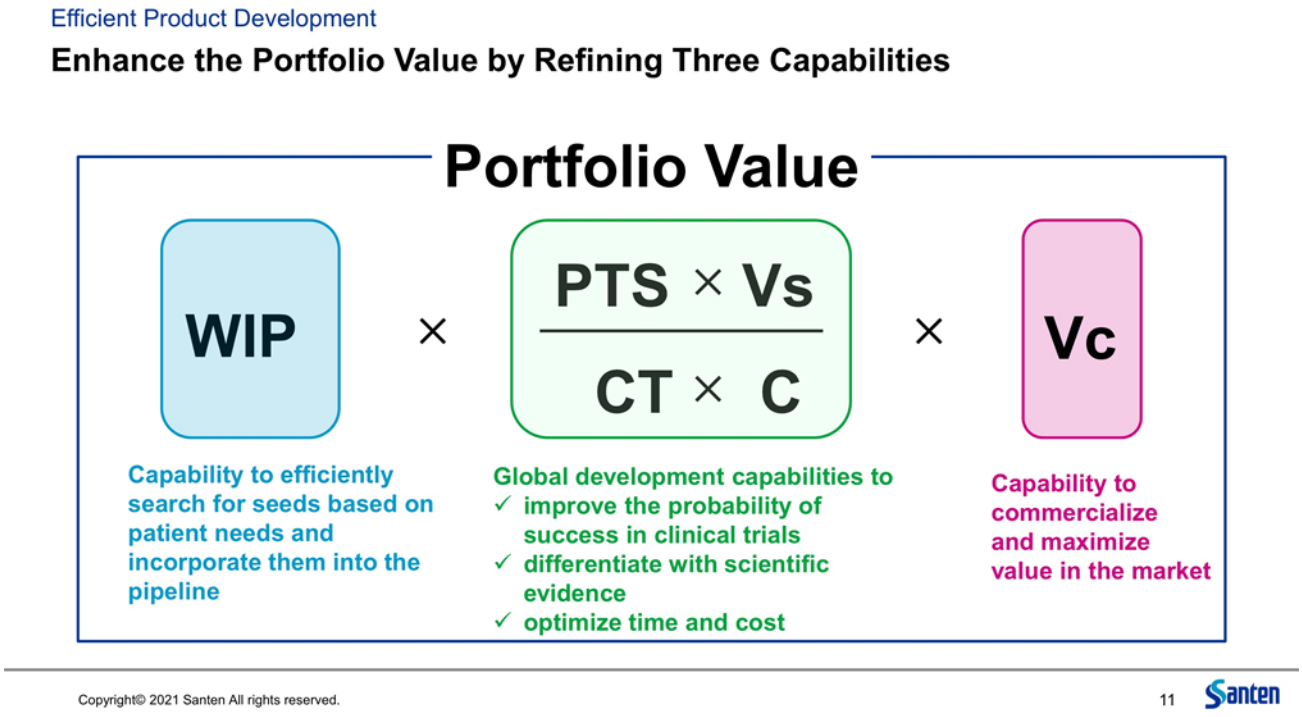
$$\text{R\&D productivity} \propto \frac{\text{WIP} \times \text{PTS} \times \text{V}}{\text{CT} \times \text{C}}$$

WIP（work in process） PTS（probability of technical success）
V（value） CT（cycle time） C（cost）

Paul, S. M. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nature Rev. Drug Discov.* 9, 203–214 (2010).

Now let me talk about the relationship between productivity and strategic product development, how we analyze our challenges, and how we try to meet improvements.

Please go to slide 10. Active R&D for future growth is an important area of investment for any pharmaceutical company. Typically, a formula like this is used for the productivity of R&D. So, with this, we are working to enhance the value portfolio and also productivity of R&D.



Please go to page 11. Number 1, on the far left, shows the patient needs.

Based on patient needs, we will explore efficiently for the seeds to capture them in our pipeline. From clinical doctors in academia and from patients and their family, we will be collecting information from them. And we will be working together with R&D and Business Development to tap into the network worldwide to capture relevant information and solutions in the pipeline to increase the number of works in process.

Today, Reza Haque will be explaining more about this to you later.

Number 2 is in the middle. This is about probability of success in clinical trials and also the realization of added value and optimization of development time and cost. This is about global development capabilities.

Over a long period of time, we have been accumulating our development experience and expertise in the area of ophthalmology. We have the partnerships that we can access, including doctors, academia, and authorities. We will continue to steadily pursue effective and efficient clinical trials so that we can bring out the best possible contribution value of our development from a science point of view. Peter Sallstig will be talking to you more about this.

Third is about commercialization after approval and launch. This is the capability to maximize value on the market. We're expanding across the globe in more than 60 countries. We are a specialty company in the area of ophthalmology. Because of that, we are able to carry on with our marketing activities and formulate strategy by product character, or like we have done with dry eye, we are also able to create and propose new value and shape new markets to maximize product value. On this, Sakai, who is responsible for portfolio strategy, will be speaking to you.

In the field of ophthalmology, I would say that Santen is the only company with all of these capabilities. That said, I understand that currently, some of you are concerned about our current situation. I also understand that there are some harsh evaluation voices coming from the market. We will take those voices to heart sincerely, and we will address them.

We will be working together. All of the 4,000-plus members will be joining forces. So how we will succeed in product development, and how we realize our growth? Today, we will explain to you those topics by giving you some specific examples.

Thank you once again for taking the time to join us this morning.

I'd like to hand things over to Reza, please.

Haque: Hello, everyone. Good morning. My name is Reza Haque. I'm the Head of the Ophthalmic Innovation Center (OIC) at Santen. Thank you very much for giving me the opportunity to talk about what we are doing here for the patient and for the society.

Today, what I'm going to talk to you about is our pipeline and how we enrich our pipeline. As for the mission of Ophthalmic Innovation Center, we consider that people are the center of all our activities at Santen, as well as responding to potential need and seeking technologies and product candidates beyond the industries.

There are three pillars at OIC that we work on. Number One is people. We know all about ophthalmic disease and understand the potential of each disease from patient satisfaction and technical sufficiency.

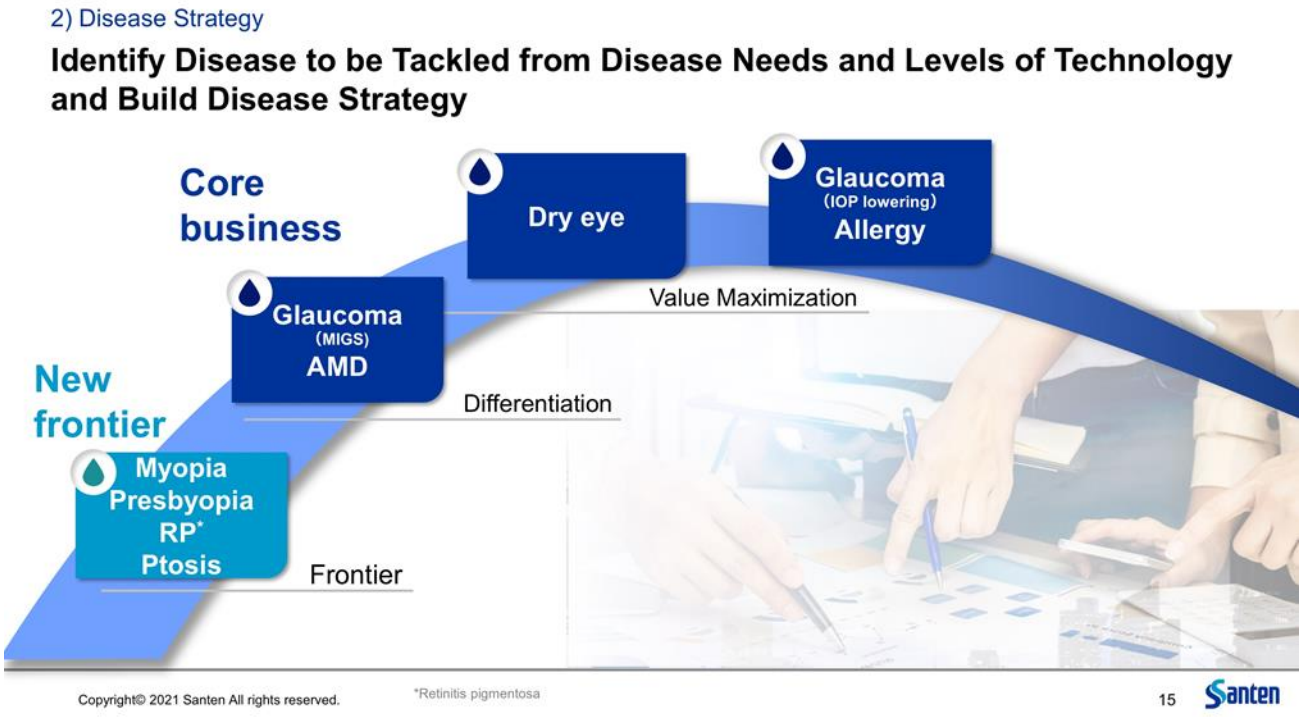
The second pillar is disease strategy. We established the disease strategy with a deep understanding of unmet medical need from the patient and the caregivers.

And the third is the networking. We evaluate and introduce the candidates and ophthalmic technology by making full use of external network that we're using it for. I will introduce the current status for such 3 perspectives.

Next slide, please. This is slide number 14. We listen to and collect the interest spectrum of the patient's voice. We hear what the patient wants 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 call it in-service of patient, which is dedicated to positively impacting patients.

In service of patients (ISOP), it's company-wide; it's called people-centered activity. 2,000-plus direct patients mobilize key technologies to capture direct patient insights from 1,800-plus survey responses and 100-plus patient interviews to enhance the understanding of patients' unmet needs and quality of life.



Next slide, please. This is slide number 15. Let's talk about the disease. We identify the disease to be tackled from the disease need and the maturity of the technologies, and build a disease strategy.

If you see the curve from left to right, on the top, you can see that the diseases like glaucoma, allergies, and dry eye are our core businesses, and we already supplied some products to the market, and we are under value maximization and differentiation.

On the other hand, the new frontiers in the left side, those are a more important disease group to achieve for Santen 2030. And those are myopia, retinitis pigmentosa, presbyopia, and ptosis. I will go through a few of them in detail in the later slides.

2) Disease Strategy

Development with Target Image for Each Disease

		Santen's target
New frontier	Myopia	Protect children from potential risk of blindness
	Presbyopia	Free middle-aged and older people from the hassle of being invisible
	Retinitis pigmentosa	Not giving up hope for treating the disease even though it is a genetic disease
	Ptosis	Better vision opens up more life (including minor patients not requiring surgery)

		Santen's target	Products for sale	Pipeline*
Core business	Glaucoma	Protect lifetime vision by minimizing the burden of eye drops	13	8
	Dry eye	Support "seeing" by eliminating discomfort caused by dry-eye	3	3
	Allergy	Make everyday life free from itchy and painful eyes	4	1

* Expected to launch by FY2025

Next slide, please; slide number 16. Before going into any disease strategy, we try to develop the image of core business and new frontier diseases.

As for new frontier, the goal for myopia is to protect children from potential risk of blindness. We always think that children with myopia wear the glass, but there is a huge risk of blindness if the condition is progressing very quickly. My fear is the parents tend to be less concerned for the children.

On the other hand, a presbyopia is the condition seen among middle age and older populations that what we call the aging condition. But goals, what is our goal? The goal is to relieve the discomfort from blurred vision that many middle-aged people in their most productive years may experience.

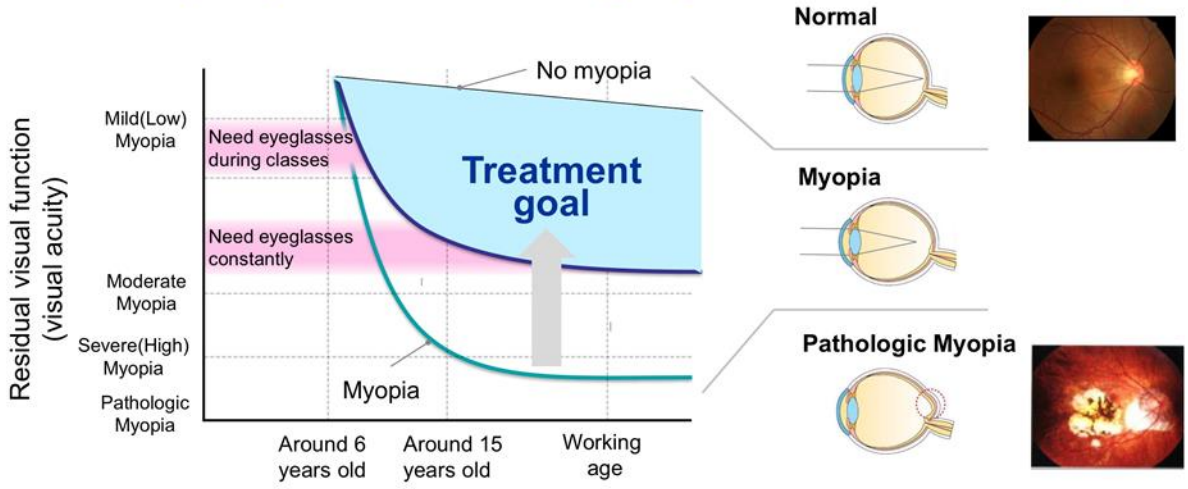
Let's talk about retinitis pigmentosa. This is a hereditary disease and has a high risk of blindness. Our goal is not giving up hope for treating the disease even though this is genetic disease.

Finally, for ptosis, the goal is to help patients live their lives to the fullest by widening the people's visibility. As for our core business, we have picked up. For these diseases, we have many drugs or products in the market worldwide, but further improvement is based on each goal.

2) Disease Strategy: New Frontier (Myopia)

Important to Prevent Progression of Myopia at School Age

One in 3 people in 2020 and **1 in 2 people** in 2050 will suffer from **myopia**[*1]



*1 *Ophthalmol.* 123, 1036-1042, 2016

Next slide, please; slide number 17. Let's talk about myopia a little bit. In the world right now, 1 in 3 people in 2020 are suffering from myopia. The rate will be 1 in 2 people in 2050. In 2010, there were 1.9 billion people suffering from myopia using glasses or contact lenses. In 2050, it will be double. Half of the population in the world will suffer from myopia. It's an epidemic.

It's epidemic in the South Asian countries. Almost 80% of the school-aged kids in Asian countries will suffer from myopia. It can be mild or moderate myopia, but it is the potential risk of pathological myopia blindness at adulthood that we would like to prevent.

2) Disease Strategy: New Frontier (Myopia)

Develop for Pre-and Post- "Treatment" Flow and After Launch of Low-dose 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**

Next slide, please;

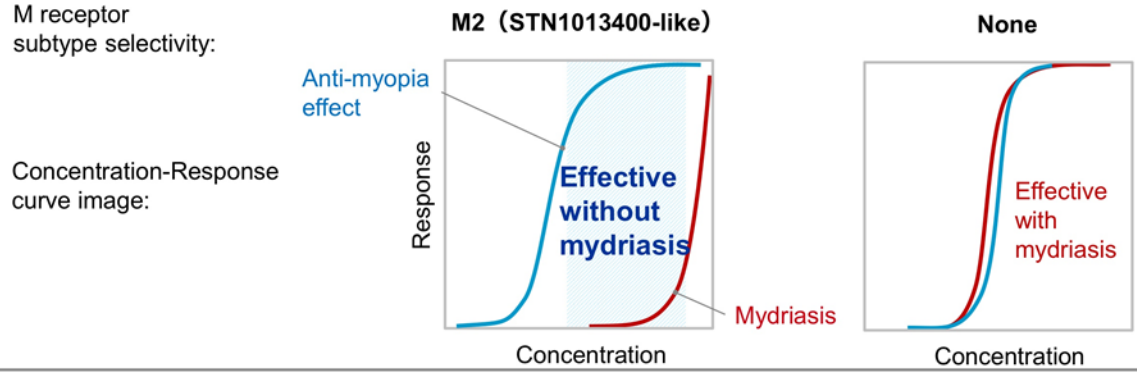
Slide 18. Our approach to myopia involves deploying a comprehensive approach to myopia by studying the patient journey, how a patient feels from early to late stage, and developing the best-in-class therapeutic options. Of course, in conjunction with the low concentration of atropine.

We want to present our approaches for protection of the children from the blindness risk of myopia before and after treatment. The enlightenment activities in collaboration and key opinion leaders in the myopia field are so important. We need to enlighten people about how serious myopia will be and the necessity of treating it so it will not progress further. Our tasks are to accelerate decision of pathology and drug discoveries through collaboration with academia, and in turn to commercialize low dose atropine under development.

2) Disease Strategy: New Frontier (Myopia)

Pursuing an Anti-myopia Agent not Causing Mydriasis-induced Glare by Increased M2 Selectivity

Receptor Subtype	M1	M2	M3	M4	M5
Anti-Myopia*1	No	YES	YES	No	No
Mydriasis*2	No	No	YES	No	No



*1 *Dis Model Mech.* 2013 Sep;6(5):1146-58. *2 *J Neurosci.* 2002 Dec 15;22(24):10627-32.

