

**Ophthalmology Is Our Singular Focus**



**R&D Day 1**

# **Santen's Contribution to Ophthalmology**

Global R&D

Santen Pharmaceutical Co., Ltd.

July 12<sup>th</sup>, 2019

# R&D Days



## Day 1

---

### **Santen's Contribution to Ophthalmology**

Introduction of Ophthalmology and Santen's Contribution  
Santen's Research and Development



## Day 2

---

### **Santen's Future R&D**

Long-term Perspective of Ophthalmology  
Santen's R&D approach

# Santen's Values and Mission Statement

Values

天機に参与する

*Tenki ni sanyo suru*<sup>1</sup>

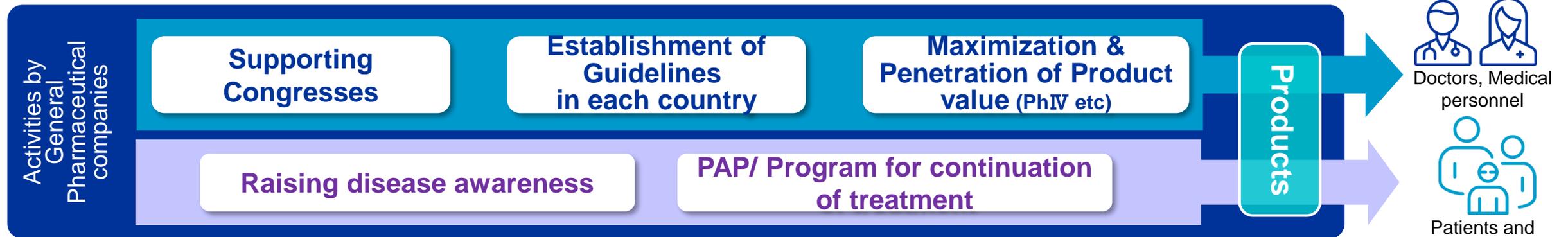
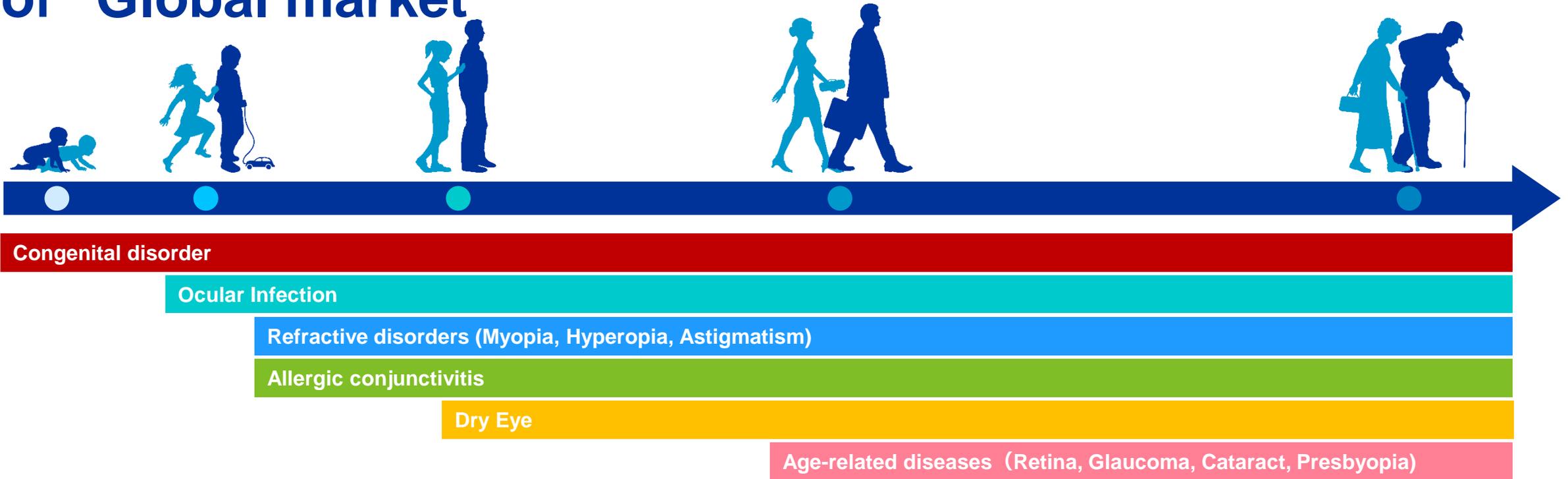
- <sup>1</sup> “Exploring the secrets and mechanisms of nature in order to contribute to people’s health”  
Santen’s original interpretation of a passage from chapter 22 of *Zhongyong (The Doctrine of the Mean)* by Confucius.

**We think carefully about what is essential, decide clearly what we should do, and act quickly.**

Mission  
Statement

**By focusing on ophthalmology, Santen develops unique scientific knowledge and organizational capabilities that contribute to the well-being of patients, their loved ones and consequently to society.**

# Genericized "Life of Vision" in the framework of "Global market"

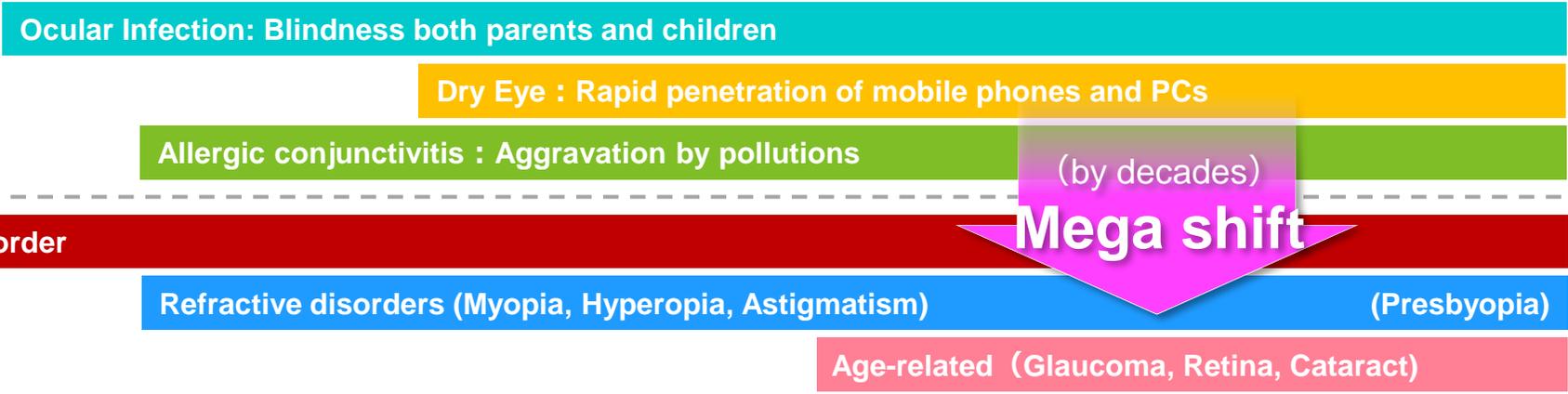


# Our original activities in Asia led Santen to No.1 in important markets

*-Up to and From today-*

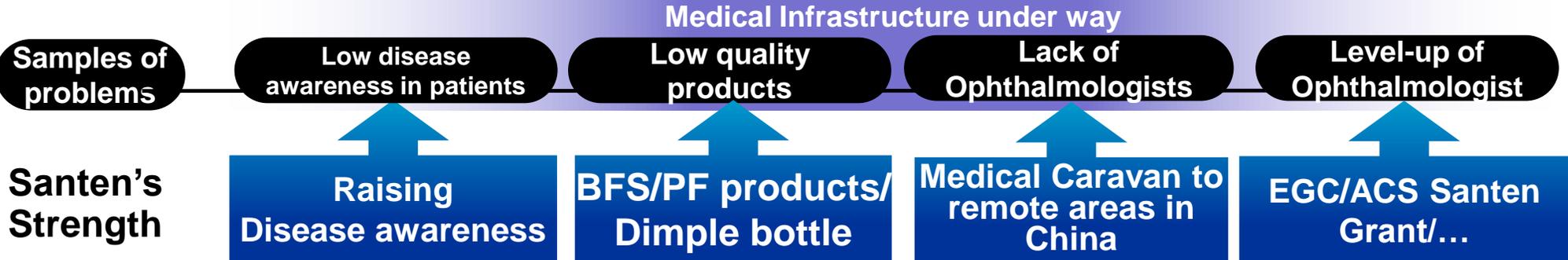


Huge economic area at the moment and in the future with over 3 billion population



Main treatment at the moment (low coverage in medical examine)

In some countries, the items below are progressing  
 -Acceleration of aging,  
 -Preventive treatment for children as important future



BFS; Blow Fill Seal, PF: Preservative Free, EGC: English Glaucoma Camp, ACS : Asia Cornea Society

