KHK4951

(Tivozanib eye-drops for retinal diseases)

R&D Day, Kirin Holdings

Dec 17th, 2025

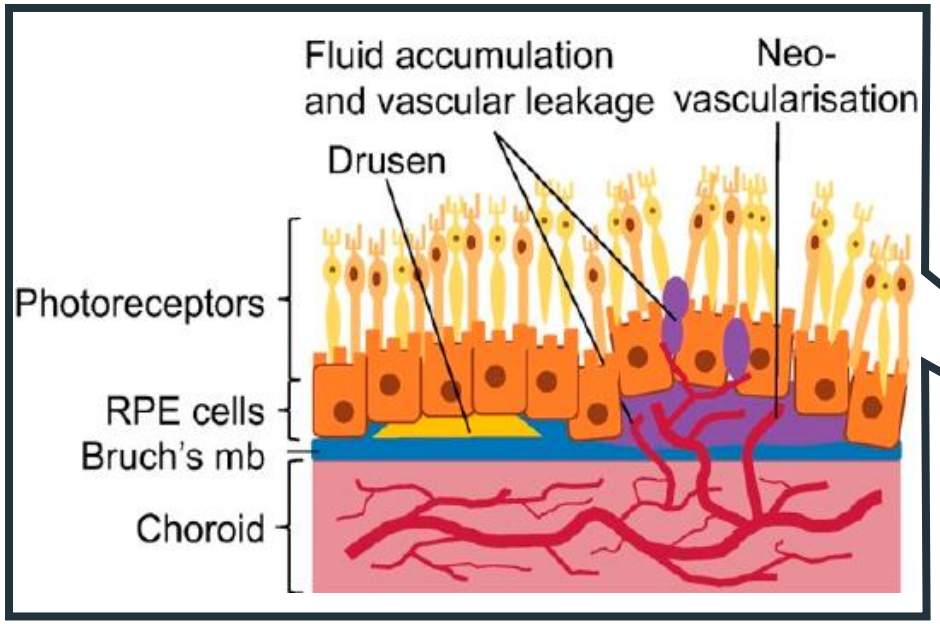
Kyowa Kirin Co., Ltd.

SHINYA HORITA

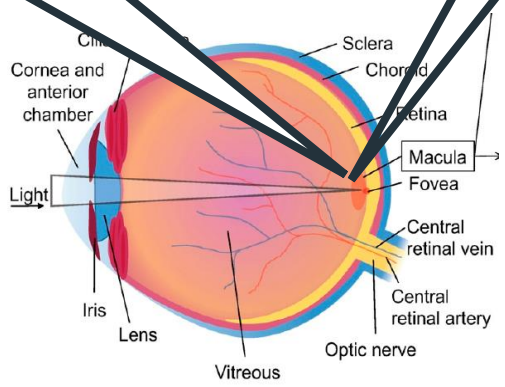
Target indications

Neovascular age-related macular degeneration (nAMD)

- Abnormal choroidal neovascularization damages the macular tissue leading to reduction of vision.
- VEGF[1] overexpression is a major cause of the disease.



Int. J. Mol. Sci. 2020, 21(13), 4627

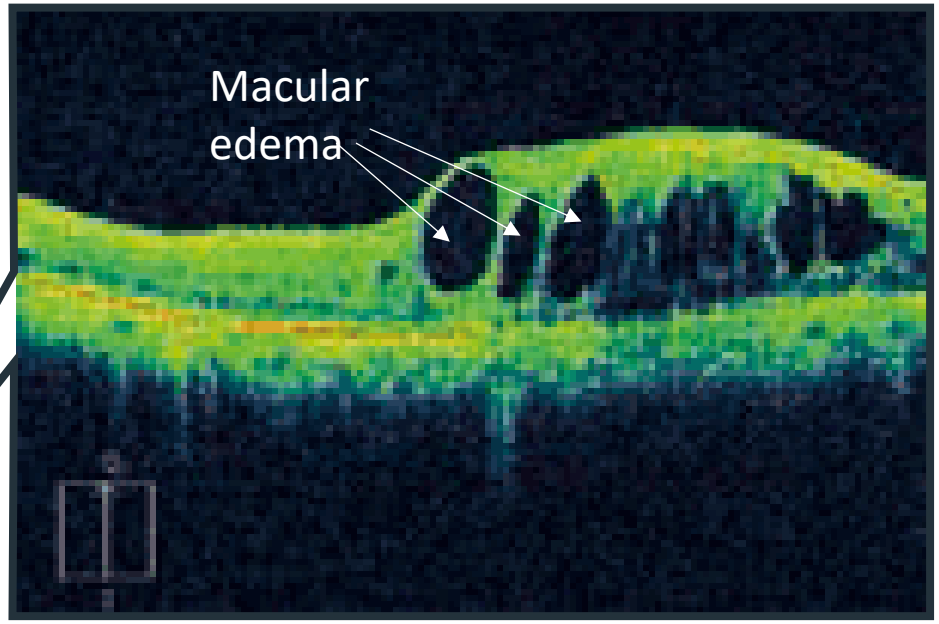


Patients treated by anti-VEGF drugs

Japan	Global
Approx. **260k**	Approx. **1870k**

Diabetic macular edema (DME)

- Hyperglycemia elevates VEGF[1] and other inflammatory cytokine leading to damage of retinal vessels, macular edema and finally reduction of vision.



https://www.jsod.jp/ippan/index.html

Patients treated by anti-VEGF drugs

Japan	Global
Approx. **150k**	Approx. **1530k**

1. *Vascular endothelial growth factor*

Unmet medical needs in nAMD and DME

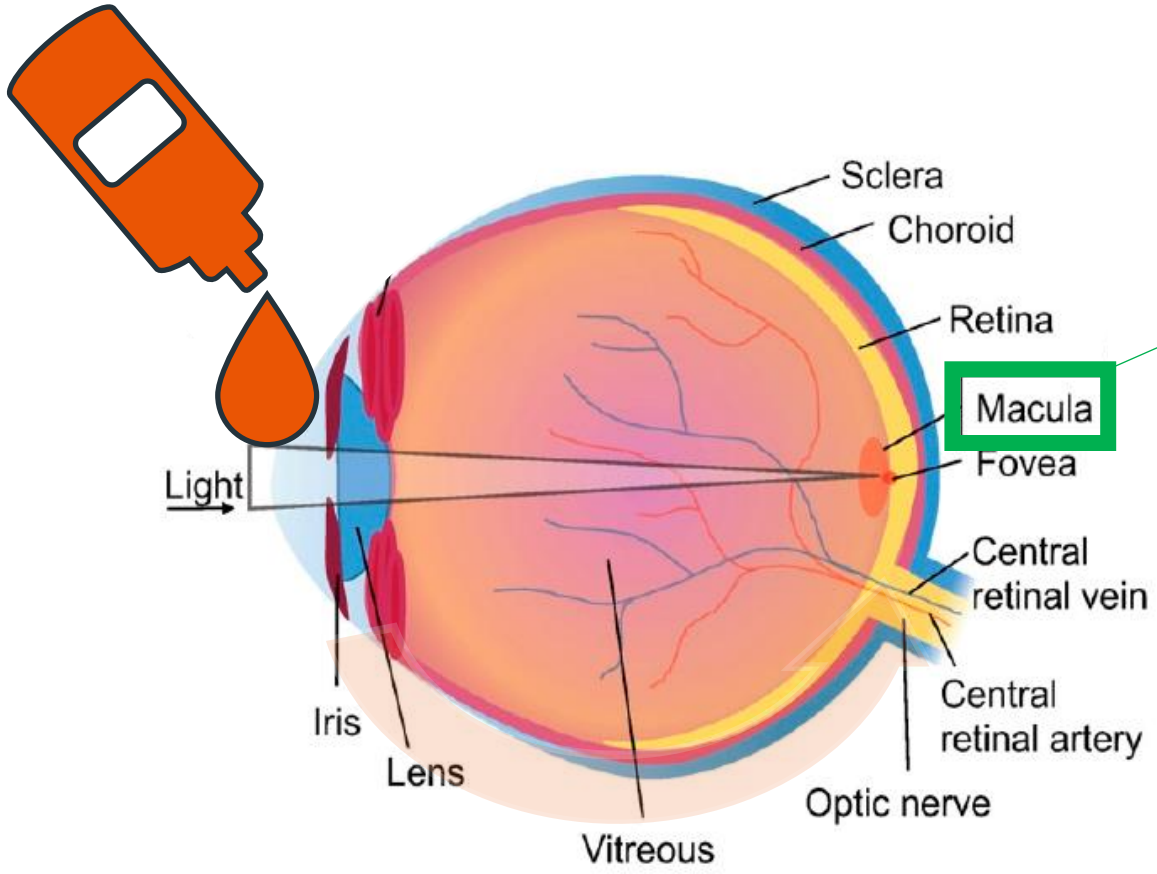
Standard of Care: Intravitreal injection of anti-VEGF drugs

Lancet 2012; 379: 1728–38

Considering the Realization of Treatment via Eye Drops

nAMD patient journey mapping by IDEA Pharma (2023)

Challenges in drug delivery to the posterior eye tissues in topical instillation of eye-drops