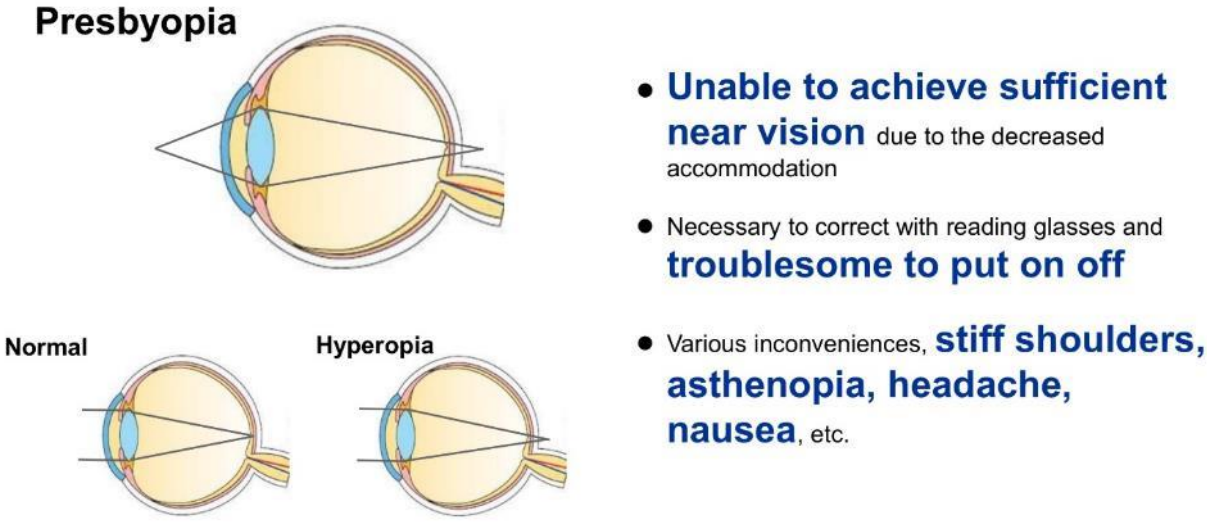
Next slide, please; slide number 19. How do you select a compound? I'll give you an example involving myopia. This is called muscarinic receptors. They are M1, M2, M3 receptors. There are 2 functions of the receptor: 1 is anti-myopia, and the other 1 is the mydriasis. So, we have to select the 1 that is not causing mydriasis but has the anti-myopia function.

If we use atropine, and the patient complains that there's too much glare to their eyes because the eye is already dilated, the pupil is dilated. They're getting more light from the sun. Our hope is that we'll get something that has more anti-myopia to prevent less mydriasis, like M2 receptors.

And we have a specific M2 receptor, which is STN1013400, which is in the Phase I stage right now. If you see the graph here, it shows the same thing that I mentioned—that if you can widen the window between anti-myopia and mydriases, it's preferable.

2) Disease Strategy: New Frontier (Presbyopia)

A Disease that Affects Everyone and Significantly Deteriorates Quality of Life



Next slide, please; slide 20. Presbyopia, a disease that affects everyone and negatively impacts the quality of life.

As I mentioned earlier, this is part of the aging process. Everyone will get this one. But this disease affects the most middle-aged and older people and significantly deteriorates quality of life.

As people continue to age, they cannot achieve sufficient near vision due to decreased accommodation. They need reading glasses when reading books and looking at mobile phones or suffer from symptoms like stiff shoulders, asthenopia, headache, and nausea.

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**

*POC (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.

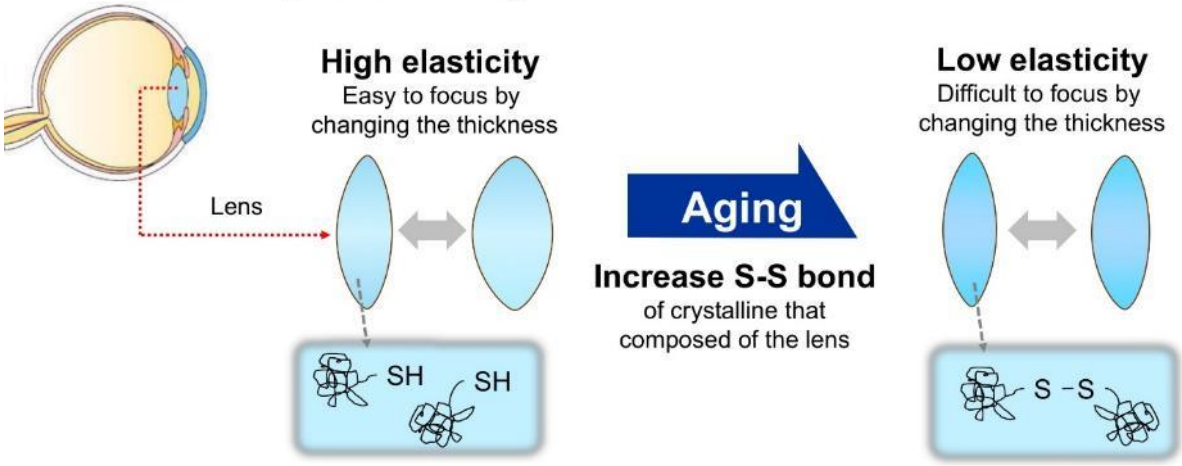
Next slide, please; slide 21. We are planning the new frontier by constructing a new evolution system.

This shows 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. Our goal is to explore the possible drugs that maintain lens elasticity. A lot of companies are working on a pinhole effect, which is just a temporary efficacy. It does not last long.

So, we achieved the development of a non-clinical assay system. We are aiming for establishment of clinical indicators and early proof-of-concept verification.

2) Disease Strategy: New Frontier (Presbyopia)

Challenge from the Most Promising Mechanism at Present. Candidate Compounds Already Identified



Development candidate have been selected based on the elasticity of the lens

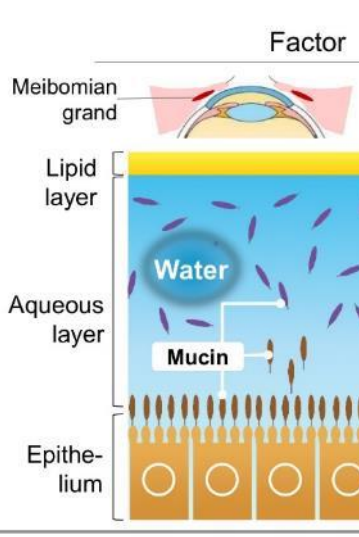
Next slide, please; slide 22. We have determined the most critical mechanism that underlies presbyopia.

Candidate compounds have been identified to reach a solution. We want to present the most promising mechanism. We are present for treating presbyopia. It is reported to restore lens elasticity lost by aging and not to change the lens thickness very much.

If you look at the slide, due to the aging, we increase in the S-S bond of the crystalline to lower elasticity of the lens. We are developing the selected candidate compound, which could modulate the lens elasticity, and we will conduct a proof-of-concept study shortly.

2)Disease Strategy: Core Business (Dry eye)

Develop and Sell Products Tailored to Factors Lead Innovation Through Further Expansion



Factor	Pharmacological effect	Santen's product	Pipeline
Meibomian grand dysfunction	**Meibum secretion**	—	**STN1010905 Others**
Lipid layer abnormality	**Water retention/ lipid layer protection**	***Hyalein***	
Aqueous layer abnormality	**Mucin secretion/ tear production**	***Diquas***	
Cornea epithelia damage	**Anti-inflammation**	***Ikervis***	

Next slide, please; slide number 23. Develop and sell products by segmentation of the dry eye, which expands our reach. Innovation will drive further market expansion. As for dry eye, it's 1 of our core businesses. We are the global leader in dry eye in terms of developing and selling products, if you consider the fact that there are 6 products in the world, and we have 3 compounds in our hand.

As we approach dry eye, there are 3 targets. 1 is the lipid layer, aqueous layer, and epithelium, which we need to consider if we're choosing the right product.

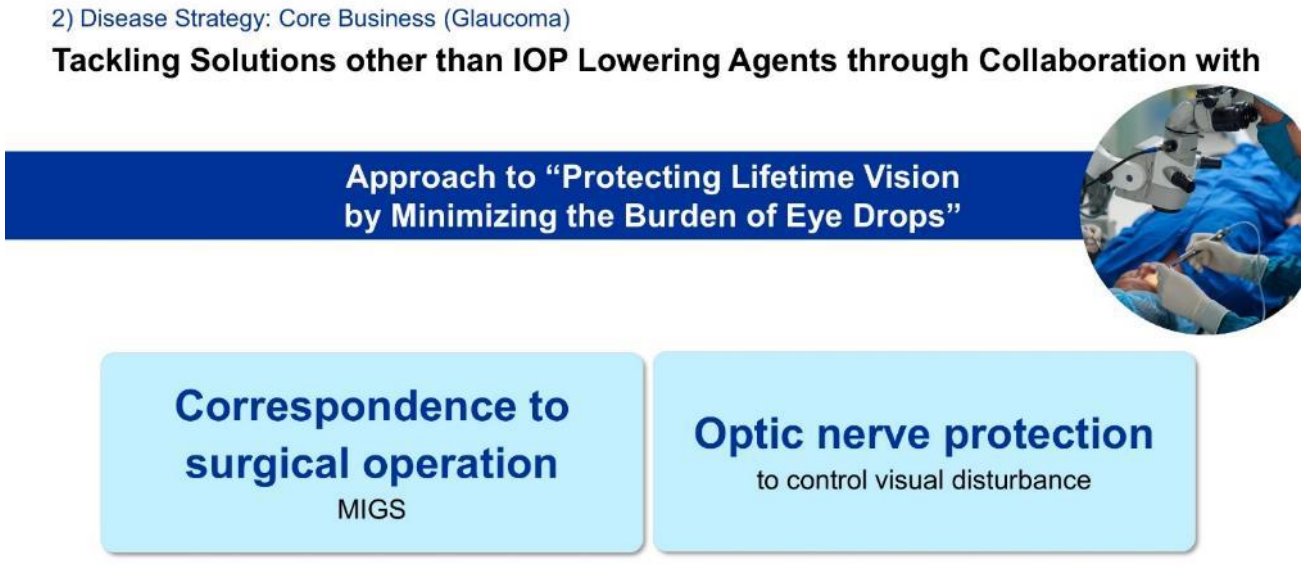
And the approach for the 3 targets is water retention. Can we prevent the evaporation of the lipid layer and mucin secretion?

And also lastly, the anti-inflammatory drugs.

On the other hand, the meibomian gland dysfunction (MGD) due to meibomian gland obstacles into the lead is a different disease from dry eye. However, the signs and symptoms are similar to dry eye. MGD is also 1 of our target diseases in the front of eye.

The regulatory requirement in each region is different, so it is hard to conduct a clinical trial globally, and the manner of treatment each region is different, such as over-the-counter deployed as self-medication.

In the US, both the signs and symptoms are regulated by the government in the same clinical study. In the EU and US, the demand of the self-medication is getting high.



Next slide, please; slide 24. We are innovating a robust new solution to the challenge of glaucoma through worldwide collaboration, which will lower our patients' treatment burden. We are also a global leader in glaucoma medication.

As for glaucoma, we progressed the collaboration with external laboratories to find a solution other than intraocular pressure lowering. Intraocular pressure lowering is 1 of the endpoints for glaucoma, but it's not all.

There are a lot of IOP-lowering agents, but even if many patients use 2 or 3 kinds of drugs or eye drops to avoid official impairment, some of these patients hardly install multi-eye drops. These are some reasons, for example, that patients with glaucoma hardly see the effects of dry-eye drops.

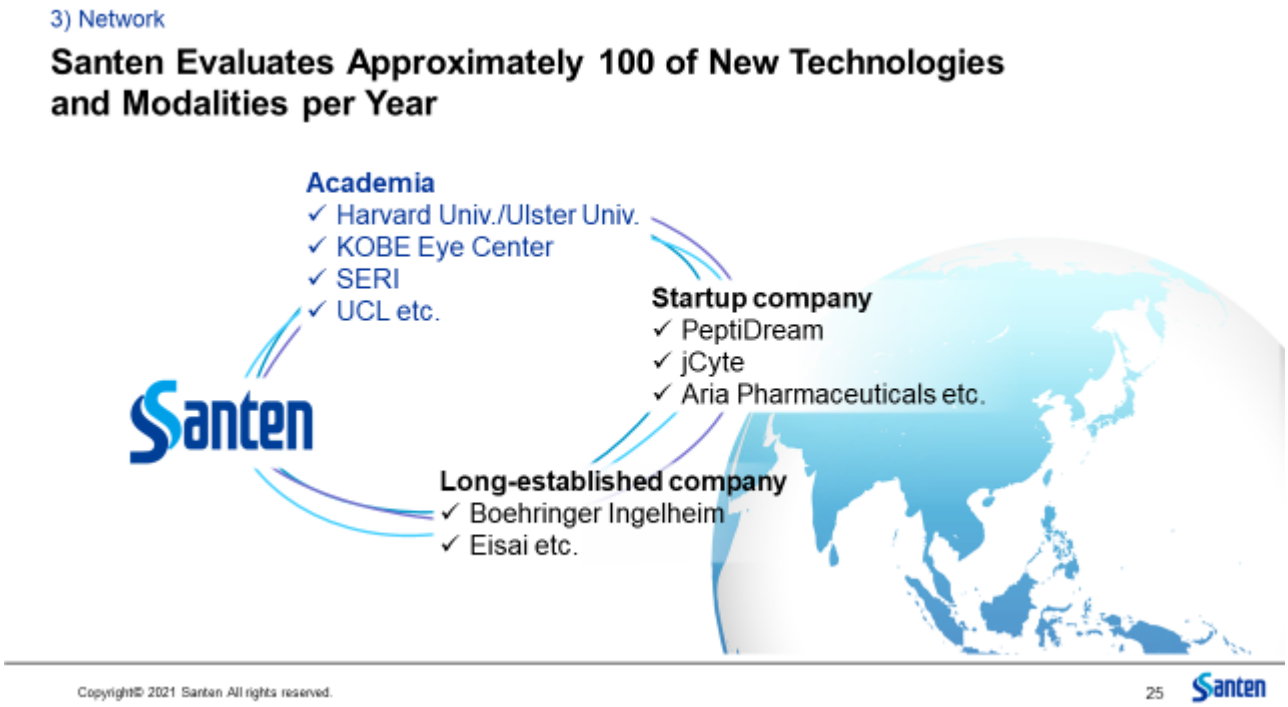
Since glaucoma vision loss occurs very slowly and without pain, it might not be useful to use multiple eye drops. Therefore, the treatment with less installation is equal. 1 of the countermeasures is surgical operation; the other 1 is optic nerve protection.

I will go into more details in optic nerve protection.

It's a very tough approach for the optic nerve protection. Many researchers in the world have been trying to find a suitable candidate with the effective mechanism of action. There are 2 reasons. 1 is the difficulty to conduct the clinical trials, and other is difficult to find the effective MOA, the candidate who can offset margin.

It takes a long time, 3 to 5 years' time, to finish the study. So, in order to prove the effect again in human clinical trials in most patients' entry and long time for development, we will need it.

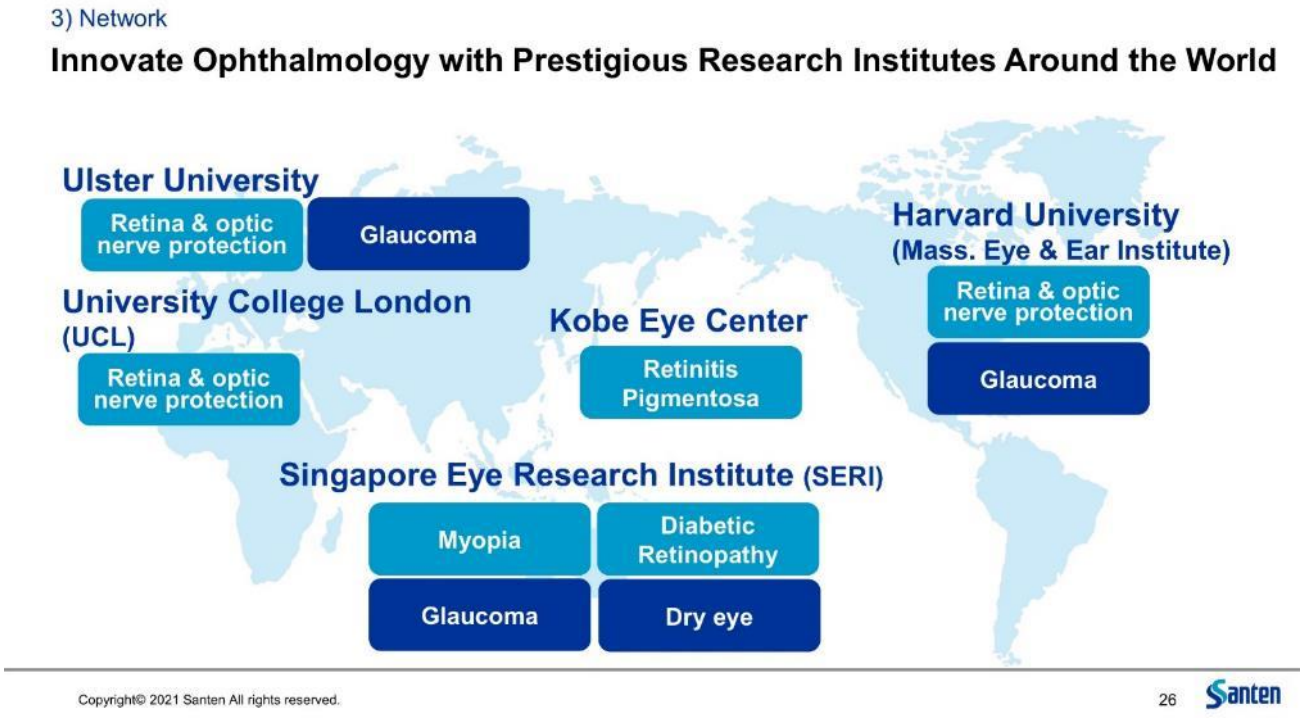
On the other hand, we have to have the candidate with enough safety and security. Efficacy is also enough. In order to solve such issues, Santen proceeded to collaborate with external research laboratories.