Establishment of Treatment guideline  
 Efforts to Myopia



# Santen's business activities aiming to protect "Life of Vision" of people around the world

Affected

Diagnosis

Treatment initiation

Treatment period

Continuation of treatment

Raising disease awareness

Improvement of diagnosis rate

Differentiated products

Improvement of compliance

Supports for stakeholders in ophthalmology

Stable supply

- Improvement of usability
- Minimally invasive

Global

Advanced Countries

Prevention

New technology for diagnosis and treatment

Recurrence prevention

• Initiatives to age-related chronic disease

Developing Countries

Eco system

Raising and Supporting of ophthalmologists

Raising disease awareness

High quality products

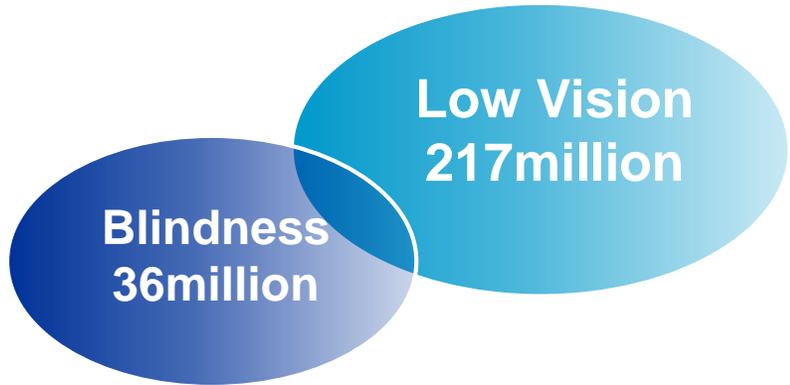
---

# Basic Policy on Santen R&D

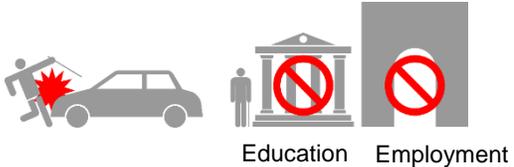
---

# Protect the Sight of People Around the World

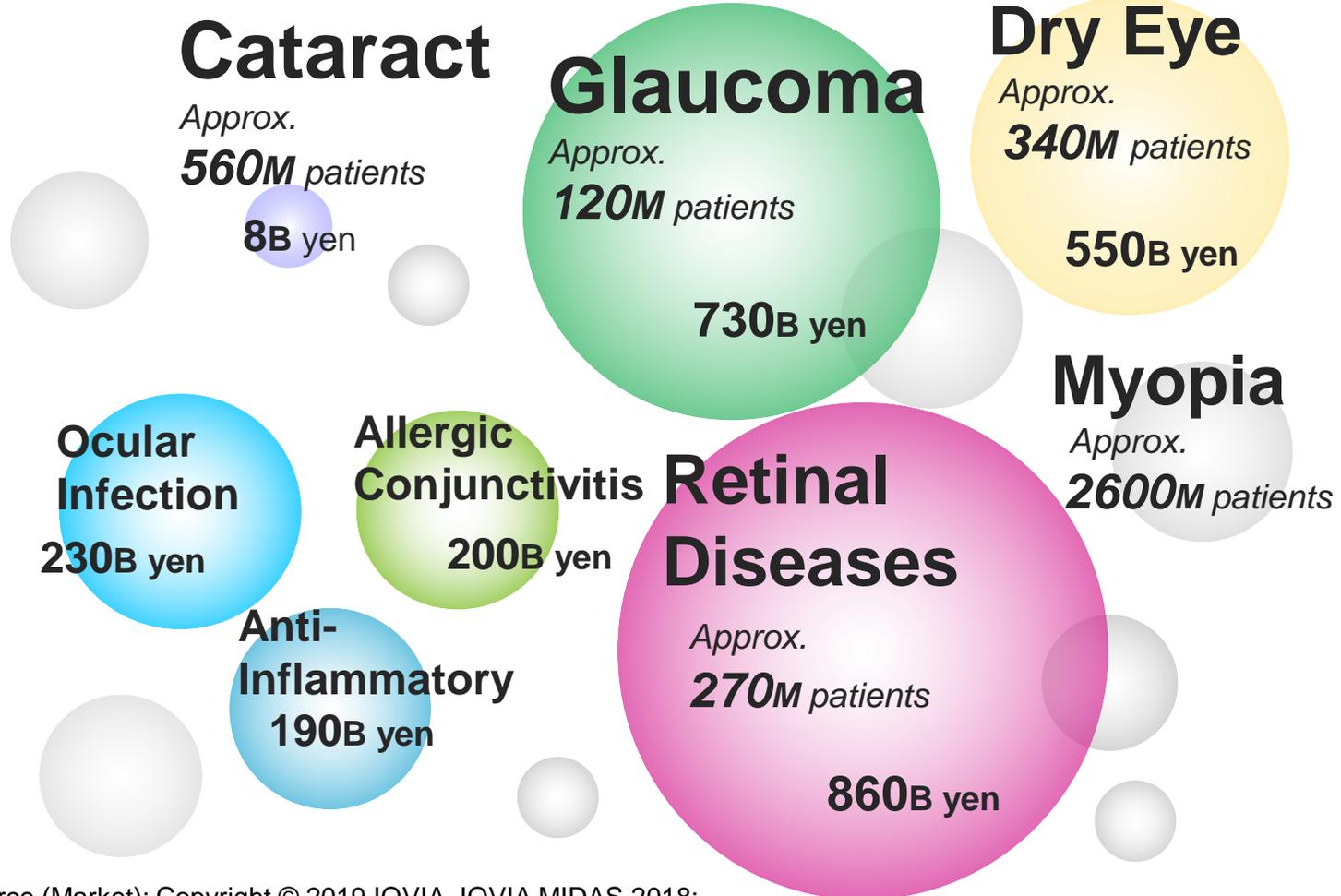
## Ophthalmic market (2018) and number of patients



Vision impairment estimated impacting 1 in 30 of world population



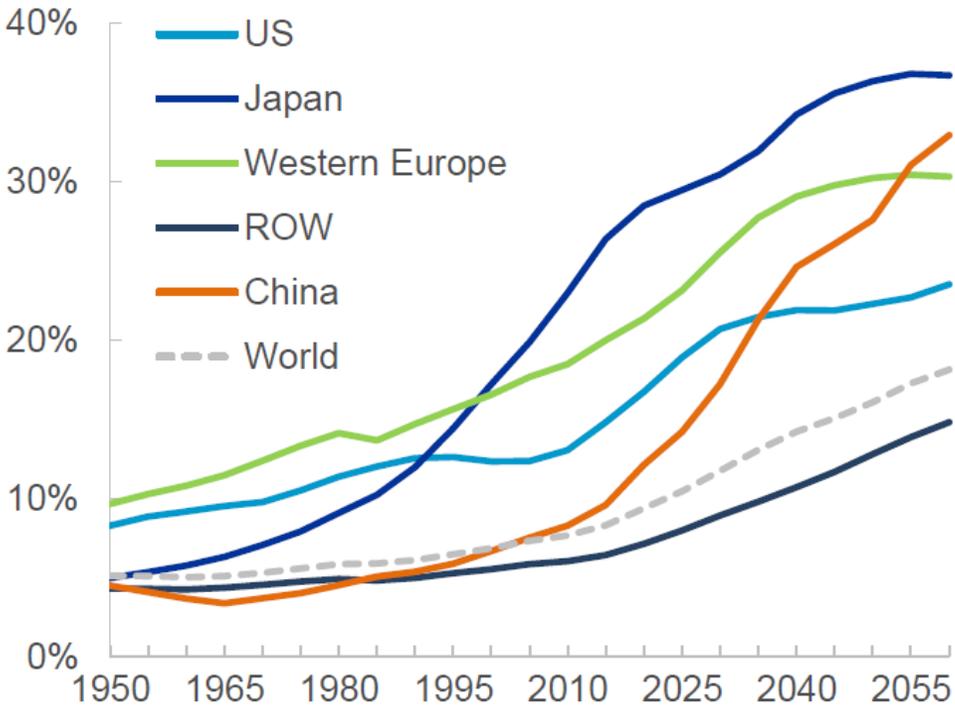
Source: WHO World Sight Day Poster



Source (Market): Copyright © 2019 IQVIA. IQVIA MIDAS 2018; Santen analysis based on IQVIA data. Reprinted with permission.

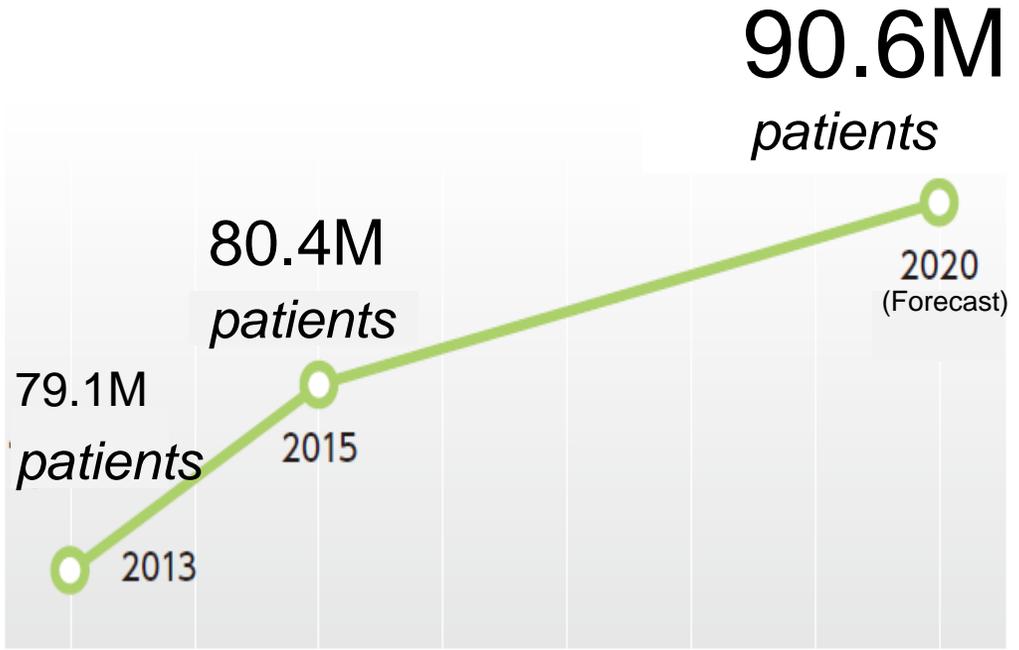
# Problem of Eye Disease Becoming Larger as the World Population is Aging

## Population Aged 65+



Data Source: United Nations, World Population Prospects: 2015 Revision

## Number of Glaucoma patients



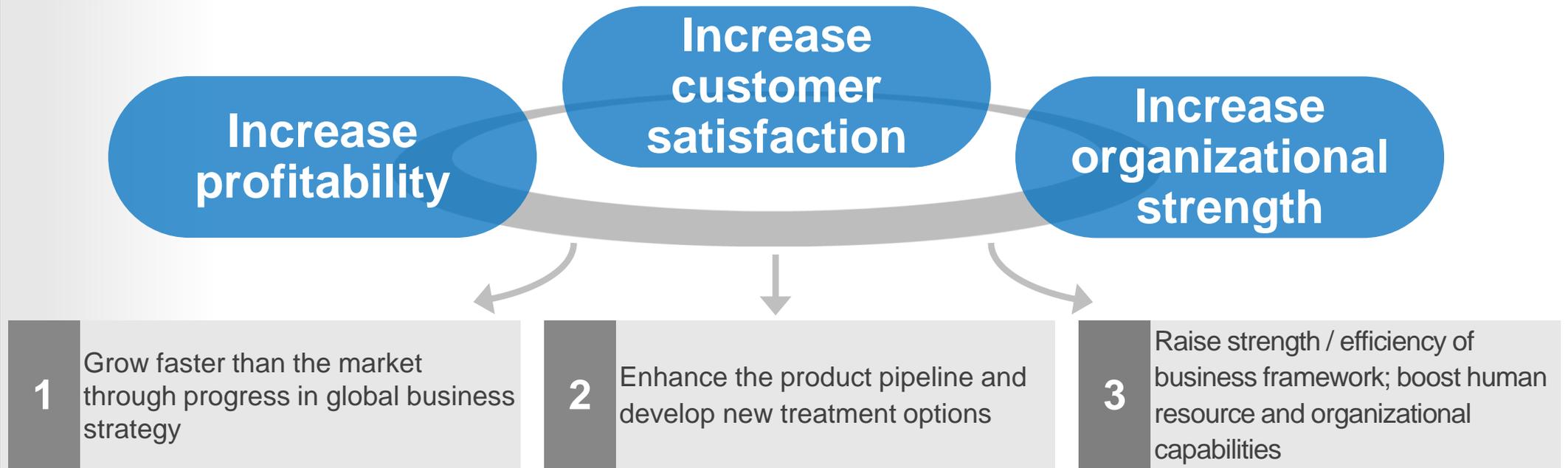
Data Source: Market Scope; Santen analysis

