SHIONOGI R&D Day 2026

November 18, 2026

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SHIONOGI's Growth Strategy

Isao Teshirogi, PhD
Chief Executive Officer

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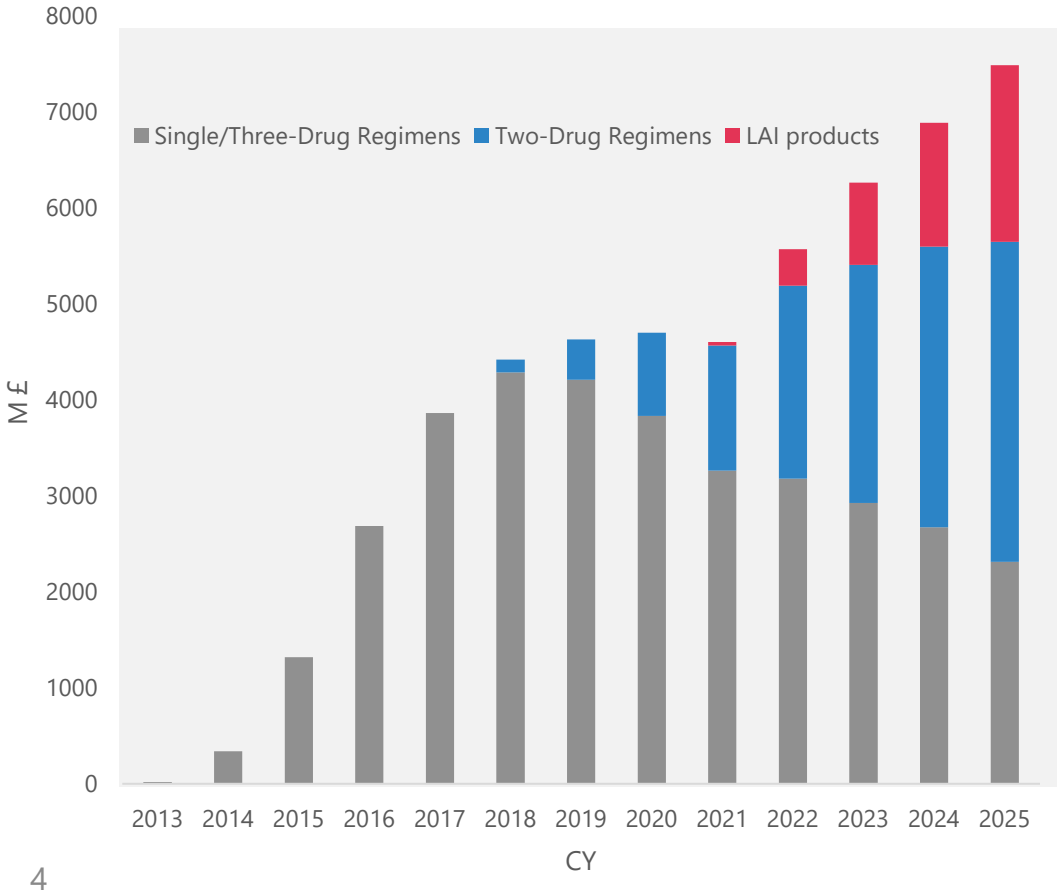
Rationale Behind the Four Major Investments

With the continued strong growth of LAI*1 products,
the HIV business will remain a stable earnings base for SHIONOGI

- Sales Trends of ViiV INSTI*2 Products -



- Growth of major products -

Dovato (dolutegravir/lamivudine)

Once-daily oral therapy
(Treatment)
Revenue (CY2025)

£ 2,678 M

YoY up

22 %

Growth is expected to continue

CABENUVA (cabotegravir; rilpivirine)

Twice-yearly injectable therapy
(Treatment)
Revenue (CY2025)

£ 1,402 M

YoY up

42 %

Apretude (cabotegravir 200 mg/mL)

Twice-yearly injectable therapy
(Prevention)
Revenue (CY2025)

£ 439 M

YoY up

62 %

LAI products are expected to continue significant growth

*1 Long Acting Injectable: Cabenuva, Apretude *2 Integrase inhibitor

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Building a Growth Foundation to Deliver In-House-Discovered Drugs Globally

Strengthen capabilities across the value chain that are essential for business growth

Value chain -Growth investments-	Research - Strengthening research capabilities -	Development - Strengthening Global Development Capabilities -	Domestic Sales -Stabilizing-	Global Sales —Rare disease business—
2025.5.7 **Acquisition of JT Group's Pharmaceutical Business*1**	■ Experienced medicinal chemists ■ Advanced technologies, including AI drug discovery	■ Akros' development expertise ■ Translational Research expertise		
2025.5.7 **Acquisition of TORI PHARMACEUTICAL*1**	■ Research infrastructure and expertise in the field of skin and allergy, centered around AIT*4	■ Domestic clinical development capabilities in the dermatology and allergy area	■ Strengthen the domestic business outside infectious diseases ■ Full-scale entry into SLIT products	
2025.12.22 **Acquisition of the Edaravone Business*2**	■ Apply accumulated RWE*5 to rare disease research	■ Key Opinion Leaders (KOLs) and Clinical Trial Physicians Network in ALS*6 Development	■ Acquisition of rights to RADICUT	■ Acquisition of rights to RADICAVA ■ Establish a rare disease business foundation in the U.S.
2026.10.5 **Acquisition of IntraBio*3**	■ Organelle evaluation technologies accumulated through levacetylleucine research	■ Development expertise that enabled successful rare disease clinical trials at overwhelming speed		■ Acquisition of rights to levacetylleucine (AQNEURSA®) ■ Synergies with RADICAVA in global sales

*1 May 2025 Press Release *2 December 2025 Press Release *3 October 2026 Press Release
*4 AIT: Allergen Immunotherapy *5 RWE: Real World Evidence *6 ALS: Amyotrophic Lateral Sclerosis

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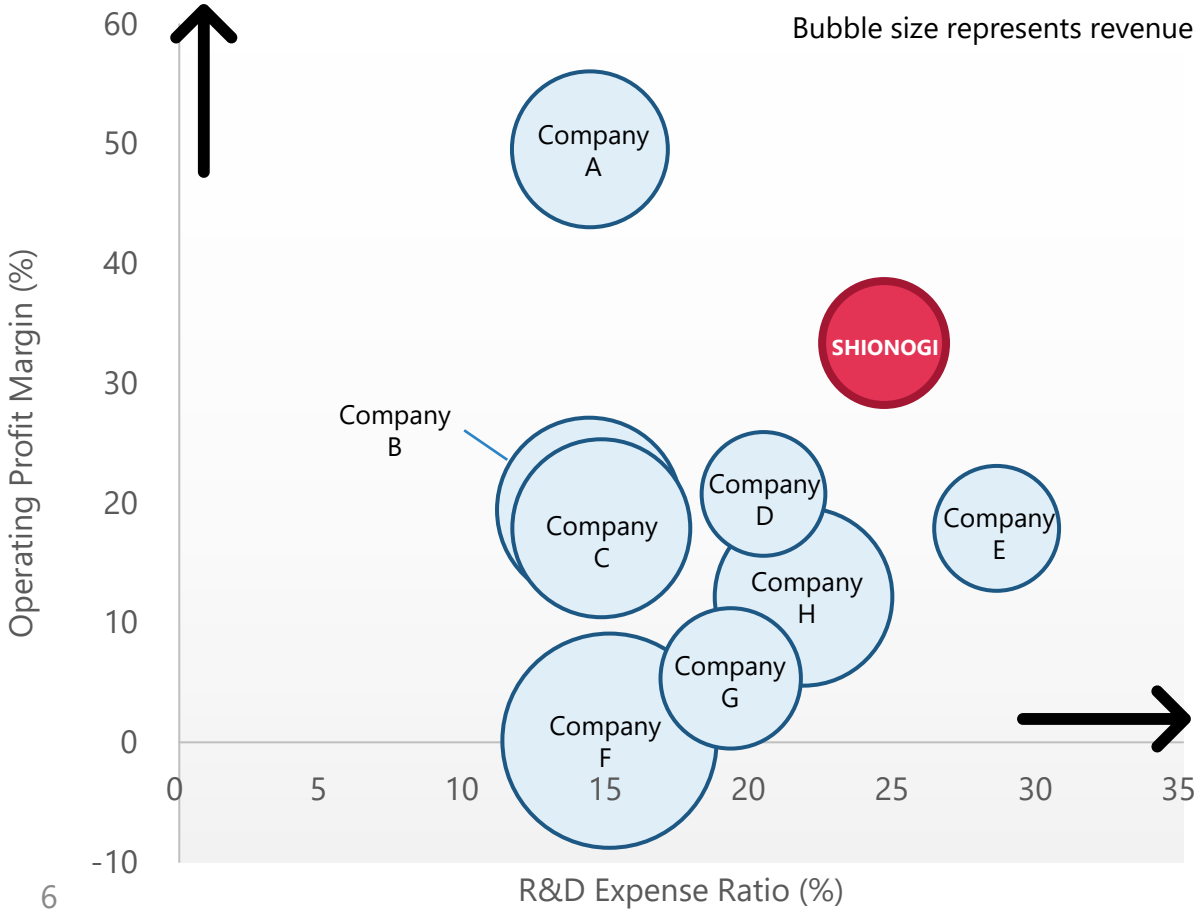
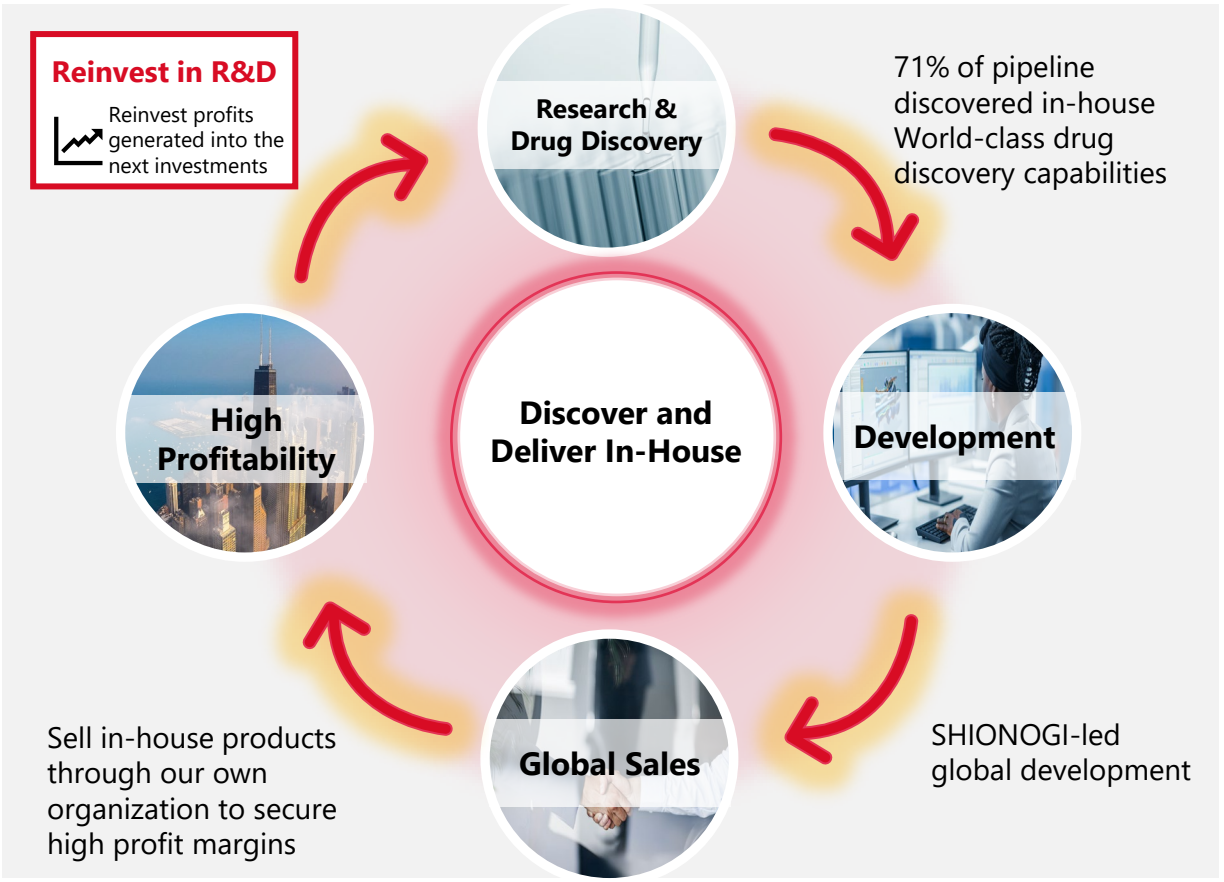
Making In-House Drug Discovery the Core of Growth

Continuously reinvest high profitability in R&D to achieve further growth through in-house-discovered drugs

Comparison of Profitability and R&D Investment among Japanese Pharmaceutical Companies (FY2025)



SHIONOGI's Unique Growth Strategy



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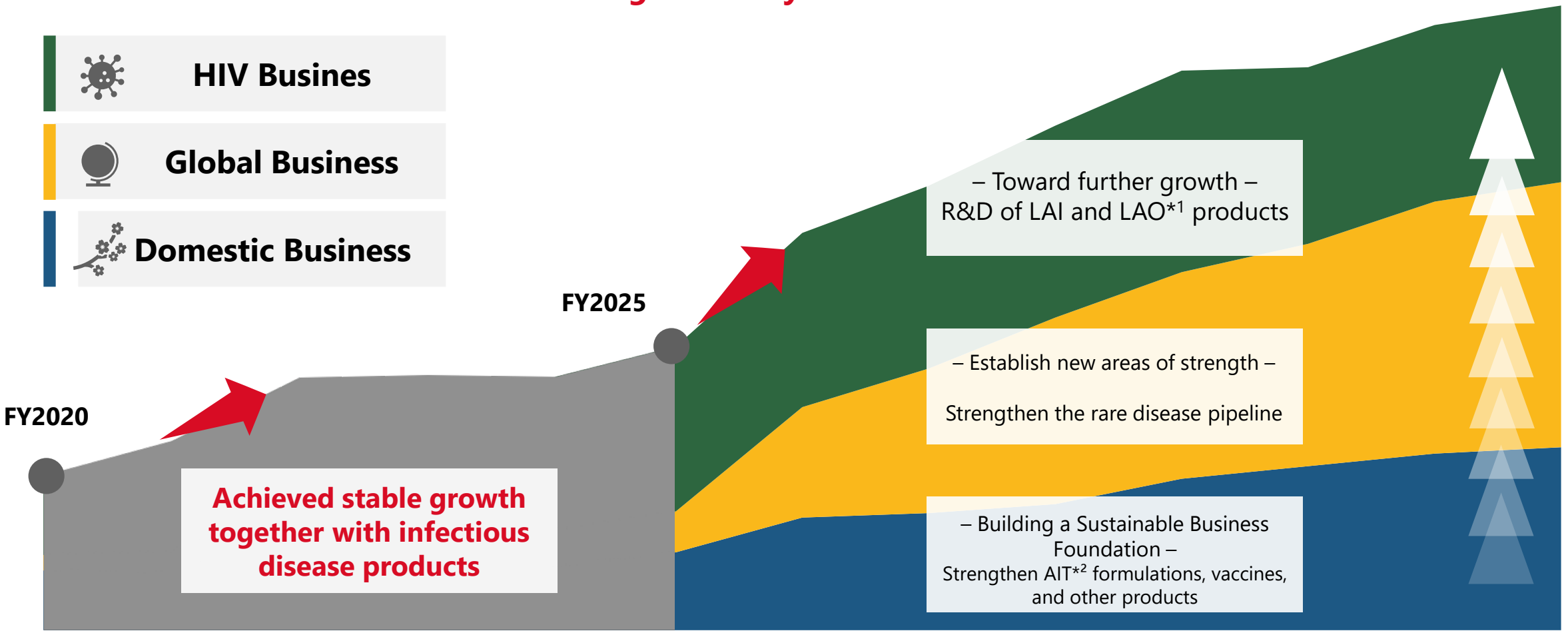
Building a Foundation for Sustainable Growth

Leverage our strengthened business foundation to develop new in-house discovered drugs into the next drivers of growth beyond HIV



※Illustrative revenue chart

*1 LAO: Long Acting Oral *2 AIT: Allergen Immunotherapy

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Driving Global Growth Based on World-Class Small-Molecule Drug Discovery Capabilities

HIV Business and R&D Strategy

I. HIV Business
II. Disease Areas of Focus

John Keller, PhD
Director of the Board, Senior Vice President, R&D Supervisory Unit

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LAIs Expected to Drive Growth Beyond 2030

Continued innovation in LAIs positions ViiV to lead the future of the HIV market

-Foundation for ViiV's sustained long-term growth

Advancing options for people living with HIV (PLWH)

Long-acting HIV treatment is the largest growth opportunity

Leading market transformation

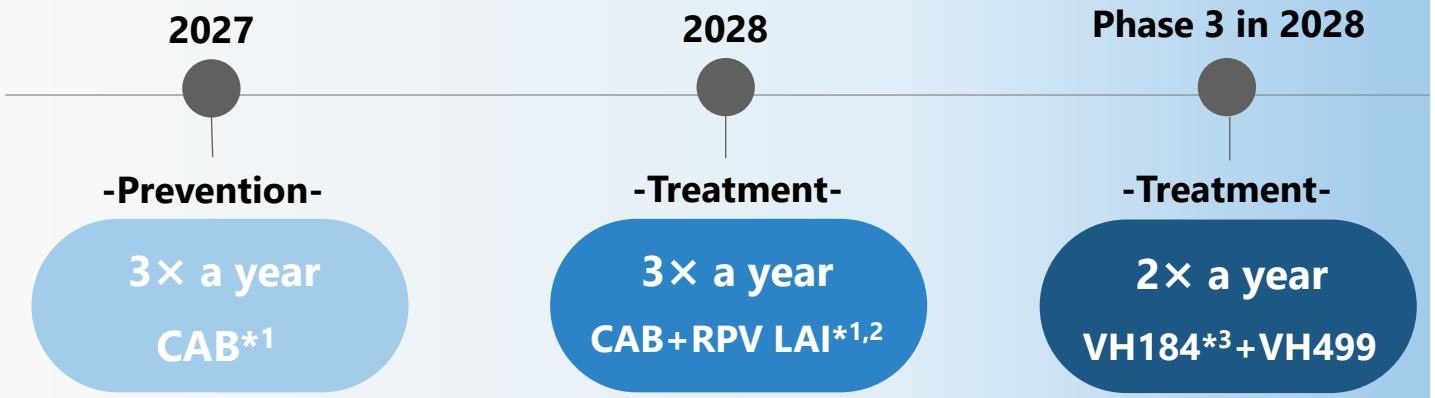
With INSTIs at the core; uniquely positioned to shape where the market goes next