Next slide, please; slide 25. Santen evaluated hundreds of new technologies, therapeutics, and modalities; every year, every opportunity is explored. As I mentioned, Santen evaluated nearly 100 new technologies. We are confident that we have many opportunities to evaluate because we believe that we have trust.

In this slide, we'd like to introduce a part of our collaboration. As a start-up company, we work with PeptiDream and jCyte, and as a long-established companies, Boehringer Ingelheim and Eisai.

As for academia, I'll talk about this on the next slide.



Next slide, please; slide 26. We partner with the leading ophthalmic centers of excellence and the most prestigious research institutes on the planet. As I mentioned, we lead ophthalmic medicine with prestigious research institutes around the world. Here are some examples.

In Japan, we collaborate with Kobe Eye Center with regards to retinitis pigmentosa. In Asia, as we have already announced, we have collaborated with SRI, Singapore Eye Research Institute, since 2017, the first comprehensive collaboration between Santen, academia, and ophthalmology.

Singapore Eye Research Institute is not only first ranked in Asia but is very well known in the whole world. In the US, we collaborated with Harvard University in 2020, and the Eye and Ear Institute as the research and teaching hospitals, as we did with Harvard Medical School and Ulster University in the United Kingdom to identify, characterize, and develop novel and unique treatments for glaucoma, targeting a component of the immune system for retina and optic nerve restoration.

In Europe, we 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. We know that we cannot do it by ourselves. We need partners. We need to do a lot of collaboration in that place.

Leadership

New Leadership Team will Further Elaborate Disease Strategies and Firmly Explore Potential Treatments

Reza Haque
Head

Takeo Hirose
Representative Head

Sreenivasu Mudumba
Vice President,
Therapeutic Modality
Innovation

Najam Sharif
Vice President,
Global Alliance and
External Research

Almira Chabi
Vice President,
Glaucoma and
Neuroprotection,
Therapeutic Area Strategy

Abu Abraham
Vice President,
Vitreous and Retina,
Therapeutic Area Strategy

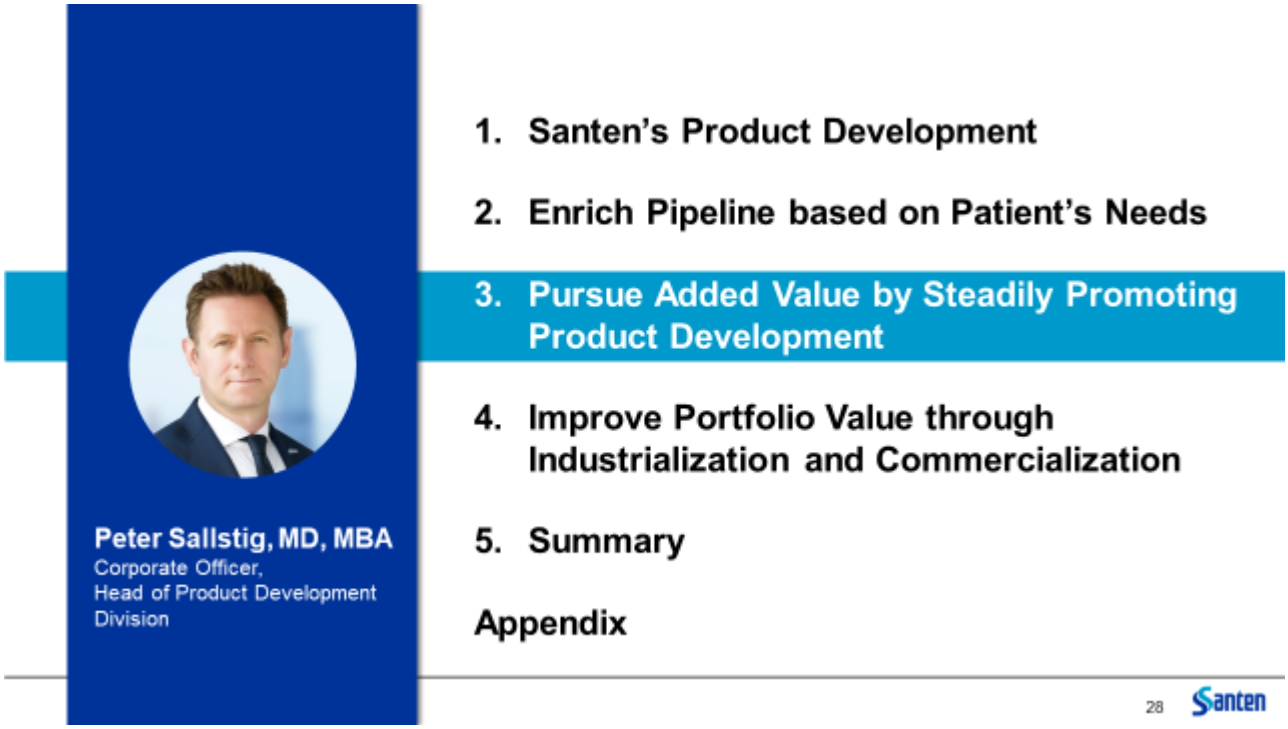
Hisao Shimada
General Manager,
Ocular Surface and
Anterior Segment,
Therapeutic Area Strategy

Takahiro Imanaka
General Manager,
Clinical Pharmacology and
Biomarkers

Next slide, please; page 27. We have a new leadership team for OIC, the Ophthalmic Innovation Center. Our new leaders, have full, elaborate disease strategies and firmly explore potential treatment.

We have someone in charge of every disease area, such as front of the eye, back of the eye, glaucoma, and neuroprotection. We have a head of mobility innovation, and also head of global external research, and also clinical pharmacology and biomarkers.

And we need a very efficient team to move forward in the year 2025 and 2030.



Sallstig: Good morning, good afternoon. My name is Peter Sallstig. I'm the Global Head of Product Development Division and Corporate Officer. It's a great pleasure having you to attend, allowing us to share with you our plans and the changes that we have started implementing within global R&D, particularly within the Development Division, which we believe will benefit physicians, payers, and most importantly, patients. So, allow me to share some details on this.

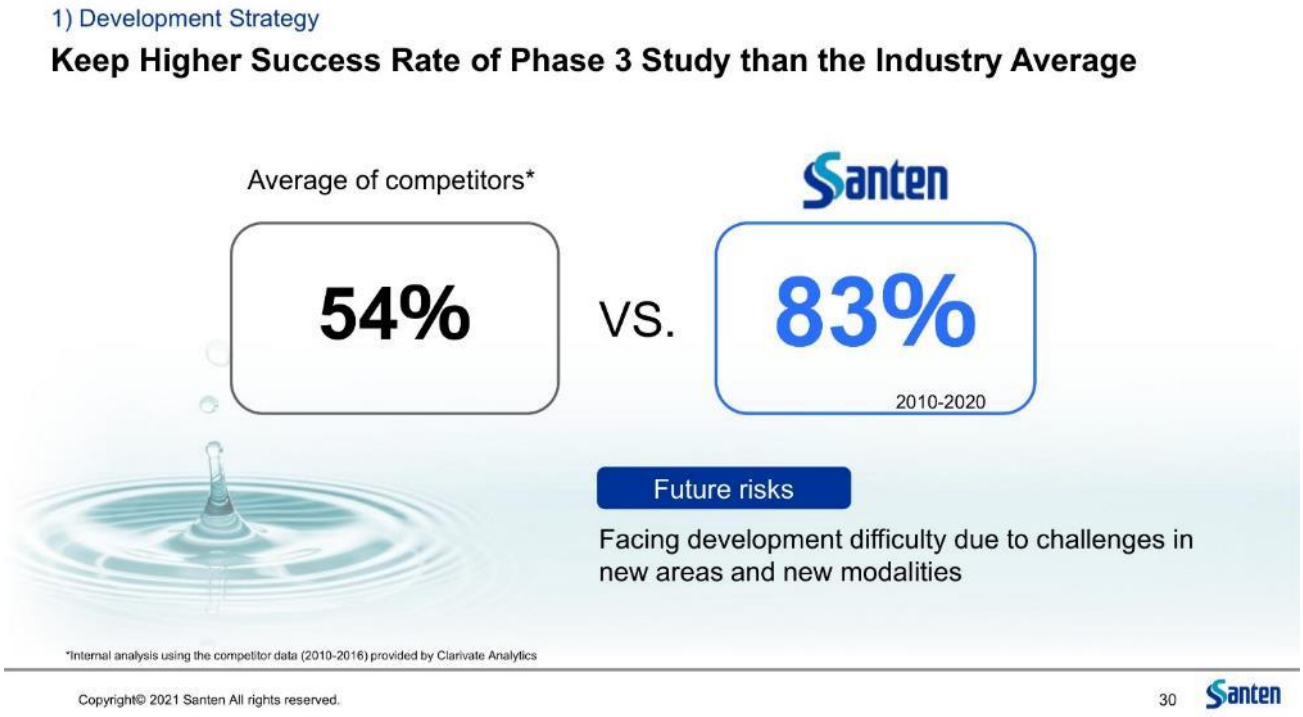
Next slide, please; slide 29. Within development, we are very much focused upon moving projects and programs as quickly as possible from the proof of concept to where we have made an initial understanding of the mechanism of action all the way until commercialization.

Our understanding of the mechanism then translates itself into a development strategy that takes into consideration, of course, 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 that we're looking for.

We're also focusing on improving our capabilities with regards to how we're maximizing the life-cycle management of our programs. As 1 of our founding blocks, we continue to invest heavily into our life cycle management. And now, we're looking to further differentiate ourselves. So, moving away from just trying to improve for instance, the shape and the way that the bottle feels for the patients, which, of course, is absolutely critical, we also believe that we have to start looking into other disease areas that we previously haven't looked into.

We are really trying to bring out here the maximum for the sake of our patients. Of course, none of this is possible unless we actually 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.

So, in the next 20 minutes or so, I'll go more into the details.

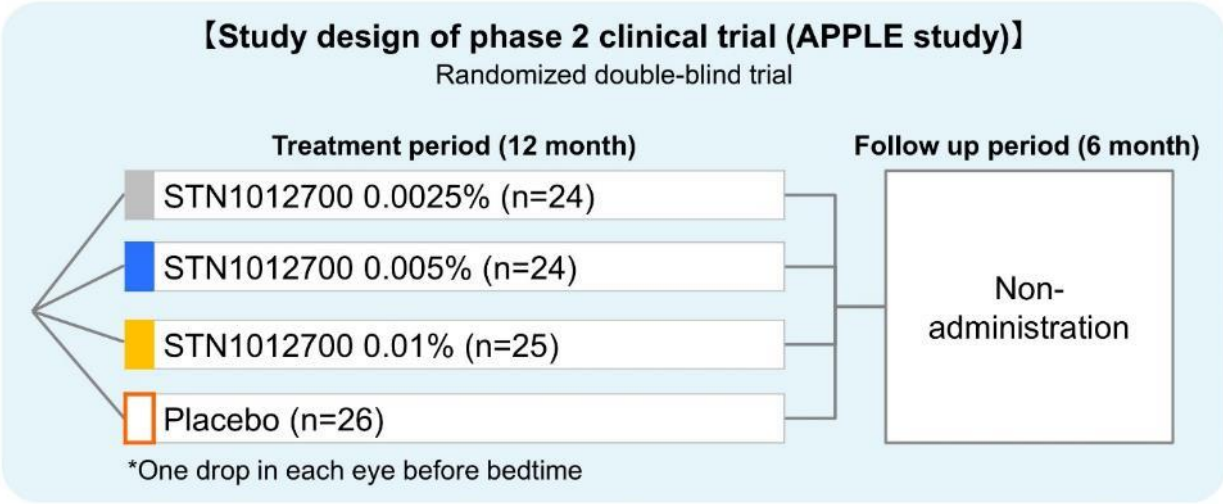


So next slide, slide 30, please. Now compared to the industry standard, we believe that we have been much more successful in delivering our projects. Particularly if we're looking at the last decade or so, the success rate is much better—54% versus 83%. In particular, we have been very successful in our home markets, that of Japan. But we've also been very successful most recently in expanding our capabilities, be it now Asia, or be it Europe.

Also, most recently, for those of you who have been following us, with the approval of *Verkazia* here in the United States. We also know, of course, that the hurdles and the requirements from the health authorities keep on rising. The expectation from payers also keeps on rising. We believe that based upon our past history, that we are quite well equipped to take it on, and we'll be talking more about how we're planning to do this.

1) Development Strategy (Myopia)

Acquire POC Early in Singapore Where There is a Well-established Clinical Trial Environment



Next slide, please; slide 31. 1 of the most exciting programs that we have is within myopia. As has already been presented to you, myopia is a condition, a disease that we believe will continue to accelerate, particularly within the Asian region.

This is why we're very grateful for having the opportunity to conduct our clinical trials in locations such as Singapore. You just heard about our collaboration with SERI. So, it all comes together quite nicely.

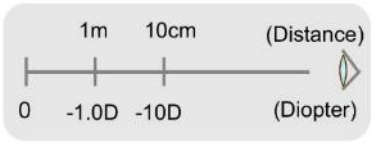
The data that you actually can see here is from our dose-finding trial that we conducted in Singapore, the APPLE study for the project STN1012700. You can see here depicted the different doses that we studied: those 3 doses in a 12-month study as a primary endpoint versus placebo, and then a 6-month follow-up.

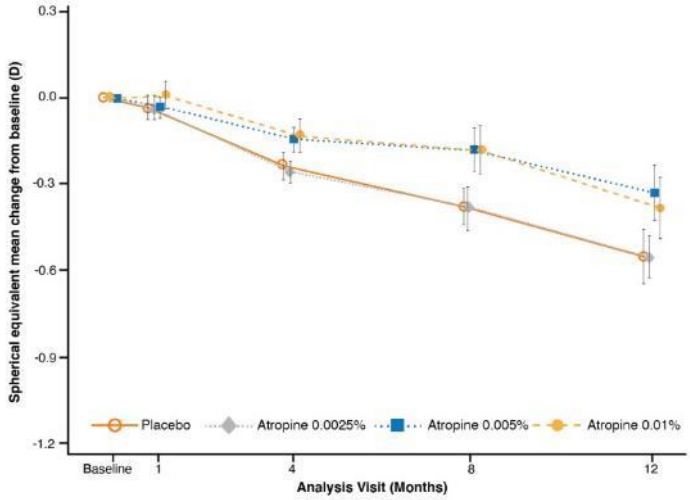
Now let me go a bit more into the details of this data. So next slide, please.

1) Development Strategy (Myopia)

STN1012700 Inhibited the Spherical Equivalent Change*

1) Spherical equivalent





* Presented at The 36th APAO 2021

Santen

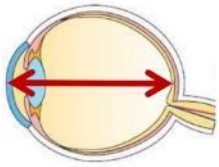
On slide 32, you can see the primary endpoint, which is the change in the spherical equivalents. What this basically shows to you is the impact that the change in diopter on your day-to-day life.

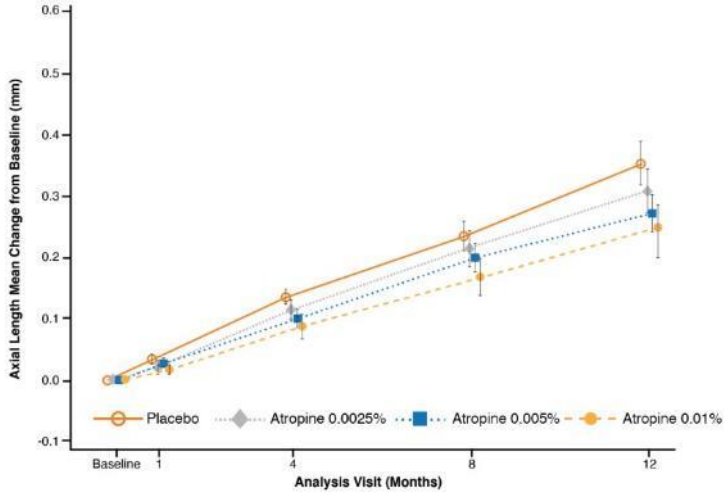
What you can see here is that the higher concentrations, the 0.01%, as well as the 0.005%, behaved quite significantly better than that of the placebo arm. So, we could really see here a drug response, which is basically what we are trying to achieve with this trial.

1) Development Strategy (Myopia)

STN1012700 Inhibited the Elongation of Axial Length*

2) Axial length





* Presented at The 36th APAO 2021

Next slide, please.

Another factor that we're looking into is the axial length. We know that in myopia, the axial length keeps on continuing to elongate itself. The result is basically that the rays coming in are not hitting the retina.

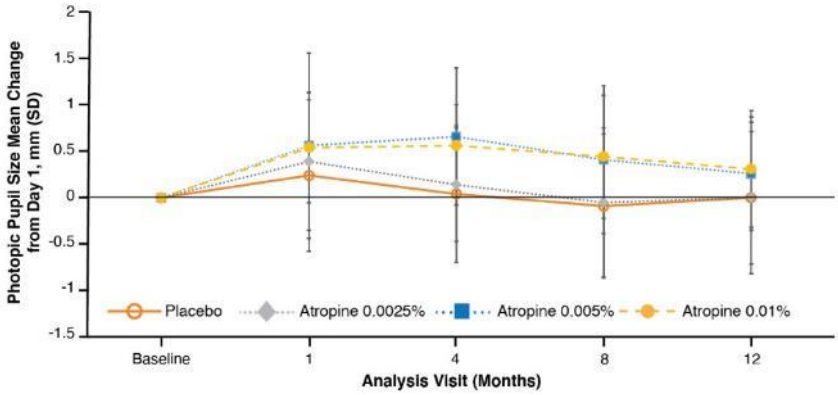
Again, what we could see here is that with the entire concentration, the 0.01% as well as the 0.05%, they performed well, statistically significant versus the placebo, and we did not see a progression of the elongation as much as we have seen with placebo.

We have now shown 2 endpoints that speak in favor of the 127 versus placebo.