# MTP2020 Fundamental Policy and Strategic Goals

## FUNDAMENTAL POLICY

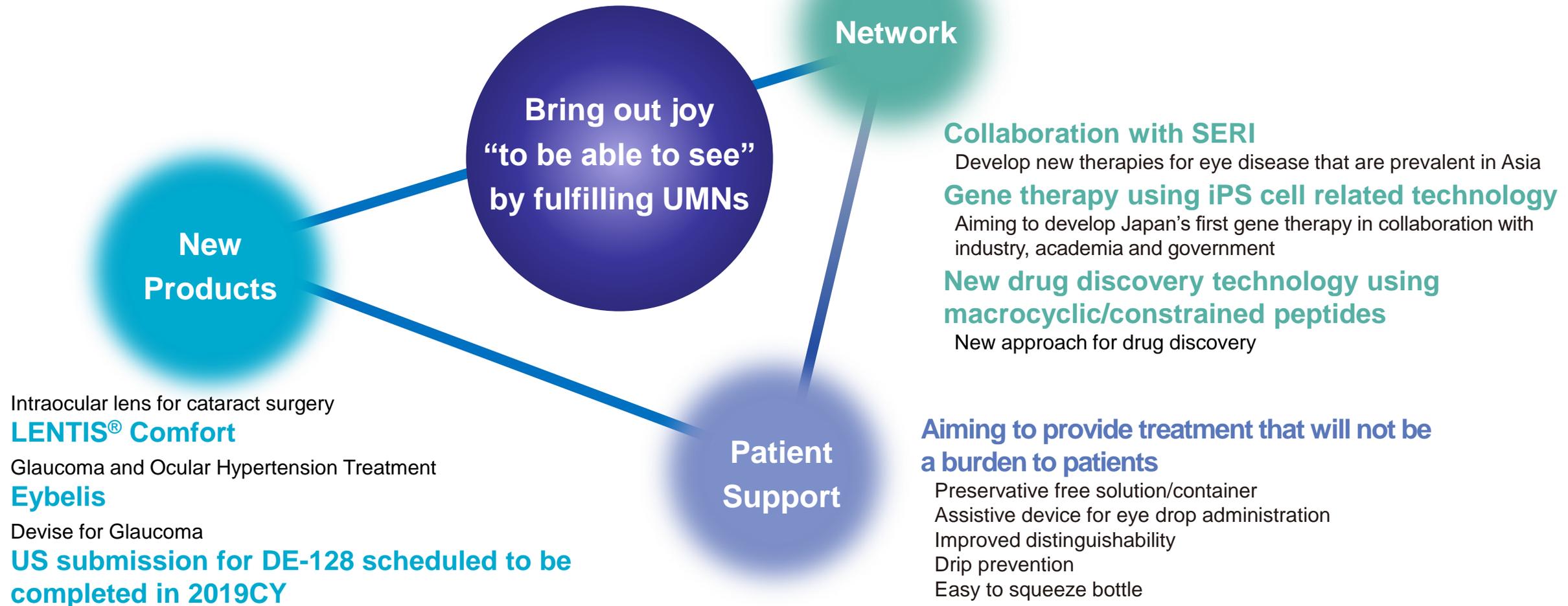
- To become a “Specialized Pharmaceutical Company with a Global Presence”
- Construct a path for sustainable growth beyond FY2020

## STRATEGIC GOALS



**Responding to the needs of patients and medical professionals worldwide, Santen will achieve reliable growth while sustainably contributing to ophthalmic treatment worldwide**

# Pursue development of much needed medical products, devices, information services by leveraging global R&D network



# Bring Out Joy “to be Able to See” by Fulfilling UMN<sup>\*</sup>

**Application of systemic drug**  
 Eye infection  
 Anti inflammatory  
 Allergic Conjunctivitis



**Therapies specific to ophthalmology**  
 Retinal disease  
 Glaucoma  
 Dry eye  
 Refractive disorder



**New modality**  
 Gene therapy  
 Cell therapy  
 Regenerative medicine  
 etc.



**Treatment for vision impairment**  
 QOL improvement



**Formulation change**  
 Low preservative  
 Combination drug  
 Dosage form change  
 Container



**Administration**  
 Intravitreal Injection

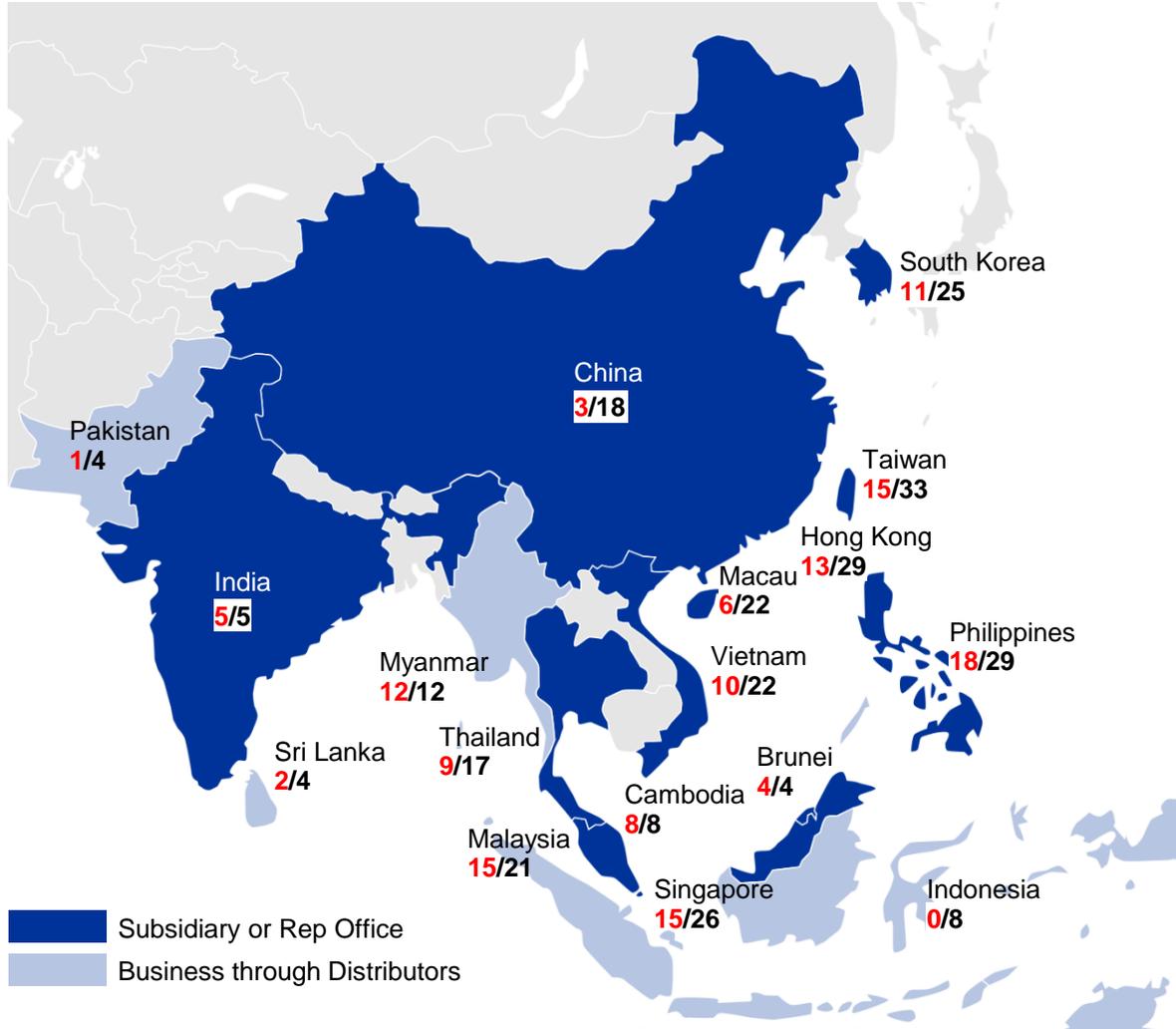


**New Dosage form**  
 Long lasting formulation  
 Drug Delivery System  
 Medical device



\*Unmet Medical Needs

# Proactively Introduce Products Approved in Japan & Europe to Asia



**No. of approved products in recent 5 years: 147 Products**  
**/ Total No. of products: 287 Products**



**Only 27 new products have been approved by China FDA**

**4,400 pharmaceutical companies, including 200 foreign companies**

**Only Santen for ophthalmic agent**

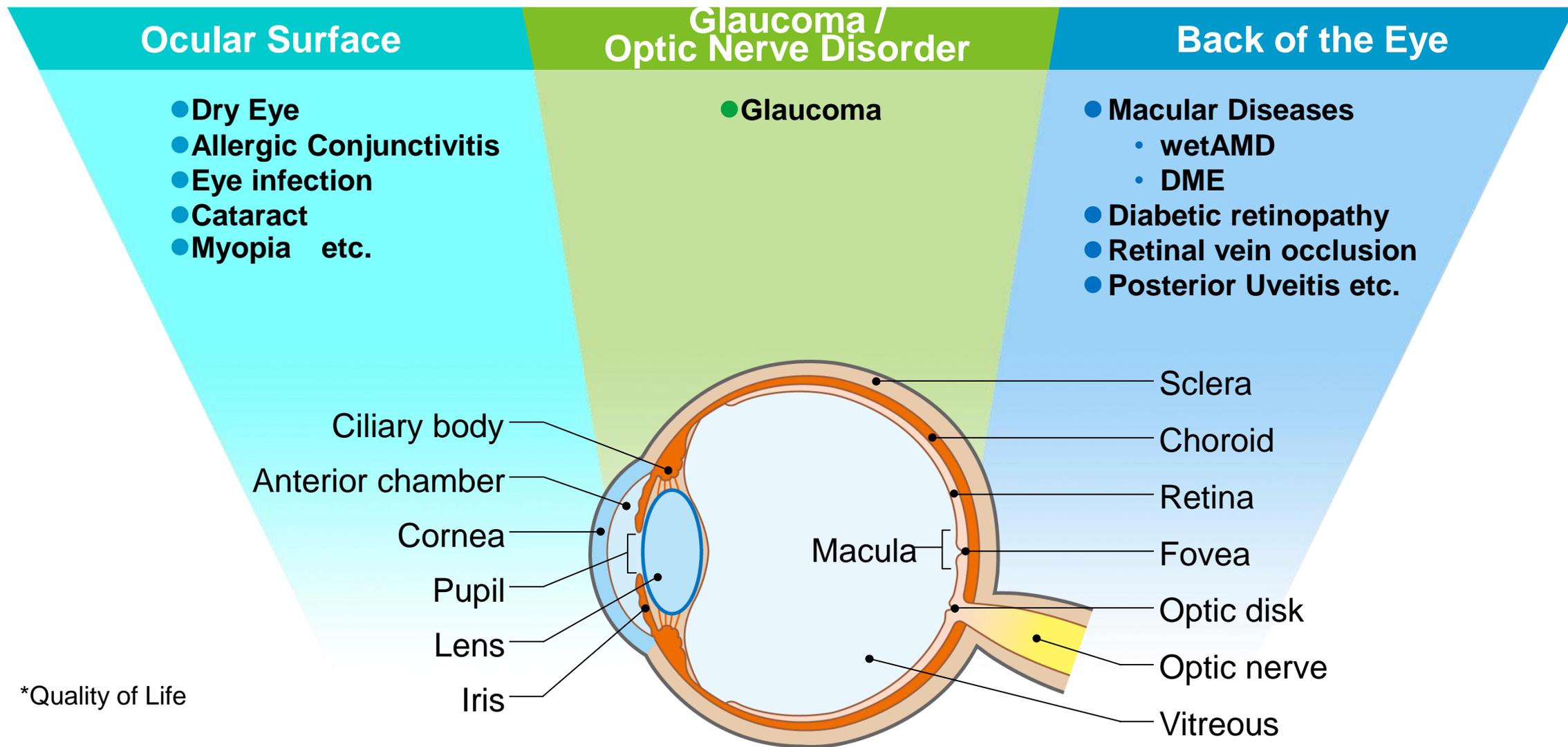


---

# Overview of Eye Diseases

---

# Conducting R&D Specific to Ophthalmology to Contribute to Improving QOL\* in Patients Around the World



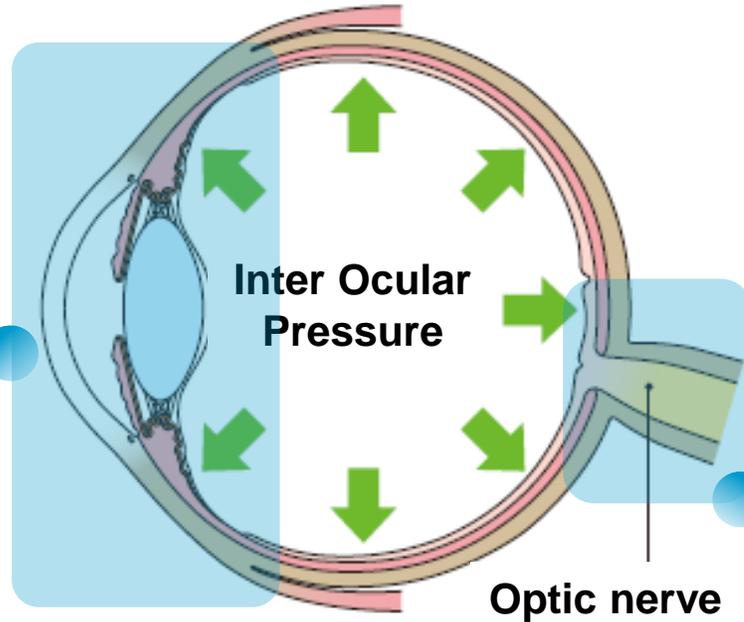
\*Quality of Life

# Glaucoma: Preserve Visual Field by Lowering Intraocular Pressure

The No.2\*1 cause of blindness in the world, No.1 in Japan\*2

Optic nerve damage due to high intraocular pressure

Inhibiting progressive visual field loss  
IOP lowering  
(Start/Continuation)