Raising standard of care

Long-acting leadership fuels next generation of treatment and prevention options

-Significant near-term growth drivers-

-Toward Sustained Competitive Growth-



*1 New IM formulations *2 RPV: Rilpivirine *3 VH184: SHIONOGI's development number: S-365598

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3× a year LAI Treatment (CAB+RPV LAI)

Transformational and addressing an unmet need for PLHIV who are not virally suppressed

Strong HCP and patient preference for less frequent administration

Two-drug regimen

Cabotegravir (CAB*1)
INSTI

＋

Rilpivirine (RPV*1)
NNRTI*2

Ⅰ **Confidence**
builds on Cabenuva's proven efficacy and trust

Ⅱ **365 → 3**
patient treatment days

Ⅲ **Doubles**
clinic LAI treatment capacity

Ⅳ **Unlocks**
substantial switch opportunity

-Development Timeline-

- **CY2026 June**：Phase 3 CUATRO well underway
- **CY2028**：Potential approval

-Robust IP Strategy-

- **Additional patents pending into 2047*3**

*1 New IM formulations *2 NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor *3 cabotegravir NCE patent expiry 2031

2× a year LAI Treatment (VH184+VH499)

Best-in-class profile transforms adherence, setting a new standard of care

-Advancing toward 2× a year LAI treatment-

Two-drug regimen

VH184
INSTI

＋

VH499
CAPSID Inhibitor

Ⅰ	Ⅱ	Ⅲ	Ⅳ
VH184	**VH499**	**Broadest**	**Ongoing**
1st third-gen INSTI with enhanced resistance profile	highly potent capsid inhibitor with low risk of DDIs*1	patient population opportunity	VH184 INNOVATE study Phase 2b

-Development Timeline-

- **CY2026 H2**: VH499 CINERGY Phase 2b start
- **CY2028**: Phase 3 start

-Robust IP Strategy-

- NCE*2 patent expiry into 2040s
- **Patents pending into at least 2047**

*1 DDI: Drug-drug interaction *2 NCE: New chemical entity

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Expanding Options to Meet Diverse Needs for PLWH

Pursue several options to meet unmet needs for PLWH

- Next wave R&D breakthroughs -

Ⅰ Long-acting Oral



Weekly oral

Ⅱ Advanced LAI



- Self-admin options
- New LAI INSTIs

Ⅲ Complementary mechanisms



New Partner Drugs

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Disease Areas of Focus

John Keller, PhD

Director of the Board, Senior Vice President, R&D Supervisory Unit

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Disease Areas SHIONOGI Will Address

Target areas where SHIONOGI can leverage its strengths and where societal needs are high

Diseases That Pose a Risk to Social Infrastructure



- Acute respiratory infections
- Infections at risk of becoming chronic
- Severe infections with no effective treatment
- Unknown infectious diseases

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Diseases with High Societal Needs

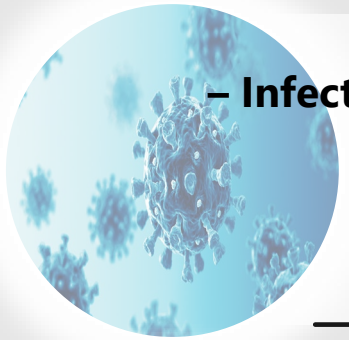


- High potential social costs
- Significant burden not only on patients but also on those around them
- Patients suffer through no fault of their own

Clarifying Priority Disease Areas

Fully leverage expertise acquired through various M&As
to clarify the disease areas that will drive the next phase of growth

Before



– Infectious Diseases –

Achieve freedom from the threat of infectious diseases



– QOL Diseases –

Contribute to a healthy and prosperous life

Acquisition of New Capabilities

1 Former JT Pharmaceutical Business / TORII PHARMACEUTICAL

- **Rare disease drug discovery experience /expertise**
- **Expertise in immunology and allergy, including SLIT**

2 Edaravone Business / IntraBio

- **Rare disease business platform established through RADICAVA**
- **Proven rapid development capabilities in rare diseases**

After

- Continue initiatives in infectious diseases
- Concentrate management resources on disease areas where our strengths can be leveraged
- Significantly accelerate the creation of a new pillar outside infectious diseases

Toward a New Disease Area Strategy

Disease Area Strategy

Create sustainable value centered on core disease areas, while developing the next growth areas

Priority Disease Areas

Three areas where SHIONOGI can fully leverage its strengths

Neuromuscular Diseases

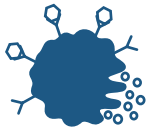


New possibilities for diseases with limited treatments

- ALS
- Pompe desease

Start with hereditary rare diseases, then expand into sporadic rare diseases and neurodegenerative diseases

Immunology / Allergy

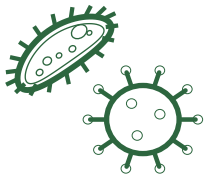


Treatments that change the immune response itself

- Allergy (SLIT)
- Cancer / Immunology
- Skin diseases

Build on SLIT products to expand into AIT and autoimmune diseases

Infectious Diseases



Freedom from the threat of infectious diseases

- HIV
- Respiratory viruses
- AMR

As a leader, leverage SHIONOGI's unique strengths in infectious diseases built over many years

Next Growth Areas (3 Selected Areas)



Sleep Disorders



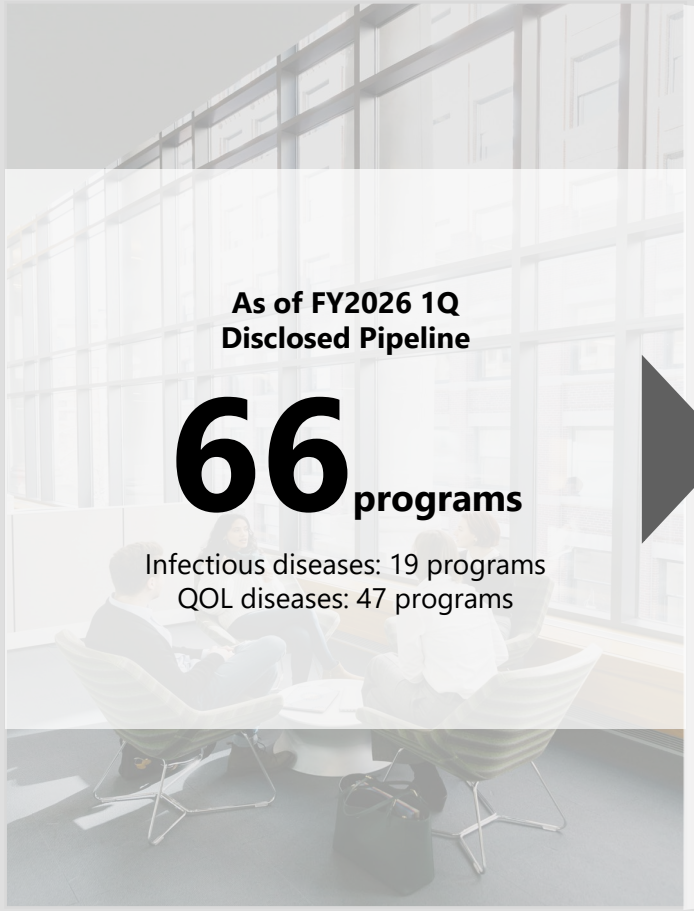
Psychiatric Disorders



Hearing Loss

Selection and Prioritization of the Development Pipeline

Restructure the pipeline in line with the disease strategy and concentrate R&D investment on growth drivers



As of FY2026 1Q Disclosed Pipeline

66 programs

Infectious diseases: 19 programs
QOL diseases: 47 programs

Alignment with Disease Strategy

Social impact / unmet needs

Scientific and Clinical Probability of Success

Differentiation / feasibility

Business Value and Competitive Advantage

Value maximization in-house / sustainable growth

Strategically Restructuring the Pipeline

Prioritized Pipeline

21 programs

– Pipeline of Prioritized Disease Area –

Neuromuscular Diseases	Immunology / Allergy	Infectious Diseases
6 programs	7 programs	7 programs

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Prioritized Development Pipeline Overview

Area	Preclinical (Preparing for Phase 1 initiation)	Phase1	Phase2		Phase3	
Neuromuscular Diseases		S-262262 Neurodegenerative diseases / ALS	S-051051 IC/BPS	S-606001 Pompe disease	Levacetylleucine CACNA1A-related diseases	Zatolmilast Fragile X sydrome
			Zatolmilast Jordan syndrome			
Immunology / Allergy			S-531011 Postoperative MRD*1-positive MSS colorectal cancer	S-531011 MSS*2 colorectal cancer(3L+)*3	TO-209 Grass pollen-induced allergic rhinitis ☆	TO-210 Acne ☆
	S-462462 Atopic dermatitis		Redasemtide Epidermolysis bullosa		TO-208 Common warts ☆	
Infectious Diseases	S-048133 Malaria	Secutrelvir COVID-19 PrEP (LAI)		S-337395 RSV infections	Secutrelvir COVID-19 treatment (Oral pill)	Olorofim Invasive aspergillosis
	S-910978 Lung MAB	S-649228 AMR (Gram-negative bacterial infection)				
Next Growth Areas			S-054502 Sleep apnea			

☆ : Japan only

*1 MRD: Molecular Residual Disease *2 MSS: Microsatellite Stable *3 Third-line treatment or later

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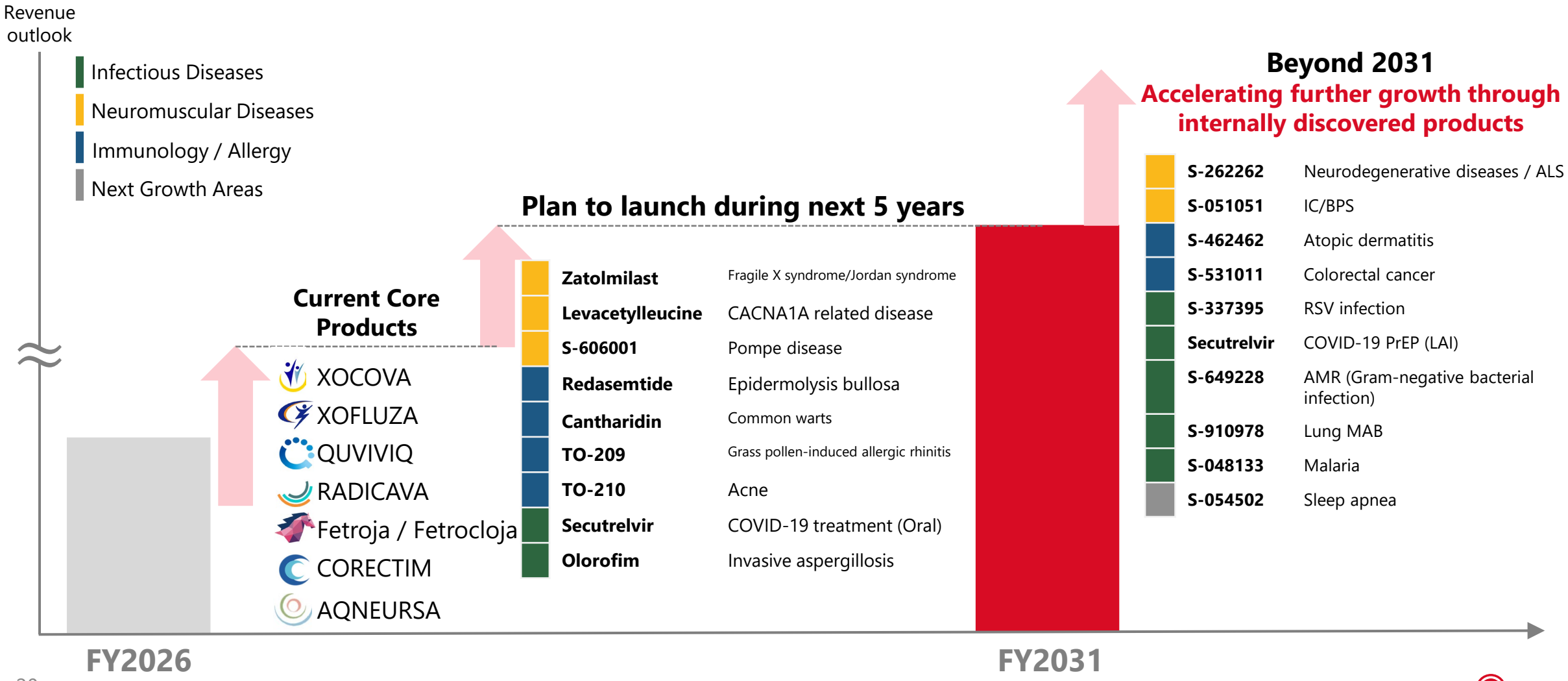
Sustainable Growth Driven by Multiple Growth Drivers

Expanding the product portfolio and further growth with in-house discovered products



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Development Pipeline

I. Neuromuscular Diseases
II. Immunology / Allergy
III. Infectious Diseases
IV. Next Growth Areas

Takeki Uehara, D.V.M., PhD
Corporate Officer, Senior Vice President,
Drug Development and Regulatory Science Division

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Priority Disease Area

– Neuromuscular Diseases –

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Neuromuscular Diseases | Vision and Unmet Needs to Address

Helping every person live life on their own terms and realize their potential, regardless of disease

Our Vision

01 Protect Growth and Development



Enable people with neuromuscular diseases to grow and develop in good health

02 Halt Disease Progression



Enable people with progressive neuromuscular diseases to live with improved survival and quality of life by halting, slowing, or reversing symptom progression

Unmet Needs

Symptoms That Diminish Quality of Life



Mobility, constipation, sleep, pain, cognition, and more

Fear of Disease Progression



Continued deterioration despite treatment

Reducing the Burden of Treatment and Caregiving



Prolonged need for clinic visits, monitoring, and caregiving

Not Adequately Addressed by Existing Treatments



Deep tissues, bone and cognitive development, and more

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Neuromuscular Diseases | Three Therapeutic Approaches

Expanding treatment options and building the next-generation pipeline through three approaches targeting mechanisms shared across multiple diseases

1 Protect Cells



—Maintaining Cellular Homeostasis—

Intervene in core disease mechanisms to protect nerve and muscle cells from damage

Key Products / Pipeline Assets

- RADICAVA Marketed
- Levacetylleucine (AQNEURSA®) Marketed / Phase 3
- S-606001 Phase 2

2 Restore Neural Function



—Normalizing Neural Circuits and Neuroinflammation—

Deliver meaningful symptom improvement to give patients more time to do what matters

Key Products / Pipeline Assets

- Zatolmilast Phase 2 / Phase 2/3
- S-051051 Phase 2
- S-262262 Phase 1

3 Deliver to the Target



—Delivering Therapeutics to Affected Tissues—

Combine drug-delivery technologies with interventions targeting abnormal proteins, substrate accumulation, and disease-causing genes

Key Technologies

- Brain Shuttle Technology
- Muscle-Targeted DDS-siRNA

Levacetylleucine (AQNEURSA®) | Target Diseases: NPC/A-T

Rare diseases characterized by progressive decline in neurological functions, including motor and coordination functions, with a substantial impact on daily life

Niemann-Pick Disease Type C (NPC)

A disease characterized by lipid accumulation in lysosomes in the central nervous system

- Neurological symptoms such as ataxia and cognitive decline
- Systemic symptoms such as hepatic dysfunction and respiratory disorders

Incidence[*1]

Approx. **1** in **100,000**

Diagnosed Patients[*2]

Approx. **400** patients
US

Approved Treatments

AQNEURSA, arimocromol, miglustat

Ataxia-Telangiectasia (A-T)

A wide range of systemic symptoms caused by impaired DNA repair and oxidative stress

- Neurological symptoms, including ataxia and dysarthria
- Systemic symptoms such as immunodeficiency and respiratory infections

Incidence[*3]

Approx. **1** in **40,000** to **100,000**

Diagnosed Patients[*2]

Approx. **1,500** patients
US

Approved Treatments

AQNEURSA

[*1] Christopher A. Wassif, et al. High incidence of unrecognized visceral/neurological late-onset Niemann-Pick disease,type C1, predicted by analysis of massively parallel sequencing data sets https://www.sciencedirect.com/science/article/pii/S1098360021042921?via%3Dihub

[*2] SHIONOGI estimates based on real-world data, epidemiological literature, expert surveys, and other sources [*3] Rothblum-Oviatt C, et al. Ataxia telangiectasia: a review. Orphanet Journal of Rare Diseases. 2016;11:159.https://ojrd.biomedcentral.com/articles/10.1186/s13023-016-0543-7

AQNEURSA is indicated for the treatment of: neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥15 kg, ataxia in adults and pediatric patients with ataxia-telangiectasia (A T) weighing ≥ 15 kg.