1) Development Strategy (Myopia)

STN1012700 Caused Only Slight Change of Pupil Size*

3) Pupil size



* Presented at The 36th APAO 2021

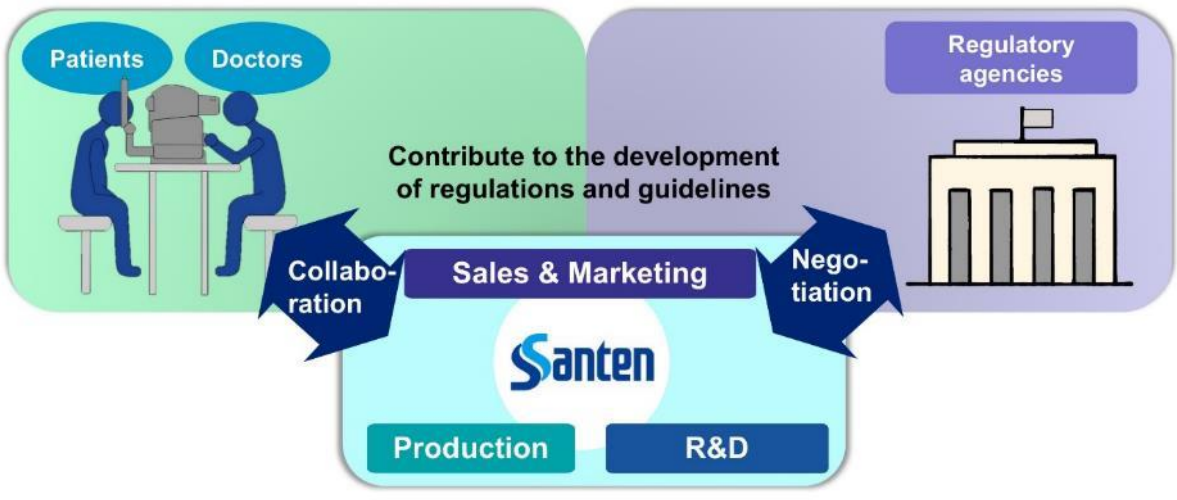
Next slide, please.

Finally, we also know that a lot of patients, of course, complain about mydriasis of glare. Looking here at the pupil size, we see a similar picture to what we've seen before with the higher concentrations having an impact. But here, of course, it's important that you're not having too much of that effect of the glare of the mydriasis.

We actually did not see that statistical significance with the higher concentration, which we believe, of course, is beneficial.

1) Development Strategy

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

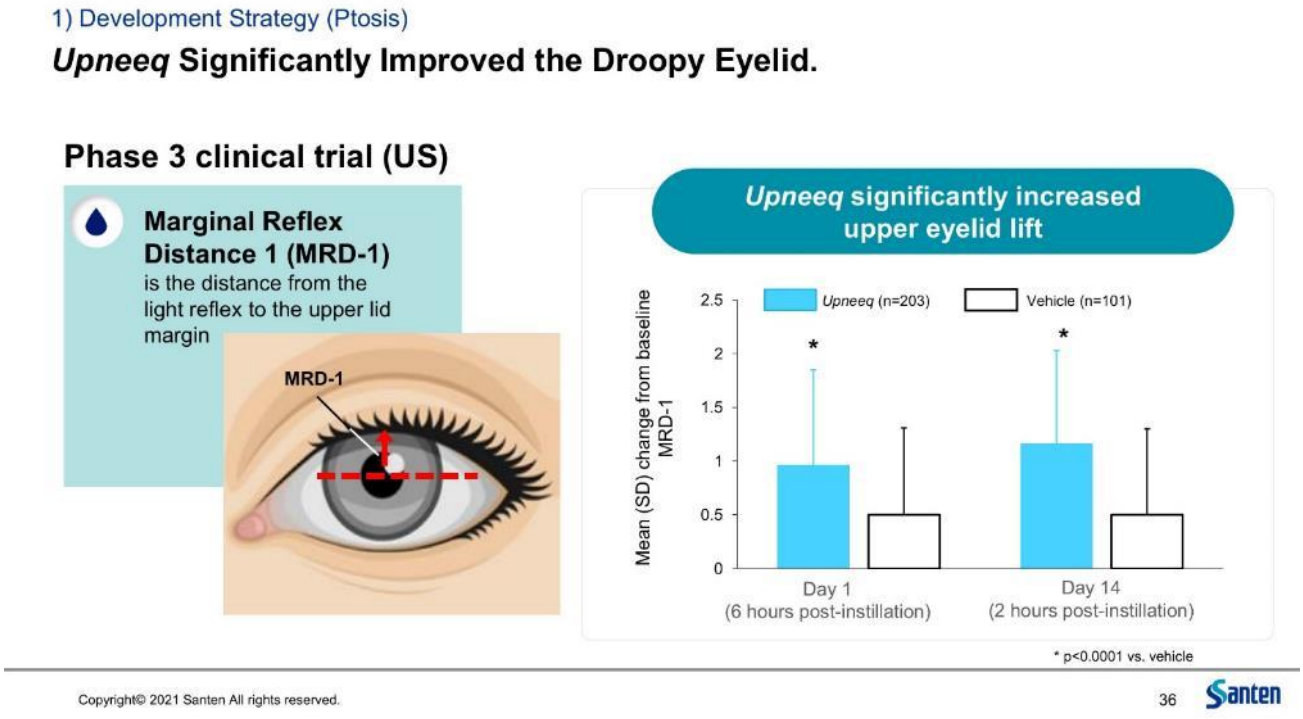


Let's move on to the next slide, please. We've talked a bit about the clinical trial data, but basically, this is just 1 piece of the puzzle. We believe that at the forefront of everything that we do has to be, of course, the patients. We want to make sure that when the patient actually comes and speaks to the physician, they get what they need, and that the physician is able to deliver on this for them.

We really take pride in communication. Particularly in the 130 years or so that we've been collaborating with physicians within and, more recently, outside of Japan, we really believe that we understand our patients' needs. Through our initiatives in service of patients', we are getting those insights and making sure that we can implement them in better clinical trials.

We are, of course, paying a lot of attention to collaborations with health authorities and are making sure that we're able to engage with them, particularly when it comes to new technologies, which is really something at the forefront for us. We want to make sure that we're on the same page, so there are no surprises.

At the end, all of this comes together internally by having a very coherent understanding with our commercial organization and our manufacturing organization so that when we're putting our products out to the market, the patients and the physicians can actually get the products with the services that they deserve.



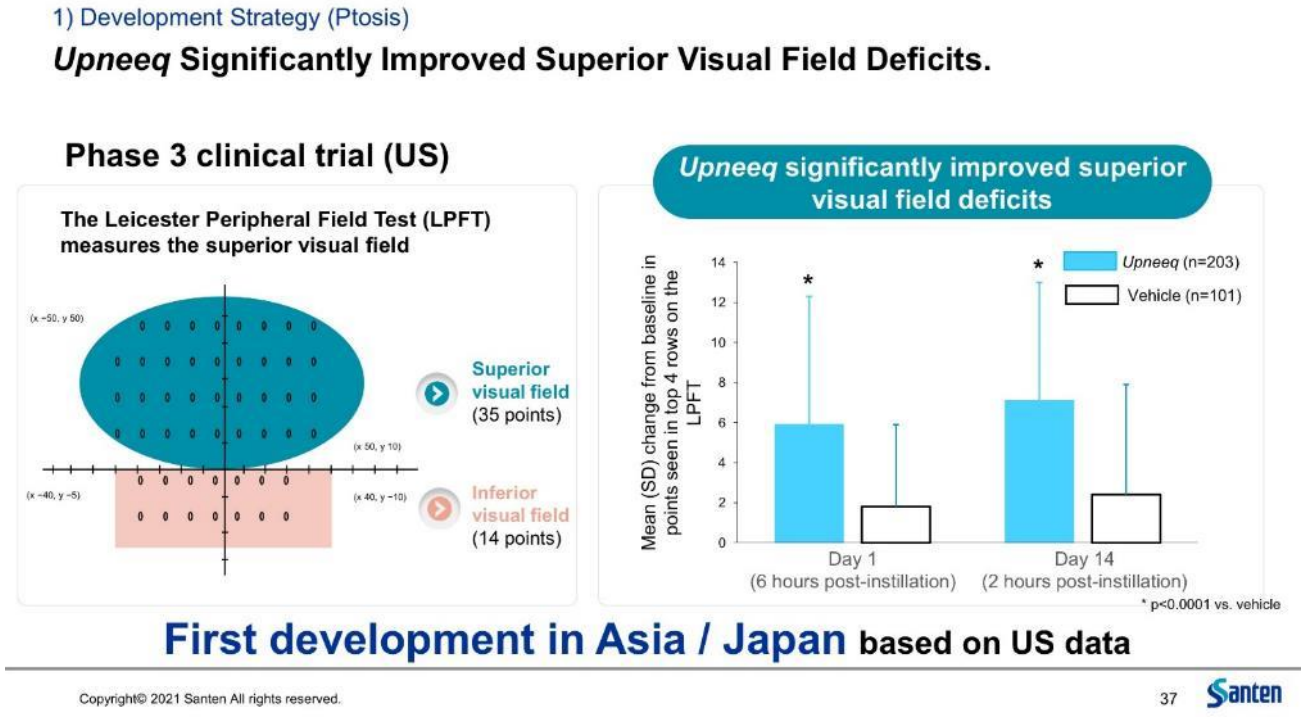
Next slide, please. 1 other very interesting program that we have going on now is in ptosis. Ptosis is a disease, as you know, that happens mainly later in life. However, you might also see this a bit earlier. There are different triggers for it, but what it's really characterized by is by droopy eyelids.

What you can see depicted here is 1 way of looking at the data. The factor that is really taken into consideration is the marginal reflex distance, which is the distance from the light that it reflects to the upper lid of the eye.

What you can see here is the data from the pivotal trial that was conducted by [Osmotic]. You can see here that even when we're testing the oxymetazoline at an early stage, be it now at 6 hours on day 1, you can actually see a statistical significance.

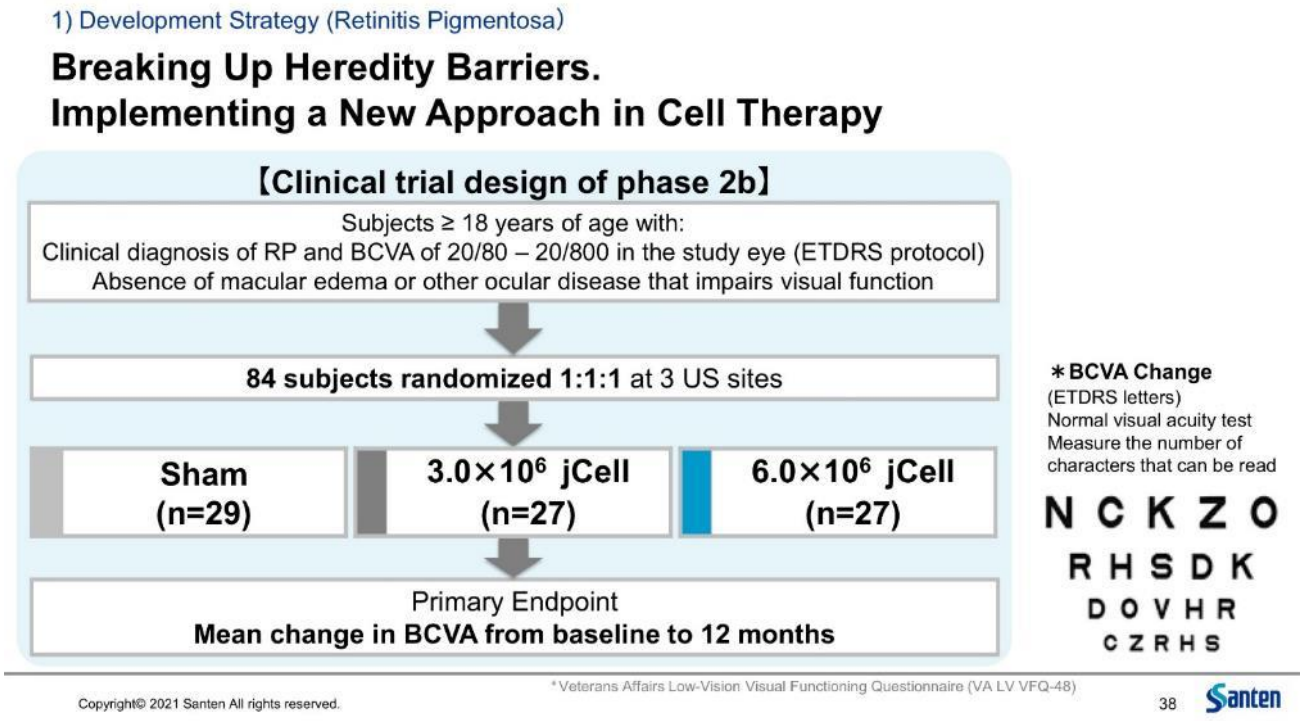
If you tested the next time, which in this study was at 2 hours at 14 days, again, you can see that statistical significance.

This is really exciting particularly for our patients. So, let's go to and see another way of looking at the data.



Slide 37 depicts what happens when we utilize what is called the LPFT, or the latest peripheral fields test. This test measures the superior visual field, which is made out of a 35-point scale. This was also used in the Phase III trial. This was another endpoint that we looked at. Basically, what you see here again is that there is statistical significance both early on at day 1 and also at day 14.

As our next steps, we're planning to move forward to utilize the certificate of the pharmaceutical product, or the CPP as it's also called, and to submit this as quickly as possible where we can, starting within Asia. This is very exciting news for the patients who actually have these droopy eyelids.

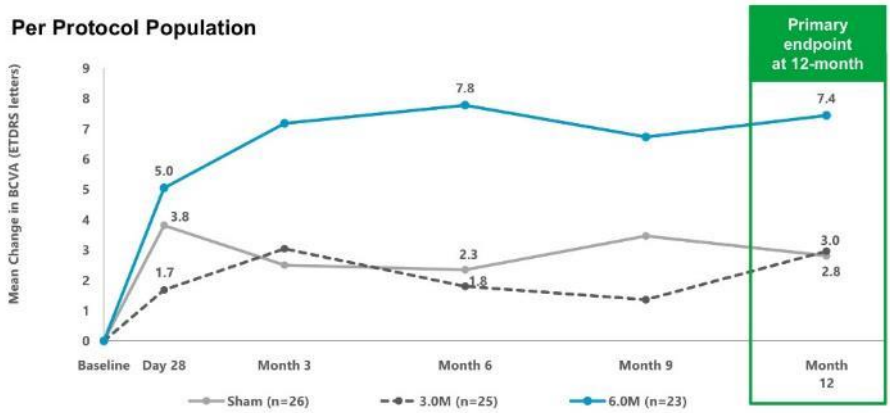


Next slide, please.

Another very impactful disease and condition is retinitis pigmentosa. As we know, this is a really devastating disease where patients suffer early in their lives from it. When they reach adulthood or even early adulthood, they're almost blind. We have a collaboration with JSAT, where we conducted a clinical trial looking at 84 subjects randomized in a 1-to-1 fashion and testing 2 doses, a 3-million-cell arm, as well as a 6-million-cell arm with the primary endpoint of mean change in best corrected visual acuity, BCVA, at 12 months.

1) Development Strategy (Retinitis Pigmentosa)

The Per Protocol Analysis Showed a Trend Towards Meaningful Differences Between the Control (Sham) and the 6 x 10^6 Group.



Per Protocol Population (n=74)
***6.0M vs. Sham**: BL to 6mo = +5.43 (p = 0.070); BL to 12mo = +4.63 (p = 0.099)*
3.0M: 3.0x10^6 hRPC; 6.0M: 6.0x10^6 hRPC

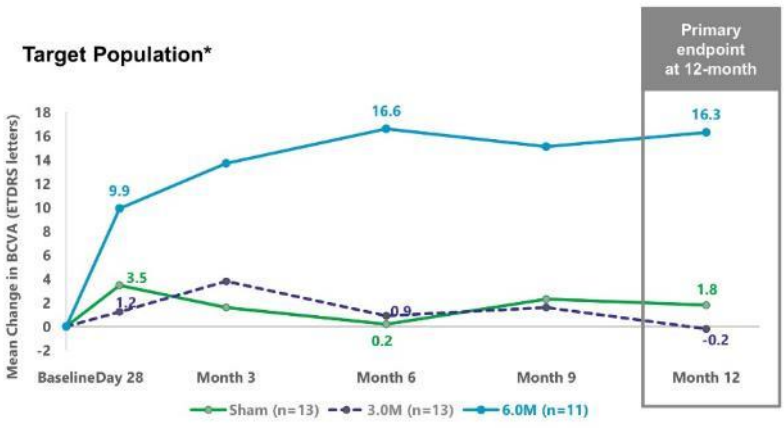
So, let's have a look at the data. Next slide, please.

Slide 39 depicts the primary analysis when you're looking at the per protocol population; you could see that there was a trend towards meaningful differences. And there was an improvement of approximately 7.4 letters, which still is quite good.

Based on this, we felt that there was still a subgroup that we could actually get a much better outcome for. So, there was some additional analysis that was done, and I'll show it to you on the next slide, please.