Visual field loss

Initial stage



Late stage



Image (Right eye only)

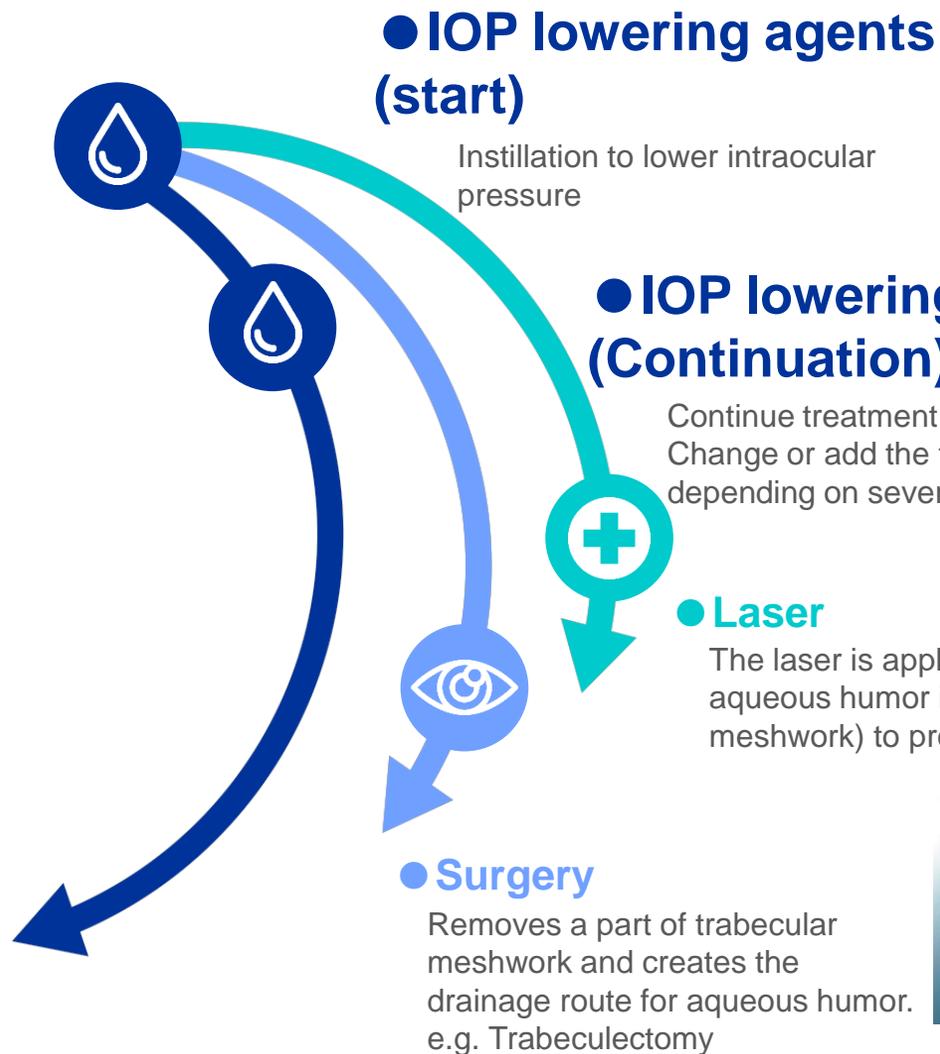
Keep and recovery of visual field

Neuroprotection

\*1: WHO Global Data on Visual Impairments 2010

\*2: Morizane et al, *Japanese Journal of Ophthalmology*, January 2019, Volume 63, 26–33

# Glaucoma: Respond to the Diverse Needs with Extensive Product Line



**Timoptol XE**  
0.5%



**Detantol**  
0.01%



**Tapros**  
0.0015%



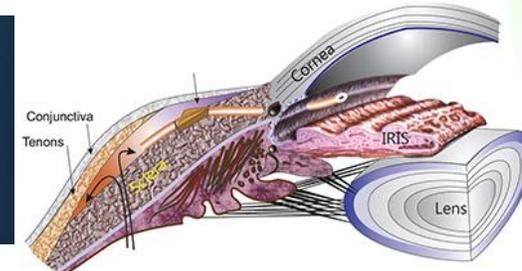
**Eybelis**  
0.002%



**Trusopt**  
1%



**Tapcom**



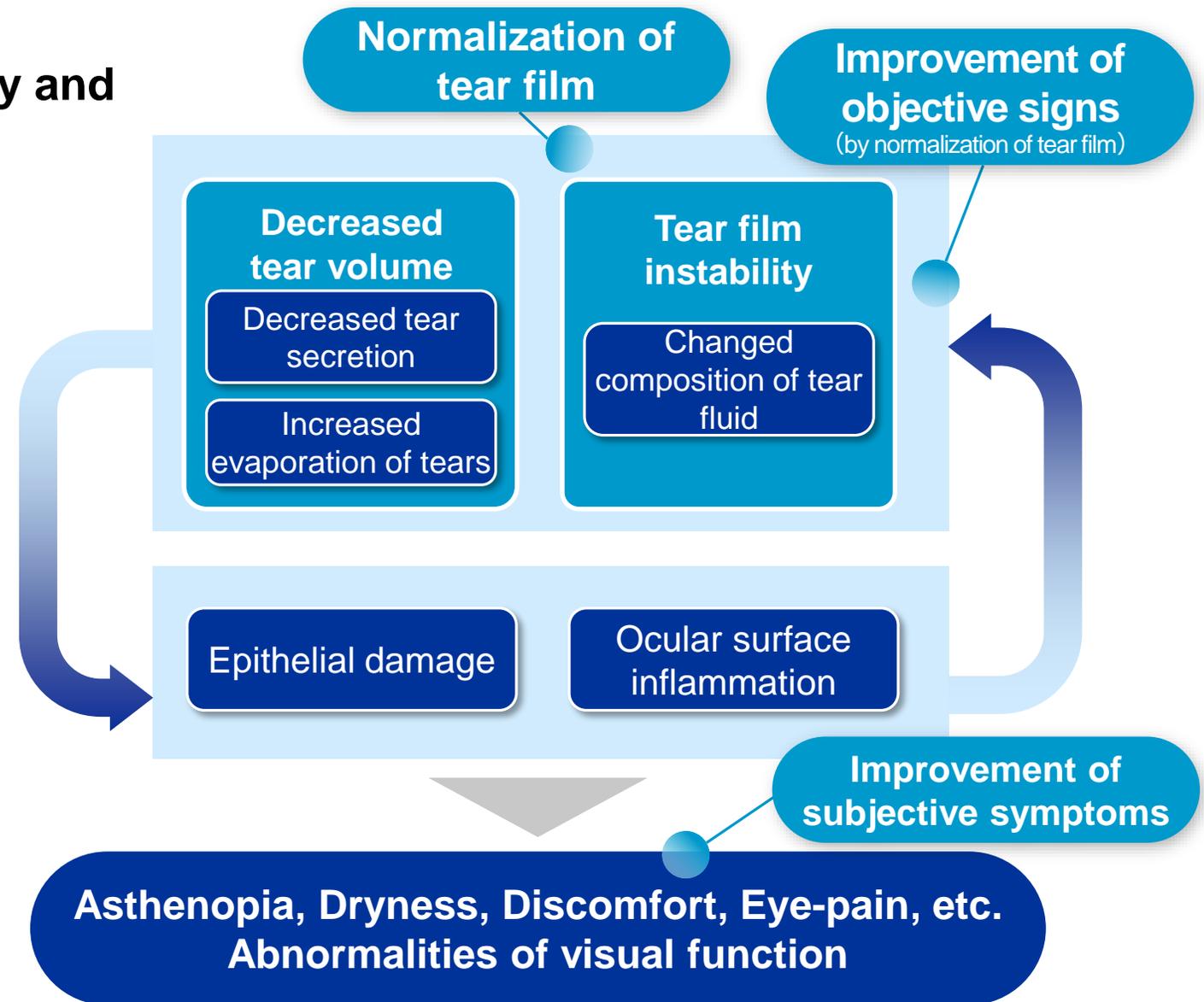
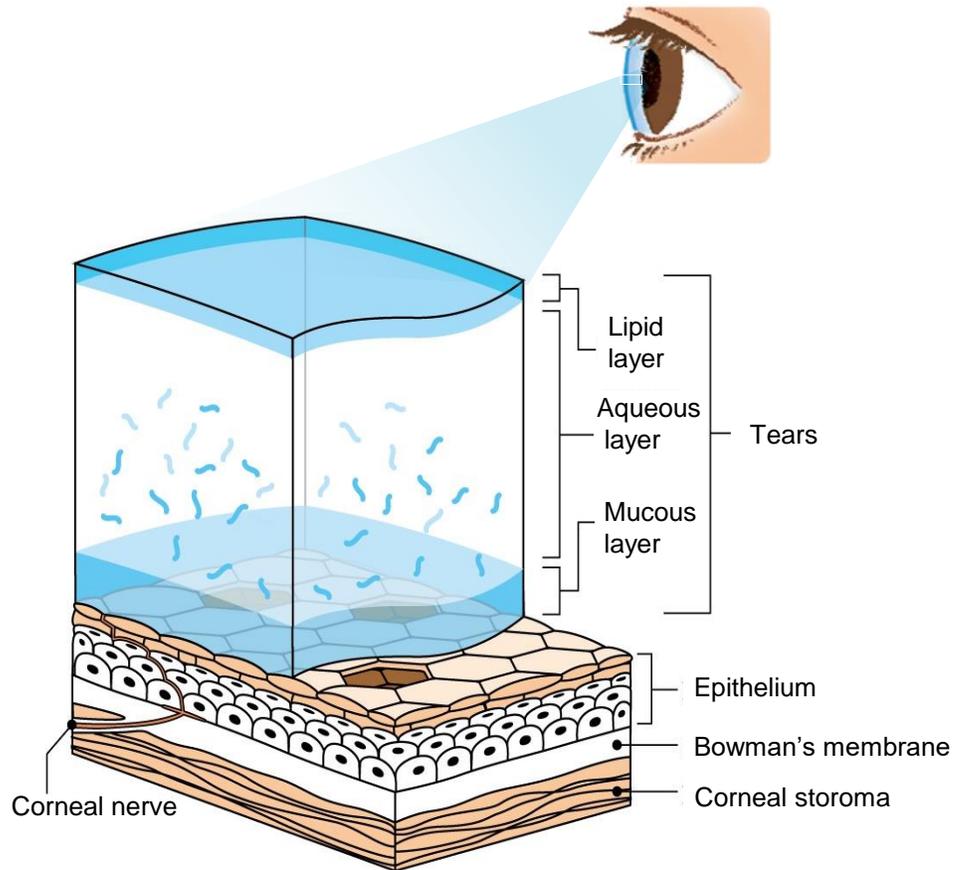
**Efficacy**  
Stronger IOP lowering agents  
Supporting to non responders

**Safety**  
Reduction and avoidance of adverse reactions  
Reduction of invasiveness and complications of surgery

**Usability**  
Improve compliance  
Reduce Patients' burden  
(Easy to drop)

# Dry-eye: Improve Condition by Targeting Causative Mechanism

A disease that can decrease productivity and worsen the QOL over time.