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Levacetylleucine (AQNEURSA®) | Potential Mechanism of Action

NPC (Niemann-Pick Disease Type C)

– NPC1/NPC2 Gene Mutations –



Impaired lysosomal transport of cholesterol and other lipids leads to their accumulation within cells

A-T (Ataxia-Telangiectasia)

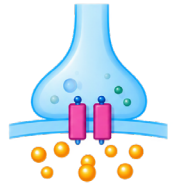
– ATM Gene Mutations –



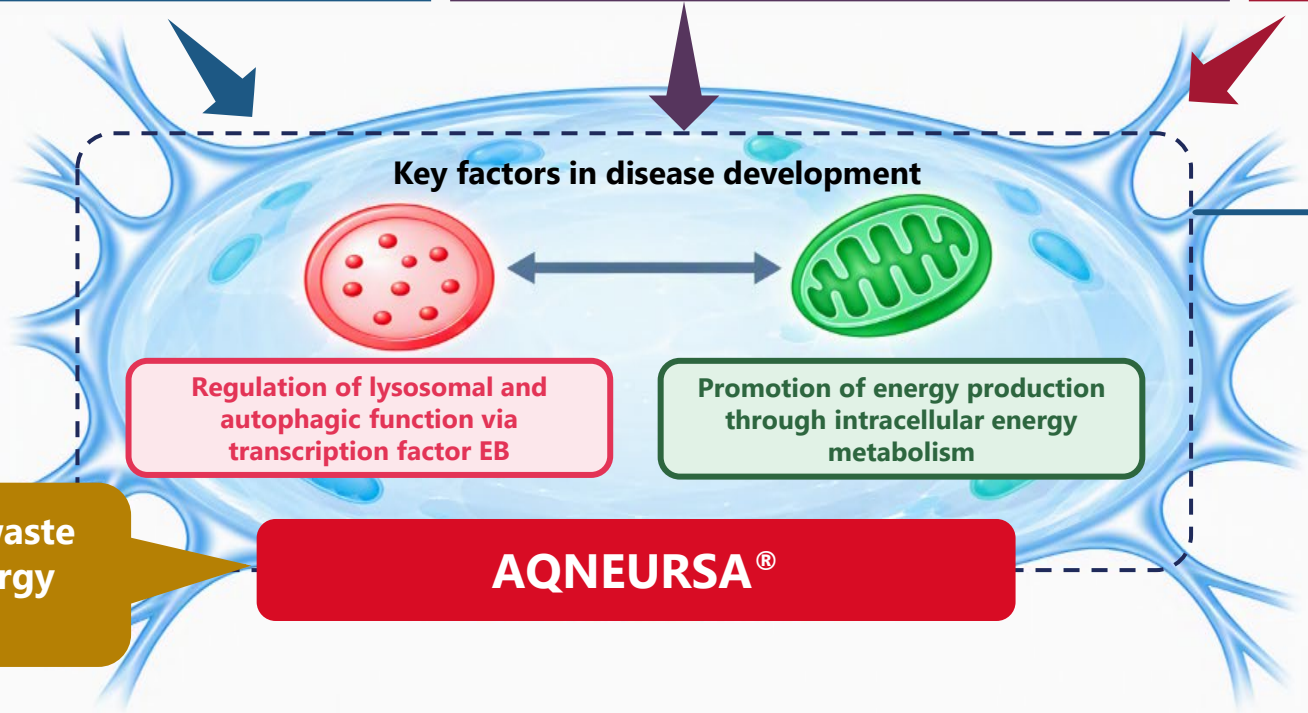
Impaired DNA damage repair and loss of mechanisms that suppress oxidative stress

CACNA1A-Related Disorders

– CACNA1A Gene Mutations –



Ca^{2+} channel (CaV2.1) dysfunction disrupts intracellular Ca^{2+} homeostasis, leading to unstable neuronal activity



Improves cellular waste clearance and energy production

Neuronal Dysfunction

Motor and Coordination Impairment
—cerebellar ataxia—
Unsteadiness, Gait disturbance, and Dysarthria

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Levacetylleucine (AQNEURSA®) | Results of Phase 3 Trials in NPC and A-T

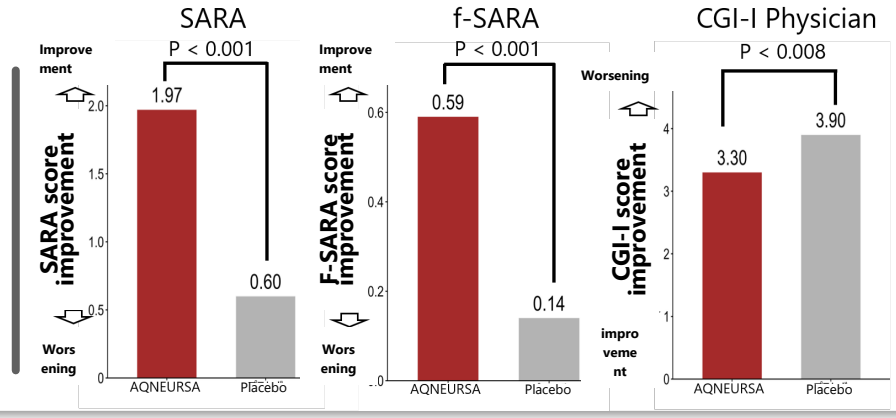
Clinical trials demonstrated a new treatment benefit: improved motor function

Phase 3 Study Overview

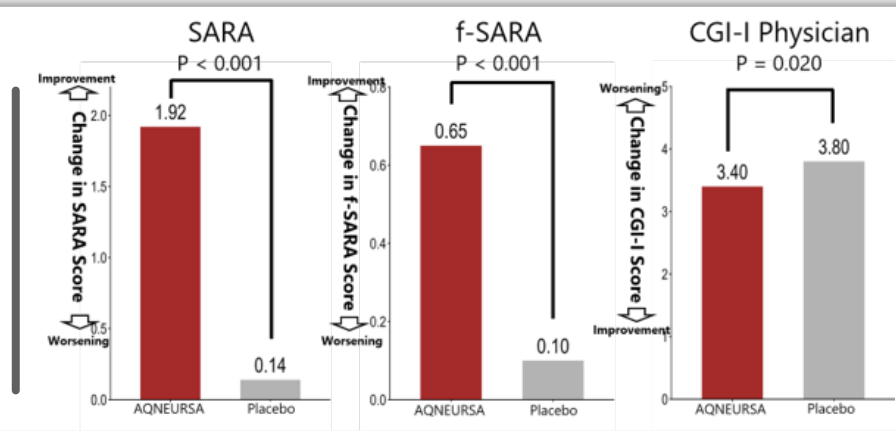
Disease	NPC	A-T
Study Design	Randomized, placebo-controlled, double-blind, two-period crossover	
Population	**Patients with NPC** aged 4 years or older	**Patients with A-T** aged 4 years or older
Endpoints	Primary Endpoints Scale for the Assessment and Rating of Ataxia (SARA): assesses the severity of cerebellar ataxia Functional SARA (f-SARA): focuses on functional impairment Key Secondary Endpoint Clinical Global Impression of Improvement (CGI-I): assesses overall improvement	
Number of Patients	60 patients	77 patients

Phase 3 Study Results

NPC



A-T



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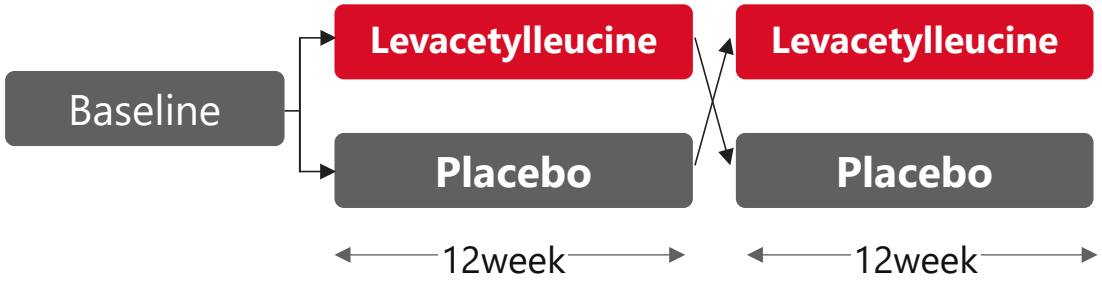
Levacetylleucine | Expansion into CACNA1A-Related Disorders

Pursuing levacetylleucine's potential to expand into additional rare-disease indications

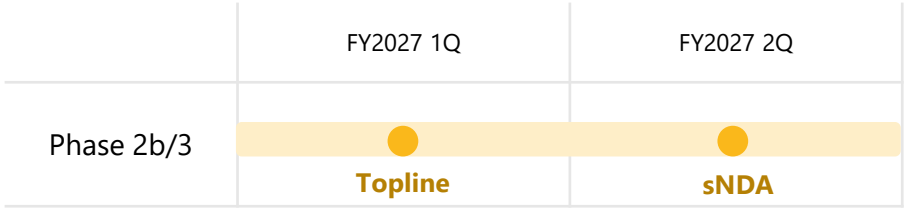
Phase 3 Study Overview

Study Design	Multinational, randomized, placebo-controlled, double-blind, two-period crossover
Population	Patients aged ≥4 years with CACNA1A-related disorders
Endpoints	Primary Endpoint • SARA*1 Key Secondary Endpoints • f-SARA • Clinical Global Impression of Improvement (CGI-I) • ICARS*2
Target Enrollment	46 patients: enrollment completed in October 2026

Phase 3 Study design



Main Milestones



*1 Objective physician assessment of cerebellar ataxia severity to evaluate treatment effect *2 International Cooperative Ataxia Rating Scale

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S-606001 | Target Diseases: Pompe Disease

A disease with substantial unmet medical needs and enzyme replacement therapy as the only available treatment option

Pompe disease is a rare, inherited lysosomal storage disorder caused by reduced or absent acid α-glucosidase (GAA) activity. Glycogen accumulates in muscles, leading to progressive loss of muscle strength and respiratory function

Disease Profile

A rare disease affecting approximately 1 in **22,000** people, with a sizable market

—Prevalence*1—	—Market*2—	—Annual Treatment Cost—
Approx. **20** K patients	Approx. $ **1.2** B (USD per year)	Approx. $ **700** K (U.S. list price)

*1 Estimated LOPD prevalence: approx. 20,000 patients (U.S., EU5, and Japan) *2 Includes both IOPD and LOPD

Unmet Needs

Sustained long-term efficacy

As a progressive disease, Pompe disease requires durable treatment benefit.

Reduced Treatment Burden

Enzyme replacement therapy requires an approximately four-hour infusion every two weeks

More treatment options

Treatment options beyond enzyme replacement therapy are needed

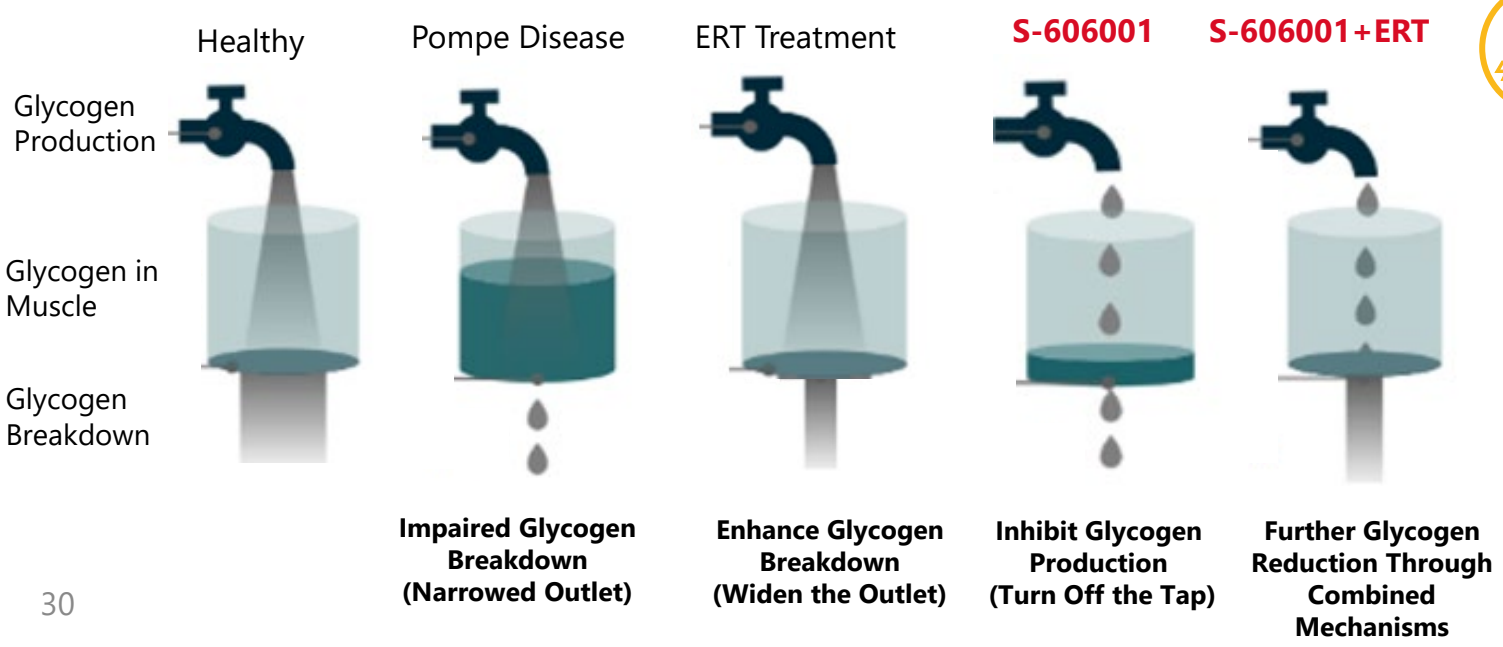
Sources: Market size: Copyright © 2026 IQVIA. Internally calculated based on IQVIA Analytics Link 2025. Reprinted with permission; Annual treatment cost: U.S. WAC for each ERT (75-kg patient); Disease overview/age at onset: Dasouki et al., *Neurol Clin.* 2014; Diagnostic delay: Lagler et al., *JIMD Rep.* 2019; Dosing interval: U.S. Prescribing Information for each ERT; Incidence: Colburn & Lapidus, *Front Pediatr.* 2024;11:1221140.

S-606001 | Mechanism of Action and Features

Providing new treatment options tailored to patient needs

Mechanism of Action

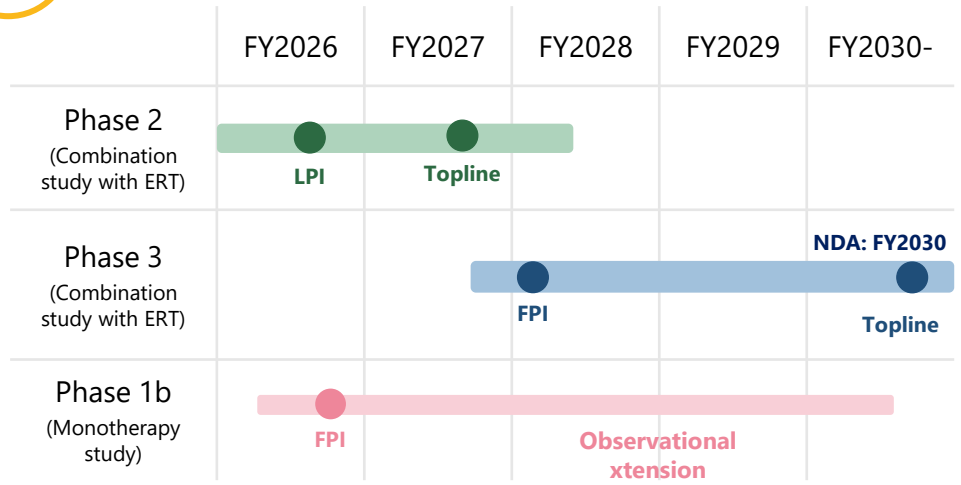
Treatment	Mechanism of Action
S-606001 (in development)	Inhibits glycogen synthase to reduce production of disease-causing glycogen
ERT*1 (standard of care)	Replaces the glycogen-degrading enzyme to promote lysosomal glycogen breakdown



Product Profile and Aspiration

- Combining with ERT*1 to enhance efficacy
- Oral monotherapy may reduce the burden of infusion visits

Key Milestones



*1 ERT: Enzyme Replacement Therapy

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S-606001 | Overview of Ongoing Clinical Studies

Assessing the value of S-606001 as both combination therapy with ERT and oral monotherapy

Phase 2 study (Add-on to ERT)

—Assessing efficacy in Combination with ERT—

Study Design	Multicenter, randomized, placebo-controlled, double-blind study
Participants	■ Adults (≥18 years) with late-onset Pompe disease ■ Receiving ERT for ≥2 years with no dose or regimen changes in the past 6 months
Treatment Period	52 weeks
Primary Endpoint	**Change in pulmonary function (%FVC) at Week 52**
Topline Results	FY2027 Q4

Phase 1b study (Monotherapy)

—Assessing safety and tolerability as monotherapy—

Study Design	Multicenter, open-label study
Participants	■ Adults (≥18 years) with late-onset Pompe disease ■ No ERT for ≥3 months
Treatment Period	48 weeks
Primary Endpoint	**Safety and tolerability**
Topline Results	FY2028

Amyotrophic Lateral Sclerosis (ALS)

A rare, fatal disease in which progressive neurodegeneration impairs motor and physical function

Progressive degeneration of upper and lower motor neurons leads to muscle weakness and atrophy, followed by loss of swallowing, speech, and respiratory function, ultimately resulting in respiratory failure.

Disease Profile

~1 in 20,000 People, with Significant Market Potential

- Patient Population*1-	- Life Expectancy-	—Market—
Approx. **60** K patients	**3-5** years	Approx. $ **750** M

Unmet Needs

Life Expectancy

Improve Not Only Symptoms, but Also Survival

Current Treatment Options

Limited Treatment Options and Persistent Unmet Need for Slowing Disease Progression

Riluzole	・Familial & sporadic ALS ・2–3 month survival benefit
Mecobalamin	・Familial & sporadic ALS ・Japan only | Early-stage ALS | ~40% slowing of ALSFRS-R decline
Edaravone	・Familial & sporadic ALS ・33% slowing of ALSFRS-R decline
Tofersen	・Familial SOD1-ALS —Gene-targeted therapy —Accelerated approval based on NfL reduction

*1 Patient population in Japan, the United States, and EU5: Amyotrophic Lateral Sclerosis Treatment Market Report, 2033

Expansion of ALS Drug Discovery

Aiming to deliver new treatment options for ALS, where unmet need remains high, through a multifaceted approach

1 Protect Neurons

—Maintenance of Cellular Homeostasis—

Target core pathophysiological mechanisms to preserve neuronal and muscle cell integrity

Edaravone



ROS

Oxidative stress

Novel Therapeutic Targets

Mitochondrial dysfunction
Reduced energy production
Increased intracellular Ca^{2+}

2 Restore Neuronal Function

—Normalization of Neural Circuitry and Neuroinflammation—

Deliver meaningful symptom improvement to extend patients' functional time

Glutamate excitotoxicity
Excessive glutamate release
Overactivation of receptors

Riluzole

Motor neuron

Activated glial cells
(microglia / astrocytes)

S-262262

CNS penetrant NLRP3 inhibitor

SHIONOGI

Edaravone | Clinical Study Results and Post-Marketing Data

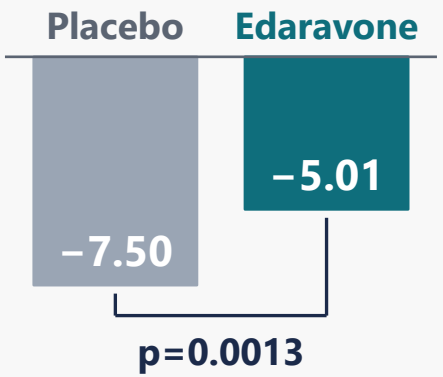
Edaravone slowed functional decline in clinical trials, and post-marketing data suggest a survival benefit; however, significant unmet needs remain

At Approval

J19 study*1

Evaluated short-term (24 weeks) functional decline

Change in ALSFRS-R (points)