1) Development Strategy (Retinitis Pigmentosa)

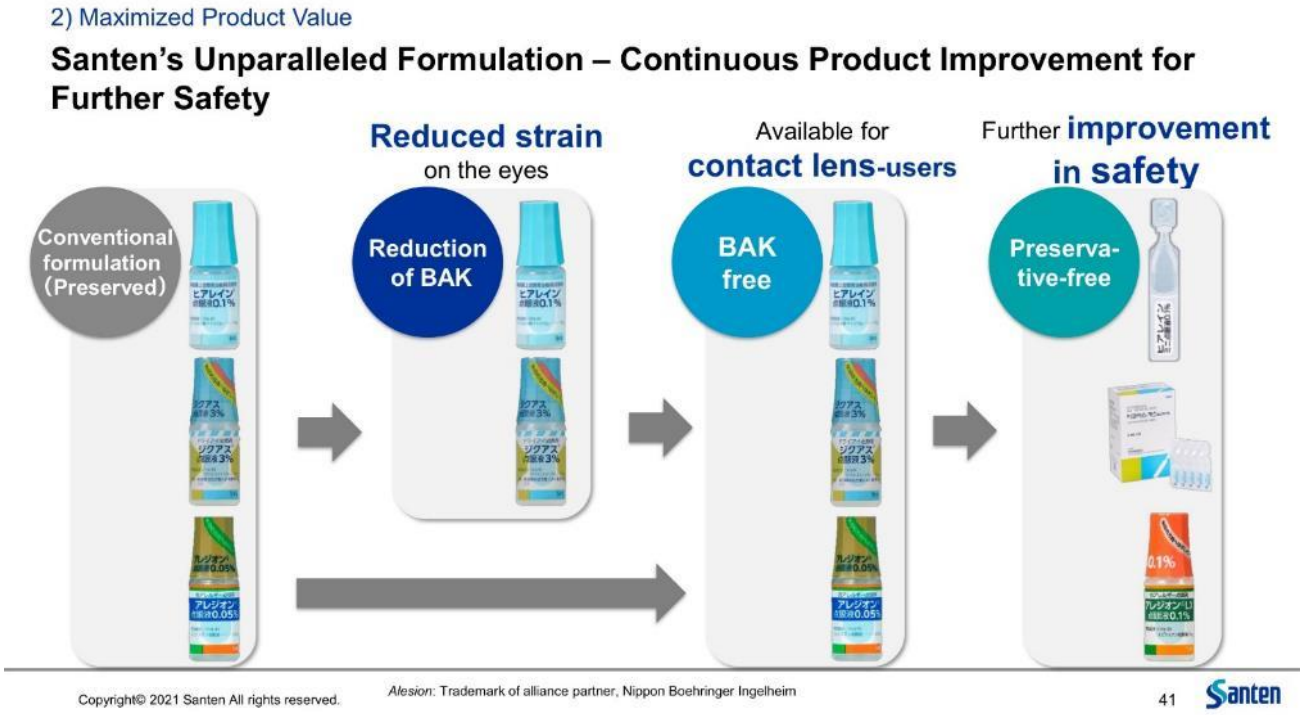
The BCVA in the 6 x 10^6 Group at 12 Months was Significantly Improved Compared to the Control (Sham) Group.



*Target patient population (n=37), 6.0M vs sham: baseline to 6 months = +16.45 (P=0.002); baseline to 12 months = +14.43 (P=0.003).
BCVA, best corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; M, million.
Santen data on file: jCyte. jCell presentation, 27 October 2020. *3.0M: 3.0x10^6 hRPC, 6.0M: 6.0x10^6 hRPC*

On slide 40, you can see that subgroup analysis that was done. There were 3 variables that went into these subgroups, and this is still to be confirmed with the health authorities, as we're going through and preparing for the next stage. At least what we were able to demonstrate in this study is that you really have a significant improvement, 16.3 letters, that you were able to increase, so basically 3 rows.

What you can see here is with a targeted approach, and in this case, for patients with retinitis pigmentosa, the impact they're going to have is really breathtaking.



Next slide, please. Now we've talked a bit about all our innovative programs, and we're really excited to try to get them as quickly as possible to our patients. At the same time, we shouldn't be forgetting about the founding strength of Santen. That really has been carrying us forward, quite frankly, in the last 130 years or so.

What we've been really good at is actually to take formulations, moving them from their original presence to a more optimal, logical, improved ophthalmological urgent. There are several steps that you can go through in trying to improve products when you're trying to get them to the patients. Often, what is being believed is that when you have the benzalkonium chloride, this actually adds to the efficacy.

In other regions, this is actually considered to not be optimal, as it's often associated with causing hyperemia. 1 of the things that we've, of course, then done is to reduce the BAK concentration.

Now for context users, they would actually prefer to have a BAK-free solution. This is, again, 1 of the capabilities that we have.

Finally, the last step, so to speak, is actually to give them a preservative-free solution, which further enhances the safety. This is really something that we've become very good at doing, and I'm sure you will see this also in our product line.

2) Maximized Product Value

Santen's Unparalleled Formulation – Improve Medication Adherence

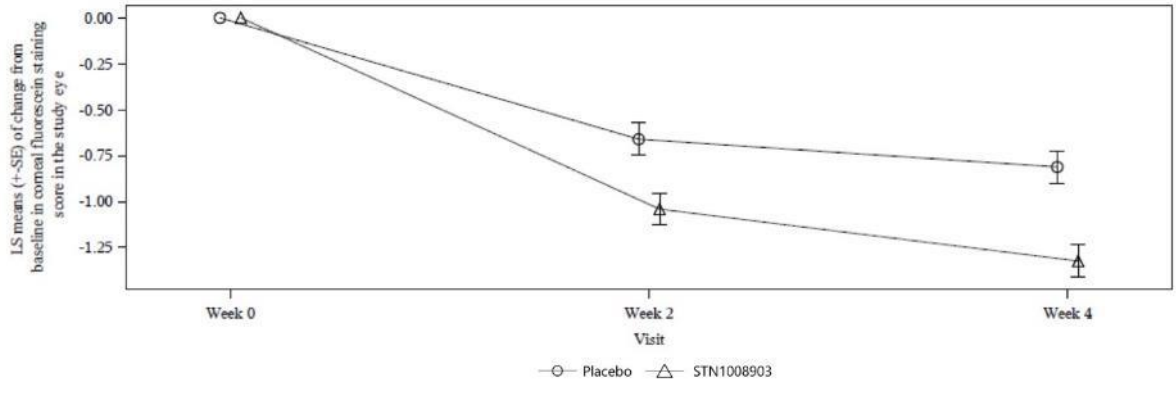
Next slide, please. Just to give you another example for our capabilities on this, if you look on the right-hand side, you can actually see the old formulation or the current formulation, I should say, of *Diquas*, which is a really good product.

We understood that patients actually might consider dosing 6 times a day to be burdensome, at least for some. Therefore, what we really wanted to achieve was reducing the installation of the drops from 6 times to 3 times a day. I'll share the data with you.

2) Maximized Product Value (Dry Eye)

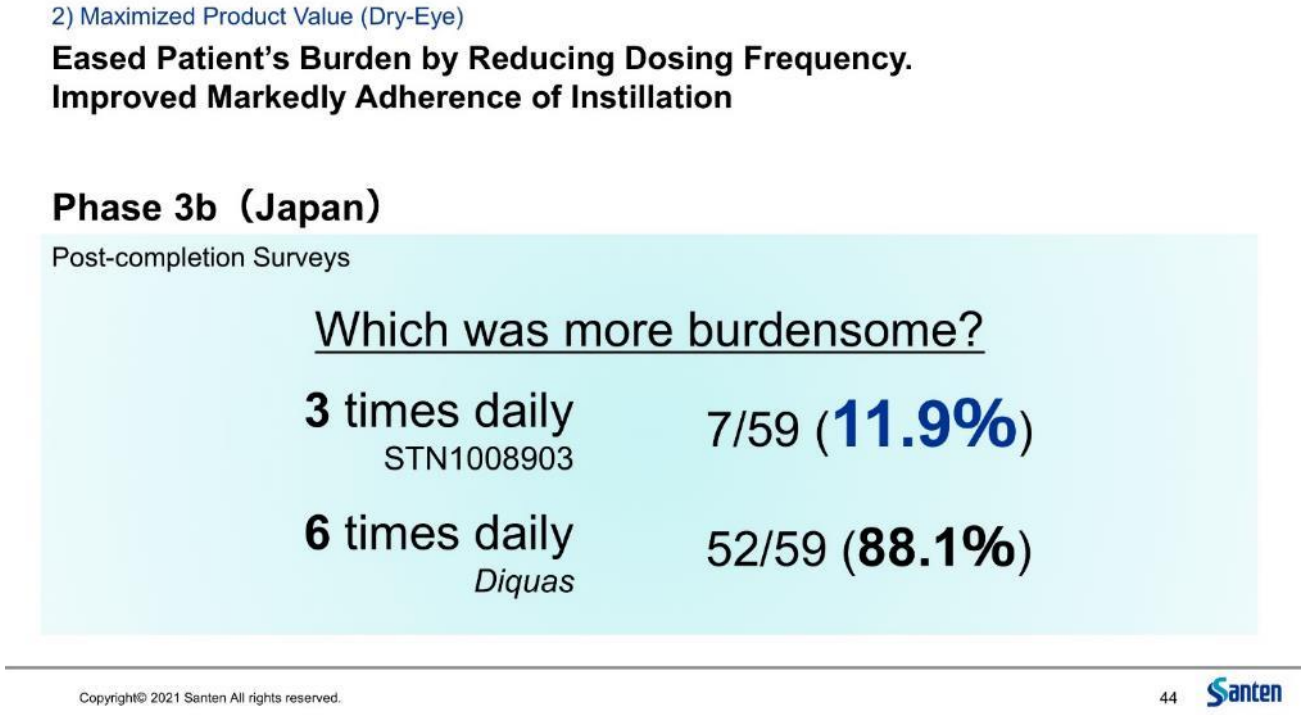
STN1008903, *Diquas* New Formulation, Maintained the Improved Effect on Corneal Epithelial Disorders. (Submitted NDA on Aug 30th, 2021, in Japan)

P3 clinical trial (Japan)



Next slide, please. This is the data that I wanted to share with you. What you can see here is that as you go down from dosing 6 times per day to dosing 3 times per day, you actually reach that statistical significance that we wanted to see here. We were able to achieve the primary endpoint and prevent damage of the cornea while also alleviating patients of their burden.

I'm pleased to say that we actually have submitted the data for this trial to PMDA as of August 30, a little more than a month ago. We're really looking forward to bringing the new, improved version of *Diquas* to our patients in Japan initially.



Next slide, please.

Slide 44 is about the burden of dosing several times a day. As part of our patient-centric philosophy, we made sure to actually ask whether dosing 6 or 3 times a day was more burdensome.

As you can see here, the numbers speak for themselves, we believe. There is a big difference here in favor of the new formulation—really exciting news about that.

2) Maximized Product Value

Respond to Various Needs as a Specialized Company in Ophthalmology

Next slide, please.

When we're talking here about the needs and trying to meet needs, I guess there are a couple of these approaches. Something that is absolutely critical for us is the impact that we're having on the environment. As part of that, 1 of the innovations that we're planning to bring forward is ensuring that our bottles are made 100% out of biomass. This is really something that we're proud of and working towards. Hopefully, we should be achieving that goal by 2030.

Also, as part of our consideration for our patients, we are considering the importance of preservative-free multi-dosing bottles required particularly in Europe as well as in Asia. So, we are working on having that replacement.

Finally, the eye-drop aid that has been a big success: we're working on an improved version. It's really great to have that combination for the patients.

We believe, at the end of the day, that making sure what's right, what's good for the environment, and what's good for the patients is going to be good for Santen as an organization.

Next slide, please.

We've talked about our programs, both innovative programs and, of course, our strengths. We also have to take into consideration the glue that brings everything together, and that's the people and the culture that is created by them.

A couple of things that we're really proud that we've been able to create, particularly in the last 2 years, and that we believe are actually going to be able to move us forward: part of our strategy, as we're moving away from just a focus on development and launching in Japan and really expanding overseas, was the establishment of a clinical global development group globally—a group that's really skilled in everything that they're doing that really can bring us to that next stage.

Part of that is the establishment of the China R&D Department. In order for us to really be able to deliver on our promises to become a global organization, we believe that these are really 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 or so. Therefore, we need to make sure that we have talents that actually can deliver on these promises.

Now of course, overseeing all of this, we have to have a global project management group. They're really 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, but the key component, as I mentioned, is the talent.

Let's focus a bit more on specific regions, starting with the US on slide 47.

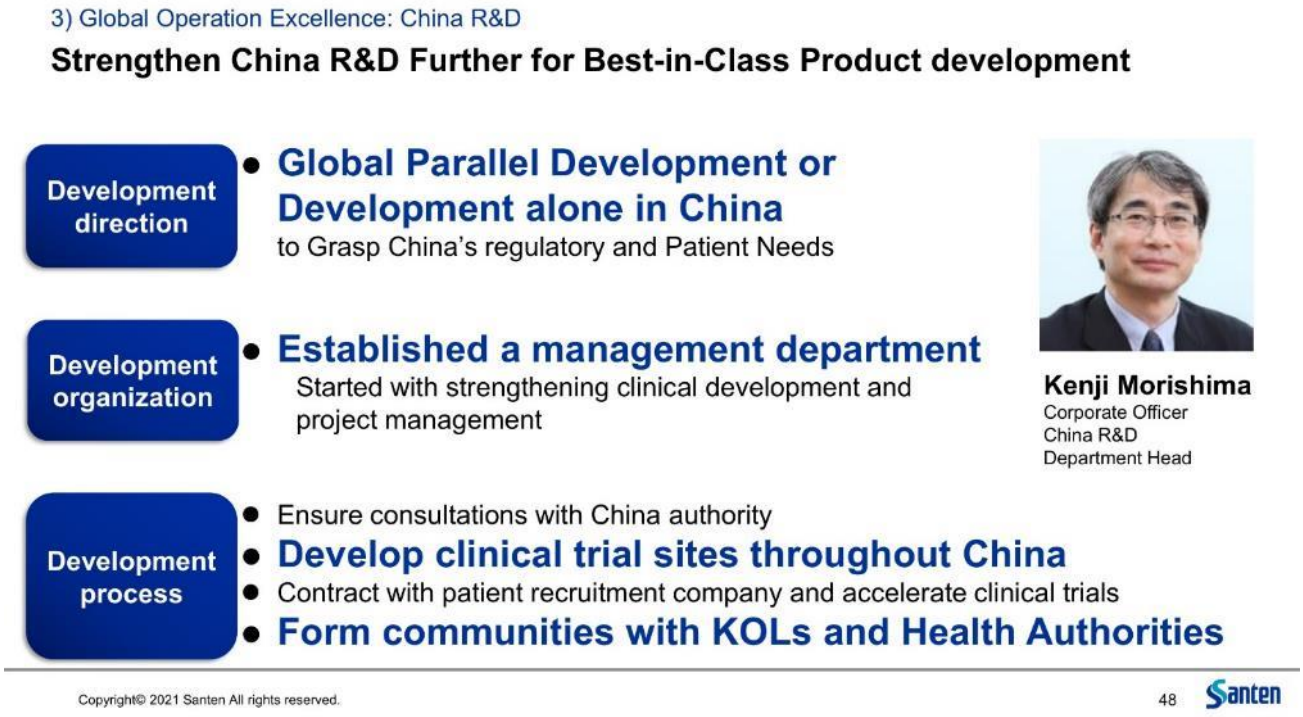
Quite frankly speaking, we haven't necessarily had that much success in the US in the past. I do believe, particularly in the US, 1 of the reasons for that has been perhaps the lack of talent—that we haven't had the right talents.

In Japan, of course, this has not been an issue, with our 130-year history and reputation with physicians, society, and talent coming onboard. In the US, as I said, this hasn't been really the case.

So, a couple of deliverables that we've been able to do so far: the establishment of strategic clinical development as well as an operations group that helps to set that strategy, operational excellence to make sure that our interactions with physicians as well as with agencies are at the top of the mind, making sure that our product as are well-vetted so that there are no surprises, and making sure that we're also talking to payers upfront.

Something else that we've been doing recently as part of the pandemic—and it was already planned, but the pandemic, quite frankly, just accelerated it—is really to see how we can digitalize things, how we can actually get to that remote clinical trial monitoring. We are really working on that, and hopefully we'll see some fluctuation of that in the near future.

And then, of course, at the end of the day, what we have to make sure is that the teams are able to deliver, and I really believe that with the talents that we have here, we'll be able to get to that next stage.



Next slide, please; slide 48. Besides the US, China is absolutely critical. And we're very fortunate that under the leadership of Morishima, we've been able to establish the Santen China R&D function. So, we actually started creating a strong group that can deliver on clinical development, can make sure that these projects are moving forward on time and on budget with the help of project management, has the right insights, and of course, reaches out to the health authority.

It's a similar approach that we've been doing here in the US most recently; now we're also doing it in China. Collaboration with health authorities, with physicians, and most importantly, with patients has really become an integral part of everything that we do within the development division.

We really believe that at the end of the day, this additional effort that we're putting forward is really going to differentiate us from the competition—having that talent and, of course, our products. Of course, all of this is only possible with strong leadership globally.

Next slide, please; my final slide, slide 49. We've actually been able to establish a leadership group, which I'm really proud of, and you can see the team here.

We've talked about Morishima, who is leading our China R&D organization. We also talked about Uday, who is responsible for the Global Clinical Development and Operations organizations, setting the clinical strategy as well as execution operationally globally. Then, of course, is Yamada-san, who is overseeing the Pharmaceutical Pharmacology Department or the formulations.

We also have a group that's overseeing the day-to-day line functions, be it medical affairs or regulatory affairs. We also have data science. We are also overseeing regions: we talked about Morishima, overseeing the China R&D, and there is also Jean Sebastian, who is overseeing the EMEA R&D.

We also have, of course, the functions which are overseeing the glue, so to speak, from an R&D capability standpoint, which is absolutely critical, and also from a strategic operations standpoint under the leadership of Matsugi.

We really believe that we have the right people here. We believe that this group will be able to help us to deliver. We believe that we started changing. Of course, we have high expectations, but I believe that we've actually started. We're going in the right direction in order for us to be able to deliver.