Hard to deliver drugs to the posterior eye tissues

Kyowa Kirin's technology overcomes the hurdle

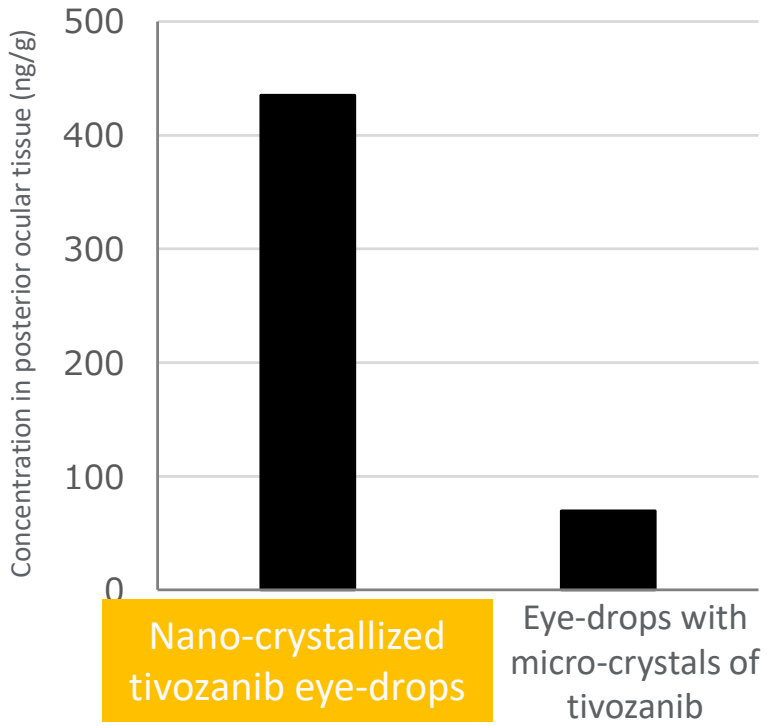
KHK4951: Nano-crystallized tivozanib eye-drops

Solution

Kyowa Kirin's **nano-crystallization technology** contributes to **efficient drug delivery to the posterior eye tissues**

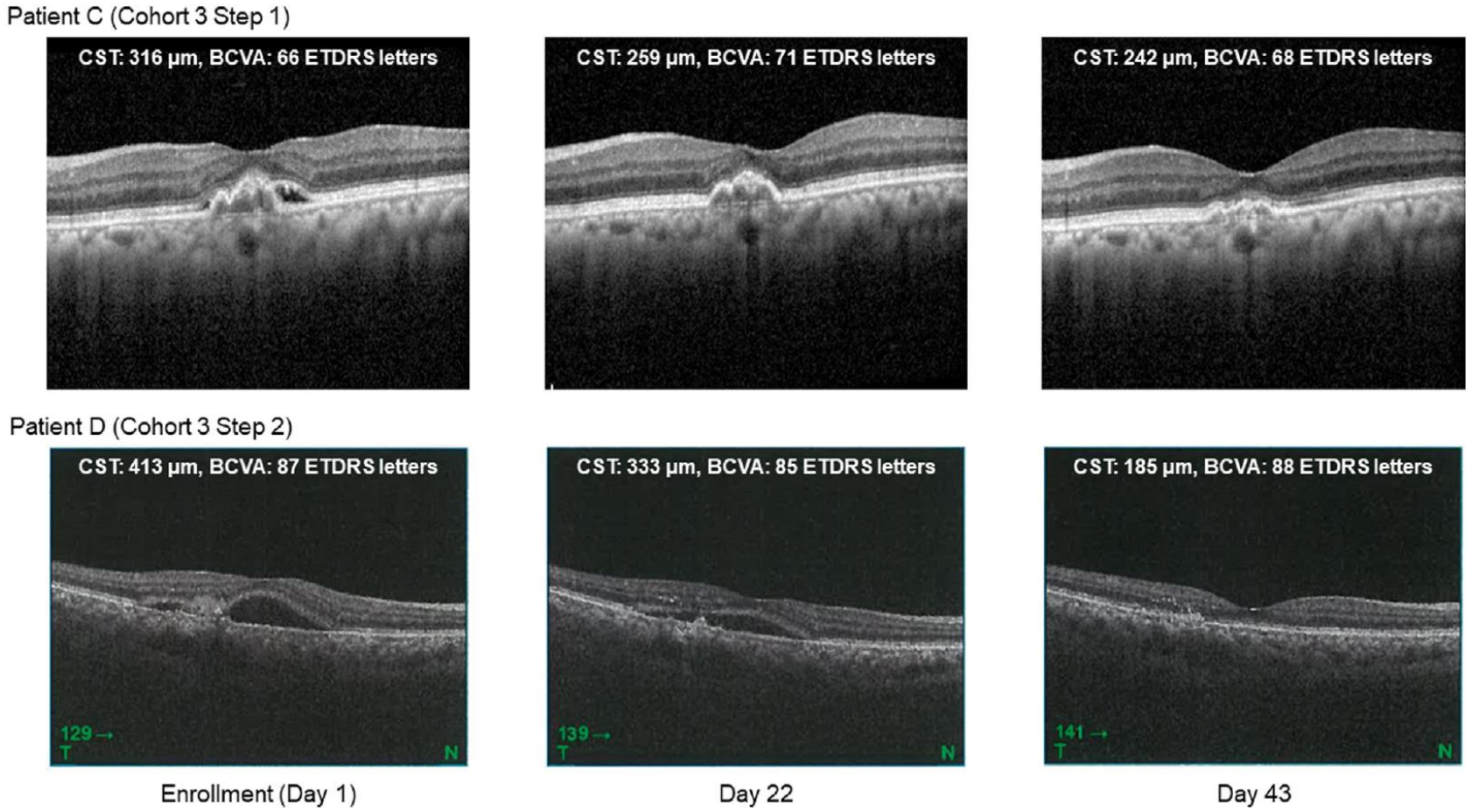
Rat ocular PK study results

Tivozanib concentration in the posterior ocular tissue after the administration of the same amounts of tivozanib to rats.



Phase 1 study: Anatomical improvement of the retinal tissues

In some nAMD patients, 3 weeks of KHK4951 treatment reduced or eliminated retinal edema.



Ophthalmology Science 2024;4:100553

KHK4951: Deliver life-changing value to patients

- Kyowa Kirin is developing KHK4951 (nano-crystallized tivozanib eye-drops) to deliver life-changing value for nAMD and DME patients.
- As of December 2025, global Phase 2 trials for nAMD and DME are in progress.

As of October 30th , 2025

Diseases under development*1	Development status	Total addressable market*3	No. of Patients*4
Neovascular age-related macular degeneration (nAMD)	P2 (JP, US)	¥500Bn-¥1Tn	3810K
Diabetic macular edema (DME)	P2 (JP, US)	¥500Bn-¥1Tn	3470K

*1 Expected indications as of the date of this document; indications may ultimately differ to expectations due status of approvals from regulatory authorities. *2 Expected year of first approval. *3 Expected total addressable market estimated by Kyowa Kirin, which is the sum of all products for the indications shown in *1, not projected sales or the Company's targets. **Colored areas represent estimates for global, and the rest are for Japan.** *4 Total number of estimated patients by Kyowa Kirin. **Colored areas represent in-house estimates for global, and the rest are in-house estimates for Japan.**

AI-driven functional simulation leveraging a DX platform for drug discovery

Kirin Holdings Company, Limited
Institute of Health Sciences

Dai Nogimura

Applying AI-driven clinical trial simulations for pharmaceuticals (QSP: Quantitative Systems Pharmacology) to the food sector

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As is

Re-evaluation

Uncertain

Product development and societal implementation

Non-physiological and localized

in vivo

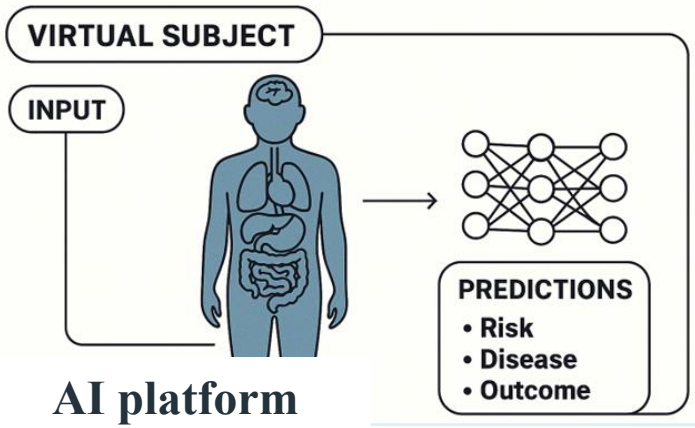
Clinical trial

③Ensuring a high probability of successful commercialization
(Cost reduction and shortened development time)

in vitro

①Efficacy prediction using virtual clinical trials

②To validate efficacy predictions



AI platform

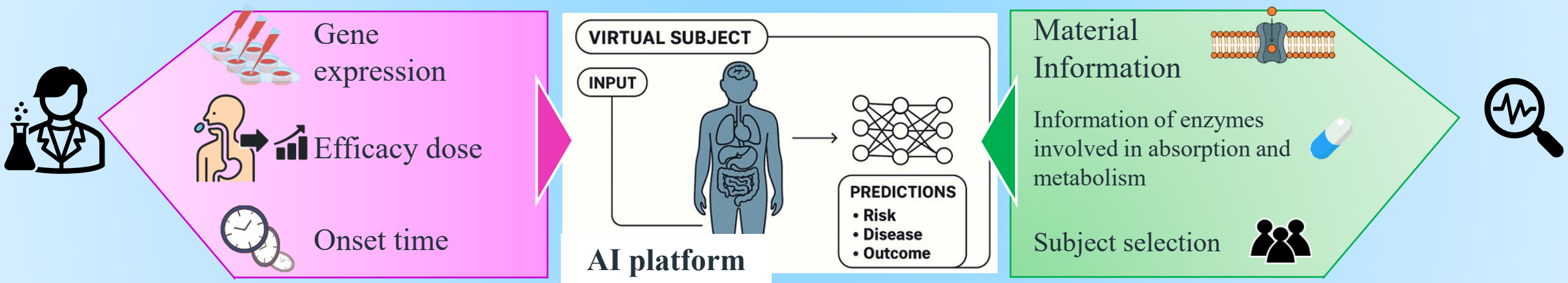
To be

Establishing QSP technology in the food sector

Realized through proprietary data and open innovatio

Proprietary data accumulated by Kirin

Achieving substantially higher predictive accuracy for therapeutic efficacy through co-creative research.



Cognizin®
For the evolution of your mind®

Functional-prediction simulations for virtual subjects

Focus on citicoline as the first target.

Kirin Group's citicoline

Cognizin® For the evolution of your mind®

Widely commercialized for overseas B2B markets as an ingredient for cognitive function

※The global market for brain-function supplements is very large — approximately ¥5 trillion.