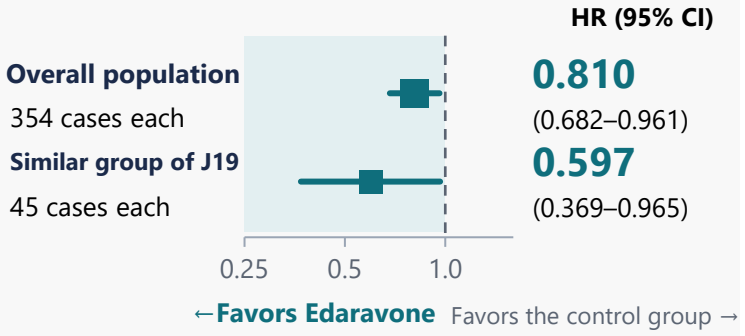
Slowed functional decline by **33%**

Post-Marketing Surveillance

SUNRISE Japan*2

Survival over up to 5 years of follow-up

Event: death or initiation of permanent mechanical ventilation



Decrease Hazard

19%

HR 0.810, p=0.0159

Event-free survival (median)

2.1 years vs **1.9 years**

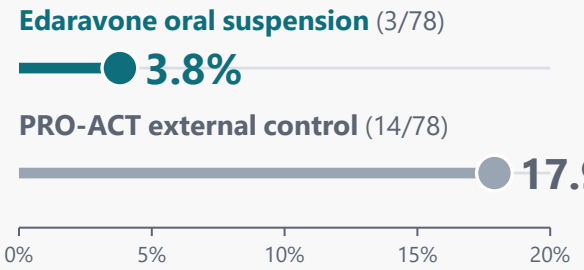
Edaravone vs **Control**

Post-Marketing Clinical Study

PRO-ACT Comparison*3

Survival over approx. 22 months of follow-up

Mortality (approx. 22 months)



Reduction in hazard of death (risk-adjusted)

84% HR 0.16 (95% CI 0.043–0.562), p=0.005

*1 J19 study: A placebo-controlled study in patients with early-stage ALS (Lancet Neurol 2017) *2 SUNRISE: Comparison of a post-marketing surveillance study with the pre-approval JaCALS registry (overall population: 354 patients per group, log-rank p=0.0159; J19-like population [patients selected based on the eligibility criteria of the J19 study]: 45 patients per group, log-rank p=0.0335). The event was defined as death or initiation of permanent mechanical ventilation (Sobue G, et al. Presented at PACTALS 2025, Melbourne, and the 43rd Annual Meeting of the Japanese Society of Neurological Therapeutics, 2025, Kumamoto; the forest plot was generated based on the data presented). *3 PRO-ACT comparison: Patients treated in a phase 3b study of the oral suspension formulation conducted as an FDA postmarketing commitment and its extension study (MT-1186-A02/A04; 7 countries) vs external controls from PRO-ACT (a pooled database of historical ALS clinical trials; patients not receiving active investigational treatment) (78 patients per group; 670 days [approx. 22 months]). HR from a baseline risk-adjusted Cox proportional hazards model. Figure created from published values in the text and Table 2 of Takahashi F, et al. Muscle Nerve 2025;72:586–596. The SUNRISE and PRO-ACT comparisons were non-randomized comparisons using propensity score matching.

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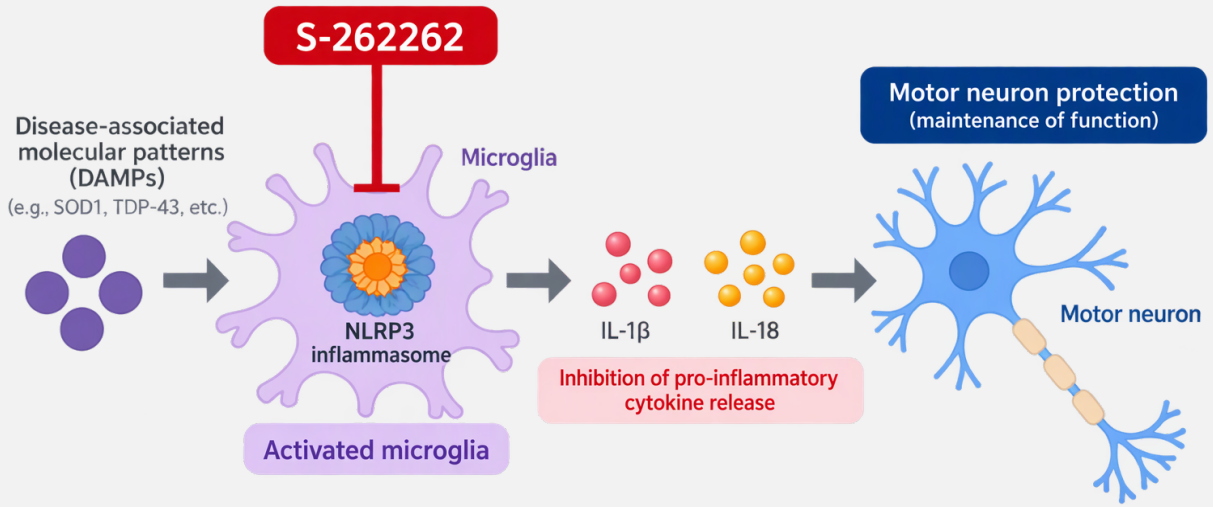
S-262262 | Mechanism of Action and Features

Favorable CNS Penetration and Potent NLRP3*1 Inhibition with Preclinical Motor Function Efficacy

S-262262 Mechanism of Action

—Suppress Neuroinflammation and Protect Motor Neurons—

Inhibits pathological protein-induced NLRP3 activation in microglia, suppressing pro-inflammatory cytokine release



Product Profile and Vision

- Favorable CNS penetration with once-daily dosing
- Potent NLRP3 inhibition at low doses
- Consistent efficacy signals from target inhibition to motor function in preclinical ALS models

Key Milestones

	FY2026	FY2027	FY2028	FY2029	FY2030-
Phase 2(a)		FPI		Topline	
Phase 2b/3					FPI

*1 NLR family pyrin domain containing 3

SHIONOGI

S-262262 | Proof of Concept as a Potential ALS Therapy

Confirm safety in Phase 1 study, aiming to achieve PoC for ALS in Phase 2a study

Phase 1 Study Overview

Population	Healthy adults
administration	Oral single and multiple dosing *Lumbar puncture CSF sampling (one multiple-dose level) also conducted

Phase 1 Study Results

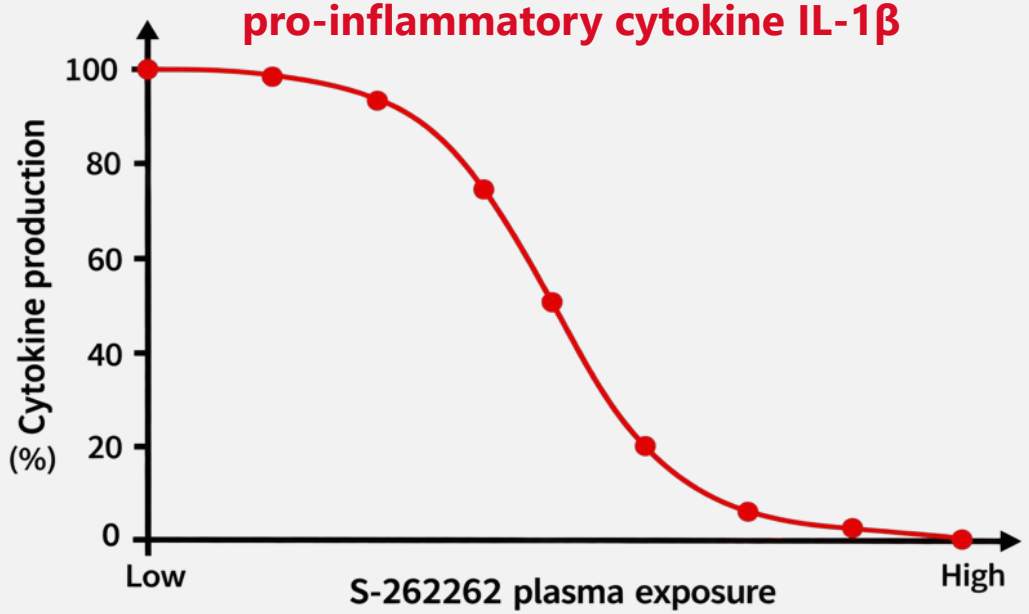
01 | Safety and tolerability confirmed

02 | Exposure-dependent suppression of cytokine (IL-1β) production

03 | CSF (cerebrospinal fluid) penetration confirmed

Data suggesting pharmacological activity in humans were obtained

Suppression of the production of the pro-inflammatory cytokine IL-1β



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Zatolmilast | Target Diseases: Fragile X Syndrome (FXS) and Jordan's Syndrome (JS)

Rare neurodevelopmental disorders caused by genetic mutations that affect a broad range of developmental domains, including cognition, language, and motor function

Disease Profile

FXS A rare disease caused by expansion of the CGG trinucleotide repeat in the X-linked FMR1 gene

—Estimated Prevalence in Males*1—

1 in **10,000**

- Developmental delay and intellectual disability from early childhood,
- A genetic disorder more common in males
- Diverse clinical symptoms, including behavioral abnormalities

JS A rare neurodevelopmental disorder caused by PPP2R5D gene variants

—Diagnosed patients*2—

Approx. **250** patients

- Characterized by cognitive and language developmental impairments from early childhood
- Diverse clinical symptoms, including behavioral abnormalities and hypotonia

Unmet Needs

No Disease-Modifying Treatment

No approved treatments; current care focuses on symptom-based treatment and support

Improved Language and Communication Function

Difficulties with communication and social participation

Mechanism of Action

Phosphodiesterase 4D (PDE4D) inhibition

*1 Fragile X syndrome (designated intractable disease 206) - National Center for Intractable Diseases Information *2 Information provided by Jordan's Guardian Angels(USA only)

Zatolmilast | Phase 2 Study Overview and Results in JS

Pursuing potential NDA submission based on study results through FDA discussions in FY2026

Phase 2 Study Overview*1

Study Design	Randomized, placebo-controlled, double-blind study
Population	■ Males and females with Jordan's syndrome ■ Aged 9–45 years
Participants	30 patients (Placebo group: n=14; Zatolmilast group: n=16)
Treatment Period	Double-blind: 24 weeks Open-label extension: 72 weeks
Key Endpoints	■ NIH-TCB*2 ■ Change in language and communication function (NRS*3)

Phase 2 Study Results

Significant improvements across multiple endpoints, including objective measures, despite small sample size

Endpoints			Between-Group Difference vs. Placebo
Objective	**NIH-TCB**	Crystallized Cognition	4.86 (p=0.173)
		Fluid Cognition	**7.35 (p=0.033)**
		Total Cognition	**4.54 (p=0.015)**
Subjective	NRS*3	Language / Communication	-0.74 (p=0.241)
		Daily Function	-0.93 (p=0.106)
	CaGI-I*4	Language / Communication	-0.50 (p=0.095)
		Daily Function	**-1.00 (p=0.008)**
	CGI-I	Language / Communication	-0.50 (p=0.065)

*1 NCT06717438 *2 National Institutes of Health Toolbox Cognitive Battery
*3 Patient-specific behavioral assessment using a numerical rating scale (NRS) *4 Caregiver global impression of improvement

Zatolmilast｜Phase 2/3 Trial Results (Fragile X Syndrome in Adult Males)

Consult with the FDA during FY2026 to determine the future development strategy

Phase 2/3 Study Overview*1

Study Design	Multicenter, randomized, double-blind, parallel-group, placebo-controlled study
Population	■ Males with fragile X syndrome ■ Aged 18–45 years
Patients Enrolled	Placebo: 58 patients Zatolmilast: 113 patients
Treatment Period and Dosing	13 weeks; twice-daily dosing
Primary Endpoint	NIH-TCB CCC*2
Secondary Endpoints	NRS*3 Language/Communication and Daily Living Functioning

Phase 2/3 Study Results

Significant improvements were observed in some subjective measures

Endpoint			Between-Group Difference vs. Placebo
Objective	NIH-TCB (Primary endpoints)	CCC	-0.35（p=0.706）
Subjective	**NRS**	**Language/ Communication**	**0.57（p=0.019）**
		Daily Function	**0.57（p=0.016）**
	CaGI-I*4	**Language**	**-0.31（p=0.021）**
		Daily Function	-0.21（p=0.116）
	CGI-I	Language	-0.22（p=0.064）

*1 NCT05358886 *2 National Institutes of Health Toolbox Cognitive Battery cognition crystallized composite score
*3 Patient-Specific Behavioral Assessment Using a Numerical Rating Scale (NRS) *4 Overall improvement assessment by caregivers

S-051051 | Target Diseases: Interstitial Cystitis / Bladder Pain Syndrome

Chronic bladder pain and frequent urination from diverse causes, greatly impacting QOL

A disease characterized by chronic bladder-related pain or discomfort and urinary frequency that substantially impairs quality of life. Its causes and pathophysiology remain poorly understood, and symptoms and disease manifestations are diverse

Disease Profile

A meaningful proportion of patients remain without a definitive diagnosis

—Patient Population*1—

Approx.
2.8 M patients

—Market CAGR*2—

Approx. **8**%

—Effective and Safe Oral Treatments—

Limited

Unmet Needs

Sustained Symptom Control

Control pain and urinary frequency and maintain long-term symptom stability

Improved Quality of Life

Chronic symptoms restrict daily activities and can disrupt sleep

Expanded Treatment Options

A lack of treatment options that combine efficacy, safety, and convenience

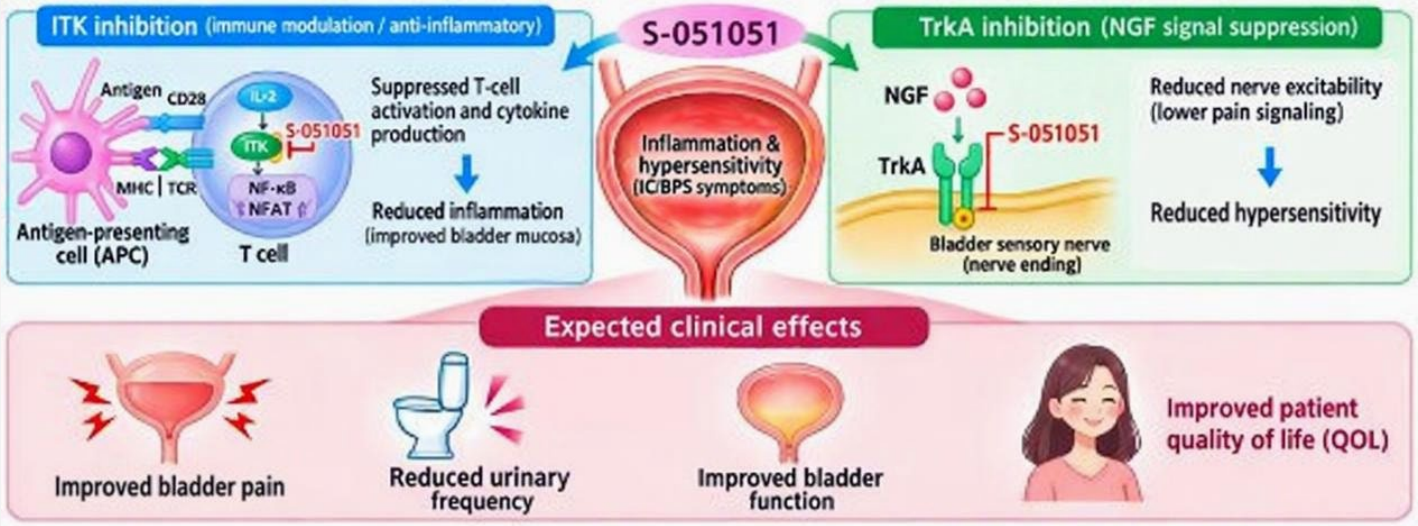
*1 Estimates by SHIONOGI based on real-world data *2 Spherical Insights and Consulting (growth rate, 2026–2035)

S-051051 | Mechanism of Action and Features

Targets inflammation and pain to become a non-invasive first-line treatment

S-051051 Mechanism of Action

Relieve patients' symptoms and improve QOL



ITK : Interleukin-2-inducible T cell kinase
TrkA : Tropomyosin Receptor Kinase A
NGF : Nerve growth factor

Product Profile and Vision

01| Targets both pain and inflammation

Inhibits TrkA and ITK to suppress hypersensitivity, inflammation

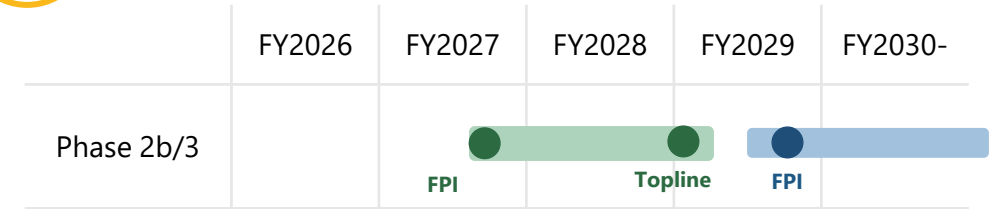
02| Targets the NGF receptor, not NGF itself

A small molecule, unlike anti-NGF antibodies

03| Once-daily oral dosing

Oral, not bladder instillation: convenient for chronic use

Key Milestones



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S-051051 | Phase 2 Study Results

PoC established in the Phase 2 study; preparations are underway to initiate global late-stage clinical development

Phase 2 Study

Study design	Placebo-controlled, double-blind, randomized, parallel-group
Patients	Patients with IC/BPS in Japan
Dosage and administration	■ Once daily oral, 12 weeks ■ S-051051 (2 doses), placebo; ~50 per group (~150 total)
Primary endpoint	The change from baseline in Numerical Rating Scale (NRS) average bladder pain score
Secondary endpoints	O'Leary & Sant symptom score (ICSI) voided volume, urinary frequency, etc.