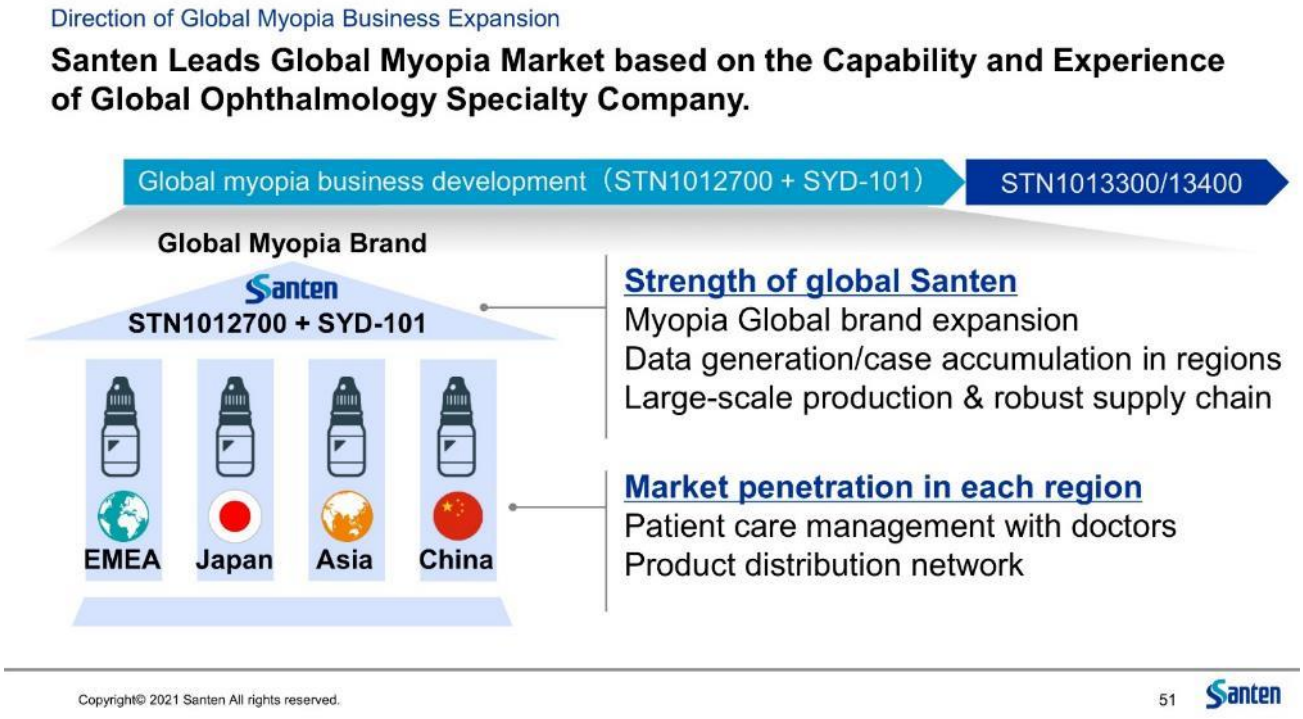
So, we're very much looking forward to working together with the physicians, and especially with the patients in delivering medications that can bring Happiness with Vision.

Thank you.

Sakai: I'm Sakai from the Portfolio Strategy and the Global Marketing Group Operating Development Division. I would like to talk today about how to build the last piece of the portfolio value, which is the commercial value.

Peter and the [inaudible] have already talked about the new frontier, which is the myopia and ptosis. The commercial value building in those areas has already started. So, you can relax and enjoy my talk.

Before considering the disease itself, do you have children aged from 3 to 15 years old? Please, have an image of your children in your mind, if you don't have that, imagine the similar age children of your relatives or acquaintances in listening to me talk.



The first 1 is myopia. Maybe you are now looking at the faces of your children. Myopia starts from very young; the visual acuity deteriorates. It is a progressive disease, and the worst outcome is losing sight. In our 130-year history, we have provided the solution, which is atropin. Actually, our myopia business is still on the way towards globalization. But now we have STN1012700 and SYD-101 introduced from Sydnexis to have a global myopia brand now.

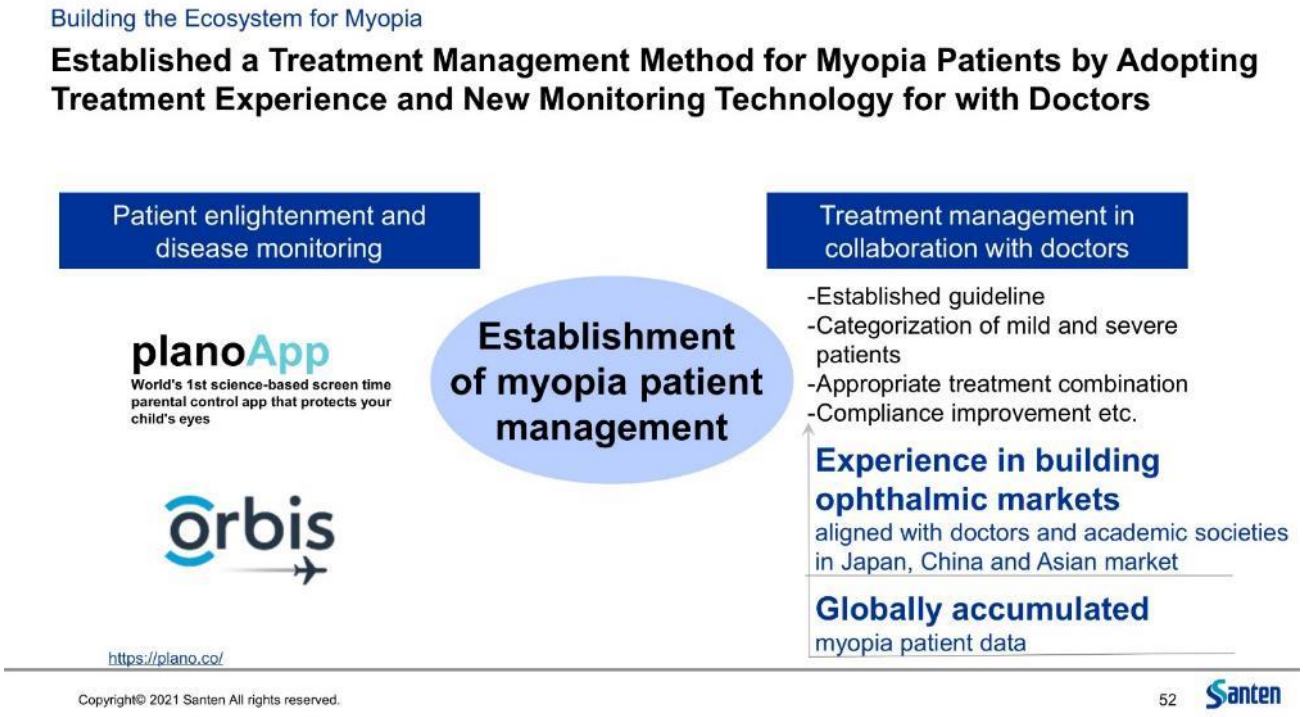
The globalization of this myopia business: already in Europe, Asia, and China, we have conducted the study in providing products in that market. We would like to provide a product to the patient globally in those areas.

In addition, to the patient, the other area, by accessing them, we are able to obtain quite a number of data. Maybe you have children with myopia or weak vision. So, to understand if the myopia is severe, you need to look into the data to identify the right information.

There are a large number of patients out there, as you may know in your experience; we should have a kind of a large scale production and the supply capability, which cannot be built very easily. So, the younger company, do they have a big manufacturing capability? I don't think so.

With this kind of product, local promotion is very important, for example, market management with local doctors. This is a chronic disease. Basically, we have strong management experience in glaucoma. Together with the physicians, we are able to provide very detailed management for patient care.

Also, supply chain development is important, not only to the patient but also the parents of the patient. We need to provide the proper information. Maybe you have experienced a diagnosis in remote treatment. This is the tool to deliver the product quickly and more swiftly to the patient.



Next slide, please; slide 52. As I have said, well, treating the chronic disease patients along with the ophthalmologists is very important, and we need to establish the monitoring technology of the patient and establish myopia patient-management technology.

There was a message to the patient from ISOP when we do the interview of the myopia patient's parents. I have heard from parents: "I have high interest in the myopia, but I don't have proper information to study." And so providing the correct information to the patient is most important; together with the development of technology, the smartphone application can be used. Also, utilizing the diagnosis network, we can provide such information.

With companies such as Plano and Orbis, we are able to provide correct information to the patient and the parents of the patient, and we will establish that methodology to do so.

And together with the doctor, we need to establish the patient care management system. We have created the market in Asia and China, mainly in dry eye. Using our past experience and already-established trust relationship with the doctor, we will be able to establish management in the myopia market as well.

So, in a broader, global area, we provide the myopia treatment modality, and the global study data accumulation is very important. Myopia patient management establishment is very important.

Manufacturing and Supply Chain System that can Meet Global Demand

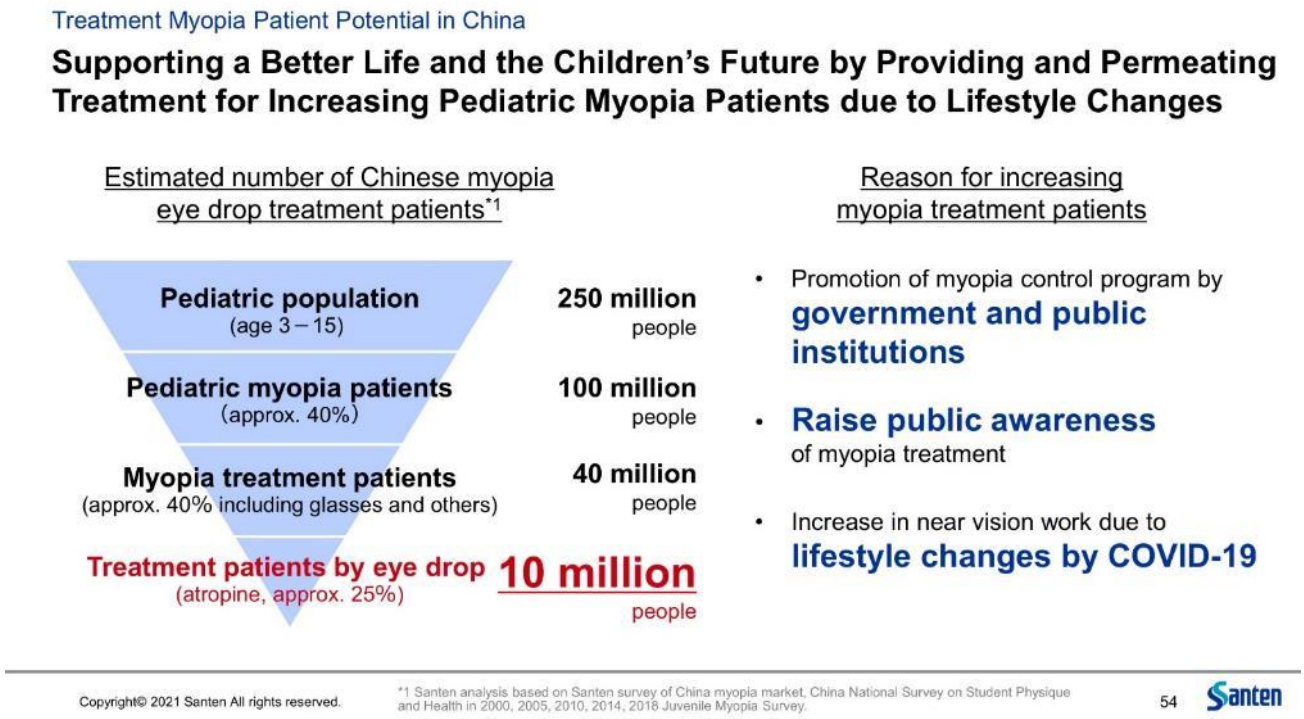
Based on the World's Largest Ophthalmic Eye Drop Production Capacity, Ensuring the Product Supply to Meet the Diverse Patient Needs

- Large-scale eye drop production:
  Approx. **400million bottles in FY2020**
- Achieved **large-scale and low-cost production** by automation and labor saving
- Suzhou plant ：
  Acquired EU-GMP, the only ophthalmic pharmaceutical company in China
  Technology / quality / production capacity
- Suzhou new plant (under constriction):
  World's largest and latest equipment
  Further strengthen the competitive advantage of product supply requiring large-scale production such as myopia

Next slide, please, about production. I said there are a great number of our patients out there, and our atropine solution is very impactful, such that if we are not able to deliver to a large number of patients, we are not able to maximize our product value.

We have 3 big facilities in Noto, Shiga, and Suzhou. So, we are able to provide the product to a great number of patients. We have that capability. In order to prepare for an increased number of patients, we are now trying to build a second Suzhou plant. So, high quality, high performance, and a large quantity of the product that can be delivered is a differentiating point from others.

For myopia in Japan, you know a good number of patients are out there. You hear about, well, a child of someone is said to be myopic already, and you are speaking about things daily.



Now looking into the Chinese myopia patient, how many patients like to have the eye drop of our drug? There are more than 1 billion people in China, but the number in the 3-to-15 year age range is about 250 million, and 40% of them are myopia. So, there are 100 million. And in China, there should be about 40 million who can be categorized as a myopia-treated patient.

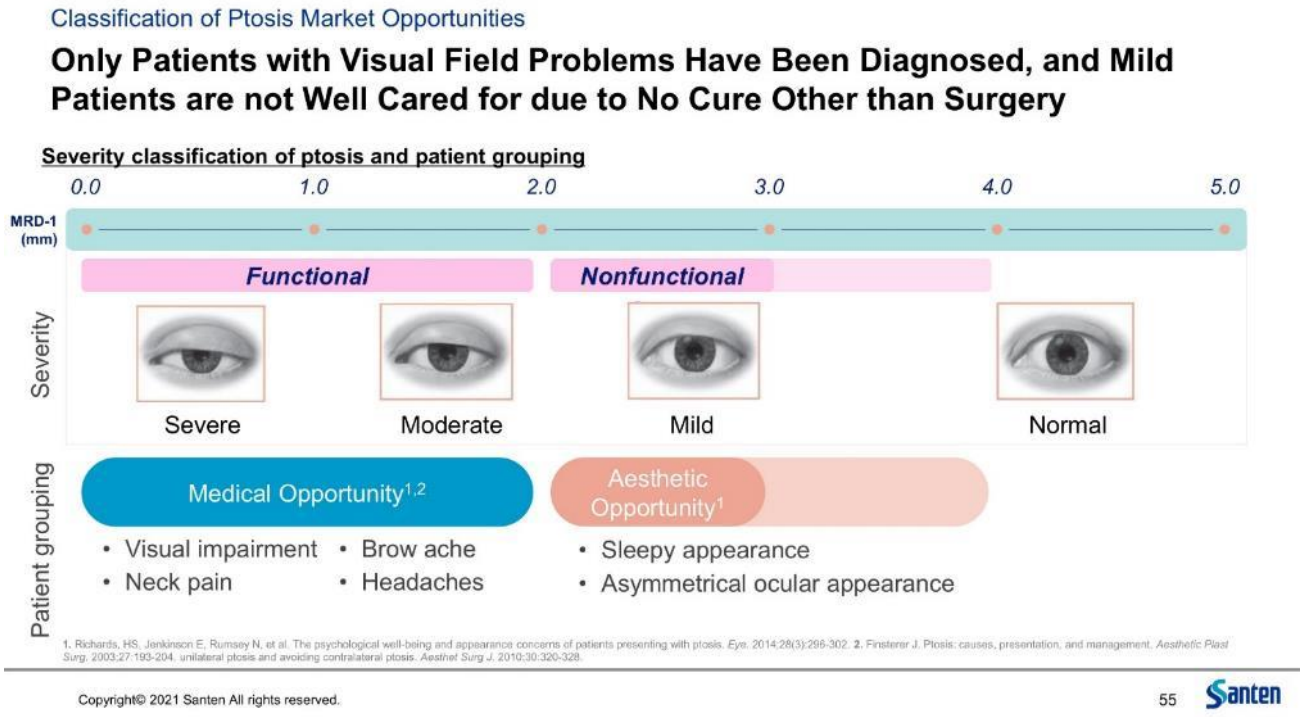
And asking them, how do you like to use the eye drop to cure myopia? A quarter positively responded. They aren't giving up glasses or lenses; they will probably use the drug together with them because it is safe, if it is proven to be safe and efficient the parents would like to prescribe the drug to their children.

As for the Chinese government, they are strongly backing our effort. Also, the public awareness is now being raised, especially because such a great number of myopic children are treated thanks to school screening. So, in a way, there is already a system to find the patient in a very well-established, composed manner.

Under COVID-19, schools are giving the remote lessons at home. Children look at the iPad, YouTube, and so on, don't they? So, in a way, near vision work is overwhelmingly increasing by the survey by some private school, or juku, asking "What do you do in your leisure time?" And the triggering answer is "Well, I look at YouTube. "

So, they study in iPad in near vision, and enjoy YouTube in near vision. So, there is much greater opportunity to expand myopia under COVID-19. So maybe you are more familiar with such a change than us.

For myopia, as Santen, we have 130 years of history. We already have the credit and the trust by the doctors. So, for the sake of the future of our children, we will provide a meaningful solution.



The second condition that I'd like to talk about is ptosis. We have the understanding that there are many patients of ptosis. So please think about yourself and also people around you, especially the seniors, perhaps your parents.

You may or may not have heard of ptosis before hearing it from us. It can be either acquired or congenital, and this is a condition where you have difficulty fully opening up your eyes. The condition is on a spectrum from severe to mild.