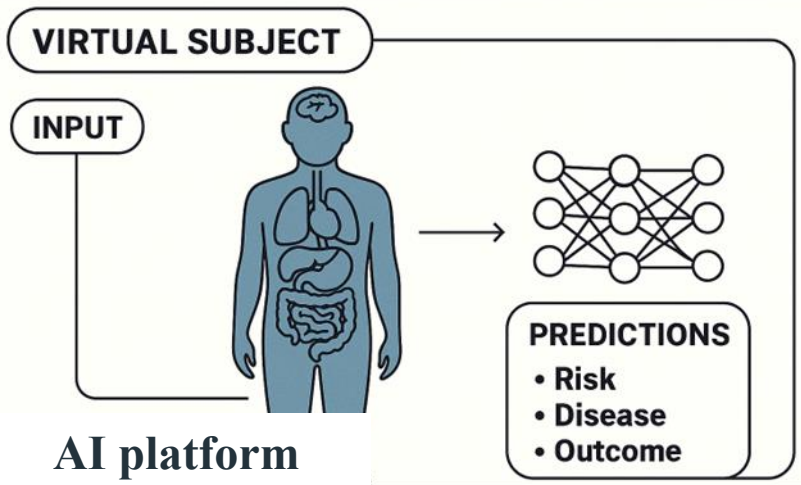
Current target areas

- Enhanced Cognitive Function
- Improved Mood
- Stress Reduction

Aiming to expand brain functionality

- Better Emotional Regulation
- Reduced Anxiety and Depression
- Improved Sleep

①Efficacy prediction using virtual clinical trials

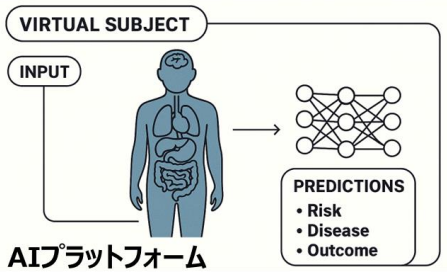


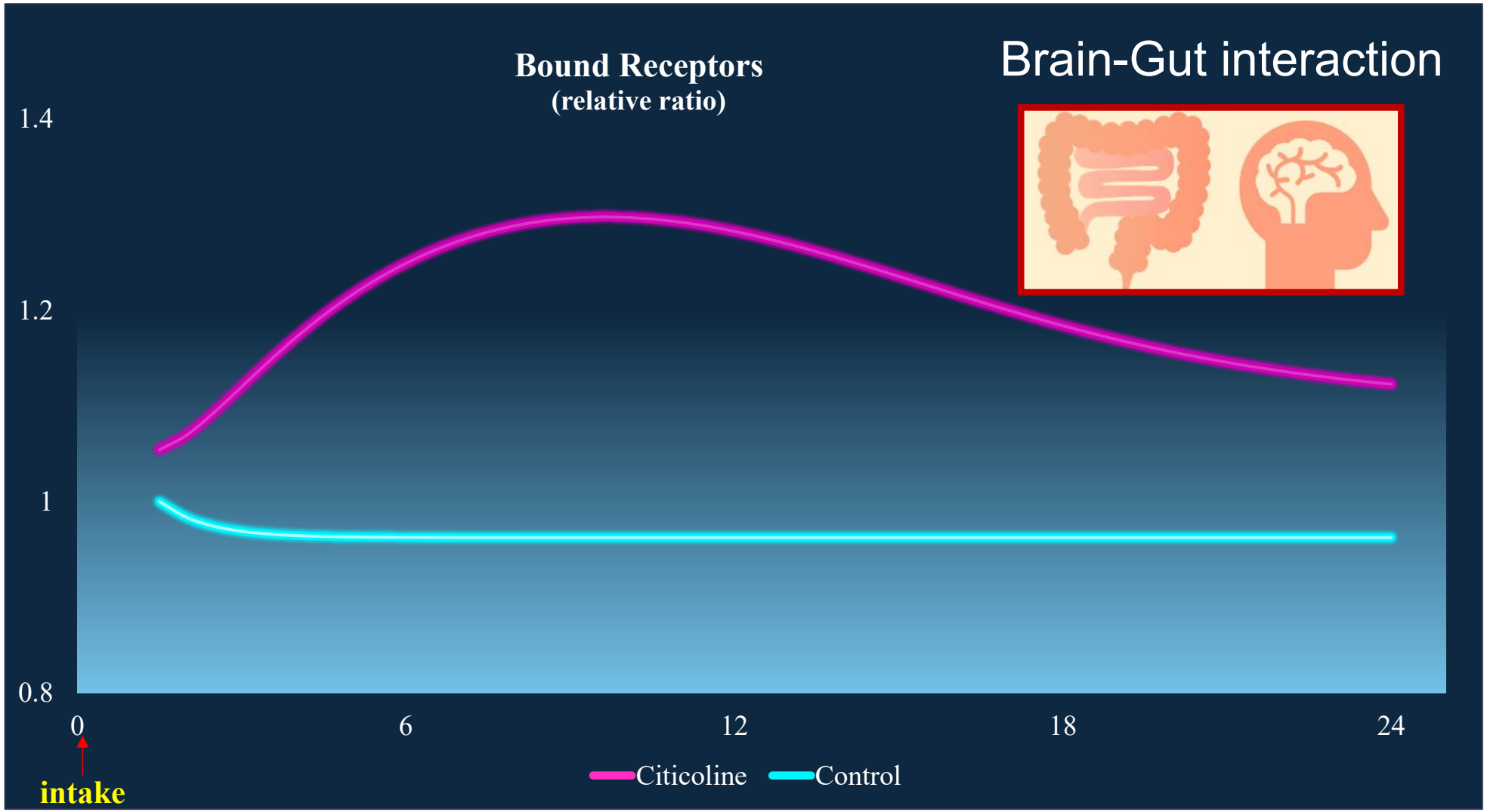
AI platform

※At present in Japan, the use of citicoline is permitted only for pharmaceutical (medicinal) purposes.

①Predictive simulations of receptor-mediated gut–brain signaling activity in virtual clinical trials