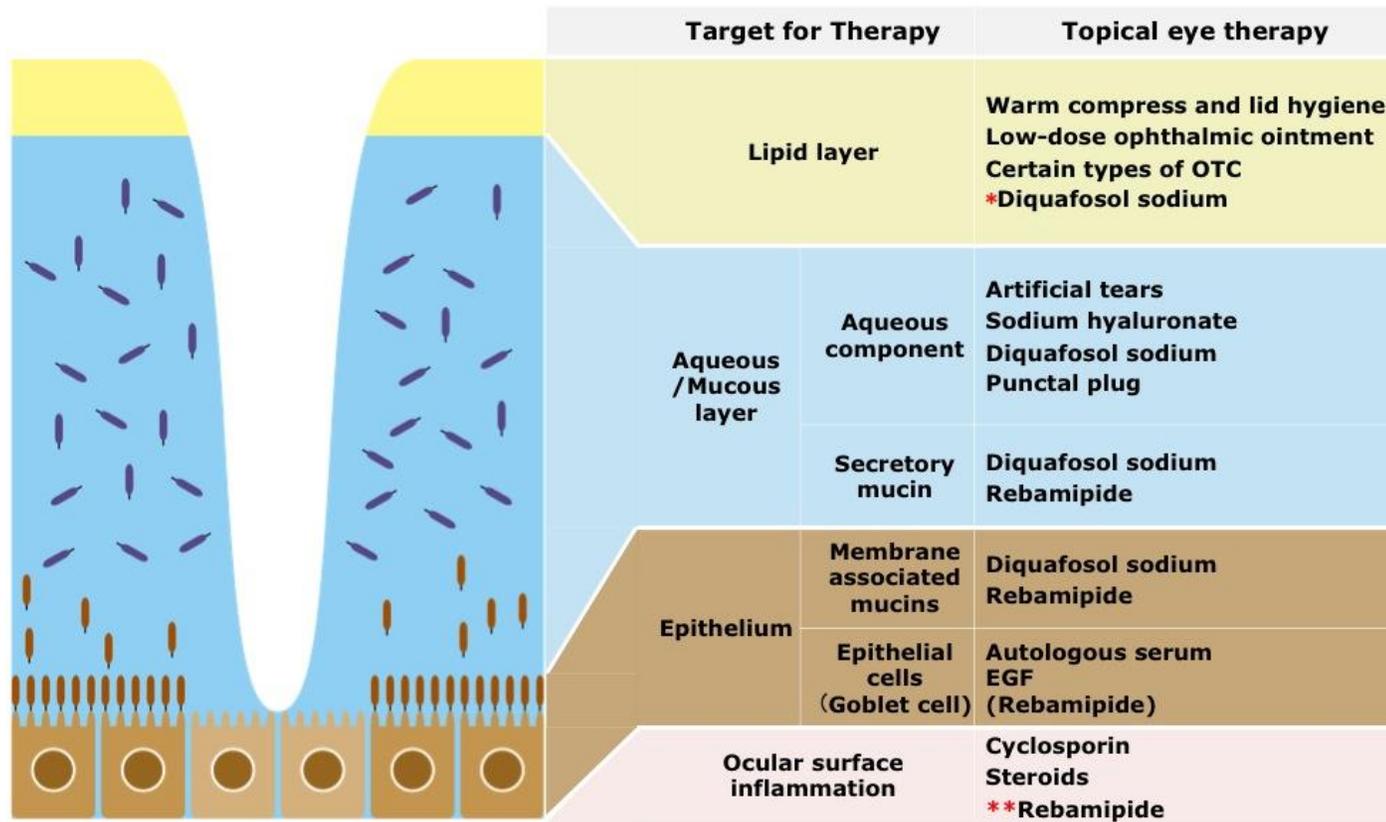


# Dry-eye: Product line for Tear Film Oriented therapy



## TFOT (Tear Film Oriented Therapy)

Ver.1



Diquas 3%



Hyalein 0.1%



Soft Santear (OTC)



Cationorm® MD / Cationorm® SD



Ikervis®

\*Diquafosol sodium may increase the function of the tear film lipid layer by promoting spreading of the lipid layer through lipid and tear fluid secretion.  
\*\*Rebamipide may suppress the inflammation of the ocular surface in dry eye by its anti-inflammatory action.

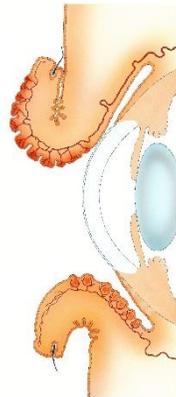
Supervision: Dry Eye Society

# Allergic Conjunctivitis: Provide Treatment to All Patients from Mild to Severe

Itching  
Hyperemia / edema



Cogan Collection, NEI/NIH



## ● Improvement of main symptoms

Anti-histamine ophthalmic solution  
Chemical mediator release inhibitors



Alegysal  
0.1%



Alesion  
0.05%



Lecrolyn® SD

## ● Improvement of main symptoms

Anti-inflammatory ophthalmic solution



Flumetholon  
0.1%



Verkazia®

PapiLock Mini  
0.1%

\* For vernal conjunctivitis

## ● Improvement of safety and usability

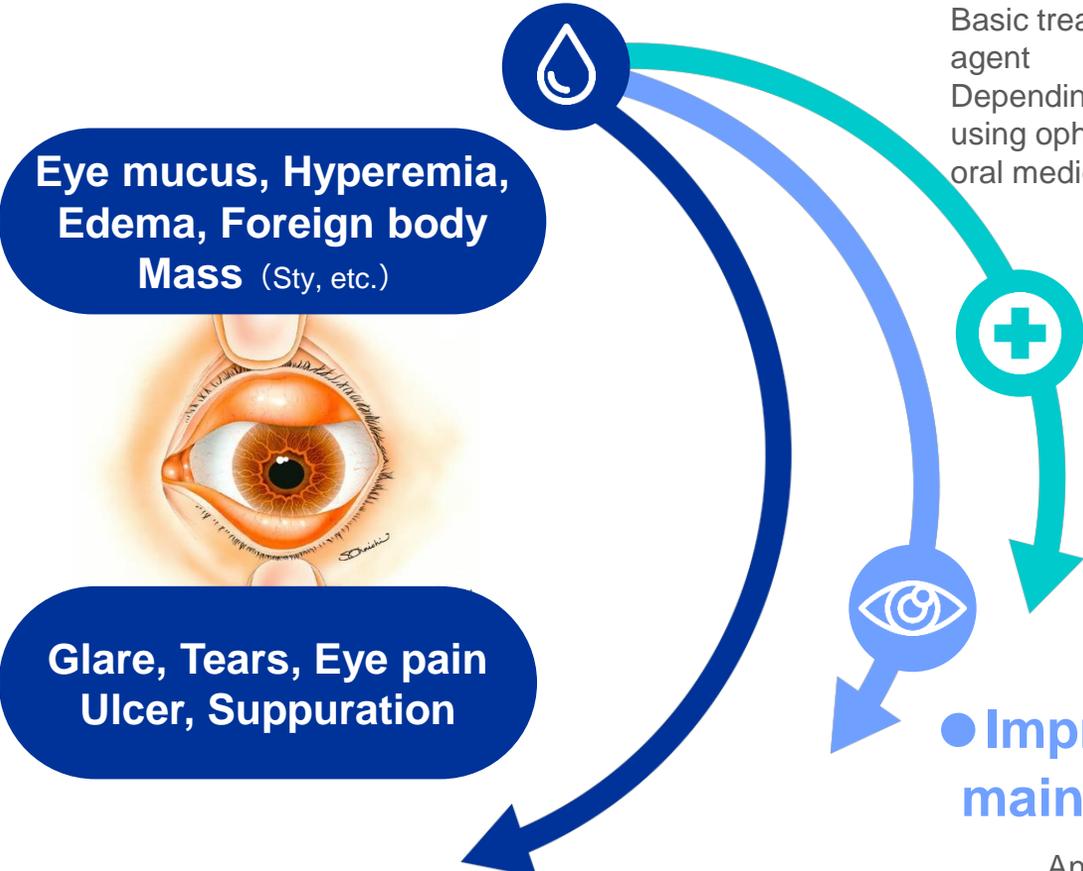
BAK free  
Reduce dose frequency



Reduce dose frequency

4 times/day ▶ 2 times/day

# Ocular Infection: Introduce Wide Range of Product Line to Emerging Countries



## ● Antibacterial

Basic treatment with antibacterial agent  
Depending on the type of bacteria, using ophthalmic ointment and oral medicine



**Tarivid**  
0.3%



**Cravit**  
0.5%



**Cravit**  
1.5%



**Ecolicin** ophthalmic ointment



**Tarivid** ophthalmic ointment

## ● Antiviral

Antiviral ophthalmic solution  
Antiviral ophthalmic ointment



**Zovirax** ophthalmic ointment

## ● Improvement of main symptoms

Anti-inflammatory ophthalmic solution



**Flumetholon**  
0.1%



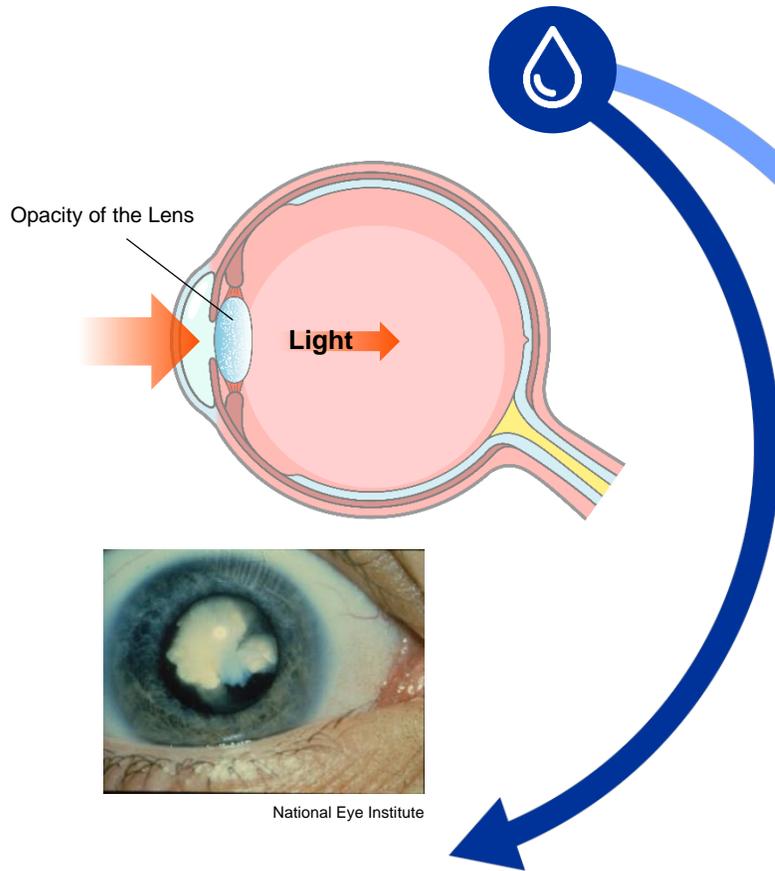
**Proranon**  
0.1%



**Santeson** ophthalmic ointment

# Cataract: New Concept Intraocular Lens

51% cause of blindness in the world\*1. Affects all over 80 years old.\*2



## ● Suppression of lens opacity

Ophthalmic agent to suppress lens opacity by stopping degeneration of lens protein