Phase 2 Study Results

Primary endpoint

Statistically significant improvement in the NRS mean bladder pain score versus placebo

Secondary endpoints

Reduction in ICSI score*, increased voided volume per micturition, decreased urinary frequency, etc.
Favorable results confirmed

Safety and tolerability

Overall, no safety or tolerability issues were identified in this study

*Score evaluating four patient-reported symptoms: pain, urgency, frequency, and nocturia

Milestones for Priority Pipeline Programs

Development Compound	Preclinical	Phase 1	Phase 2	Phase 3	Milestones through FY2027	Expected Stage in FY2030
Levacetylleucine Ataxia-telangiectasia (A-T)					European approval	Launch
Levacetylleucine CACNA1A-related disorders					sNDA	Launch
Zatolmilast Fragile X syndrome					Phase 3 completion	NDA
Zatolmilast Jordan's syndrome					Phase 2 completion	Approval
S-606001 Pompe disease					Combination with ERT: Phase 2 results Monotherapy: Phase 1 ongoing treatment and follow-up	Combination with ERT: Phase 3 to NDA Monotherapy: Phase 3
S-051051 IC/BPS					Initiation of Phase 2b/3	Phase 3 through NDA submission
S-262262 Neurodegenerative diseases/ALS					Initiation of Phase 2a	Phase 3

Priority Disease Area
– Immunology / Allergy

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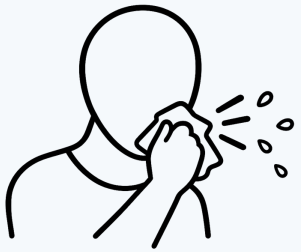
Immunology / Allergy | Vision and Unmet Needs to Be Addressed

Free from chronic symptoms and fear of relapse, so patients can stay in school, at work, and engaged in society

Our Vision

01 Fundamentally Change Allergies



Aim not only to control symptoms, but also to modify the allergic response itself

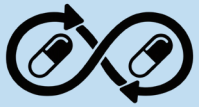
02 Freedom from Chronic Symptoms



Enable patients to continue their daily lives without being controlled by symptoms or concerns about recurrence

Unmet Needs

Lifelong treatment



Chronic diseases characterized by repeated exacerbation and remission
Long-term impact from childhood through adulthood

Symptoms that reduce QOL



Severe itching, sleep disturbance, and reduced QOL
Large interindividual variability in treatment response

Burden of continued treatment



Financial burden associated with hospital visits and biologics. Physical burden of injections and concerns about the long-term safety of medication

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Immunology / Allergy | Three Therapeutic Approaches

Optimize Immune Regulation According to Disease and Create New Therapeutic Value

1

Regulate systemic immunity



Maximizing AIT and expanding into the next generation

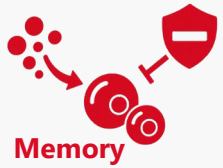
Maximize the value of SLIT (sublingual immunotherapy) and leverage the existing platform to expand target allergens and treatment technologies

Key Products / Pipeline Assets

- CEDARCURE Marketed
- MITICURE Marketed
- TO-209 Phase 3

2

Regulate Local Immunity in the Skin



Controlling immune memory to suppress recurrence

Suppress local Th2 activation in the skin to provide long-term control of chronic inflammation and recurrence

Key Products / Pipeline Assets

- CORECTIM Marketed
- VTAMA Marketed
- S-462462 Preclinical

3

Establish an immunosuppressive environment



Advancing Regulatory T-Cell Research

Apply knowledge and technologies related to regulatory T cells gained through cancer immunology research to other immune and allergic diseases

Key Products / Pipeline Assets

- S-531011 Phase 2

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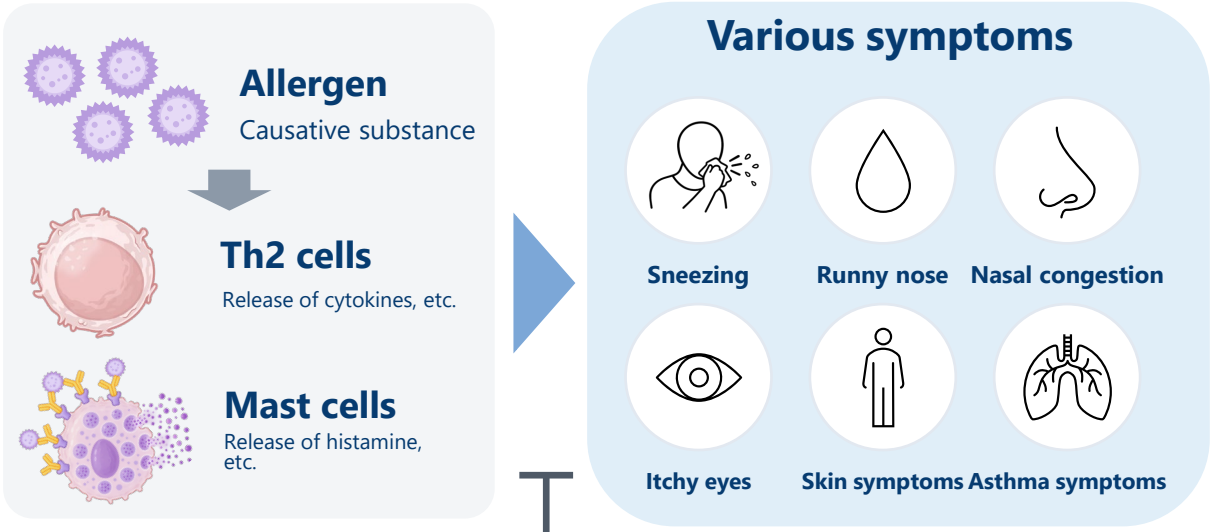
Mechanism of Allergen Immunotherapy (AIT)

Suppress excessive responses to causative allergens and shift toward a state in which allergic reactions are less likely to occur

Symptomatic treatment (antihistamines, intranasal corticosteroids, etc.)

Temporarily suppress symptoms caused by allergic reactions that have already occurred



Examples of medications that control symptoms

- Oral antihistamines
- Intranasal corticosteroids
- Antihistamine eye drops
- Topical antihistamines Corticosteroids

Allergen Immunotherapy (AIT)

Continuous administration of allergens to modulate the immune response

Continuous administration → Sustained symptom relief



Restore balance in the immune response and shift toward a state in which allergic reactions are less likely to occur

Routes of AIT administration

- **Subcutaneous immunotherapy** Administered subcutaneously
- **Sublingual immunotherapy** Administered under the tongue
- **Oral immunotherapy** Primarily for food allergy

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What Is Sublingual Immunotherapy (SLIT)?

Acts on the body's response to allergens, aiming to alleviate symptoms and achieve long-term improvement in allergic predisposition

What Is SLIT?

An allergen immunotherapy in which a small amount of allergen is administered under the tongue after diagnosis at a medical institution and treatment is continued at home over a long period

Diagnosis → **Administered under the tongue** → **Continued at home**

Why Sublingual Administration?

- **Utilizes the immune environment of the oral mucosa, making it possible to aim for immune tolerance**
- **Convenience of administration at home**

What Is CEDARCURE?

A sublingual immunotherapy treatment for Japanese cedar pollinosis



- **Only SLIT Treatment** for Japanese Cedar Pollinosis in Japan
- Approx. **1.0** million patients — **Most widely prescribed SLIT**
- **Covered by health insurance** Japanese Cedar Pollinosis (Allergen Immunotherapy)

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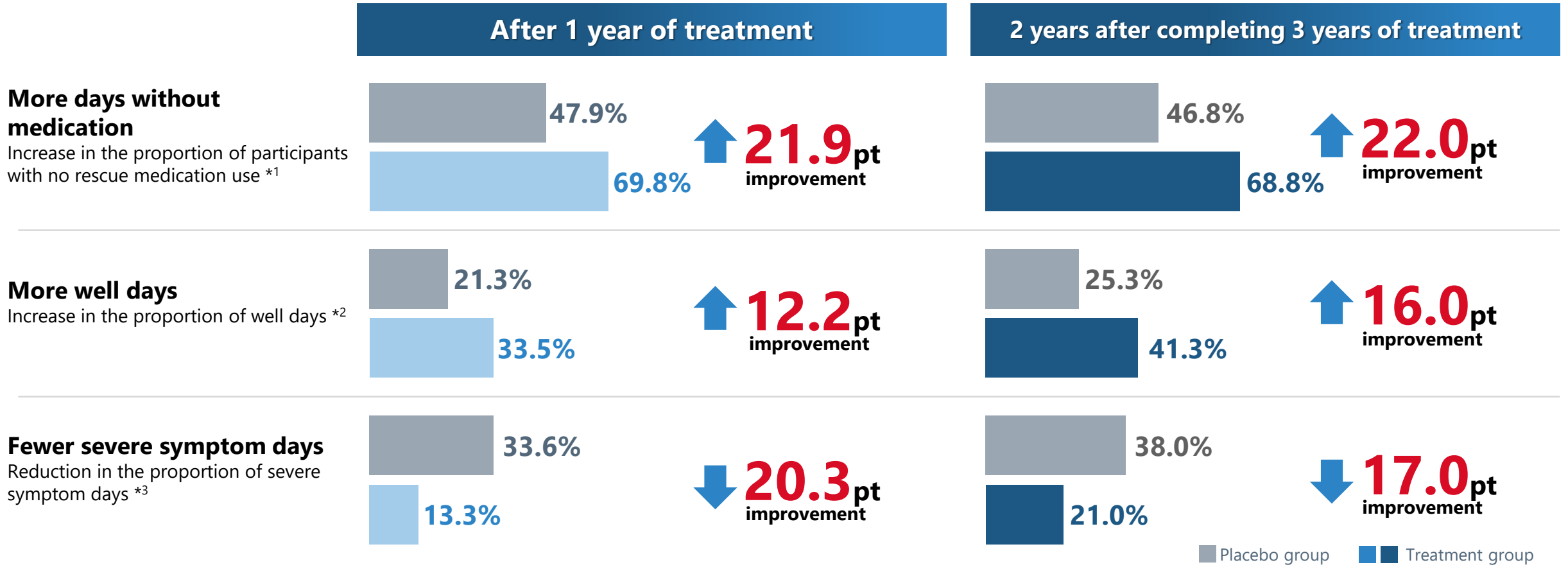
Treatment Value of CEDARCURE

Clear efficacy is observed from the first year of treatment, with the disease-modifying effect sustained after treatment completion



Yonekura S, et al.
Disease-Modifying Effect of Japanese Cedar Pollen Sublingual Immunotherapy Tablets. J Allergy Clin Immunol Pract.

*1 No rescue medication used at any time
*2 A day on which sneezing, rhinorrhea, nasal congestion, itchy eyes, and watery-eye scores were all – or 1+, and no rescue medication was used
*3 A day on which any of the sneezing, rhinorrhea, or nasal congestion scores was 4+, or either the itchy-eye or watery-eye score was 3+

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Growth Potential of CEDARCURE

Deliver the value of CEDARCURE to more patients with Japanese cedar pollinosis and pursue further growth

Current number of patients prescribed CEDARCURE among patients with Japanese cedar pollinosis

Continued for 3+ Years[*1]

470,000 patients

Approximately 1% of Japanese cedar pollinosis patients

Prescribed CEDARCURE[*2]

1 million

Approximately 2% of Patients with Japanese Cedar Pollinosis

Visited a medical institution[*3]

18 million

Japanese cedar pollinosis[*4]

47 million

Key Issues to Monitor

Long-term treatment continuation required

Long-term daily treatment is important to obtain a disease-modifying effect that continues after treatment completion

A certain period is required before the effect is observed

Unlike symptomatic treatment, approximately 3 months are required before an effect on rhinitis symptoms is observed

Expanding access for patients in need

Leveraging SHIONOGI's manufacturing capabilities, we plan to expand supply in phases.

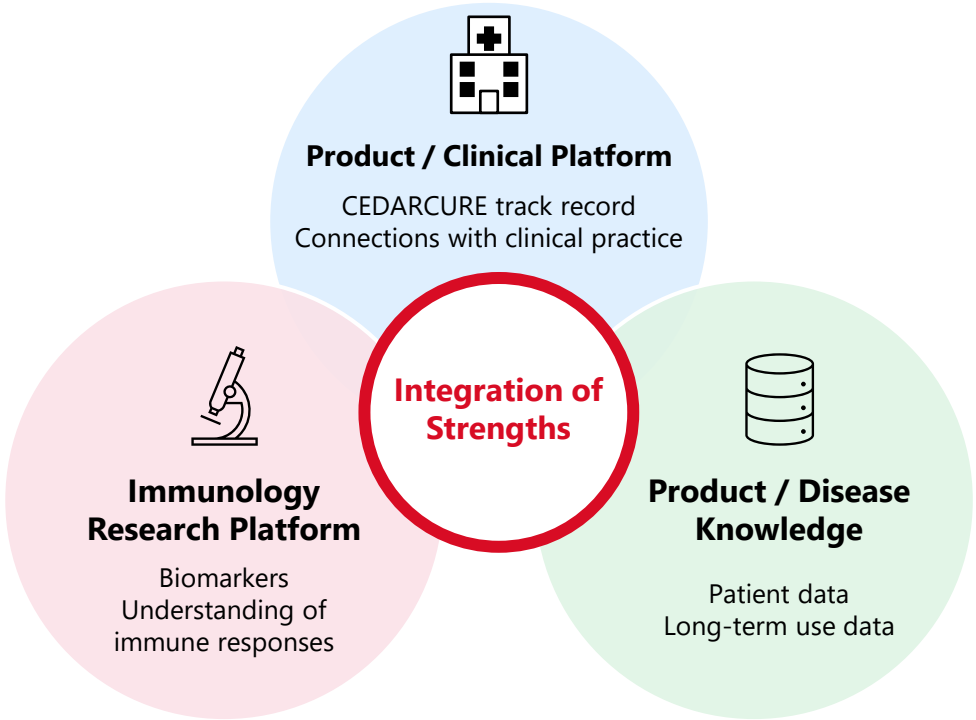
[*1] JMDC health insurance claims data [*2] Estimated from CEDARCURE sales data, June 2026 [*3] Physician questionnaire survey / Internet survey on Japanese cedar pollinosis patients nationwide, Allergy 74(3):124–132, 2025 [*4] Prevalence based on epidemiological data, Ministry of Health, Labour and Welfare

Initiatives to Maximize the Value of CEDARCURE

Leverage SHIONOGI's research capabilities to deliver the value of CEDARCURE to patients of all ages in Japan

Addressing the Challenges

Integrate SHIONOGI's research capabilities with Torii Pharmaceutical's product platform



Treatment Optimization Using Biomarkers

During Treatment

Assess treatment response

Assess functional changes in addition to antibody levels
Early monitoring and adherence

At Treatment Completion

Assess durability of effect

Monitor recurrence and response thresholds after treatment completion

Utilize Biomarkers to Support Decision-Making from Treatment Initiation through Treatment Completion and Provide Optimal Treatment for Each Patient

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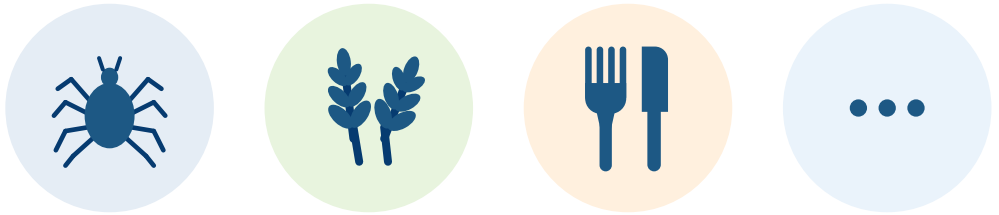
Optimization and Further Expansion of AIT

Optimize AIT and expand treatment options across allergies

Expansion to Other Allergies

Expand Target Diseases



House dust mites | Pollens | Food allergy | Others

×

Further Advancement of AIT



Antigen optimization | Use of adjuvants | SCIT / SLIT | Evaluation of long-term efficacy

Targeted next-generation AIT

Significantly suppresses symptoms with minimal burden, while ensuring a high level of safety

Collaboration concept with ALK*1

Leveraging antigen assets and expertise in SLIT/SCIT; discussions initiated regarding expansion into food allergies

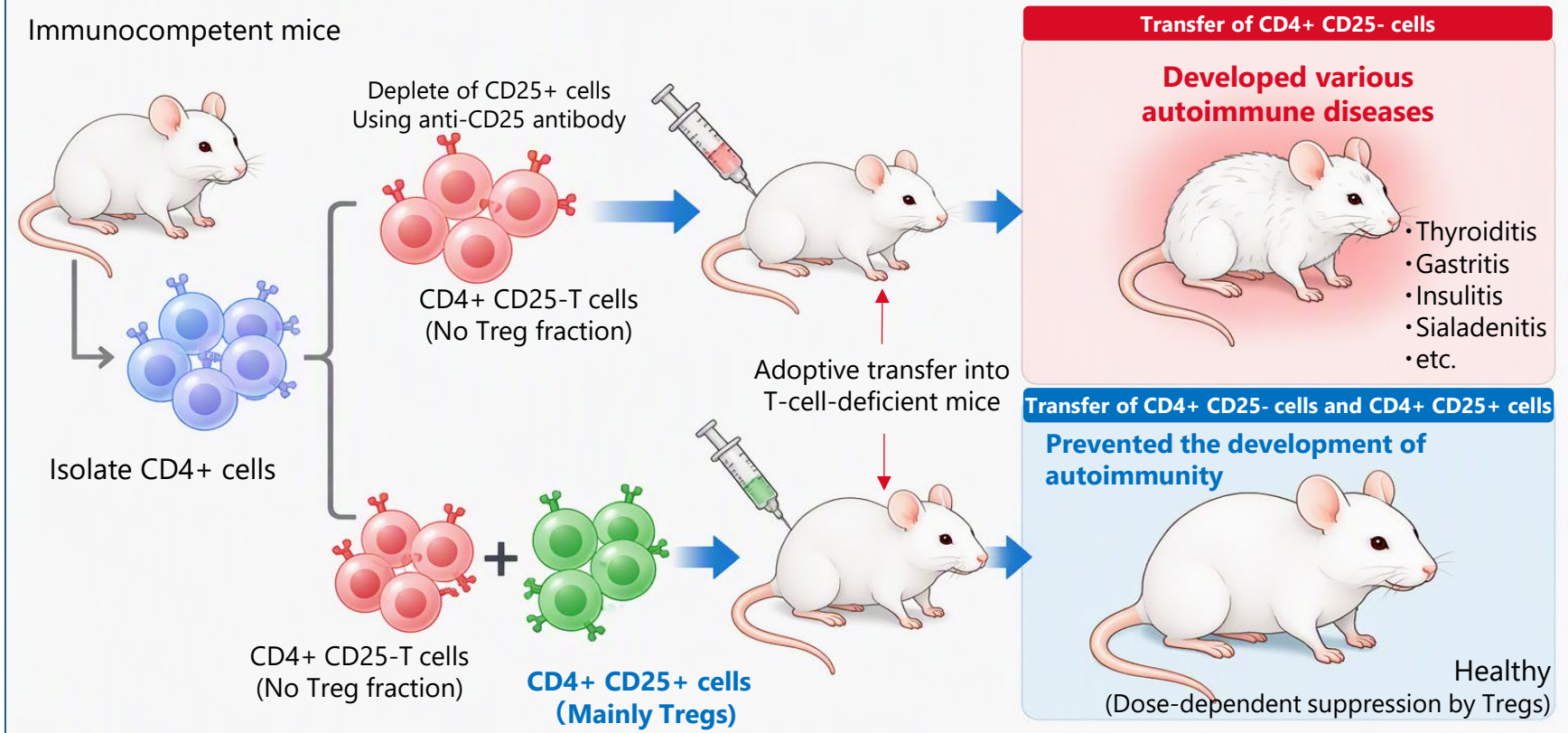
*1 Denmark-based specialty pharmaceutical company focused on allergy: https://www.alk.net/

S-531011 | Discovery of Regulatory T Cells

Tregs are critical for immune homeostasis, and excessive Treg depletion may increase the risk of autoimmunity

Key experiments leading to the discovery of Tregs by Prof. Shimon Sakaguchi*1

(*Sakaguchi S. et al., J Immunol. 1995; 155: 1151-1164*)



Removal of CD4+ CD25+ cells

Development of autoimmunity

Prevention of autoimmunity by re-constitution with CD4+ CD25+ cells

Identification of a T-cell population that suppresses autoimmunity

The discovery of FOXP3 helped establish this population as Tregs

*1 Shimon Sakaguchi: Recipient of the 2025 Nobel Prize in Physiology or Medicine

S-531011 | Overview

An anti-CCR8 antibody designed to achieve durable antitumor activity while maintaining a favorable safety profile

Current Treatment Landscape of Colorectal Cancer

Colorectal cancer is a common malignancy. Early-stage disease is potentially curable with surgery, whereas chemotherapy is the mainstay for advanced or metastatic disease.