①バーチャル臨床で有効性予測

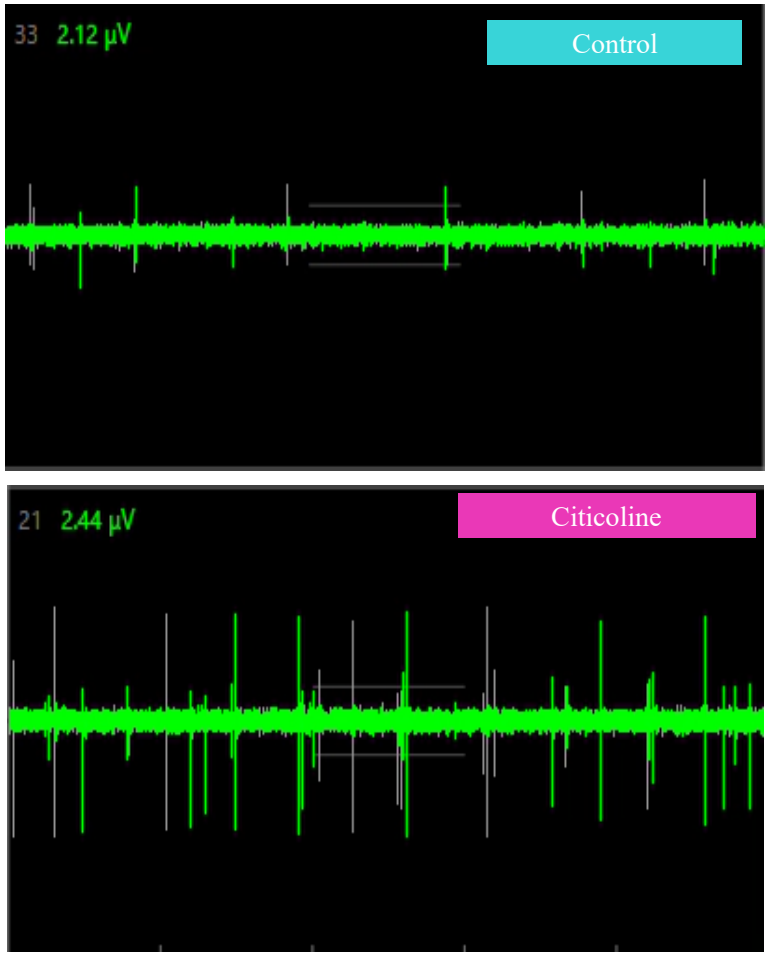




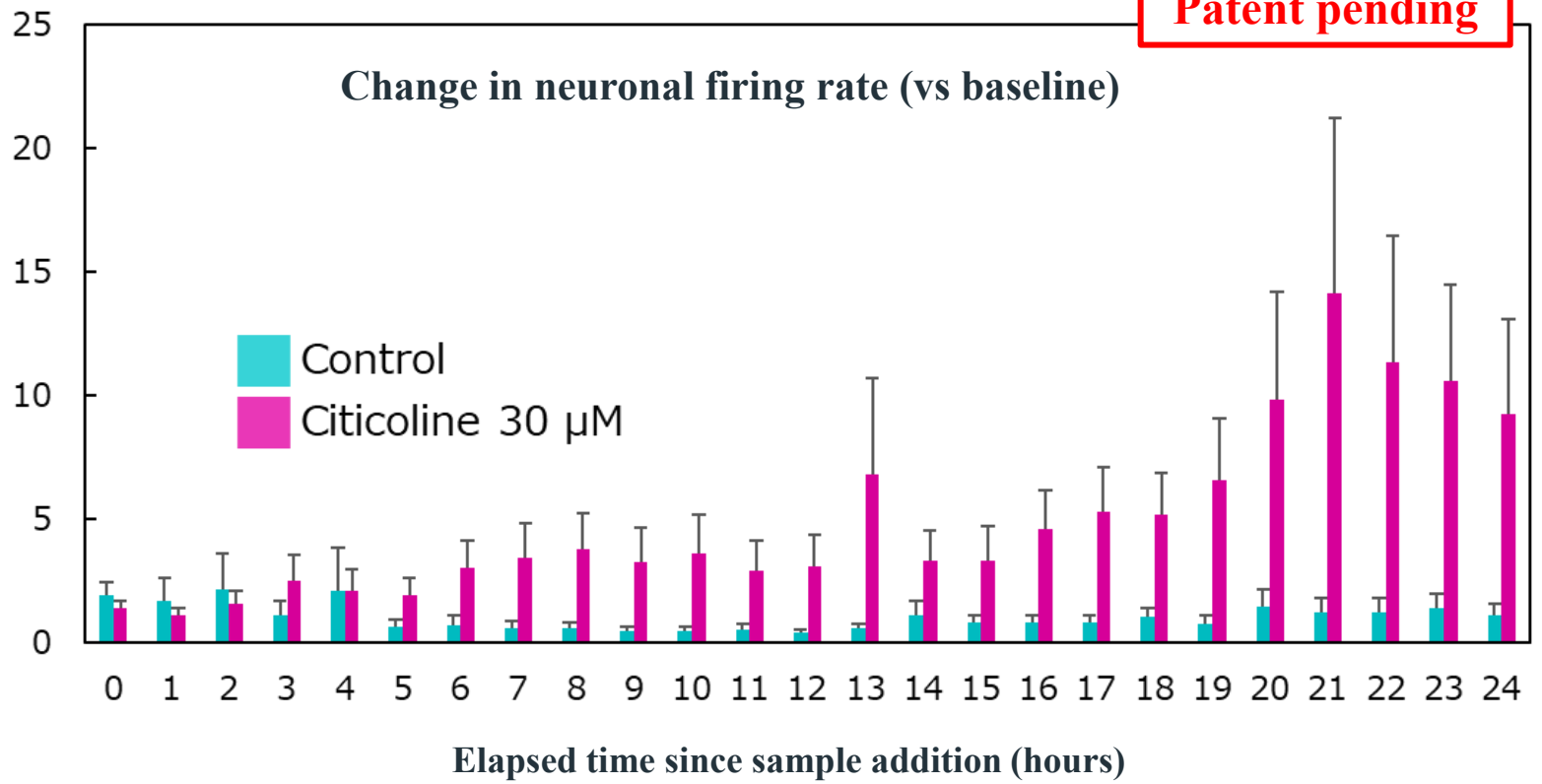
②Supporting evidence for efficacy prediction results

microelectrode array (MEA)

Assessment of gut-mediated neural activity (neuronal firing)



Patent pending



Results supporting the predicted efficacy

Successfully applied drug-AI clinical-trial simulations (QSP technology) to the food sector.

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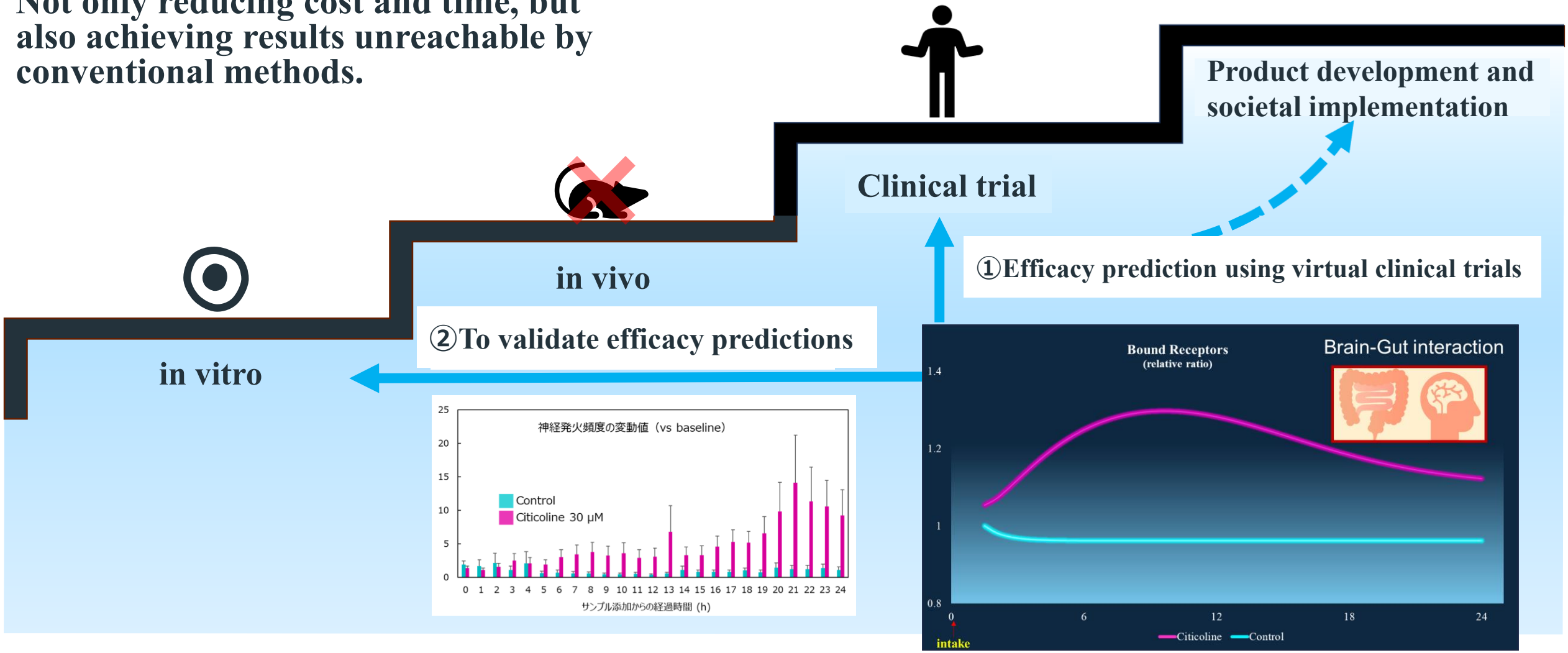
Not only reducing cost and time, but also achieving results unreachable by conventional methods.

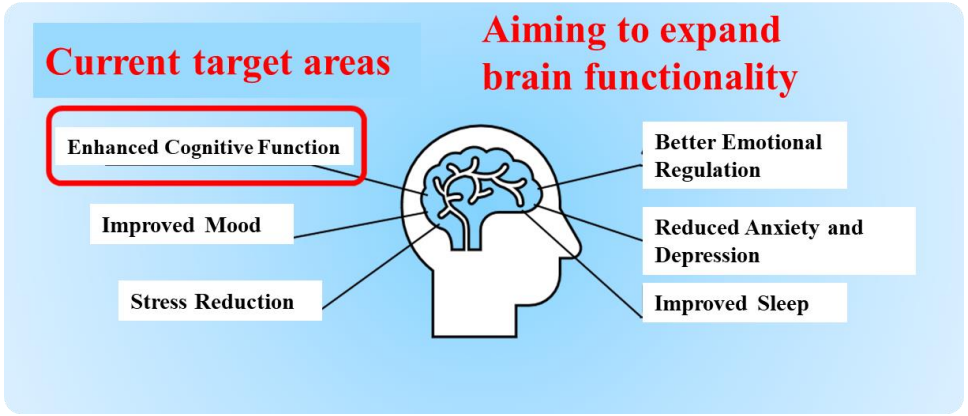


③Towards high-confidence product launch: Research timeline

2026 | 2027 | 2028

Functional prediction by model simulations

Clinical trial plan → Trial conduct → Product launch



Clinical trial

Product development and societal implementation

Clinical trial

LC-Plasma :
Driving global expansion through R&D

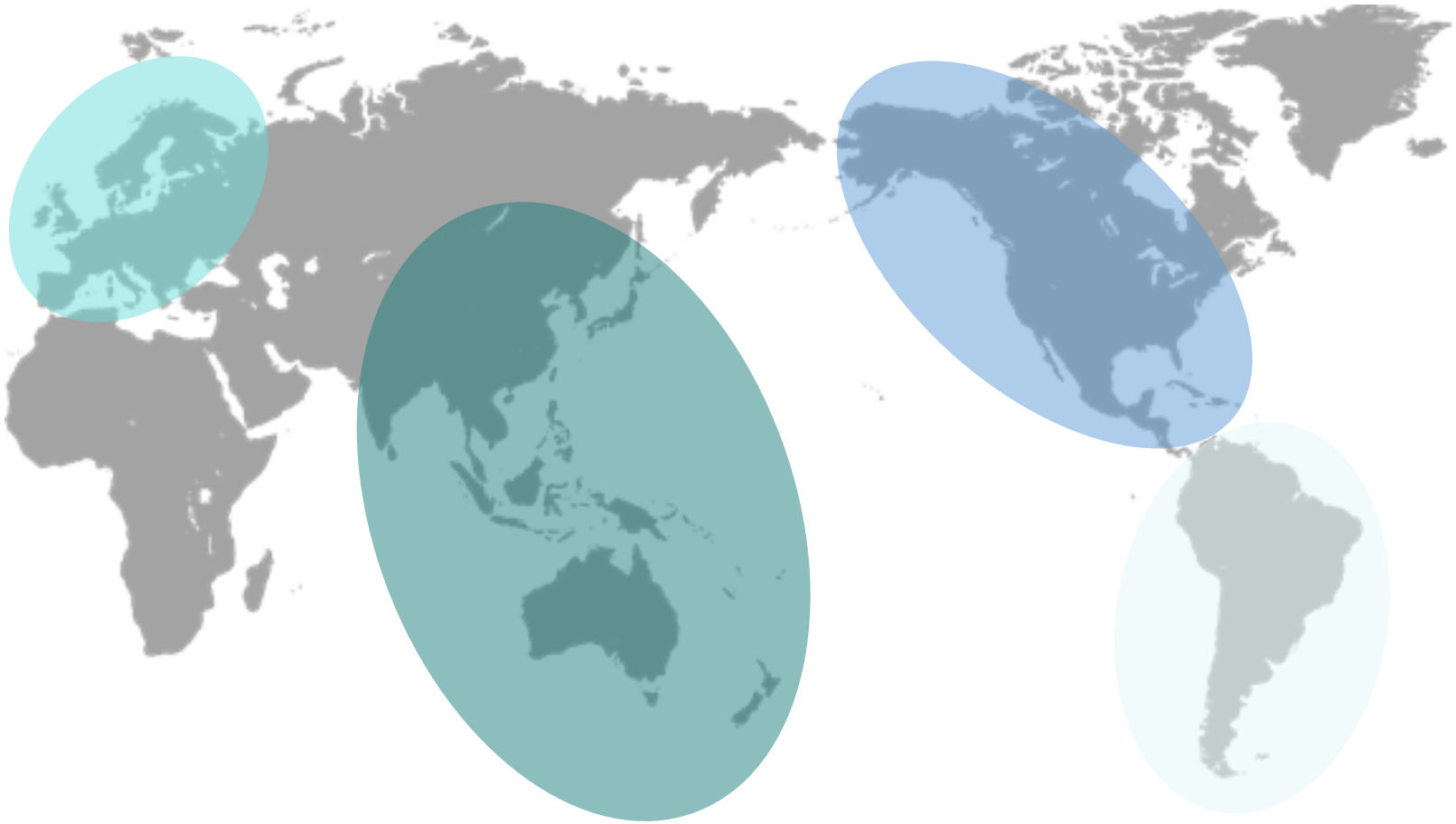
～Clinical Trials to Support Global Health Claims～