Kary Uni  
0.005%

## ● Cataract surgery

The lens that has become cloudy is removed and replaced with an intraocular lens

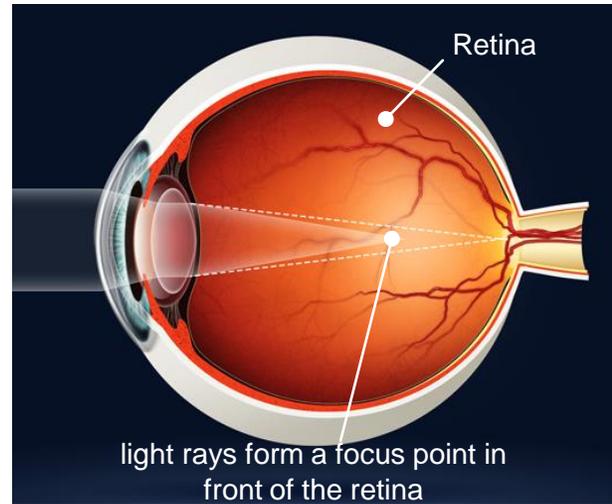


\*1: WHO Global Data on Visual Impairments 2010

\*2: 科学的根拠 (evidence) に基づく白内障診療ガイドラインの策定に関する研究 2002

# Myopia: Aim to Develop and Provide the World's First Treatment

27% of the world population is estimated to have myopia\*. Forecast to increase in the future.



**Suppression of the axial length elongation**

Low dose atropine

**Vision Correction**

Eye glasses, Contact lenses, LASIK

**Axial length growth**

**Pathologic myopia**

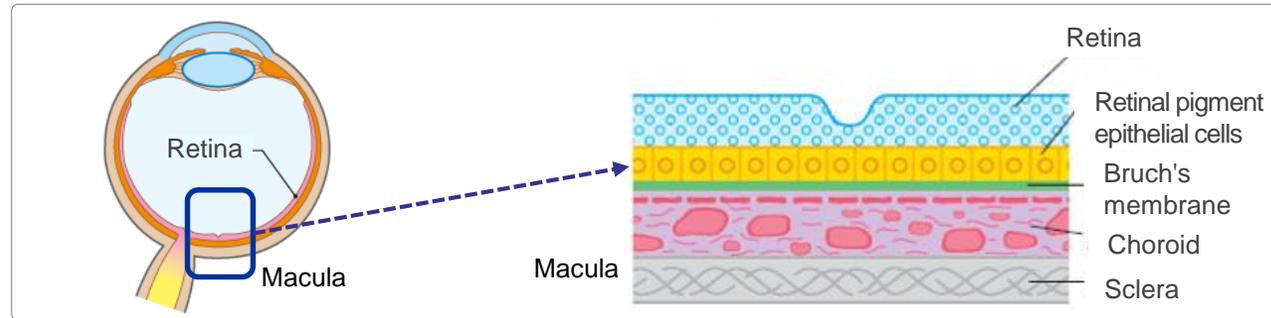
**Vision loss**

**Treatment of the cause of vision loss**

Regression of neovascularization (Anti-VEGF therapy)

\*: IMPACT OF INCREASING PREVALENCE OF MYOPIA, Report of the Joint World Health Organization

# Retina/Uveal Diseases: Aim to Provide Better Treatment Option



## wet Age-related Macular Degeneration (wetAMD)

Abnormal blood vessels begin to grow toward the macula. Then, the macula is impaired and can result in a severe loss of central vision.

## Diabetic Retinopathy (DR) Diabetic Macular Edema (DME)

The retina is damaged due to diabetes. If edema develops in macula (DME), it directly linked to vision loss.

## Central Retinal Vein Occlusion (CRVO) Branch Retinal Vein Occlusion (BRVO)

Retinal hemorrhage and edema caused by the retinal vein occlusion. If this extends to the macula, vision loss occurs rapidly.

## Posterior Uveitis

Inflammation occurs in the uvea (choroid) due to various causes, resulting blurred vision, ocular floater, photophobia and vision loss.

### Anti-VEGF therapy

Regression of the neovascular vessels and inhibition of neovascularization

### Laser photocoagulation

Laser cauterize the lesion or related tissue.

### Photodynamic therapy (PDT)

### Steroid

### Anticoagulant (Oral)

### Anti-TNF $\alpha$ therapy

### Steroid

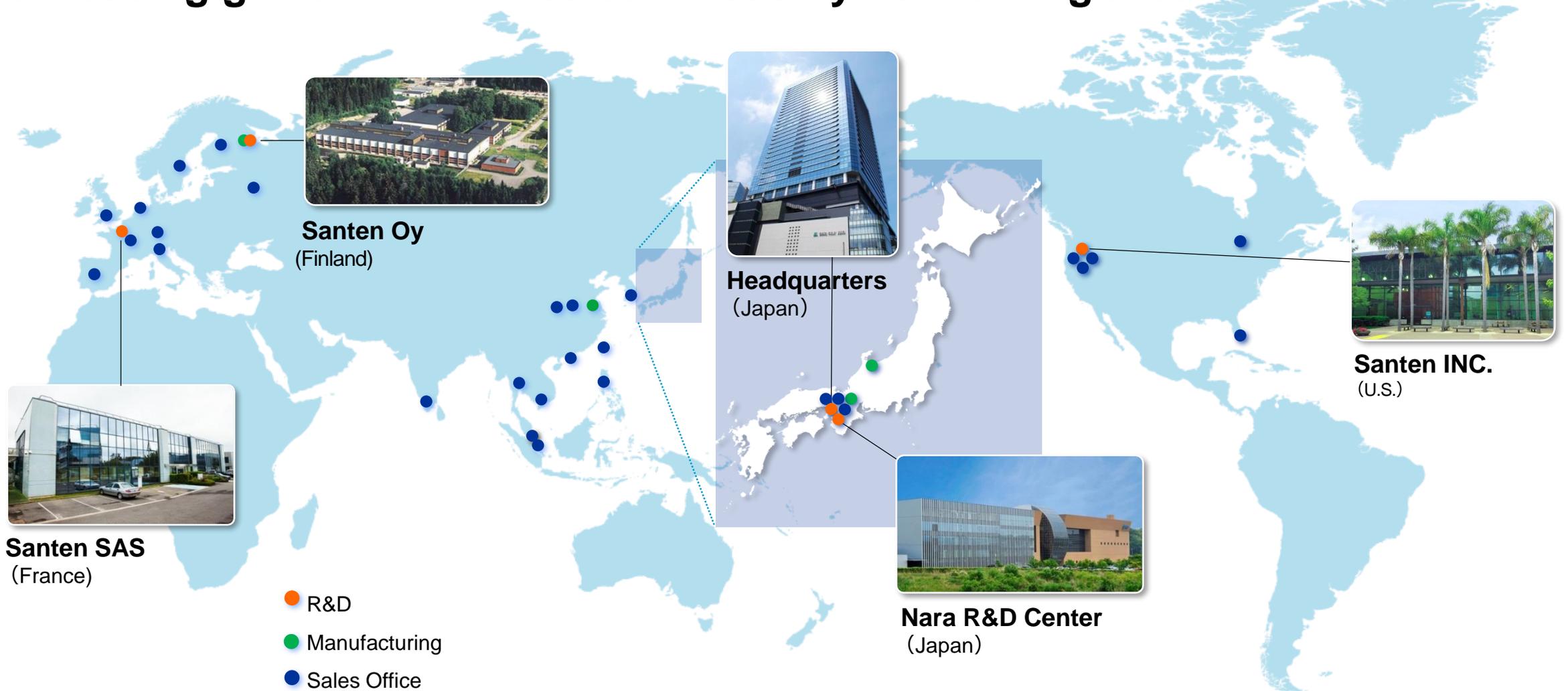
---

# **Global R&D Network and Expedite Product Creation**

---

# Santen's Global R&D Network

Addressing global unmet medical needs by networking around the world.



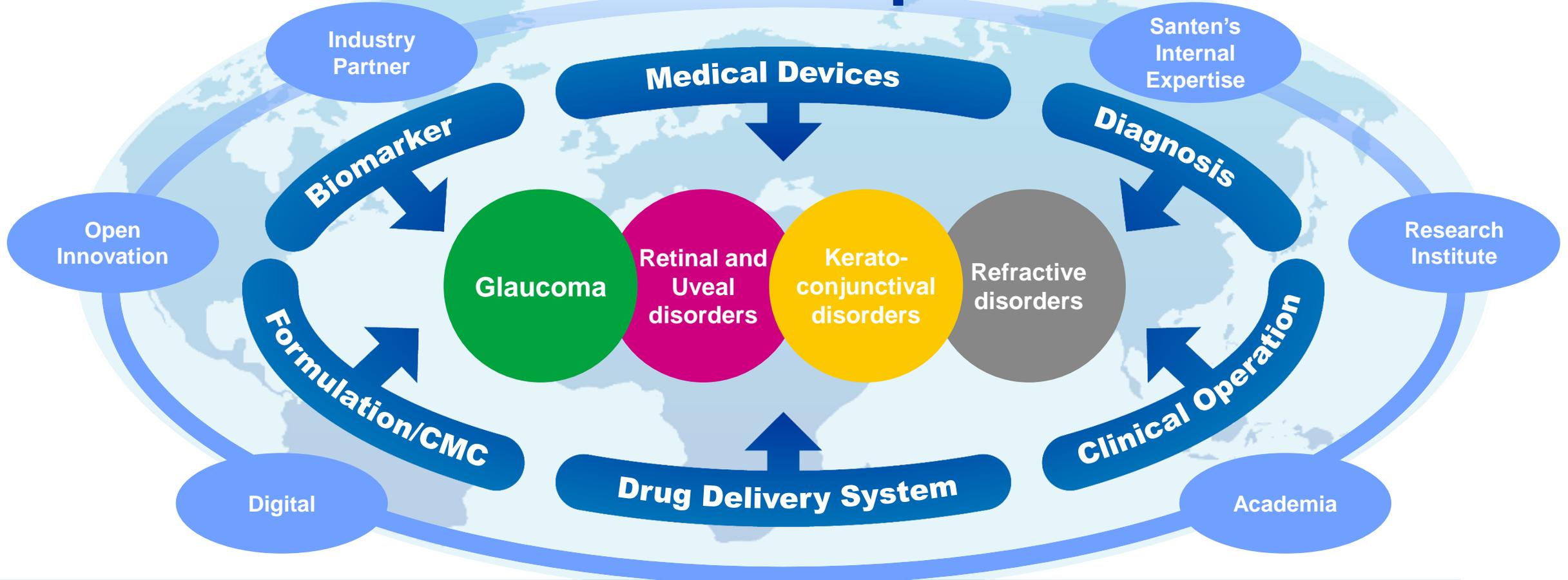
# Expedite Product Creation by Leveraging Global R&D Network