As you can see on the slide, when the condition is severe, you can see that the eyelid is quite droopy. And looking at moderate and mild, at the very center of the pupil, it is somewhat covered because of the eyelid coming down, and this starts to impact your visual acuity visual field.

Now even with the current treatment, it is very difficult to handle. Surgery is the only option available today. And for the milder vision, this is nonfunctional. And oftentimes with these mild-case patients, they are not diagnosed as ptosis patients. There's MRD-1 mentioned by Reza in his presentation.

So, when the distance from center pupil to eyelid is about 2 millimeters, this is when you start to see a compromise in visual field function. Once you start to reach this distance, you may start to see functional disabilities, and may seek a solution.

But with these milder patients, we believe that there is need for aesthetic solution or aesthetic opportunity.

Blepharoptosis Market Opportunity Classification by Age

Most of Medium-Severe Patients are Elderly, but There Are Great Opportunities When Including Young People with Mildly Patients

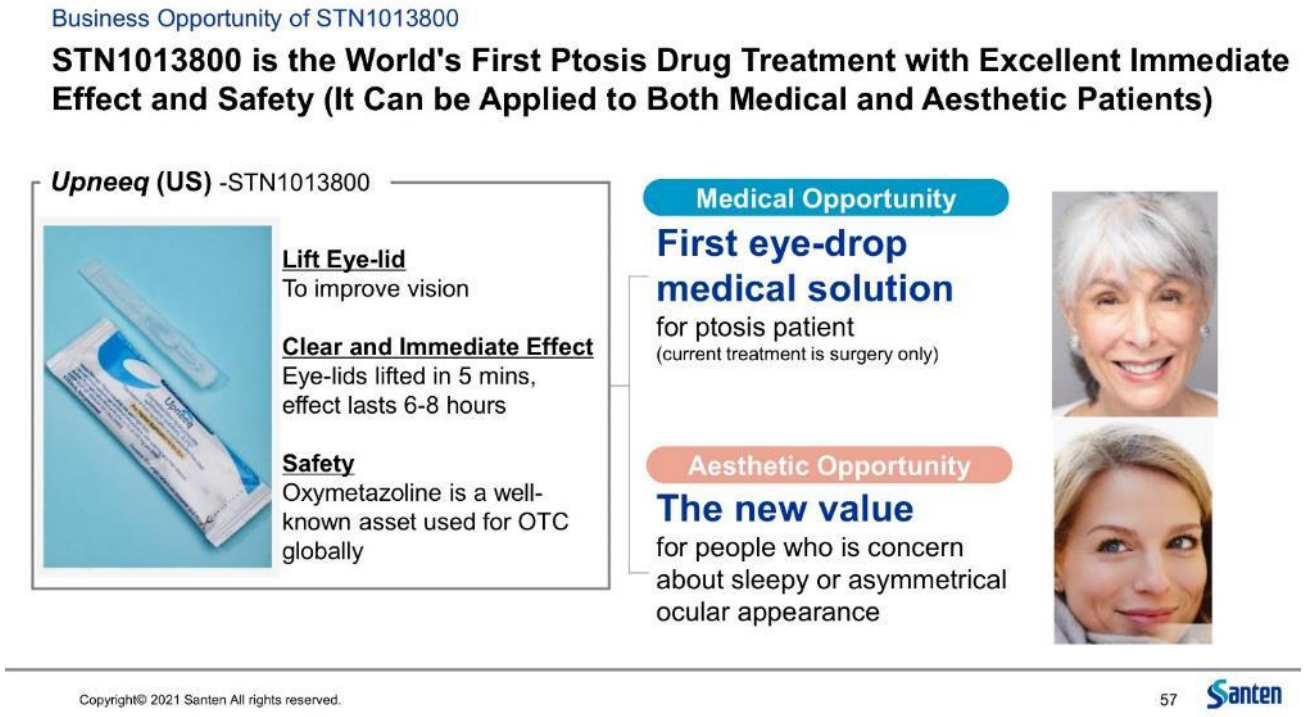
1. Paik JS, Han K, Yang SW, Park Y, Na K, Cho W, Jung SK, Kim S. Blepharoptosis among Korean adults: age-related prevalence and threshold age for evaluation. *BMC Ophthalmol.* 2020 Mar 13;20(1):99. Kim MH, Cho J, Zhao D, et al. Prevalence and associated factors of blepharoptosis in Korean adult population: the Korea National Health and Nutrition Examination Survey. *Eye (Lond).* 2017;31:940-946.

Please go to the next slide. This is looking at the segmentation of patients. As you can see, when we think about the condition and how this is age-driven condition, you can easily imagine that the proportion of patients will go up as the age goes up.

But at the same time, there's a certain percentage of patients who are younger with the aesthetic opportunity, and we understand from literature that the prevalence is different amongst countries. But we could say that 20% to 30% of the people aged 30 and above are set to have ptosis.

And for this aesthetic opportunity, whether the standard should be 3mm or 4mm is pretty much dependent on the size of your face or eye. Therefore at this moment, there are not definite standards by countries. It is also true that the surgical option is the only treatment option available today.

Now with regards to ptosis, it's not always both eyes that are impacted by ptosis. There are cases where only 1 of the 2 eyes is impacted, which you might feel more familiar with.



Please go to the next slide.

As treatment to ptosis, we are developing STN1013800. This has actually been developed by Osmotica and approved by the FDA in the US. The product name is *Upneeq*—"up" and "unique" together is *Upneeq*.

There are YouTube movies uploaded that discuss the usage of *Upneeq* if you are interested.

So, through the use of *Upneeq*, you are able to lift up your eyelids. It is efficacious, it is fast acting, and also safe. It takes only 5 minutes for lifting up of the eyelid, and the benefit is sustained for a period of 6 to 8 hours and is quite safe as well.

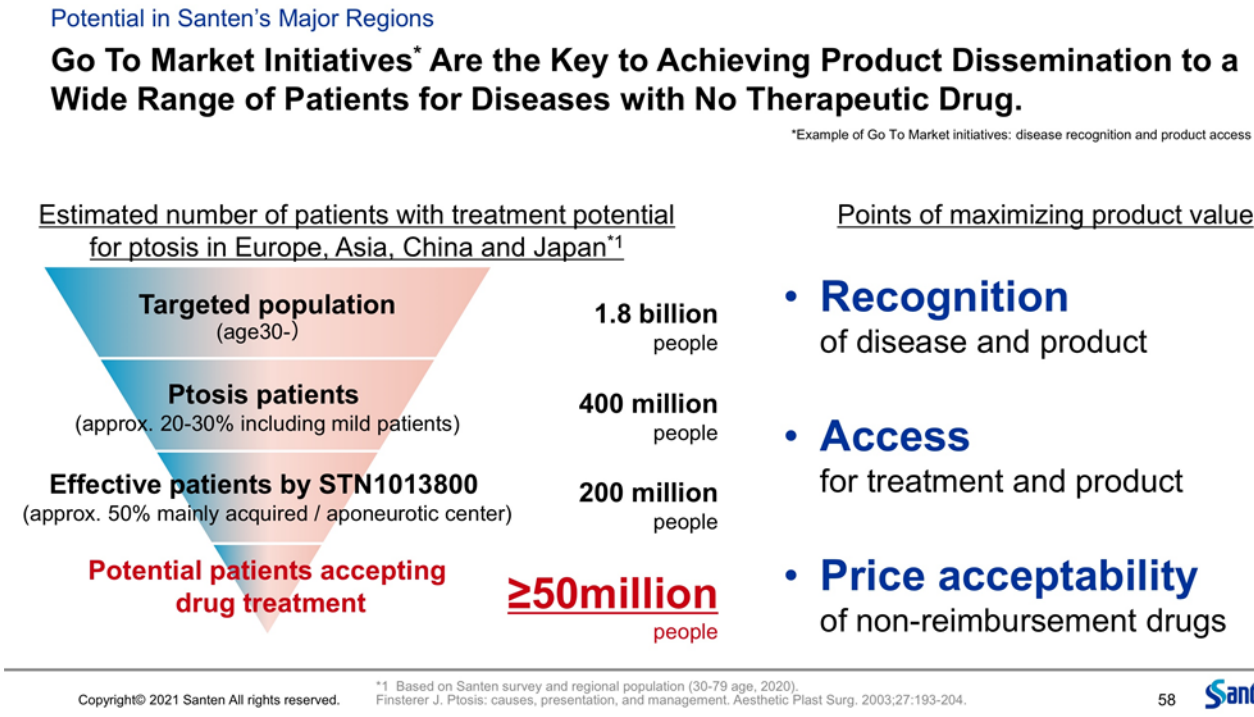
Oxymetazoline is the API used. This is used in various OTCs, so it is quite safe as well.

I mentioned the medical opportunities and aesthetic opportunities. So again, such a core treatment is the only available option today. This is going to be the very first eye drop of its kind in the world to treat ptosis.

Currently, patients with aesthetic needs are not being addressed. For example, there may be people who are concerned about looking sleepy or having an asymmetrical appearance. These needs could be addressed with this product as well.

There is a surgery option available today, but that means it is expensive. And also, you may find it to be somewhat scary. It is not that you need to make just 1 visit to get your surgery and you are done. No, that is not the case. After the surgery, you will need to go back the following day for a checkup and 1 week after and 2 weeks after.

Also, there will be a consultation prior to surgery as well. There is also downtime where your eyes may swell and may not be able to go out in the public. And so, although our solution level might not be exactly as the same as that of surgery, but we believe it is a very efficient way in that it is very comfortable.



Next slide. This is looking at the major regions of Santen: the EU, Asia, China, and Japan. As I said, the target population we are assuming is 30 years old and above, that is 1.8 billion people globally. The prevalence of ptosis is about 400 million.

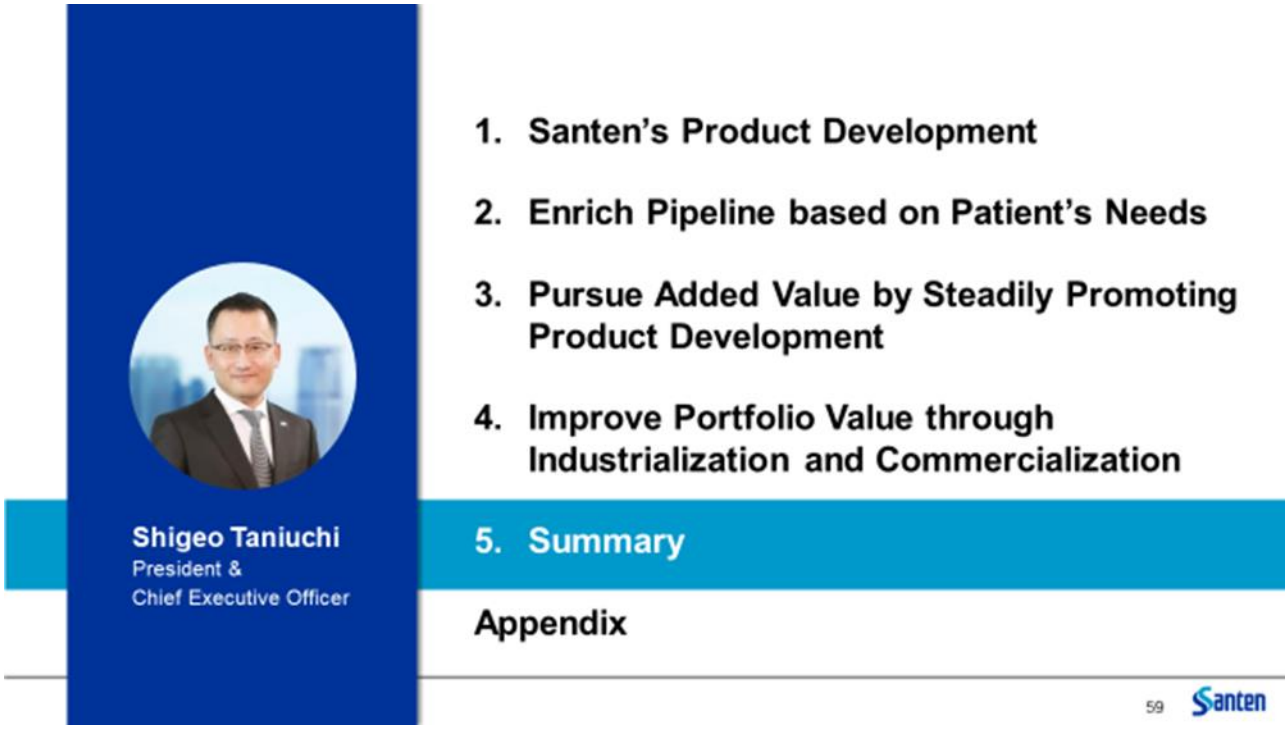
The agent works on Muller muscle. It may be efficacious on some, and not so efficacious on others. So with that in mind, of the 400 million people with ptosis, we estimate that 200 million people would find *Upneeq* to be beneficial.

And of that, we estimate 50 million people, based on our research, are having interest or treatment intent using the product.

Now this is only a potential number that we are estimating. We also need to make sure that we enhance the recognition of the disease and product and also create access to the treatment and product this year through commercialization. So, this is a commercialization challenge for us.

We need to look into the economics of each vision and market as well. We want to get as close as possible to 50 million. And this is up to our commercialization capabilities. We would like to overcome the various hurdles and challenges so that we can deliver other treatments to many patients.

That's all. Thank you.



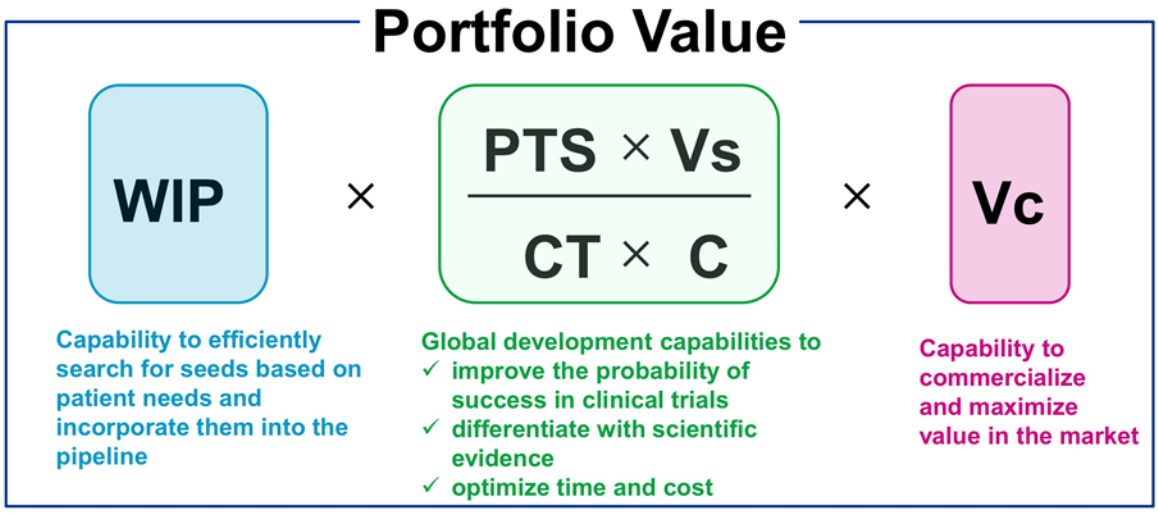
So, we have talked about the product development strategy to Santen 2030, what we are aiming at, and how this will contribute to our profitability.

As I said in the beginning, there should be the improvement of core products, and we are promoting the new frontier as well. For example, for glaucoma, we have *Eybelis,* improved *Tafluprost, Microshunt, Rock inhibitors and others and* for allergy, we have *Alesion*.

Also, the myopia and the ptosis new areas and glaucoma as well, this should be included in the mid- term strategy.

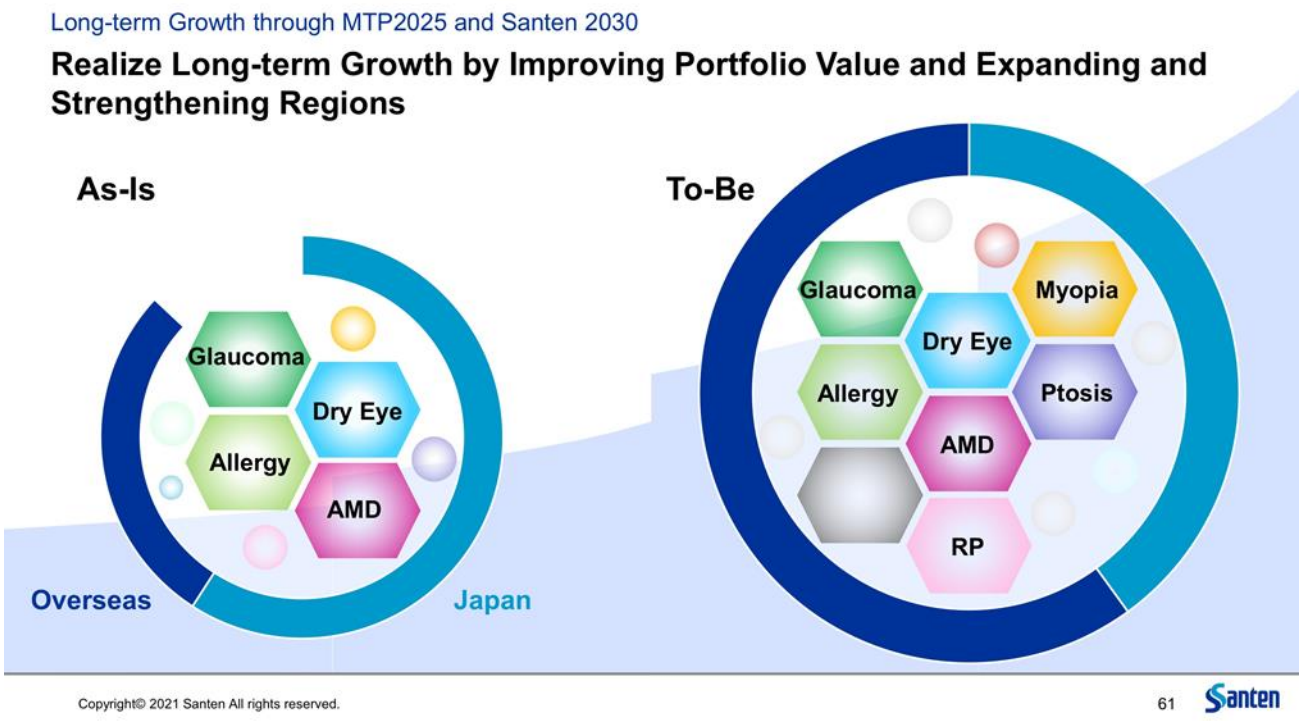
Efficient Product Development

Contribute to Future Profitability from Product Development



Please look at page 60. As I said in the beginning, we try to promote process innovation and medical innovation. The 2 perspectives to address the medical issue. As for the medical innovation, we try to refine the 3 capabilities, working more on process and the productivity of the development and maximizing the commercial value.