Kirin Holdings Co., Ltd.　Institute of Health Sciences

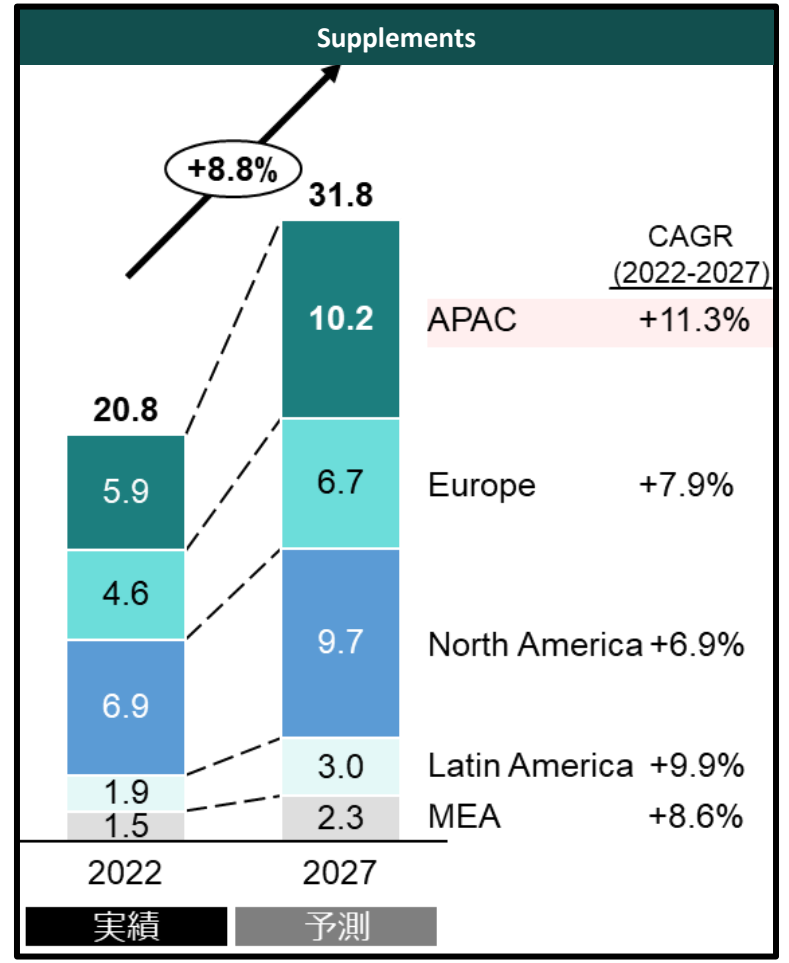
Emiri Hiramoto

Globalizing LC-Plasma Value Through R&D

Expanding LC-Plasma into high-growth markets



Regional market size and growth rate of immunity-related products
(2022-2027、Billion USD・%)



Source: Arizton「IMMUNE HEALTH SUPPLEMENTS MARKET

Challenges for Global expansion

Evidence of efficacy that complies with the requirements of relevant national guidelines must be provided

- Confirmed Effectiveness in Western countries
- Efficacy in Reducing Infectious Disease Symptoms
- Safety Data for Long-Term Consumption

◆**Currently conducting two clinical trials in Australia**

Blackmores: Collaborative Clinical trial

Griffith University: **Joint Research**

◆**Advancing the understanding of LC-Plasma mechanisms through world-class research**

Clinical trials in Australia to drive social and economic value

Blackmores

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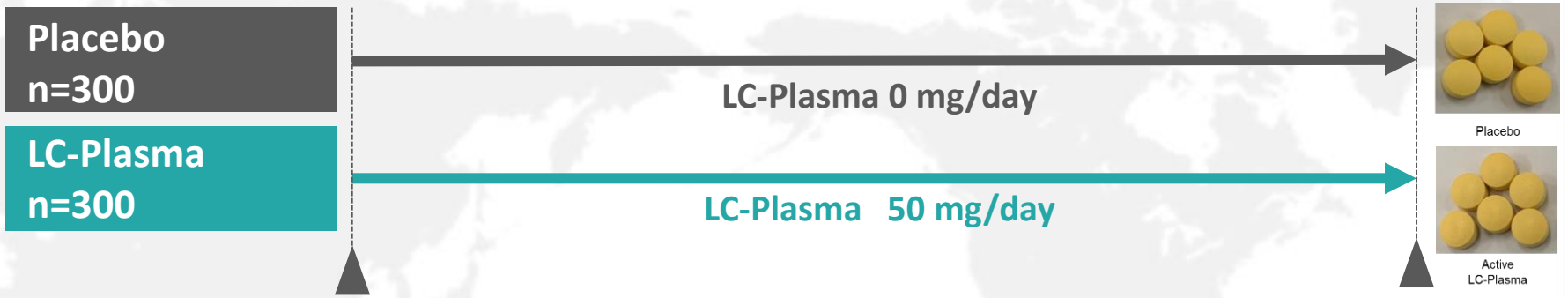
● Outline

Healthy adults aged 18–60 in Australia

n=600



Measure upper respiratory injection symptoms (duration, occurrence, and severity)

Product launch expected in 2026 or thereafter.

Strong claims not approved in Japan for social implementation.

Clinical trials in Australia to drive social and economic value

Griffith University

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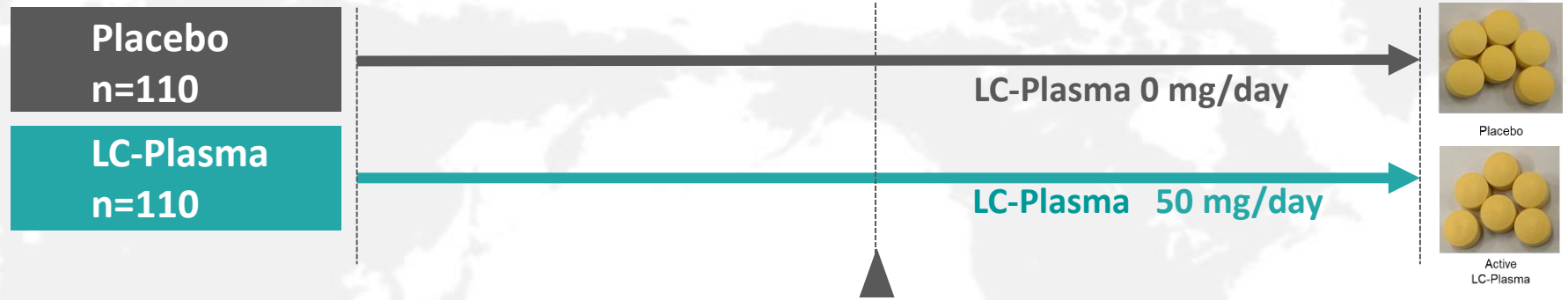
● Outline

Healthy adults aged 18–60 in Australia

n=220



- Measure upper respiratory injection symptoms
- Antigen detection of Influenza A/B, RSV, and Coronavirus
- Immune markers including pDC activity (broadly assessed by CyTOF to identify novel markers)

Application to new health claim

Increasing the global value of LC-Plasma by advancing its mechanistic insights

Publication expected in Q4 2026

Pioneering LC-Plasma science with cutting-edge technology

Griffith University

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CyTOF (Cytometry by Time-Of-Flight)

Cutting-edge analytical technology delivering scientific proof of action mechanisms

(widely utilized in vaccine development and other advanced applications)

Decoding immune system dynamics to elevate LC-Plasma research to a world-class scientific standard

Driving business growth through academic partnerships

Academia	Unveiling the effectiveness of plasma lactic acid bacteria against the Southeast Asian threat of “dengue fever”, in collaboration with world-renowned infectious disease expert Prof. Abu Bakar of University of Malaya.
KOL	Partnering with Prof. Suresh of Griffith University as a KOL 

Strategic alliances with immunology experts to drive global growth of LC-Plasma

Approaches to Immunity Visualization and Immune Care Awareness

Kirin Holdings Company, Limited
Institute of Health Sciences

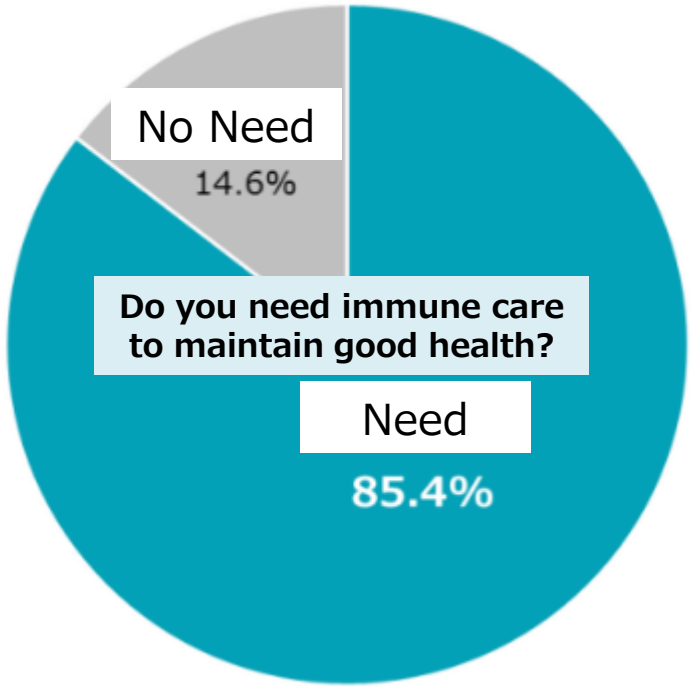
Yukiko Kato

Immune Care in Japan: Awareness–Behavior Gap

CONSCIOUS

Approx. **85%**

Immunity is necessary for good health.