Improving Treatments

Unmet Medical Needs

Reducing Patient Burden

## Santen's Product Development



# Network Product Development



## Expanding Partnerships globally



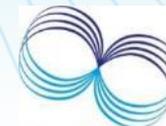
Academia



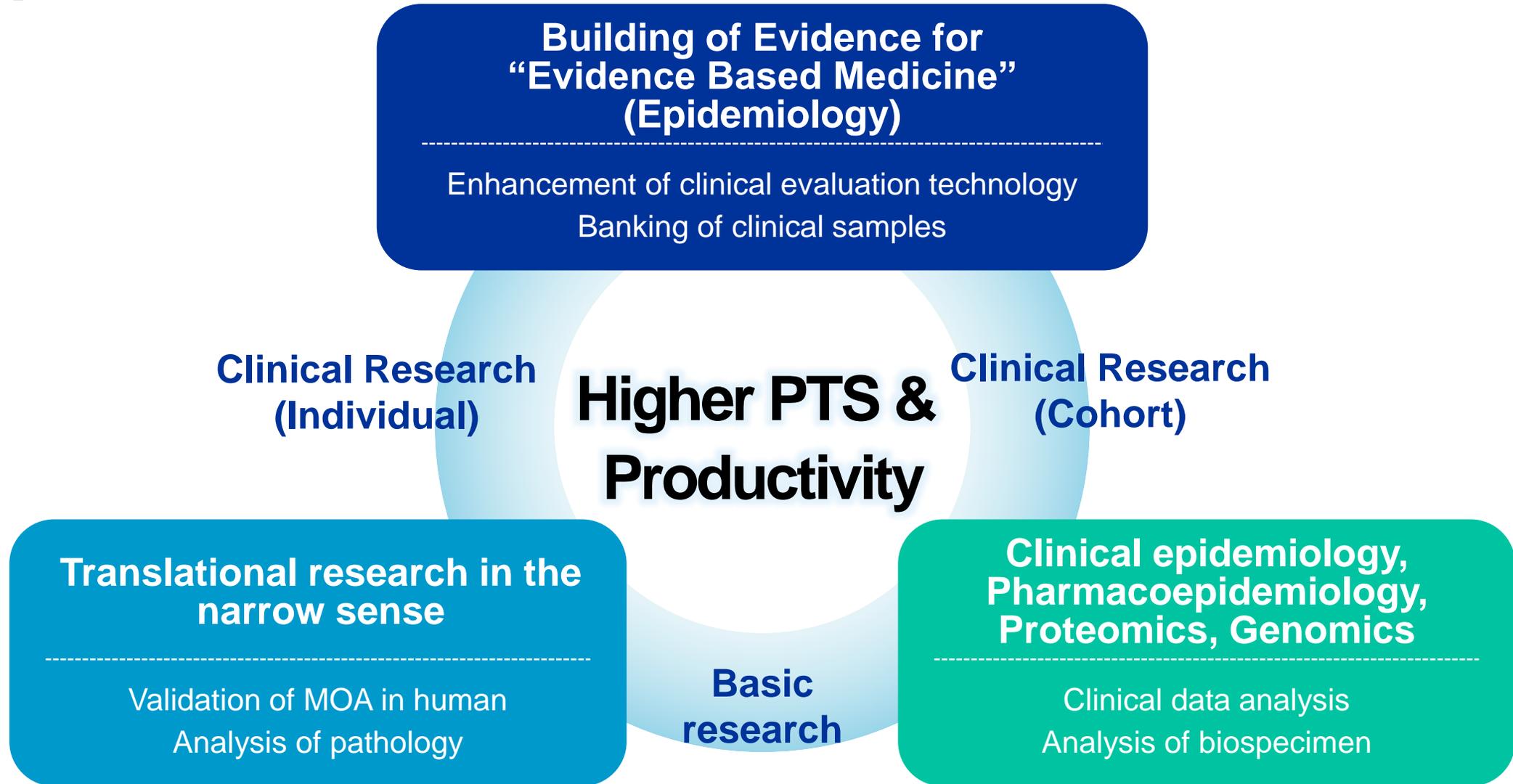
Research Institute



## Industry Partner



# Improve PTS\*



\*Probability of Technical Success

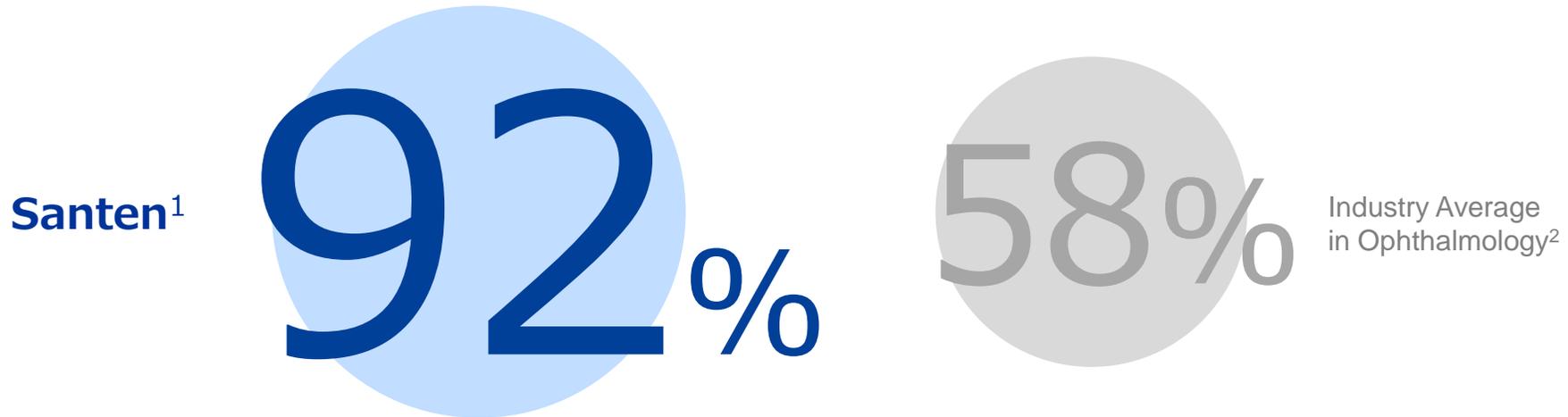
# Clinical Development that are Fast and Have Higher Success Rates



## ● Speed of clinical trials DE-117 clinical trials (Glaucoma)



## ● Phase 3 success rates in ophthalmology



1. Internal analysis in 2006-2018

2. Clinical Development Success Rates 2006-2015, Bio, Biomedtracker, Amplion, 2016

---

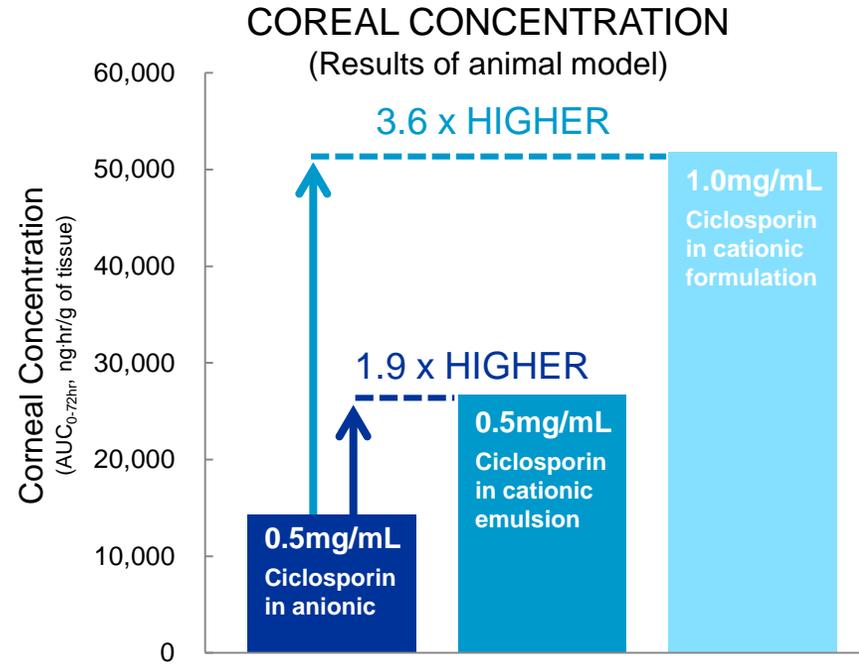
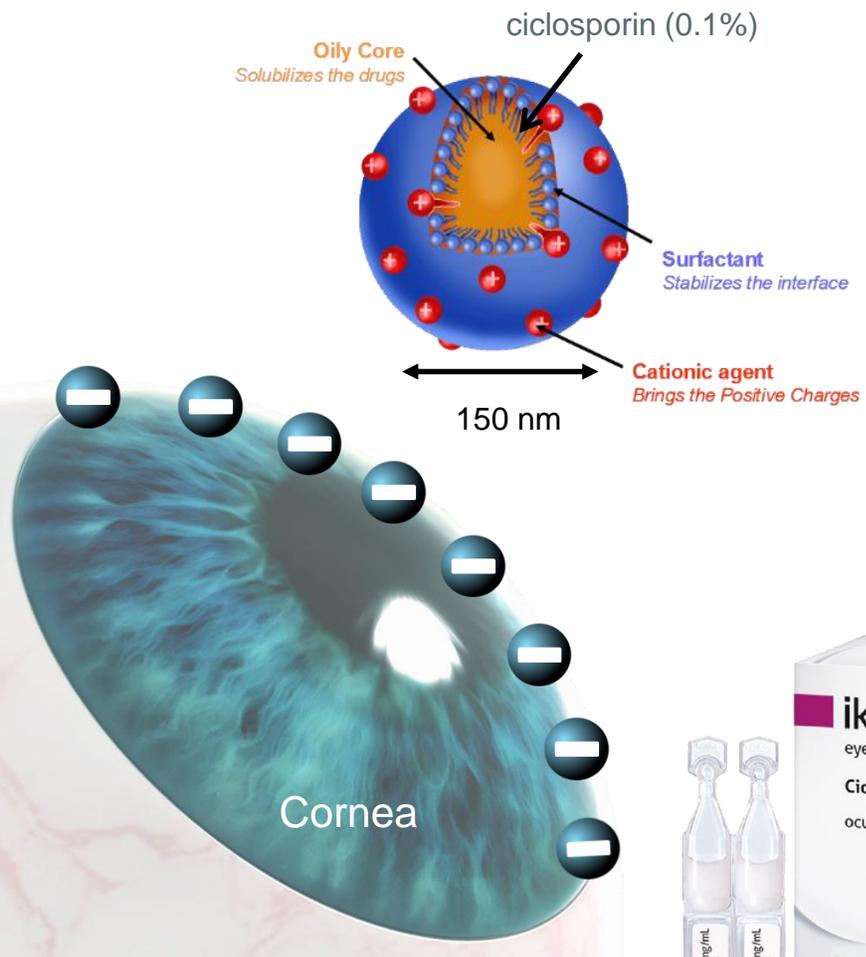
# Pharmaceutical Development