Those 3 capabilities must be improved to contribute to the value maximization for the patient, as well as our own growth.



Next slide on page 61. Together, we see enhancement of our portfolio value. We are expanding geographically to achieve MTP2025 in Santen 2030. So, from now, 5 years and 10 years to come, the portfolio will develop from the current status greatly; taking in the growth opportunity, we will be a global company. I strongly believe in the global growth.

So with regards to continuously listening to the voices of the patient and the medical professionals, and providing the solution to the challenges to attain long-term growth, we'd like to make our utmost effort together.

I solicit your continued guidance and support.

Question & Answer

Q-1-1

I have a question about the idea of development of myopia treatment. On slide 16, there is a goal to protect the children from the risk of myopia, or losing sight.

So, are you targeting the severe patients who are at the risk of losing sight? For atropine, you have a broader scope of a goal, but there is another item, and the first goal of development is on page 16. So, you are targeting the patients who are at such a severe stage?

A-1-1

Taniuchi: First of all, for myopia, the goal we are targeting is not just on the atropine, but I am explaining the stance for myopia or something as a whole. The goal is to try to suppress the progression of myopia for children, and to try to prevent the possible risk of losing sight in the far future.

The first step to achieve is the atropine. It is for suppressing the progression of myopia for children and for more severe targeted patients. How do we stop the progress from severe patient to very severe? Well, it is too early to discuss today, but we have a portfolio as a whole.

And in the end, for milder patients, they get rid of the spectacle in their daily life. And for severe patients, we tried to minimize the number of severe patients who are at the risk of losing sight. So, we have the portfolio. Peter or Reza, if you have any additions, please.

Sallstig: Yes. Peter speaking here. Thank you so much for the question. I think as we're trying to approach this, this is still at the early stages for us, as was already pointed out also in the presentation. So initially, of course, with our clinical trials, we're trying to address the patients who are still at an early stage in their disease.

I think it's absolutely critical to be aware that these patients need to be treated as early as possible. We also know that many of these patients, of course, are rapidly progressing. So, if we're looking at our data that we're currently have, and that I also presented from STN1012700, those patients were, quite frankly, more at the early stages, so the mild to moderate myopic patients. And this is our first initial goal.

Then, of course, we're hoping, as was alluded to, to have a portfolio with other follow-up compounds that are much stronger in their efficacy, where we could also be targeting patients that are more progressed in their disease and much more severe. But nonetheless, I think it's absolutely critical to recognize we need to treat these patients as early as possible.

Q-2-1

The first 1 is about jCyte's early data, which was presented. I don't recall looking at this data before, but I have a question about how this data should be looked at.

So, the overall conclusion here, I guess this would be, is it BCBA, a change of 7.4% versus 3%? So, there's this data, and then there's stratified data as well. In conducting future clinical studies, your conclusion was that 7.4%, was not good enough. And so, you moved on to do the stratification analysis to get 16.3% for this will be conducted.

I want to know the approach for future clinical study and how we are to conduct a stratified analysis, please.

A-2-1

Sallstig: Thank you very much for the question. You're absolutely right. I mean, in this patient pool, in the initial, so to speak, the para-protocol population, what we saw there was that there was that trend towards achieving those differences.

But 7.4%, as you say, while it's an improvement, it's really not differentiating in itself. And you have to also understand for these patients, which are quite rapidly progressing, as I was saying, they actually have a quite significant impact later on in their life.

We recognize that there is another way of looking at this patient pool that is a better way, and what we believe will also help us actually to move forward in the Phase III.

Now as I mentioned, we're still here at the early stages. We still need to actually talk to the agency. So, if we go to the next slide, please, slide 40. So, this is actually looking then at that target population. Literally, there are 3 criteria that we were looking at in order to come to this 16.3%. 1 was to make sure that between, for instance, the study eye and the fellow eye that there was at least a 3-letter difference.

Then we also needed to ensure that there was the centralization. So, there are a couple of these variables that we looked upon. These, of course, still need to be validated and discussed with the agencies before we move forward.

But we believe that once the agency agrees to this, and once that we can actually see the impact that this has, particularly with the 6-million cell-arm here, we will move forward, because you could see with the 3-million-cell arm, we did not see that same response.

So, moving forward, I think it's the 6-million-cell arm with this specific population that we've been able to select, but again, it needs to get the buy-in also from the agency.

Q-2-2

I do have another question about presbyopia.

So currently, it seems like you have already identified a candidate. So, I'd like to know about the development timeline of preclinical, clinical, if you have a timeline in place already for presbyopia?

That's my second question. Thank you.

A-2-2

Haque: Thank you very much. As I mentioned in my talk, we decided to start the POC study very soon for presbyopia. We will move on to Phase II and Phase III. It will take some time.

And as you've seen, there are a lot of other companies working on the pinhole effect. But our program is not on pinhole. It is on the lens elasticity, which stays the pathophysiology of the disease, not for 1-hour improvement. We're not doing that.

Q-2-3:

So POC means that the clinical study is being done already? Or is that to be conducted, reanalyzing?

A-2-3

Haque: We are planning to do the POC very soon.

Taniuchi: So, to your first question, Peter did respond to that, and we do have data available. We are working together with jCyte on this. We have a team that is dedicated to cell therapy, and we are working on that.

In October, we had staff join us from Novartis, and so we have a very good team that we are working with. So, as for development and commercialization for this, we would like to see acceleration. We are working very hard.

And presbyopia: Reza responded to your question. We do not have specifics yet that we will need to go through agency consultation, but we would like to accelerate the clinical studies. So please do look forward to some good data. We are taking a unique approach, and so we are very excited as well.

Q-3-1

Well, first 1 is STN1012700, which is the myopia treatment drug. So, what is the development of the situation in China of this drug? In a way, the competitors, some competitors are ahead of you. But even in the case the competitor comes ahead of you, in terms of the quality, in terms of the performance, are you able to establish the competitive advantage over them?

Would you explain about your strategy?

A-3-1

Morishima: Yes, there are 2 competitors who were ahead of us in China and also other companies are now applying. So, the competitive landscape is very tough now. But we are in a process of collecting global data, not just providing the treatment drug, on what kind of a treatment of modality and methodology is appropriate. We have a kind of a multifaceted data accumulated. That is our strength.

As Mr. Sakai mentioned earlier, there is a population of 1 billion, a great number of patients. So, they were developing a unique dose. A stable supply of a drug can be done by something only, I guess. Of course, we import from the beginning, but we'd like to expand the Suzhou plant; we would like to locally manufacture and locally provide.

And our supply capability is superior to others. So not just the drug itself, but inclusive of treatment modality, stable supply, information provision, we think we are competitive enough to compete in the Chinese market.

Taniuchi: For myopia, yes, as Mr. Sakai touched upon, we need to create the kind of environment, so creating a market is important, as is contacting doctors, schools, parents, how we involve all those players, not just trying atropine. We go out to the market, and we show our posture we are carrying for you.

So, we need to tie up with the academia, and we need to be very kind of a detailed approach in a localized area. And we have that capability already established in China. So, we are able to differentiate in a comprehensive way. I think what the local company can do is very different from our capability.

So of course, differentiating the product itself for quality is important, but moreover, a kind of overall approach to be able to differentiate in the myopia and Chinese market.

Q-3-2

The second question, may I? So, jCell therapy, I want to ask. You mentioned data over 12 months. It shows the very stable efficacy until 12 months. But what about after that, the longer-term efficacy, what is your assumption? And is it possible for a second dose?

A-3-2

Sallstig: The way that the data was designed and is presented, we can present the 12-month data as of now. There is a long-term extension, which is being looked upon. There is also additional dosing, so to speak, that is being looked upon. But this is part of the program.

So unfortunately, we can't share that data as of right now as it's still ongoing. So, my apologies, but that's the best we can answer right now.

Q-4-1

I have 2 quick questions. I wonder if you have any update on *Eybelis* in the US, I think that looking at the past programs in the US, unfortunately, there were some failures in the past. And so, when it comes to interaction with the authorities, I wonder with the new team, if you're having better interaction with authorities.

That's my question.

A-4-1

Sallstig: So, the PDUFA date as of today is set at November 19. From that perspective, we're approximately now a month and a half out, give or take.

You're absolutely right. I think 1 of the lessons learned that we have done is a very proactive approach with the agency. So, we went and talked to them upfront about the 3 pivotal trials that we submitted. So, the pay-only trial, Spectrum 4, as well as Spectrum 3, just to ensure that the data is comprehensive enough for the agency.

And in those discussions that we had it was considered that it was adequate for us to be submitting. We have gone through now, as I mentioned; we are about a month and a half out from the finish line, if I can call it that.

We have had very good interactions with the agencies. We have responded as quickly as we can to questions that they might be having. Of course, you know, there is never a 100% guarantee, but we've done every single step that we can do in order for us to have that partnership with the FDA.

And hopefully, it's actually going to result in a positive approval, but as of today, there is no indication that we wouldn't be meeting the PDUFA date of the 19th.

Q-4-2

My next question is about STN1012600. Phase II is to be moved up is what you mentioned, if I understood correctly. And so, I wonder if you could elaborate on that. Is it that you saw a speedy enrollment of subjects than you expected? Was that the case?

A-4-2

Sallstig: As I was trying to allude to, I think 1 of the things that we've been very much focused upon is lessons learned. So, we obviously had the opportunity already with STN1011700 to have some sights really participating that really were able to deliver.

Combined with the new team that most recently joined us, which really comes from some good ophthalmological backgrounds—such as Alcon, Novartis, and so forth—and also different capabilities knowing the CROs, knowing besides all of this combined, I think, actually has helped us to accelerate the STN1012600

recruitment quite significantly.

So, we're really optimistic about moving this forward. Of course, we still need to wait for the data, but we're quite optimistic at least about the interest that we have seen with regards to this data.

Taniuchi: Especially in the US, in the past, over the last 10 years, we have had some struggles, which is true, and you may be concerned. And that is why we have been working so hard the last 2, 3 years. So, including Peter, we have a very good team structure in place now, and we have been making positive improvements.

We have been changing people, and we have been modifying our relationship with CROs as well. And whether or not this is sufficient, we're not sure, but it's true that we have been making progress steps forward.

And also, it's true that I'm not completely 100% satisfied, but we have been making improvements. And we have started STN1012600 with the new setup. And so that is why we have been able to accelerate.

And also, *Verkazia* approval was 1 as well. And so, I want to believe that we are improving. We feel that we are improving, but then again, we still need to wait for the results. We are constantly thinking about possible different scenarios. And so, I guess all we can do now is wait for some good results.

So, we have high expectations. We are very positive, and we will continue to work to enhance and improve market abilities

Q-5-1

First 1: as ptosis, the commercialization of the ptosis on slide 58, it says that there is a kind of applying issue for this. The ptosis has a medical opportunity and an aesthetic and cosmetic opportunity, but will it be like an OTC in commercialization? Is it the main scenario? If it's the case, like OTC marketing, maybe it can be done by Santen alone in Japan. But in Asia and AU Europe, is it possible to pursue the OTC upload in those other markets?

A-5-1

Sakai: First of all, we don't consider selling this product right away at OTC because it has been approved as an Rx prescription drug. So, it is difficult to sell this at OTC market which approval is by Rx drug. We will continue selling prescription, having certain data accumulated, and then advance into the OTC afloat. That should be reasonable.

And for our strategy in Asia, well, it is difficult to start OTC right over there. Maybe we have to sell other than the ophthalmology goods, then there will be, of course, a new chance for Santen. Maybe we will look for another company who has that capability, maybe if it is the case.

Q-5-2

So, you are going to pursue the Rx that is a medical, kind of ethical drug opportunity first? Then mid-term and longer term, you're going to appeal cosmetic aspect? Can I safely assume that?

A-5-2

Sakai: If I supplement or Rx, we are able to upload 2 ways. Yes, my writing has some kind of a long point. We just pursue the Rx medical, but it is not that we can't approach a kind of cosmetic purpose. That's up to the physicians, the judgment.

There are patients who have drooping eyes, and they are very much annoyed by that. And if the doctor thinks that should be cured or treated, the doctor would provide the drug for that purpose.

Taniuchi: So as the Rx development and also the reimbursement, let's separate the 2. So first for approval as in Rx, and then how it's going to be reimbursed, how it's going to be listed in the NHI price list. I think we need to streamline the story in a very clear way.

Q-5-3

Second question for myopia data: M2 receptor has the low mydriasis potential. So, by just selecting M2 only, as compared to the 1 who has the activity to have 1 way with 3, what would be the difference? Just selecting M2 would be very different from the other selection, M1 or M3.

A-5-3

Morishima: Well, this is still the preclinical. So that link about the mydriasis and collecting myopia, we have a broader opportunity, I guess.

So, if the atropine concentration is effective higher. But because mydriasis is concerned, the window is becoming smaller. But if we just select the M2 selectivity, we don't need to worry about mydriasis and can move more positively treating the myopia. That is our strategy.

Thank you very much. That's all.

Q-6-1

I'd like to just ask 1 question with respect to atropine, or maybe 2 questions. Slide 31. After follow-up, I wonder if data after follow-up has already been disclosed somewhere.

After the administration period, maybe there was exacerbation, or I think there's been some report of deteriorated visual function. So, I think those studying and the administration period, how should they be understood?

And also, for how long could you administer the agent. And I think I understand that you're targeting China, but I'd like to understand the philosophy of development going forward, please.

A-6-1

Morishima: So, the progression of myopia. That's been reported. So that does happen sometimes. The administration period is less than 2 years. And after that, subsequently, there is a follow-up. But in clinical practice, there is the timing of the growing of the eyeballs, which is considered. But that's not been clarified in the clinical studies.

So, as I said, after launch, we will continue to study the optimal approach to treatment. So, this study will continue. After the eyeball stops growing, we will need to see how that is going to be impacting the treatment. Aside from the clinical study, we will continue with the study to generate data.

And your concern was about rebound. And so, we would like to look into that, as well, to see if there is a rebound.

Q-6-2

In order to get approval, there is no data required on rebound?

A-6-2

Morishima: Per the guideline, it's 2 years plus follow-up that needs to be included in the submission package. And so, we will be providing that data into that package.

Q-6-3

Okay. Thank you. Just 1 more question, please. Atropine, I wonder about the IP when you commercialize. In other words, the data protection period, what is that going to be like in China? Could you talk about IP of atropine in China?

A-6-3

Morishima: The drug itself is quite old, so there is no patent around it. There are prescription patterns of each of the companies, and we have the same. We don't believe that there are going to be any products with the same prescription. But in terms of IP, I don't believe that that should be an issue.

So, it's not that we want a monopoly, but it's more about information provision where the doctors would want to come to us. This would be the aim of atropine.

Q-6-4

So, there is no set time or duration for data protection?

A-6-4

Morishima: So even if you get a patent, there is no data protection period. From a regulatory affairs perspective, there is a data protection period for each of the countries. In China, there is new regulation, and so, there are uncertainties we still need to clarify. But we should be able to get some time secured for data protection.

Q-7-1

The early project evaluation, the ROI or some index. Well, I guess are you controlling ROI for M&A and some cost issue. You had the large, fixed asset 1 time. So, I have some doubts about your ROI index and what is going on there.

A-7-1

Taniuchi: Well, I am not too concerned with this. In the early and also the later, R&D cost, the balance sheet impact, yes, we decide the investment and the merger and acquisition. Yes, in the past, as you're concerned, there was kind of a bad figure in a fixed asset enlargement; I really know that. And in the midterm plan, we have to be cautious.

So, we have a hurdle rate and also the impact on ROI, and also the credit recovery, account receivable recovery, so forth; we are now severe, more looking severe. And Sakai is facilitating this, and if you have any additions, please.

Sakai: The early-phase investment, well, the impact upon the return on investment we look at very severely from an accounting perspective, M&A, and also the in-licensing of the compound from others, it's very difficult to evaluate on an equal footing.

But it is not that we have kind of our own long-term possessed assests, and Reza, as a team, is looking into this severely. Reza as a team is doing research and the global BD team will receive that.

So, in actual practical aspect, if Reza has anything to add, please go ahead.

Haque: We are doing a lot, as I mentioned, in our core business and also on new frontiers. And also, there are a few things that I cannot say right now. We are looking into all the venues in ophthalmology possible. And we're working very closely with the BD Group to find a gap, and also with your Global Alliances Group to find out more indications, and all of things we are doing, as I mentioned, clearly, that is all for unmet need.

Q-7-2

I have a confirmation with Mr. Sakai. So, you have a budget well controlled and strictly abiding by the budget line?

A-7-2

Sakai: Yes, I do so. I am doing that.

[END]