Unmet needs in advanced/metastatic colorectal cancer*1

–5-year survival rate*2–

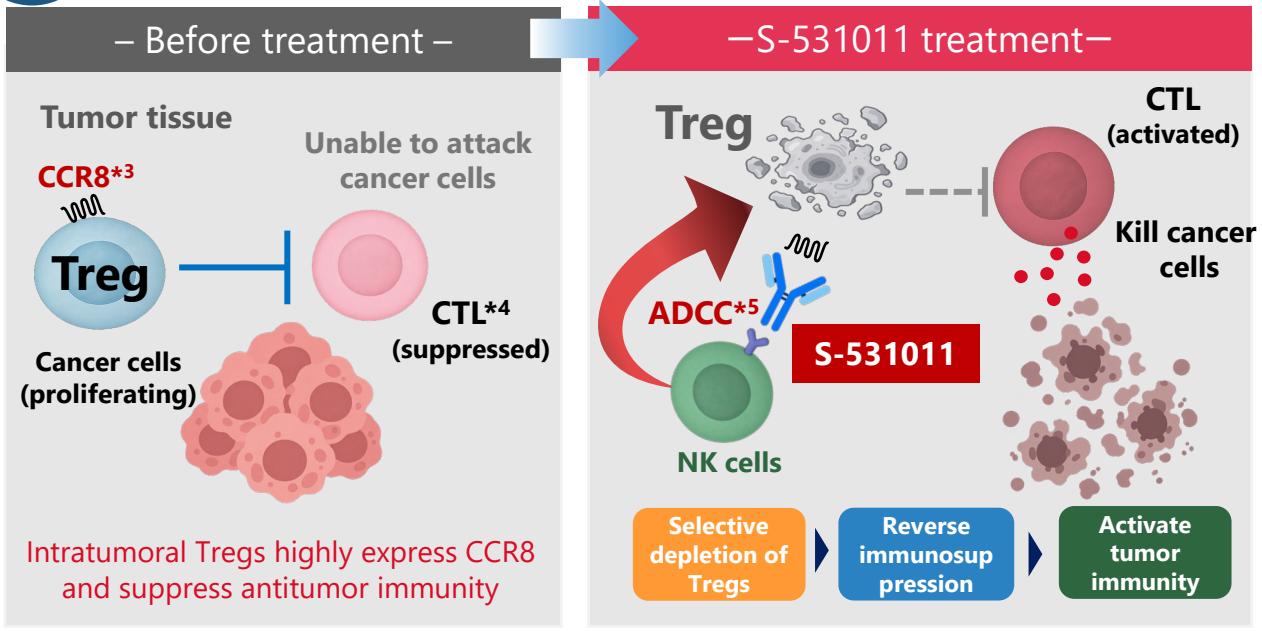
Approximately **15**%

– Standard of Care–

Safety concerns

Chemotherapy and angiogenesis inhibitors only

Mechanism of Action



Product Characteristics

- Anti-CCR8 humanized monoclonal antibody
- Durable antitumor activity with a favorable safety profile

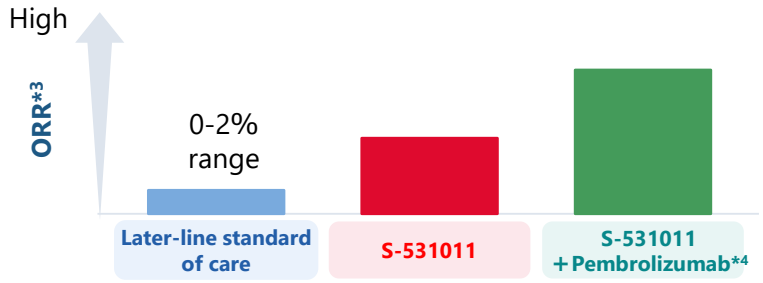
*1 Microsatellite Stability (MSS) Colorectal Cancer *2 American Cancer Society (Five-year survival rate after diagnosis of distant metastasis: 13% for colon cancer, 18% for rectal cancer)
*3 C-C motif chemokine receptor 8 *4 Cytotoxic T lymphocyte *5 Antibody-Dependent Cellular Cytotoxicity

S-531011 | Phase 1b/2 Study Results in Colorectal Cancer

Promising efficacy signals with an excellent safety profile in colorectal cancer*[1,2]

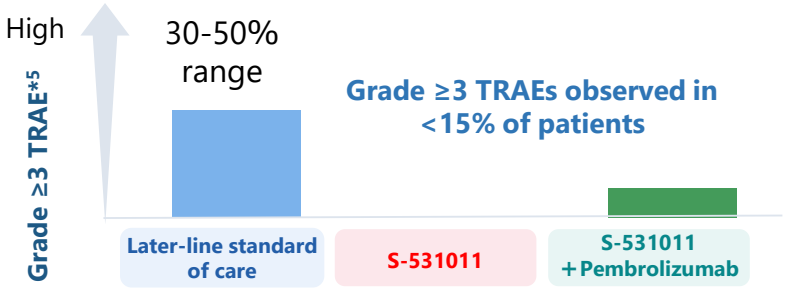
① Promising efficacy signals in colorectal cancer

Signals suggestive of antitumor activity observed in colorectal cancer, which is largely unresponsive to existing checkpoint inhibitors



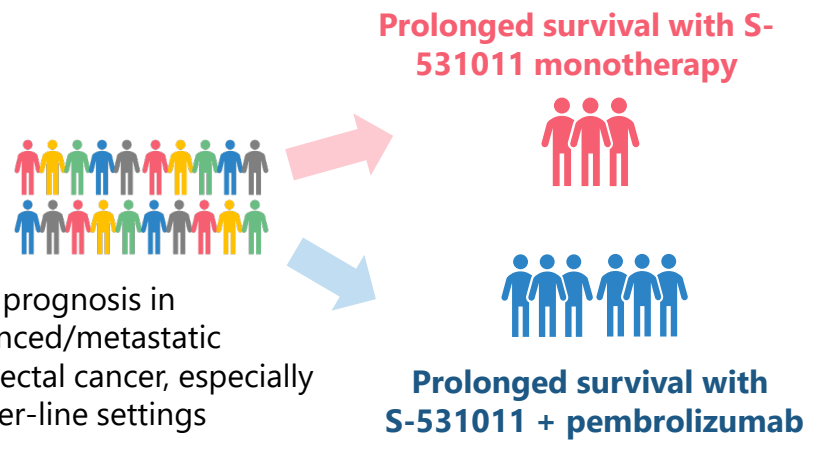
② An excellent safety profile

Limited severe TRAE with S-531011 alone or in combination with pembrolizumab



Prolonged survival observed in some patients

Clinically meaningful prolonged survival observed with S-531011 monotherapy and in combination with pembrolizumab



*[1] Colorectal cancer: Data for MSS colorectal cancer, including objective response rate and survival, are from ongoing single-arm studies. Caution should be exercised when interpreting cross-trial comparisons due to differences in patient populations and study designs. *[2] Data source: S-531011 Phase 1b/2 study, Parts B/C (as of September 3, 2026)
*[3] Percentage of patients who achieved a complete or partial response *[4] Pembrolizumab combination: jointly developed with Merck *[5] Treatment-related adverse event

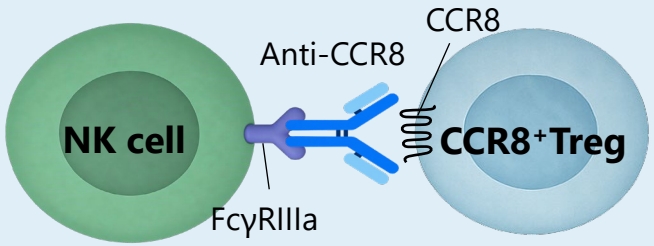
SHIONOGI

S-531011 | Strategic ADCC Design Differentiated from Competitors

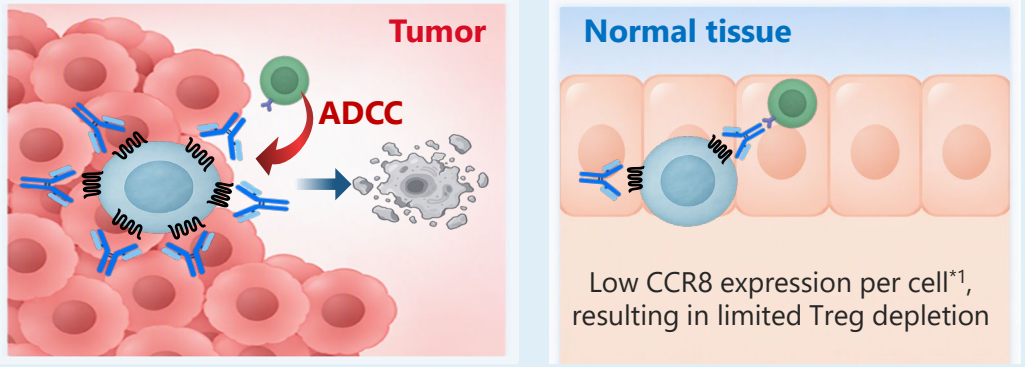
Strategic ADCC design to balance efficacy and safety by avoiding excessive Treg depletion

Anti-CCR8 strategic ADCC S-531011

Conventional FcγRIIIa binding affinity

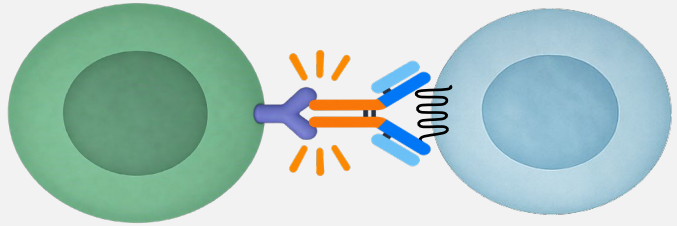


Potential for improved safety with limited impact on Tregs in normal tissues

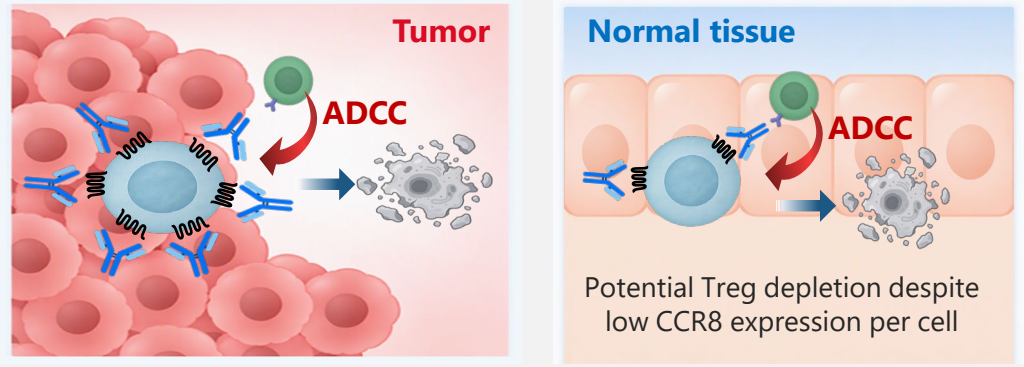


Anti-CCR8 Antibody with ADCC Enhanced (afucosylated, etc.)

Enhanced FcγRIIIa binding affinity



Risk of excessive depletion of Tregs in normal tissues, potentially leading to increased toxicity



*1~2.2-fold higher CCR8 expression per Treg in tumors than in normal tissues (*Weaver JD et al.,Oncoimmunology, 2022; 11: e2141007*)

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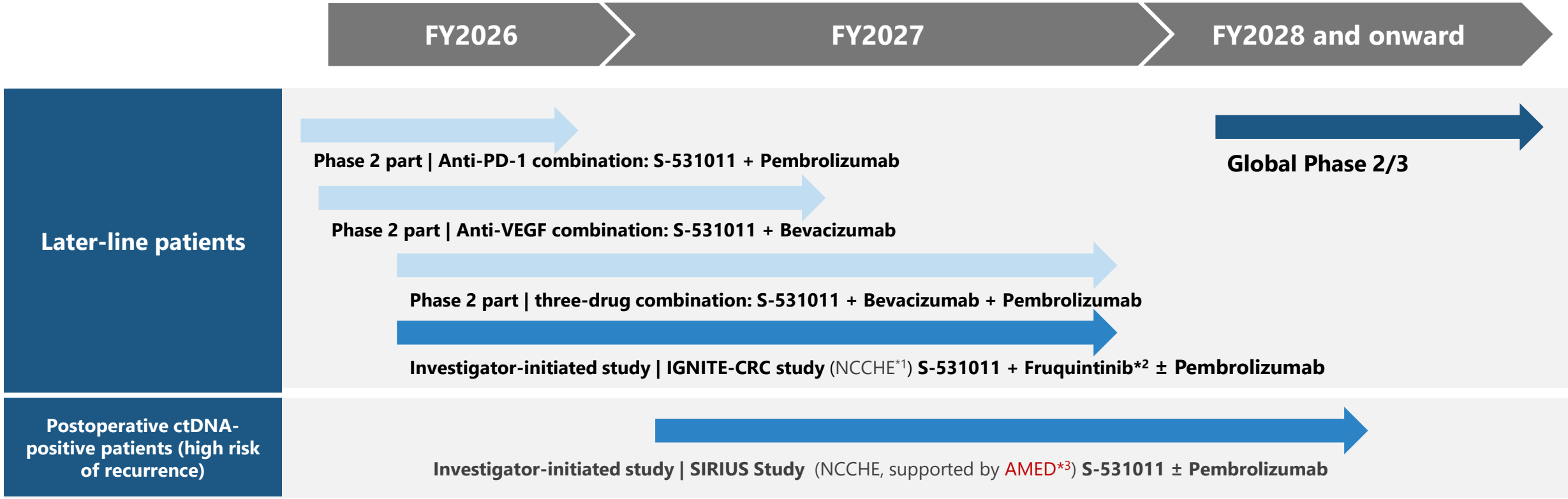
S-531011 | A new treatment option for colorectal cancer

Identify the optimal regimen and rapidly advance to late-stage development, while exploring expansion into the adjuvant setting



*1 National Cancer Center Hospital East *2 Angiogenesis inhibitor with a mechanism distinct from bevacizumab
*3 Japan Agency for Medical Research and Development FY2026 Research Project for Practical Application of Innovative Cancer Medicine

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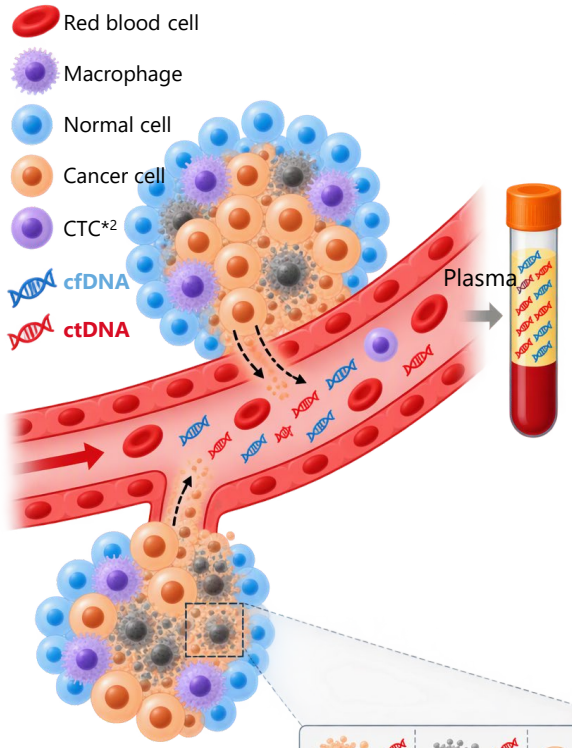
S-531011 | Expanding into MRD-Positive Colorectal Cancer

Identify post-surgery MRD[*1]-positive patients by ctDNA to enable intervention before recurrence

Relationship Between MRD and ctDNA



MRD positive
(ctDNA detected)

ctDNA detected
▼
Suggests residual cancer cells remain; linked to poor prognosis

MRD negative
(ctDNA not detected)

ctDNA not detected
▼
Suggests no detectable cancer cells remain; linked to favorable prognosis

ctDNA (circulating tumor DNA)
Cancer-derived cfDNA; may indicate MRD
cfDNA (cell-free DNA)
Free DNA released into blood by cell damage

Growing Momentum in Pre-Recurrence Therapy Development for MRD-Positive Patients

Large-scale observational study in Japan

MONSTAR-3.5:MONSTAR-MUGEN[*3]

Multicenter biomarker study using ctDNA analysis in resectable solid tumors

Prospectively evaluates the association of molecular profiles, including MRD, with recurrence and prognosis

Enroll MRD-positive patients

SIRIUS Trial: Investigator-Initiated Study of S-531011

Planned for colorectal cancer patients identified as MRD-positive through ctDNA monitoring

*1 Molecular Residual Disease *2 CTC: Circulating tumor cell *3 Study led by National Cancer Center Hospital East

S-531011 | Expanding into MRD-Positive Colorectal Cancer

Industry–government–academia collaboration opens a new opportunity: recurrence prevention

SIRIUS Trial Overview

Target	Postoperative MRD-positive colorectal cancer patients
Study design	Investigator-initiated trial (randomized controlled trial)
Sample size	40 (S-531011 monotherapy: 20 / S-531011 + pembrolizumab: 20)
Primary endpoint	ctDNA clearance rate at 6 months
Other endpoints	DFS (disease-free survival) / OS (overall survival) / Safety