---

# Innovative Pharmaceutical Development to Meet Customer Needs



# Less frequency: Reduce Patient Burden



AUC = Area under curve  
Rabbit cornea  
Cornea, 2013;32:345-354



Tapros  
0.0015%

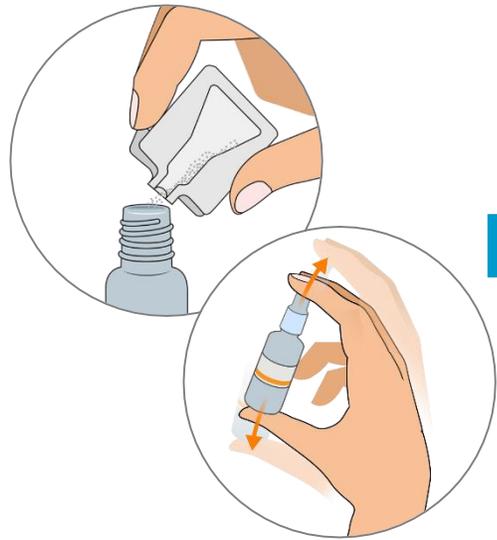
Timoptol  
0.5%

Combination Drug



Tapcom

# Improve usability: Support Patients' Adherence to Treatment



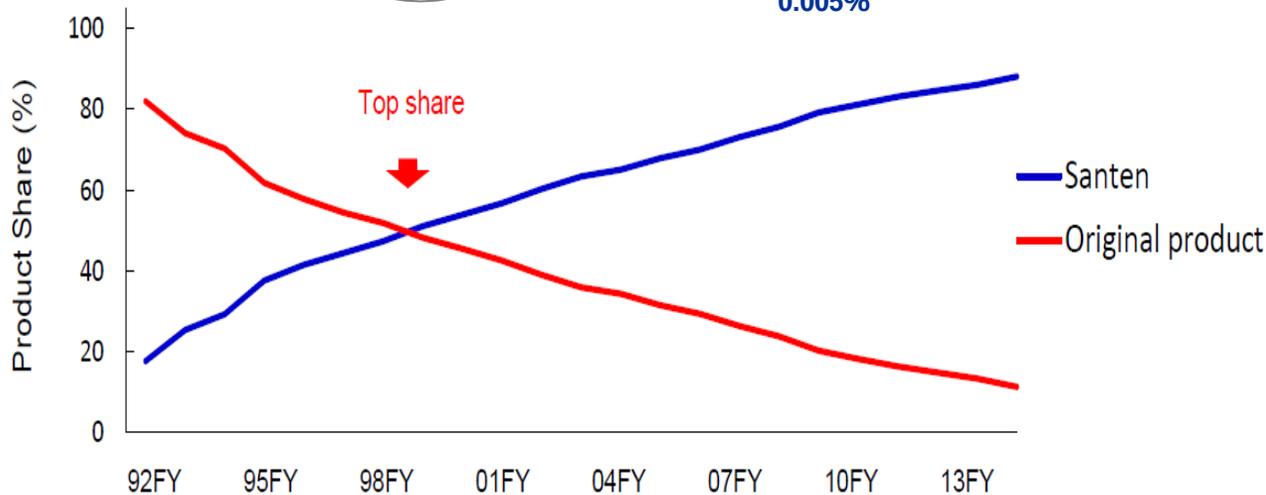
**Kary Uni**  
0.005%



**Cationorm® SD**



**Cationorm® PFMD**



Source: Santen analysis



**Lecrolyn® SD**



**Lecrolyn® PFMD**

# Ophthalmic Solution with High Safety: Prevent Treatment Withdrawal

Low BAK

BAK Free

Preservative Free

Conventional preservative

Low Preservative in new formulation

Other Preservative in new formulation

Preservative Free in new formulation

Benzalkonium Chloride

Benzalkonium Chloride (Low Concentration)

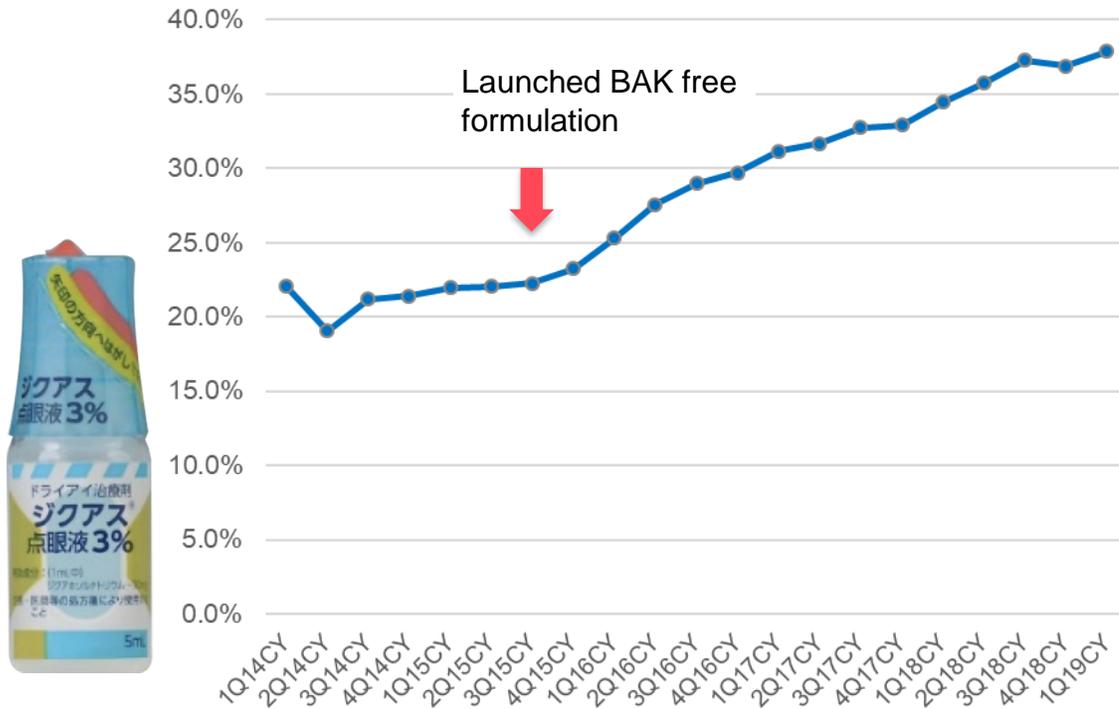
Chlorhexidine gluconate solution

N/A

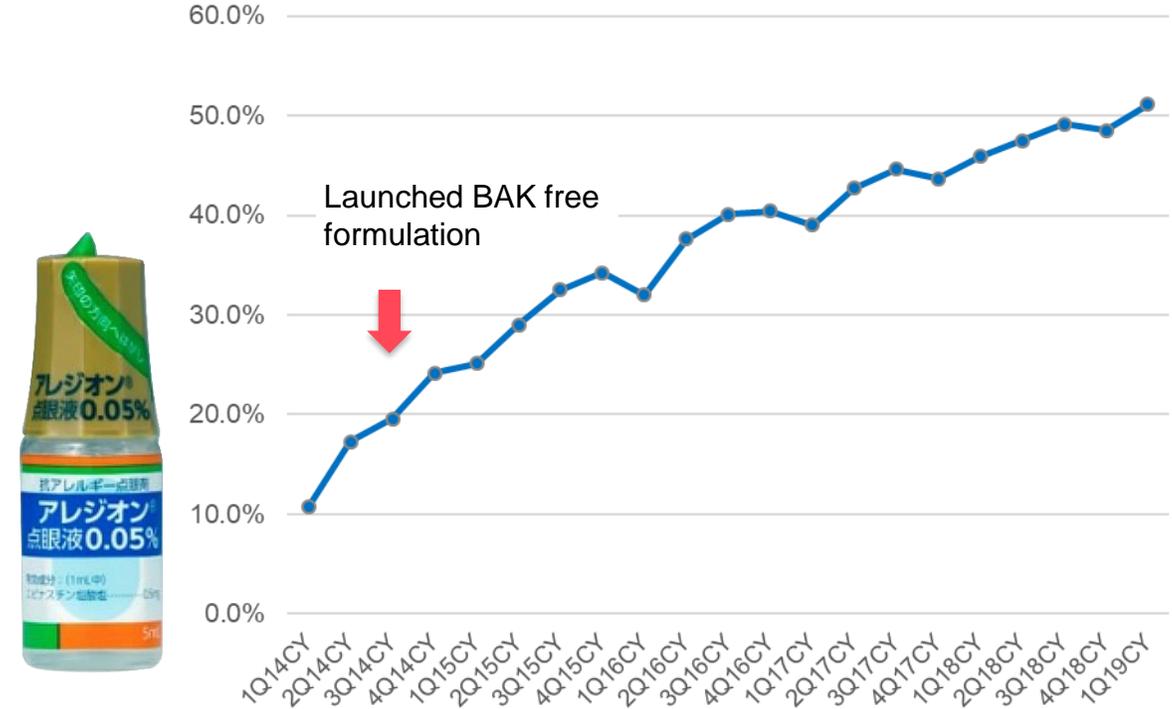


# Ophthalmic Solution with High Safety: Promote Continuous Business Grow

### Sales Share Trend of Diquas in Japan



### Sales Share Trend of Alesion in Japan



Source: Copyright © 2019 IQVIA. IQVIA MIDAS 2014/1-2019/3; Santen analysis based on IQVIA data. Reprinted with permission.

# “Dimple Bottle” was Developed by Bringing in Voice of Patients

1977~  
Bottle pack



1992~  
Chip & Cap



2002~  
Dimple bottle



Instillation success rate  
**52%**

Easy to drop



2019~

Assist tool for instillation  
Just In



Instillation success rate  
**84%**



Easy-to-see display

Concentration display on the top of the cap  
Product name labeling on top of the shrink label

With the design of holding position



Front



With the line of the same cap's color

Back

Sentence-enlarging labels

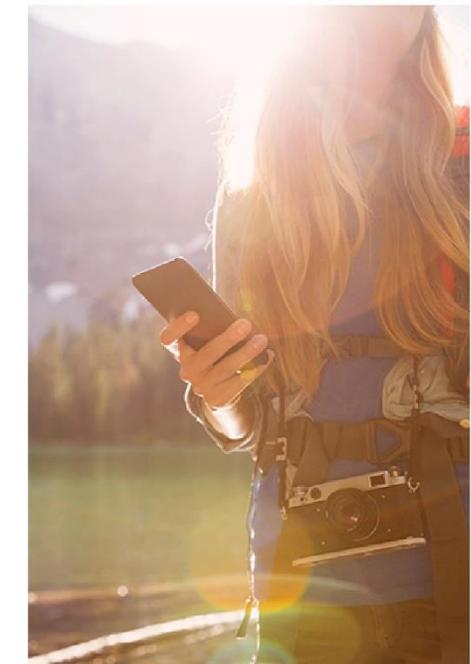
Easy to see residual volume



Slits on both sides



**VISION  
EVERY  
DAY.**



SANTEN R&D:

# VANGUARDS OF VISION

**Santen**

# R&D Leadership Members



**Naveed Shams**

Senior Corporate  
Officer & CSO,  
Head of R&D Division



**Reza Haque**

Senior Vice President,  
Head of Biomedical  
Strategy & Research



**Kenji Morishima**

Corporate Officer,  
Head of Pharmaceuticals &  
Pharmacology  
Representative, Asia R&D



**Peter Sallstig**

Senior Vice President,  
Head of Product  
Development



**Takeshi Matsugi**

Head of R&D Strategic  
Operations

The logo for Santen features a stylized 'S' in a light blue color, followed by the word 'Santen' in a bold, dark blue sans-serif font.

*A Clear Vision For Life™*