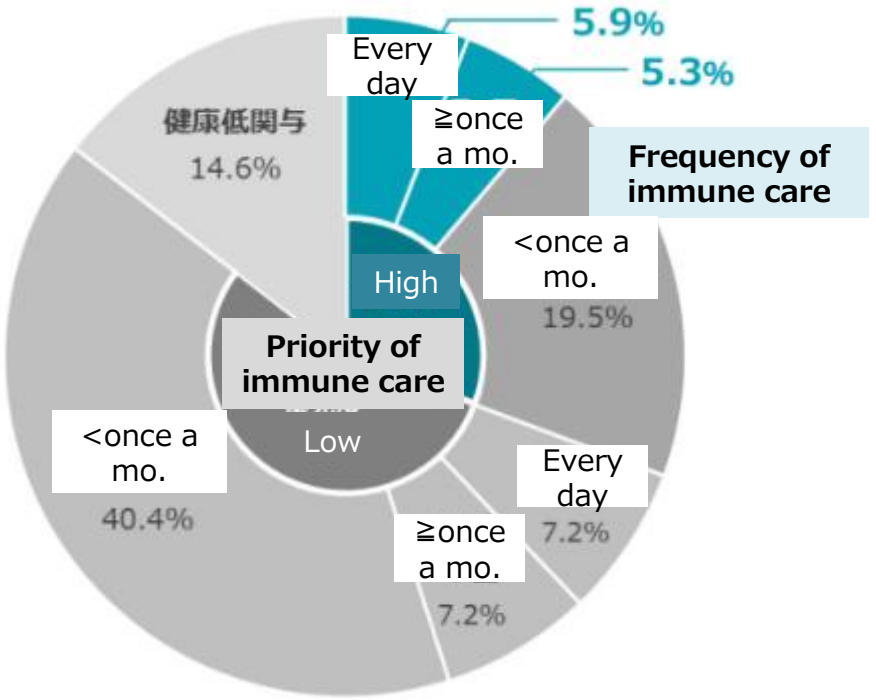
ACTION

Approx. **11%**

With immune care habits

Why the discrepancy?

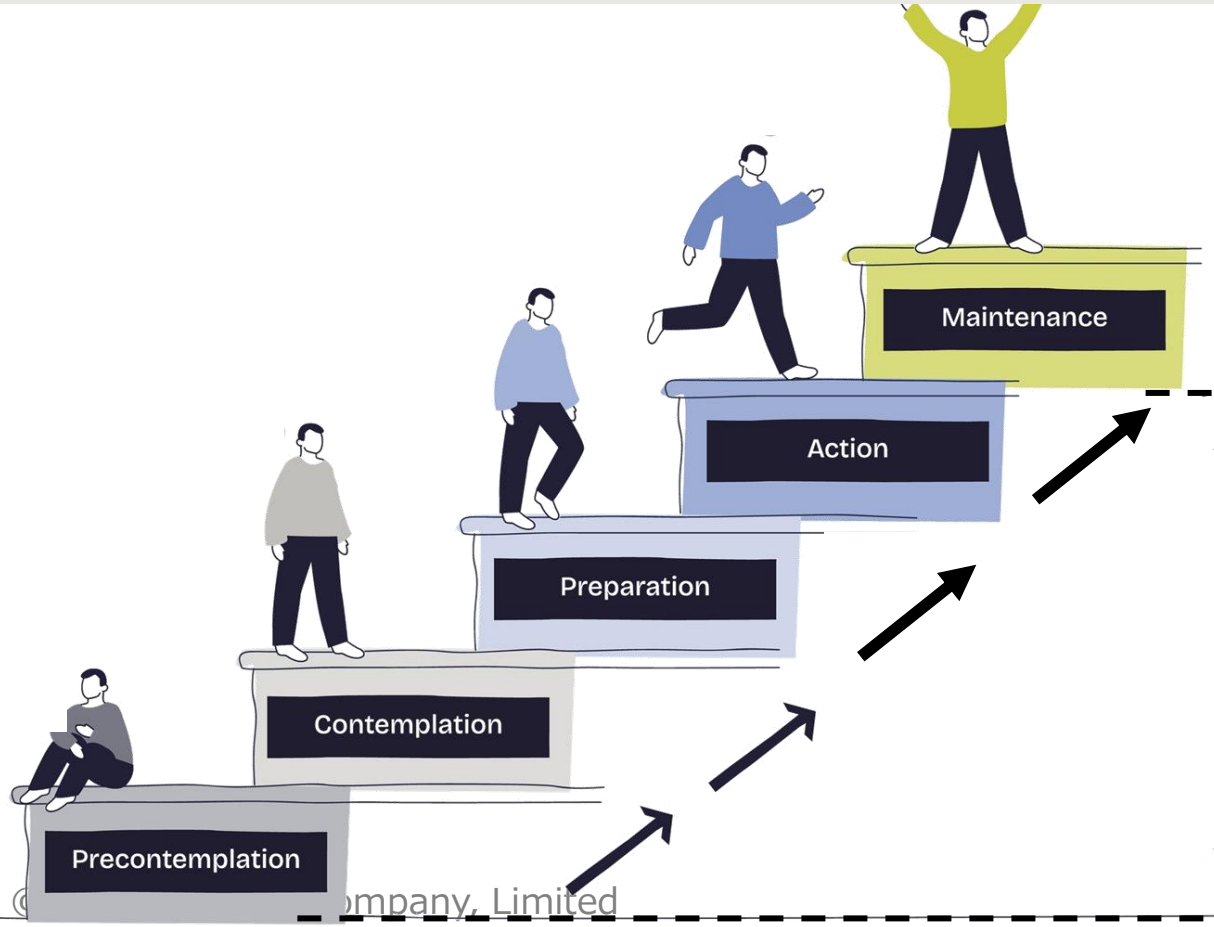
- People don't think immune care is essential ?
- It is difficult to be aware of our own immune status ?



Turning awareness into action is the key to **spreading immune care habits.**

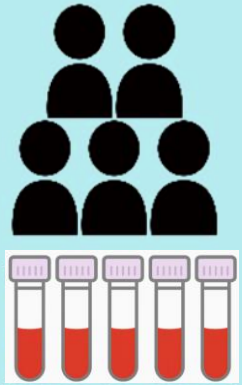
Barriers to making immune health care a habit

Barriers to Habit Formation
Immunity is **“invisible”** and therefore often neglected.



Wakayama Health Promotion Study

Participants: N=223 (aged 51-55 years)

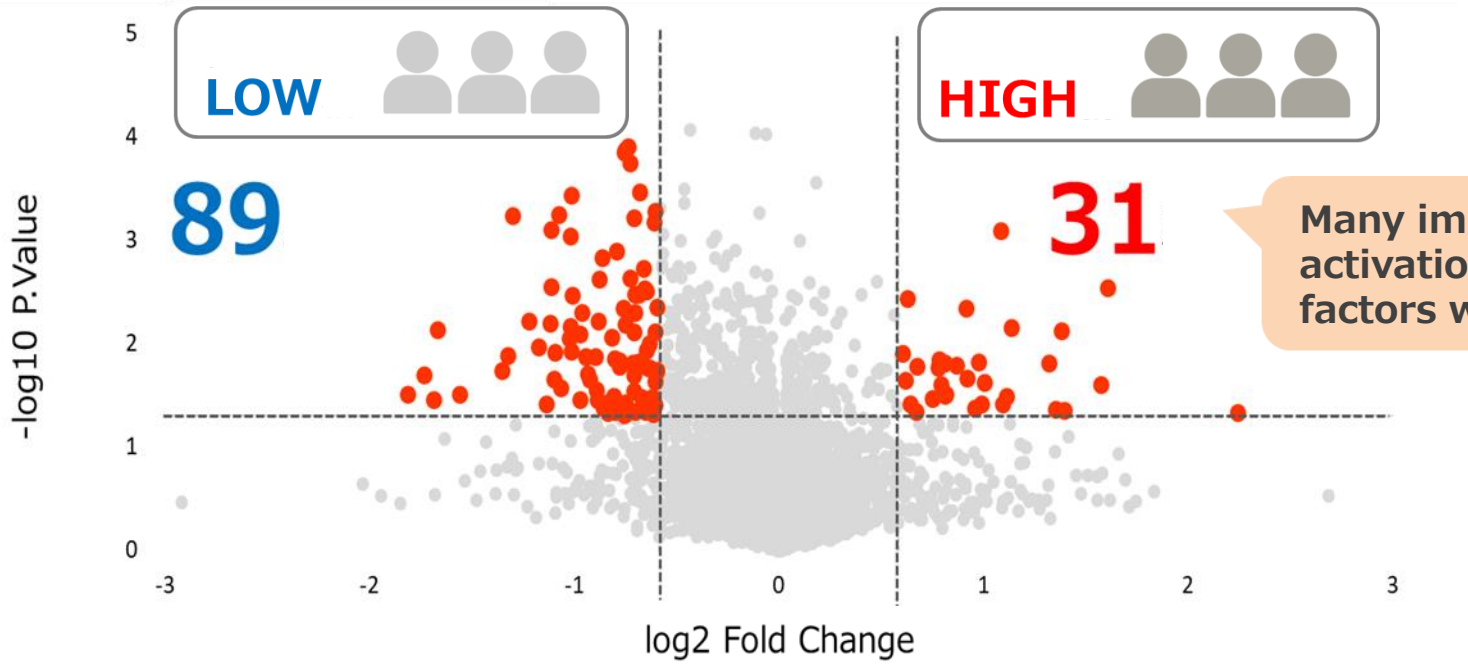


Measurement of pDC activity

Visualization
using Kirin’s technology

Shutterstock（ライセンス取得済）

First Discovery Worldwide of Urinary Factors That Visualize pDC Activity



Many immune activation-related factors were included.