Industry–government–academia collaboration drives SIRIUS

AMED Trial support	**NCCHE + 14 sites** Trial conduct	**SHIONOGI** Drug development
Supported by the Practical Research for Innovative Cancer Control program	Trial conducted at multiple sites in Japan, centered on NCCHE	Provides S-531011 and supports the trial with prior clinical data and know-how

Future Outlook

- **Now** — MONSTAR-MUGEN launch
- **Late 2026–early 2027** — SIRIUS trial start
- **2028** — PoC*1 to be confirmed by 6-month ctDNA clearance
- **2029 onward** — Proceed to company-sponsored trial based on results

Aiming to achieve early PoC in postoperative MRD-positive colorectal cancer patients

*1 PoC: Proof of Concept

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S-462462 | Atopic Dermatitis

Unmet needs remain for long-term remission of symptoms and a reduced patient burden

Disease Overview | Atopic Dermatitis

- A chronic inflammatory skin disease with relapsing-remitting eczema and pruritus
- Skin barrier dysfunction and immune abnormalities are intricately involved; rash and severe itch greatly impair patient QOL, including sleep and daily life

Disease Profile

Beyond conventional steroids, diverse options are available, including biologics and oral therapies

– Prevalence*1 –

~**46** million

JP・US・EU4+UK

– Market*2 –

~**$15.5** billion

JP・US・EU5

– Treatment Options –

Rapidly expanding

Unmet Needs

Higher treatment goals

High-level remission of rash and pruritus

Long-term disease control

As a chronic disease with repeated flares and remissions, preventing relapse and maintaining a favorable condition long term is important

Lower treatment burden

AD requires long-term treatment, so long-term safety and ease of administration matter as much as efficacy

*1 Internal research

*2 Copyright © 2026 IQVIA. Calculated internally based on IQVIA Analytics Link 2025 Reprinted with permission

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Developing a Next-Generation Atopic Dermatitis Therapy

Combining our dermatology expertise with JT's strength in kinase drug discovery to create innovative therapies

Current Strengths

Dermatology & Topical Treatment Platform

Shionogi	**Topical Steroids** RINDERON Ointment/Cream/Lotion, etc.
Former JT	**Topical Janus Kinase Inhibitor** CORECTIM Ointment

Accumulated expertise

- Kinase drug discovery capabilities
- Topical formulation design and development
- Infant and pediatric development
- Insight into remaining unmet needs

Source of Differentiation

Strengths built through multiple kinase drug discovery programs

Target selection × High selectivity Drug design = Efficacy / safety balanced

Mekinist MEK*1 inhibitor Launched 2016	**CORECTIM JAK*2 inhibitor** Launched 2020

Advancing Topical Drug Development Capabilities

- Experience in developing multiple topical formulations
- Optimization of local and systemic exposure/ Formulation design tailored to patient needs

Growth Portfolio

Next-generation therapy

S-462462

Combining the technologies built in kinase drug discovery to address needs that remain unmet after CORECTIM's launch

Kinase drug discovery + Topical drugs

Multiple target molecules identified

- Advancing exploratory research on multiple novel targets
- Evaluating optimal treatment approaches, including oral drugs

*1 Mitogen-activated protein kinase / Extracellular signal-regulated kinase Kinase *2 Janus kinase

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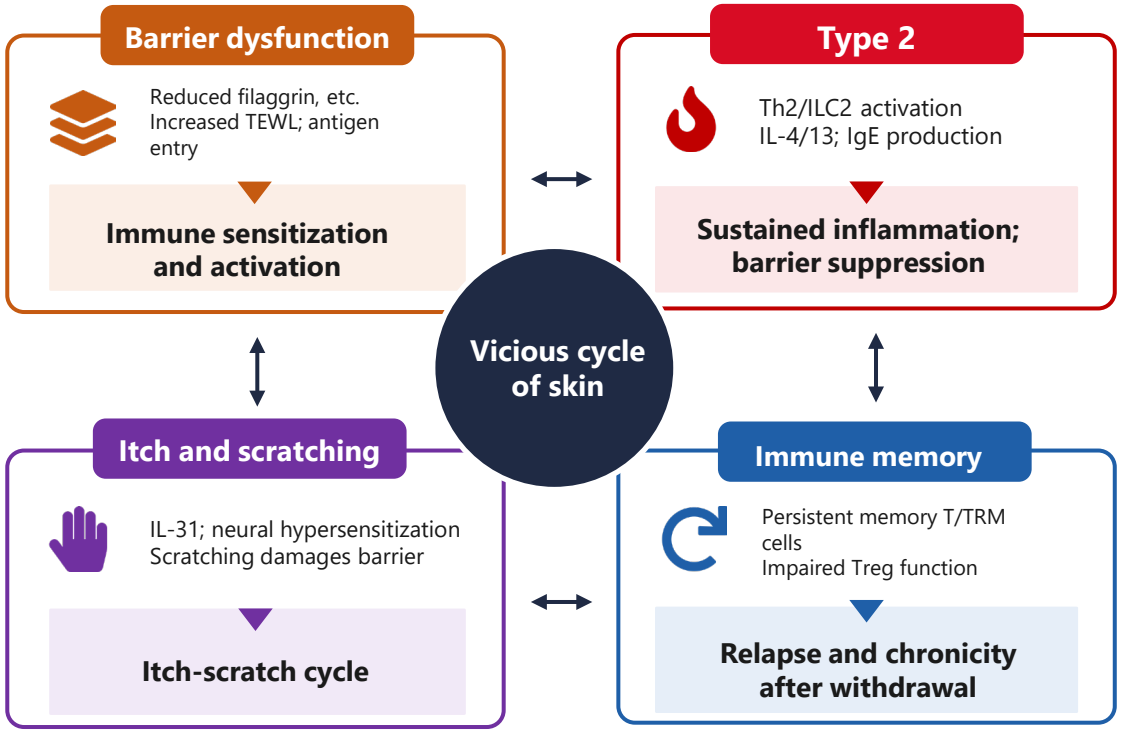
S-462462 | Atopic Dermatitis

Beyond symptom control: targeting immune memory to prevent relapse after treatment discontinuation

Challenges in Atopic Dermatitis

– Beyond Biologics: Relapse After Withdrawal –



Evolving Treatment Approaches and Remaining Challenges

IL-4/IL-13 signaling inhibition	Type 2 inflammation selectively suppressed; improves rash and pruritus Challenge	Mainly continuous dosing; room to address relapse after withdrawal
OX40/OX40L signaling inhibition	T cells and immune memory targeted for durable effect Challenge	Safety risks from systemic immune modulation
Kinase inhibition	Differentiation possible through target selectivity and formulation design S-462462	NIK inhibition aims to suppress OX40 signaling and safely prevent relapse locally

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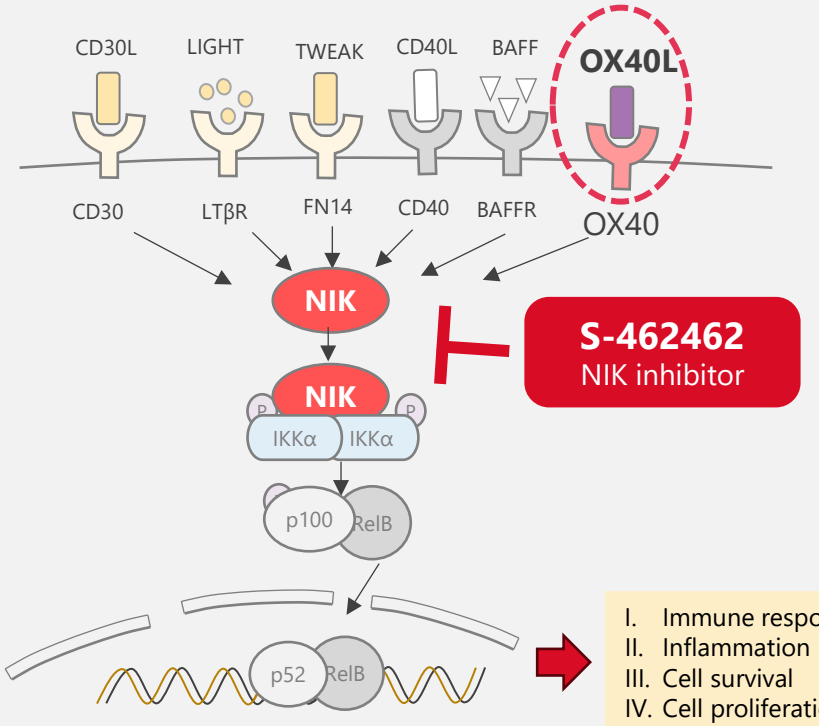
S-462462 | Mechanism of Action and Profile

Achieving Sustained Disease Control After Treatment Discontinuation with Topical Therapy

S-462462 Mechanism of Action

Targeting an upstream kinase rather than individual cytokines



I. Immune response
II. Inflammation
III. Cell survival
IV. Cell proliferation

NF-κB-inducing kinase (NIK) activation of multiple receptors, including OX40

Inhibition of NIK suppresses downstream immune and inflammatory genes

Improves skin symptoms (itch and eczema) and prevents flares

Product Profile & Target Product Concept

01 | Once-daily dosing

Convenient topical cream for long-term use

02 | High efficacy

Superior efficacy versus existing non-steroidal topicals

03 | Addressing unmet needs

Aiming to prevent post-treatment flares while maintaining safety

Key Milestones

	FY2026	FY2027	FY2028	FY2029	FY2030~
Healthy adults		Phase 1 FPI			
Adult patients		Phase 1b Topline		Phase 2b FPI → Topline	
Pediatric patients*					Phase 2b FPI

* Ages 2–11

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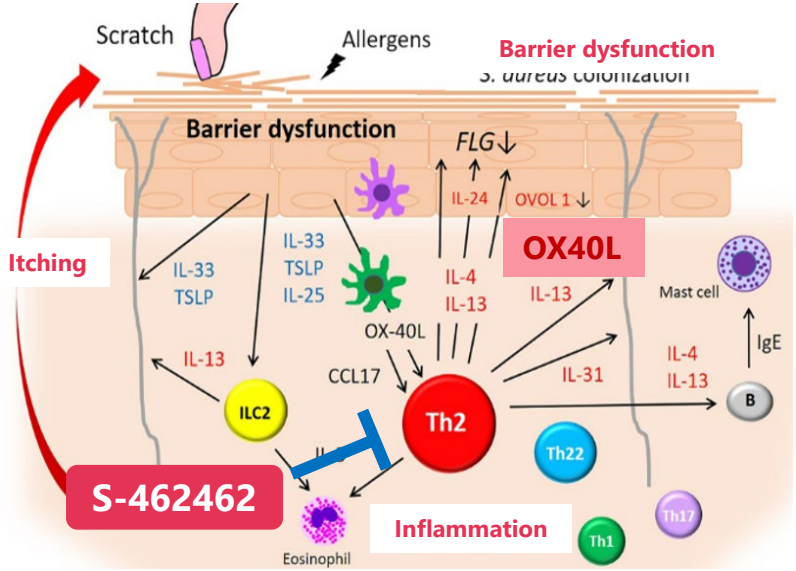
S-462462 | Therapeutic Hypothesis Based on OX40 Signal Inhibition

NIK inhibition for symptom improvement and sustained remission after treatment

Mechanism of Action and Therapeutic Hypothesis

–S-462462 inhibits NIK, thereby suppressing OX40 signaling–



Atopic Dermatitis Pathophysiology

Suppresses Th2 cell activation, proliferation and survival in the skin

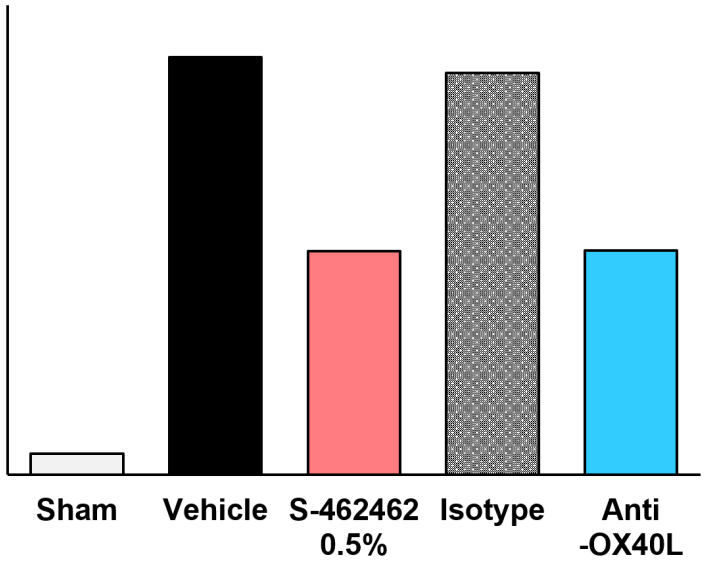
Reduces memory T cells associated with chronic inflammation and flares

Improves atopic dermatitis symptoms

Safe, sustained remission after treatment

Preclinical Data Supporting the Therapeutic Hypothesis

Efficacy in atopic dermatitis model*1



- Comparable efficacy to anti-OX40L antibody
- Sustained dermatitis suppression after treatment, accompanied by reduced memory T cells
- Favorable local safety with topical cream

*1 Mouse Biostir AD-induced dermatitis model

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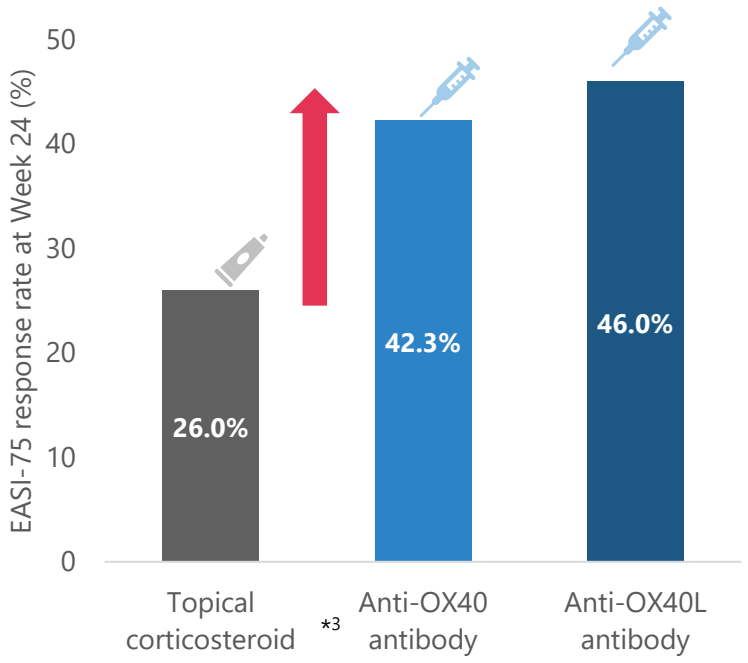
S-462462 | Target Profile

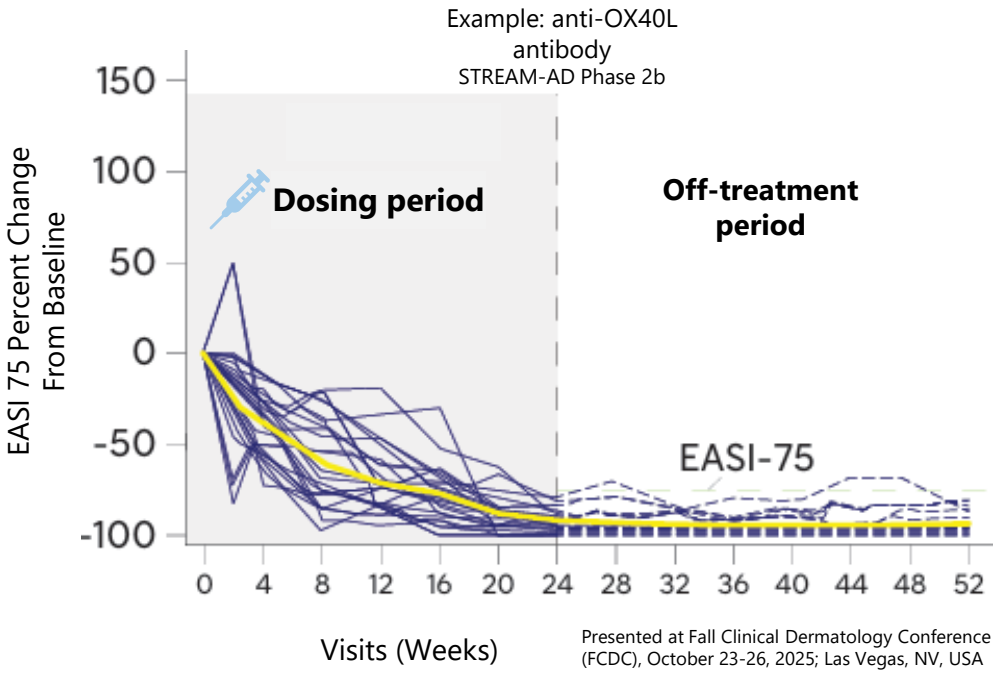
Achieving the efficacy of anti-OX40*1/OX40L*2 antibodies in a safe topical drug

Efficacy of anti-OX40/OX40L antibodies

– Efficacy exceeding existing non-steroidal topicals –



– Sustained relapse suppression after off-treatment –

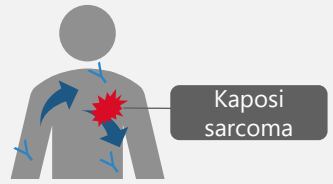


Presented at Fall Clinical Dermatology Conference (FCDC), October 23-26, 2025; Las Vegas, NV, USA

Safety

Systemic administration
Anti-OX40/OX40L antibodies

Kaposi sarcoma reported

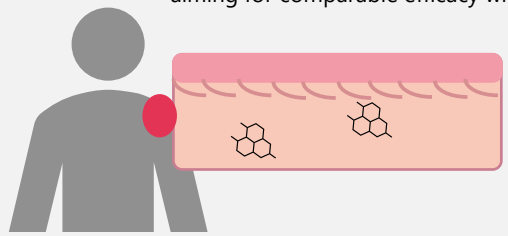


Well tolerated, but systemic safety risks remain

Topical drug
S-462462 cream

Avoids systemic **risk**

Limits pharmacologic action to the skin, aiming for comparable efficacy with safety



*1 Anti-OX40 antibody: rocatinlimab 300 mg, every 4 weeks, ROCKET IGNITE
*2 Anti-OX40L antibody: amlitelimab 250 mg, every 4 weeks, COAST 1
*3 Topical corticosteroid: medium potency (≈ existing non-steroidal topical): tapered as needed, once-daily TCS, LIBERTY AD CHRONOS