Activated commander cells

∝

Correlated with pDC activity

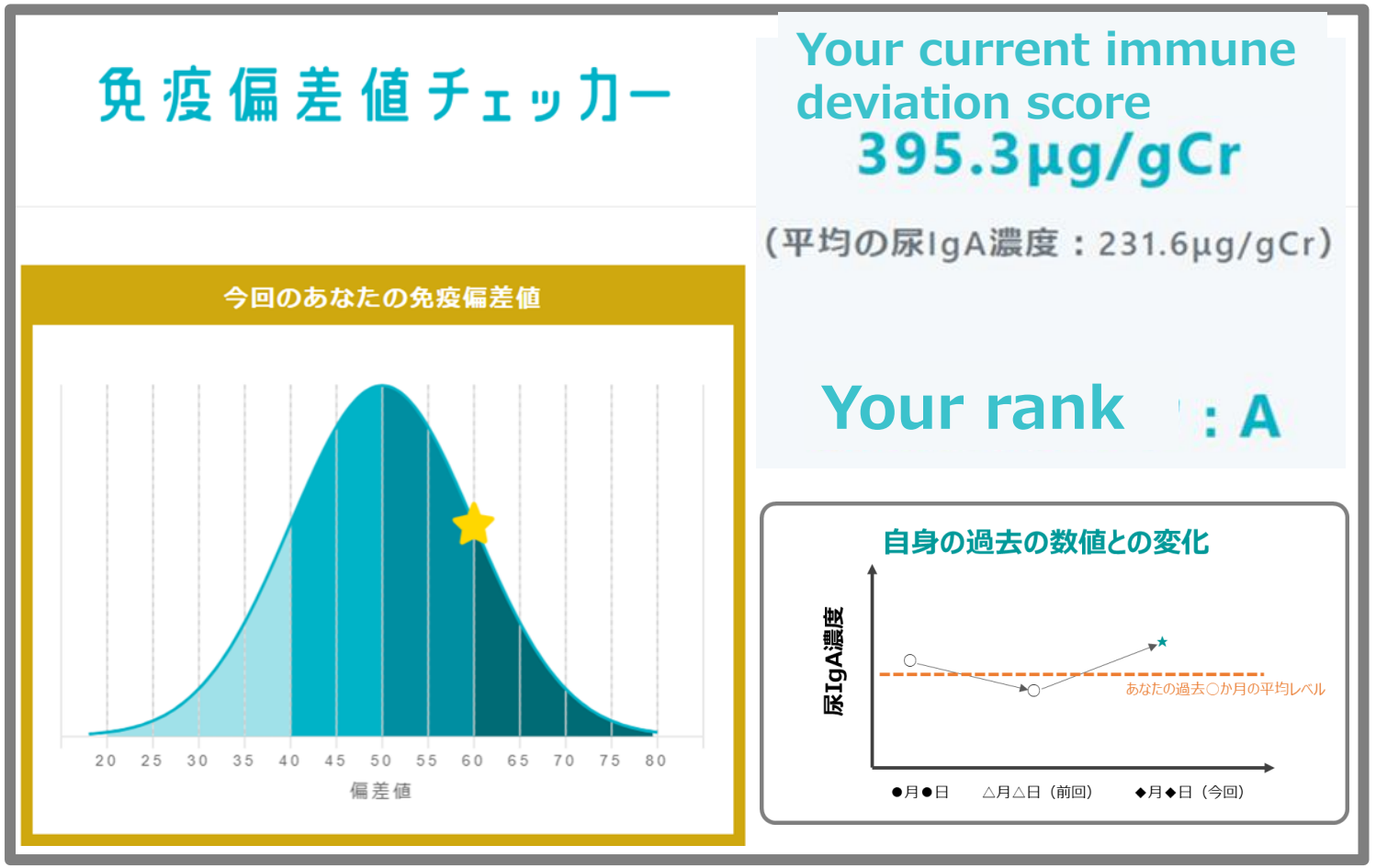
Urine samples

Toward Establishing a Service to Visualize Immunity Through Urine Testing

(Publication planned for Q2 2026)

How to Interpret and Utilize the Results of Kirin's Unique "Immunity Visualization" Test

Shows your current immune status, trends over time, and recommended immune care to help you move closer to your desired future state.



Know

Deepen

Take Action

The service is planned for a test launch in Q3 2026 in partnership with **KIRIN, FANCL and Healthcare Systems.**

Driving Behavioral and Social Change Through Awareness Activities

Resolving challenges and promoting awareness in each domain,
co-creating social value together.

@Community

Co-creating with municipalities to advance immune care

@Workplace

Immune Care Challenge for Employees

hallenge implemented with approximately 1,700 Kirin employees.

@Educational Domain

Addressing challenges in kindergartens and learning centers

Considering implementation of immune care promotion programs

Toward an Immune Care Society Driven by Both Social and Economic Value

Realizing an Immune Care Society

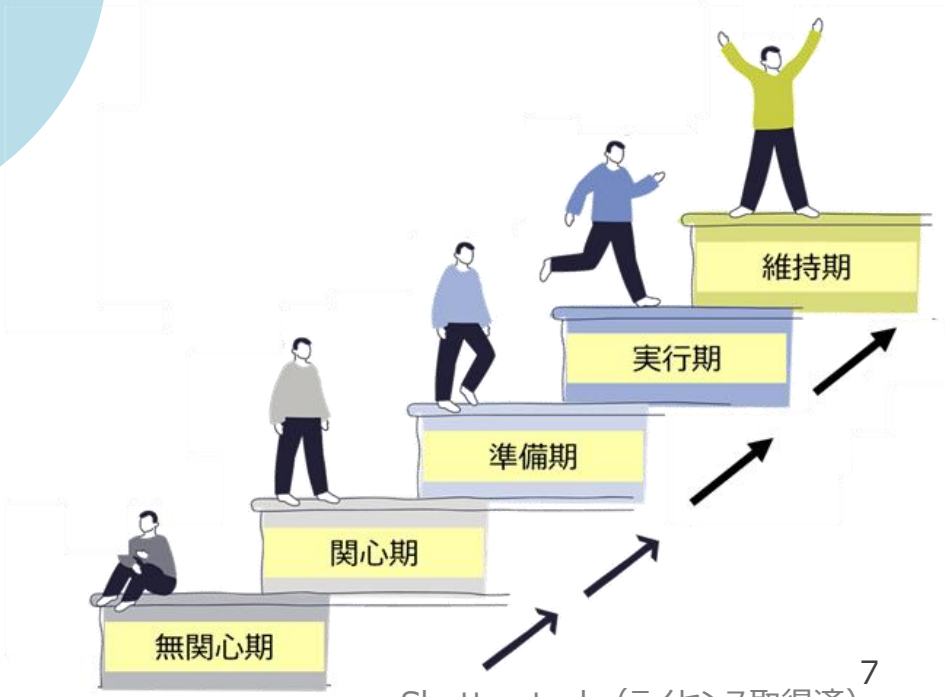
Awareness:
Community, Workplace, Educational Domain

Social Value

Economic Value

Visualization of Immunity

Visualization of immune status
(Habit Formation for immune care)



Shutterstock（ライセンス取得済）

Advancing Beer Flavor Innovation with Kirin's Preference AI "FJWLA"

Kirin Holdings Co., Ltd.
Institute for Future Beverages

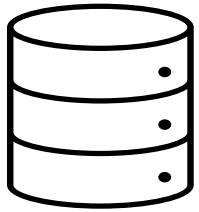
Yuto Fujiwara

What Is the Preference AI “FJWLA”?

Proprietary datasets

Consumer research data

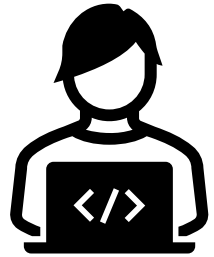
Component analysis data



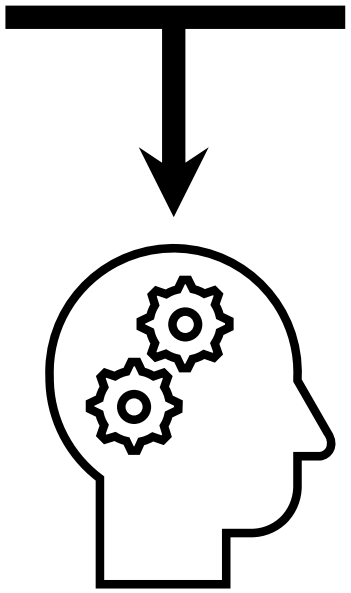
Data accumulated through Kirin’s consumer-first philosophy — over 1 million records

In-house AI development

AI system development



Kirin’s platform built for predicting consumer preferences



Preference AI：FJWLA (Flavor Judgement for Whole Liking Analysis)

AI that identifies which components should be controlled to enhance consumer preferences

How FJWLA Creates Competitive Advantage

Preference AI

Proprietary datasets

Consumer research data

Component analysis data

Data accumulated through Kirin's customer-first philosophy — over 1 million records

In-house AI development

AI system development

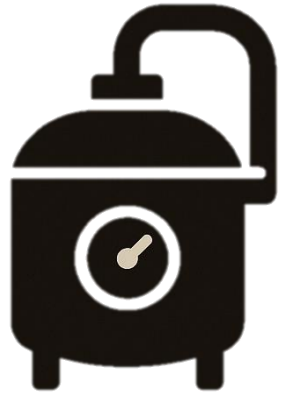
Kirin's platform built for predicting consumer preferences

Preference AI：FJWLA (Flavor Judgement for Whole Liking Analysis)

AI that identifies which components should be controlled to enhance consumer preferences

What only Kirin can do

Kirin's brewing expertise



Advanced brewing expertise that precisely controls components

What cannot be done without Kirin

Realizing truly "consumer-first" beer development

FJWLA Enables Discovery of Components that Drive Taste

Preference AI

Data input and AI analysis

Predicts research results!

Input
Component data

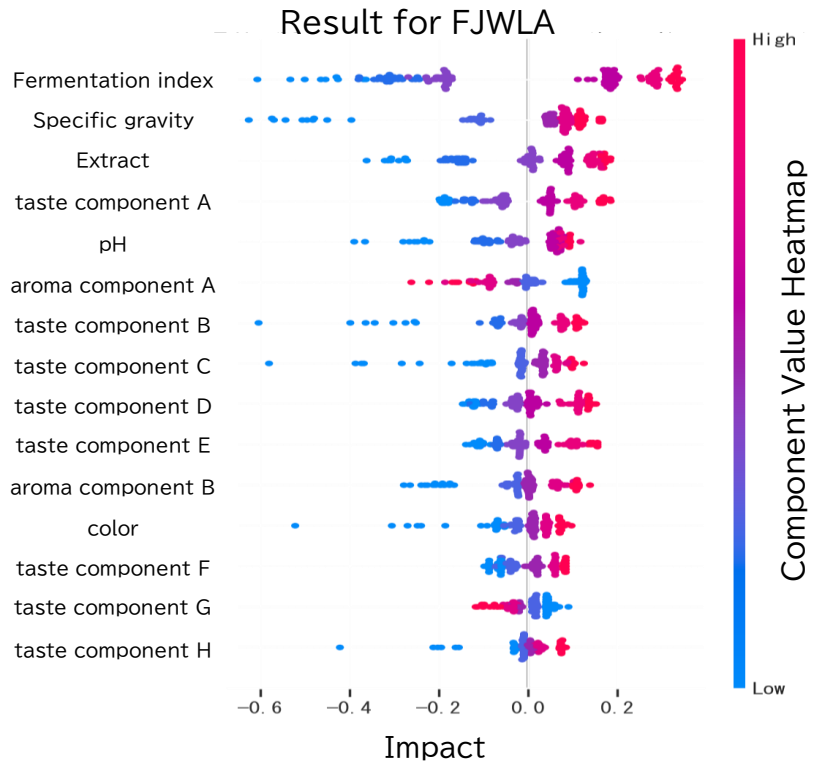
Output
Consumer research data

Preference AI (FJWLA)

Calculates the impact of each component!

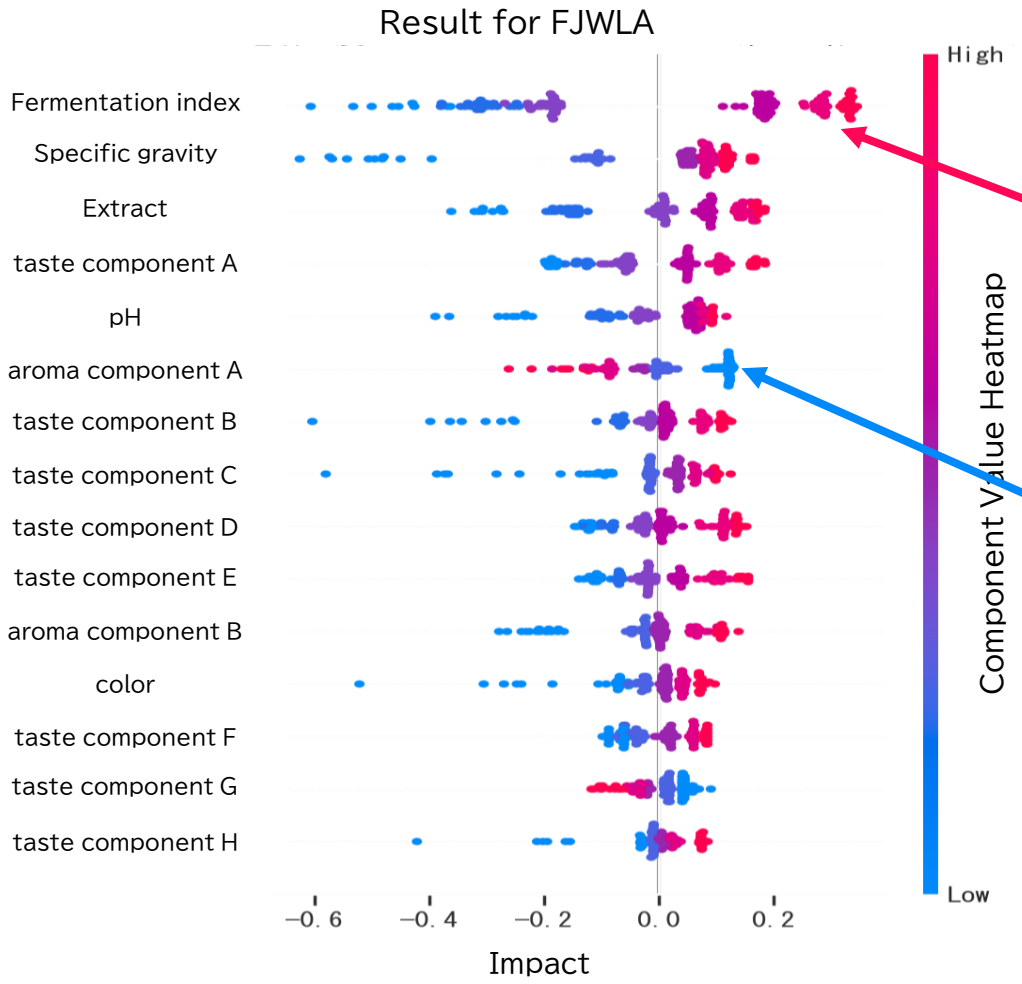
※ FJWLA (Flavor Judgement for Whole Liking Analysis)

Output of analysis results



Shows which components have the biggest impact on consumer preferences.

Brewing Control of FJWLA-Identified Components



An increase in Fermentation index value has a positive effect on “like.

Lower the fermentation index

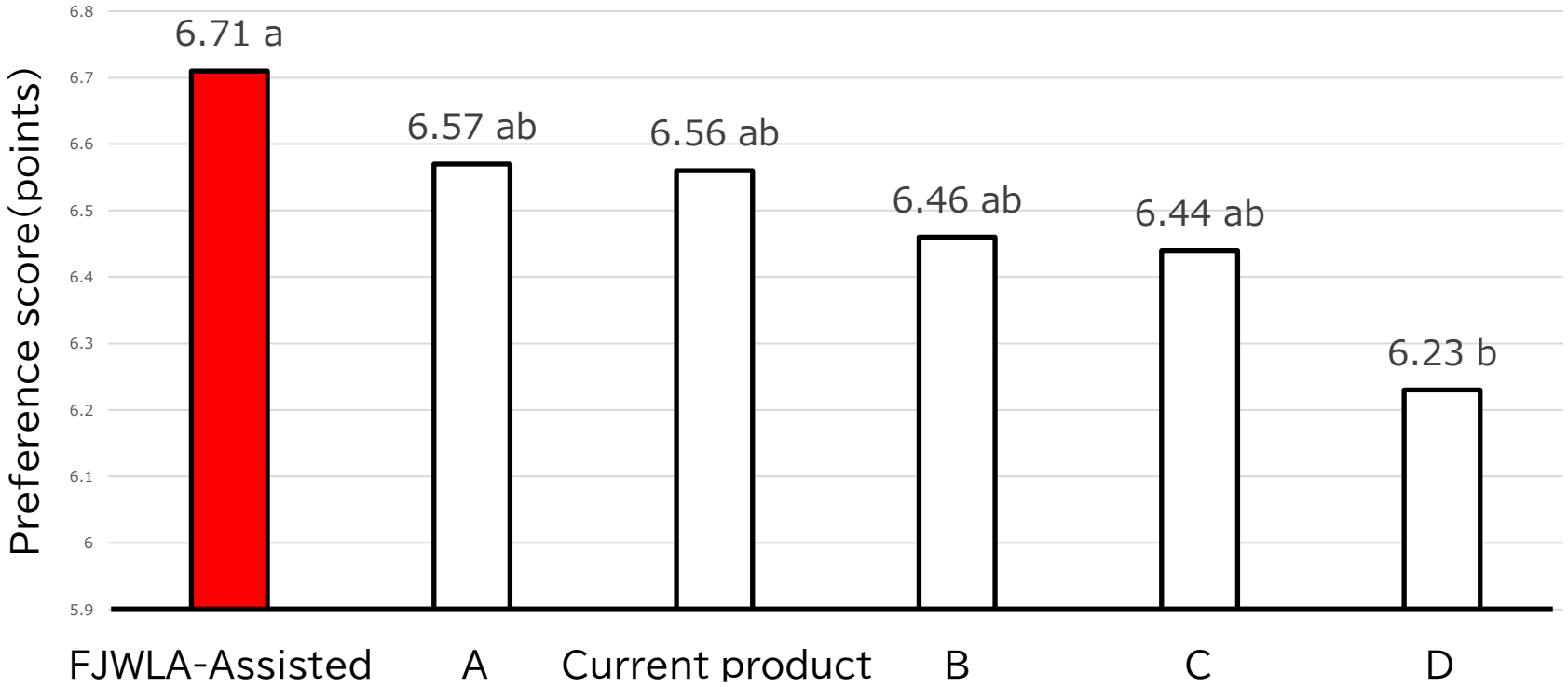
A decrease in aroma component A value has a positive effect on “like.

Control aroma component A

By controlling these components, we can brew a highly preferred beer.

FJWLA-Assisted vs Unassisted

Consumer evaluations of products developed with FJWLA



FJWLA × brewing expertise
to develop
more preferred flavors

※A~D:FJWLA-Unassisted
※Research conducted with
120 consumers
※Test at the 5% significance level

Product Launches Using FJWLA Set for 2026

AI-driven product development

FJWLA → Brewing → Research

Multiple rounds of consumer research

Launching in 2026

Applied to ¥XXB/year brands with strong business impact

Kirin's Long-Term Roadmap for AI Development