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Redasemtide | Overview

A novel therapeutic approach aimed at improving skin lesions throughout the body

Indication: : epidermolysis bullosa

An inherited disease in which genetic changes impair the function of collagen that holds the skin together, causing blisters, erosions, and ulcers throughout the body with even minor mechanical trauma

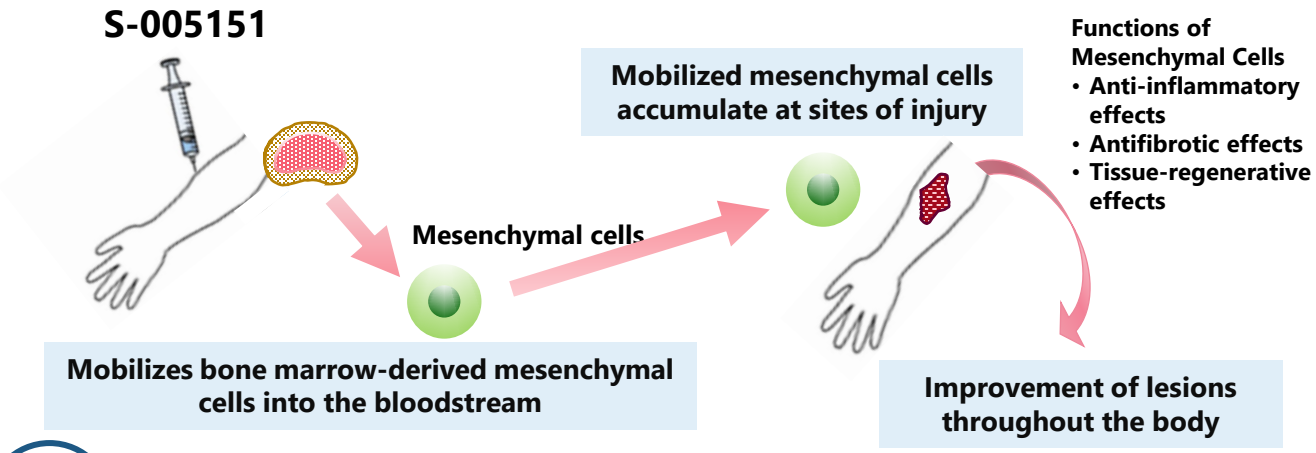
Number of Patients in Japan*1

Approximately **300**

Curative Treatment

None

Mechanism of Action of Redasemtide



Product Characteristics

Administration | Intravenous formulation expected to exert systemic effects

Efficacy | Suggests closure of refractory ulcers and improvement of skin lesions throughout the body

Product | Relatively straightforward quality control compared with cell therapy

*1 FY2020 MHLW Health and Labour Sciences Research Grant, Research Program on Rare and Intractable Diseases, Nationwide Epidemiological Survey of Epidermolysis Bullosa (estimated number of patients)

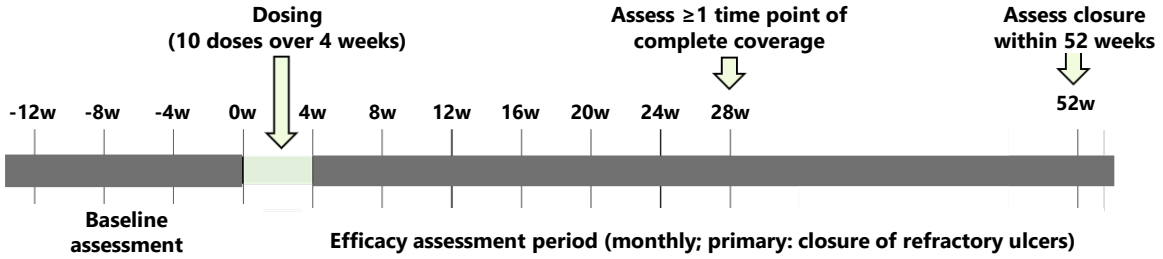
Redasemtide | Results of an Additional Phase 2 Study

Primary endpoint achieved; plan to file for approval in FY2026

Study Overview

Country	Japan
Patients	Patients with dystrophic epidermolysis bullosa with refractory ulcers
Study design	Multicenter, open-label, uncontrolled study
Dosage and administration **Number of patients**	• 1.0 mg/kg by 30-minute intravenous infusion 10 doses over 4 weeks [Week 1: 4 days, Weeks 2–4: 2 days/week (once every 3–4 days)] • Redasemtide group: 4
Primary endpoint	Closure of refractory ulcers*1
Secondary endpoints	Efficacy on overall condition (Total area of skin lesions in one selected region*2, total area of skin lesions throughout the body, QOL assessment [CDLQI or DLQI], etc.)

Study Results



Primary endpoint

- Closure of refractory ulcers confirmed in 3 of 4 patients

Secondary endpoints

- Consistent improvements, including reductions in lesion area in the selected region / throughout the body and improvement in QOL, were observed in some patients

*1 At least one time point of complete coverage within 28 weeks after treatment initiation and whether closure occurs within 52 weeks after treatment initiation. Closure is defined as complete epithelial coverage of the ulcer surface maintained at two time points at least 2 weeks apart.
*2 The entire body was divided into seven regions, one of which was selected.

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Cantharidin (YCANTH®) | Overview

Indication: molluscum contagiosum

Japan's first and only treatment for molluscum contagiosum

– Diagnosed patients –

Approximately **3** million*1

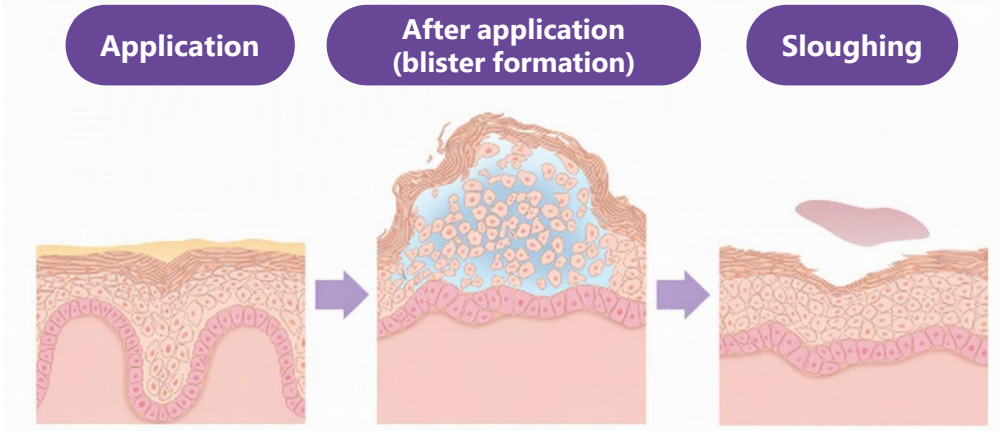
Approximately 83% of viral warts

– Approved drugs –

None

Mechanism of Action

Through activation of neutral serine proteases, desmosomes in the epidermis are weakened and the epidermal structure is disrupted, forming blisters at the application site. This is thought to cause the lesional skin to slough off, thereby removing virus-infected tissue.



Product Characteristics

- **Healthcare professional-administered topical formulation containing 0.71% cantharidin**
- **Single-use applicator for local application to lesions**
- **Can be used in a broad range of patients from children aged 2 years and older to adults**

Future Development

■ Indication expansion to common warts
✓ Global Phase 3 Studies Ongoing

*1 Internal calculation based on JMDC data

SHIONOGI

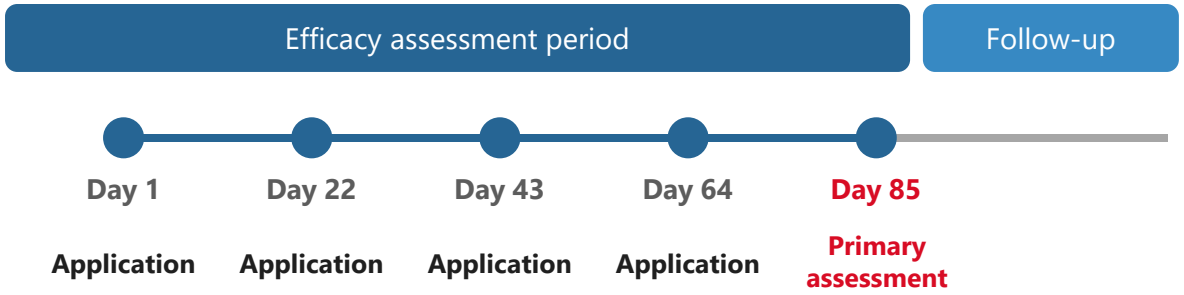
Cantharidin | Phase 3 Study Design in Common Warts

Advance two Phase 3 studies for indication expansion, aiming for regulatory submission in Japan

Study Design*1

Countries	U.S. and Japan
Patients	Patients aged ≥2 years with common warts
Study design	Multicenter, placebo-controlled, double-blind comparative study
Dosage and administration **Number of patients**	• Up to four applications every 21 days • **COVE-2 / COVE-3***2 300 patients each
Primary endpoint	Proportion of participants achieving complete clearance of all treatable common warts at Day 85

Efficacy Assessment Period / Follow-up



Key Milestones

- ✓ COVE-2 study, U.S.: **topline results expected in Q1 2027**
- ✓ COVE-3 study, U.S. and Japan: **topline results expected during 2027**

*1 Phase 3 study in the U.S.
*2: Phase 3 study in the U.S. and Japan

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Milestones for Priority Pipeline Programs

Program	Preclinical	Phase 1	Phase 2	Phase 3	By FY2027 Milestone	Expected Stage in FY2030
TO-210 Acne vulgaris					Phase 3 completion	Launch
TO-209 Grass pollen allergy					Phase 3 completion	Launch
Cantharidin Common warts					Phase 3 results available	Launch
S-531011 MSS colorectal cancer (3L+)					Phase 2 part, results from two-drug combination[*1] Phase 2 part, results from three-drug combination[*2]	Phase 3
S-531011 Postoperative MRD-positive MSS colorectal cancer					Completion of Enrollment in Phase 2 Investigator-Initiated Study	Completion of Phase 2 Investigator-Initiated Study
Redasemtide Epidermolysis bullosa					Approval in Japan	Launch
S-462462 Atopic dermatitis					Phase 1 completion	Phase 2

[*1] Two-drug combination: S-531011 + pembrolizumab
[*2:] Three-drug combination: S-531011 + pembrolizumab + bevacizumab

Priority Disease Area
-Infectious Diseases-

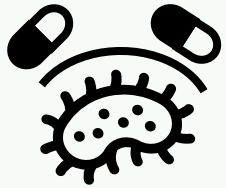
SHIONOGI

Infectious Diseases | Our Vision and Unmet Needs to Be Addressed

Realizing a healthy and sustainable society in which people around the world are not constrained by infectious diseases

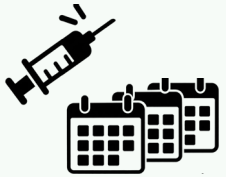
Our Vision

01 Ensure Continued Availability of Treatment Options



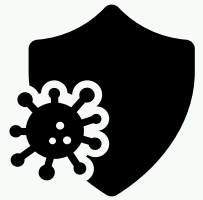
Even when drug resistance or mutations emerge, effective treatment options remain continuously available

02 Preventing infection, disease onset, and progression to severe disease



High-risk patients can live without concern about severe disease, functional impairment, or death caused by infection

03 Prepare for Unknown Infectious Diseases



Even when emerging or re-emerging infectious diseases occur, the spread of infection can be contained and social activities maintained

Unmet Needs

Loss of Life or Function



Loss of the lives or physical functions of patients and their families

Disease Outbreaks Disrupt Society



Isolation and stigma caused by quarantine and social division

Insufficient Preparedness for the Next Threat



Insufficient countermeasures and systems for outbreaks and biological threats

Outbreaks disrupt society



Increased anxiety, Secondary health impacts, Increased burden on society

Infectious Diseases | Priority Infections

Focus on infectious diseases with high unmet needs and aim to address social challenges through both treatment and prevention

1

HIV Infection



—Addressing the Fundamental Needs of PLWH*1—

- S-365598/VH184 (HIV)
- LAO (Long Acting Oral)

2

AMR*2



—Preventing the Loss of Treatment Options—

- Cefiderocol, S-649228
- Olorofim

3

Biothreats



—Preparing for Unknown Infectious Diseases and Pandemics—

- Cefiderocol
- Research on broad-spectrum antiviral agents

4

Acute Respiratory Infections



—Providing More Convenient Products—

- Secutrelvir
- S-337395

5

NTM/TB*3



—A New Option for Difficult-to-Treat Infections—

- S-910978

6

Malaria



—Addressing Global Health Challenges—

- S-048133

*1 PLWH: People Living with HIV *2 AMR: Antimicrobial Resistance *3 Nontuberculous Mycobacteria/Tuberculosis

Cefiderocol | Overview

A SHIONOGI-discovered infectious disease treatment approved in 38 countries, with continued expansion into additional countries and regions

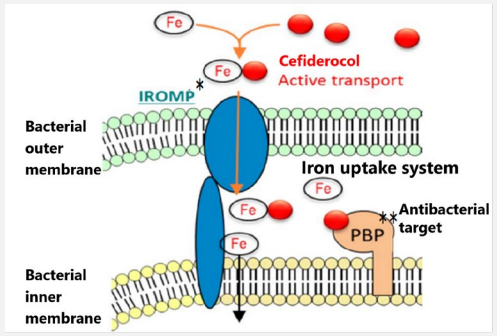
Disease Overview: Gram-Negative Bacterial Infections

Various infections caused by carbapenem-resistant bacterial strains

Product Characteristics

An injectable treatment useful for various infections caused by multidrug-resistant pathogens, including carbapenem-resistant Gram-negative bacteria

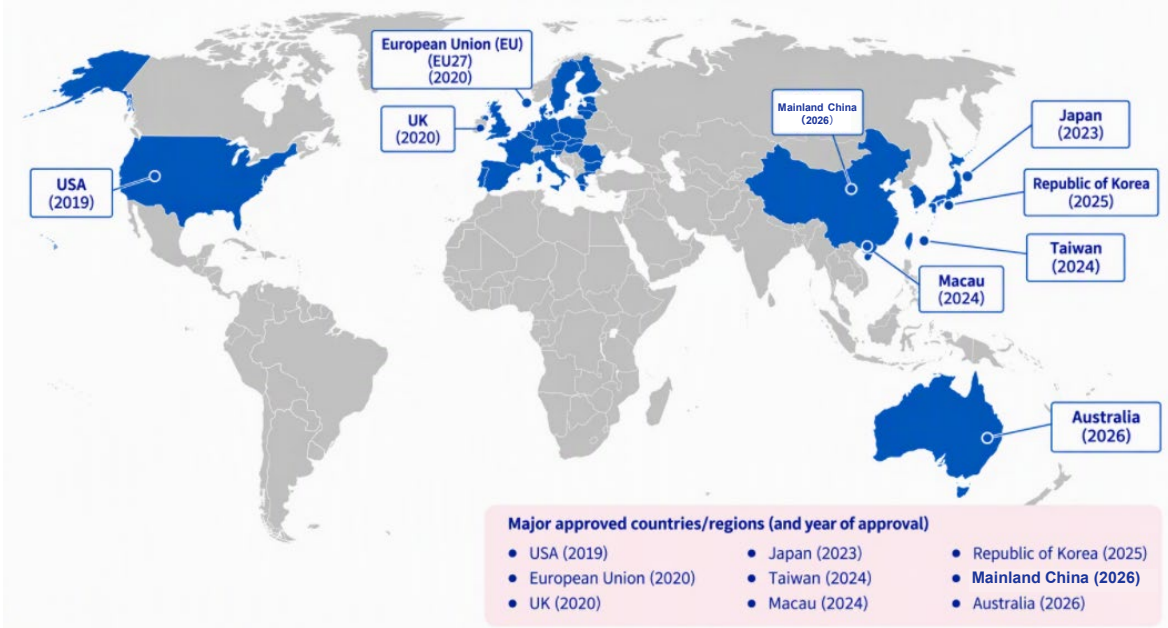
Mechanism of Action



Inhibits bacterial cell wall synthesis

Uptake into bacterial cells via the iron transport system of Gram-negative bacteria

Countries and Regions Where Approved



Pediatric Development

- **FY2026: Filing in the U.S.*** and Europe completed**
- **Regulatory approval in FY2026**

*** This project has been funded with Federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. 75A50126C00004

* Iron regulated outer membrane protein ** Penicillin binding protein

SHIONOGI

Cefiderocol | International Value of the Drug as Preparedness Against Threats

Strong activity against melioidosis and plague pathogens strengthens preparedness for infections with limited treatment options

Melioidosis*1

Causative pathogen: *Burkholderia pseudomallei*

- Zoonotic infection caused by bacteria living in environments such as soil and water
- Can cause pneumonia, sepsis, etc.
- Has been studied in the past for application as a biological weapon

In vitro activity against clinical isolates

Number of strains	MIC_{90} (μg/mL)	MIC range (μg/mL)	Test medium
246*2	**0.12**	**≤0.03–16**	Iron-depleted medium (ID-CAMHB)
272*3	**≤0.03**	**≤0.03–32**	Iron-depleted medium (ID-CAMHB)

Plague (Black Death)*4

Causative pathogen: *Yersinia pestis*

- Mainly carried by rodents and transmitted to humans via fleas
- Has a history of use as a biological weapon
- Worst-case bioterrorism scenario (WHO)
  : 50 kg of plague bacteria released over a city of 5 million or more people results in 150,000 infections and 36,000 deaths

In vitro activity against clinical isolates

Number of strains	MIC_{90} (μg/mL)	MIC range (μg/mL)	Test medium
30*5	**2**	**≤0.03->8**	MHB supplemented with apo-transferrin

*1 Glanders and Melioidosis – Ministry of Health, Labour and Welfare Research Group Bioterrorism Response Website *2 Antimicrobial Agents and Chemotherapy, 65(2), Jan 2021.
*3 Antimicrobial Agents and Chemotherapy, 67(6), May 2023. *4 Plague – Ministry of Health, Labour and Welfare Research Group Bioterrorism Response Website *5 IDWeek 2016

S-649228 (Cefiderocol+Xeruborbactam) | Overview

While cefiderocol maintains its efficacy,
advancing development of combination therapy with xeruborbactam as preparedness against further AMR

Product Profile

- Combination injectable of cefiderocol and xeruborbactam
- New treatment option against highly resistant bacteria that may emerge in the future
- Under development for patients with infections caused by multidrug-resistant Gram-negative bacteria

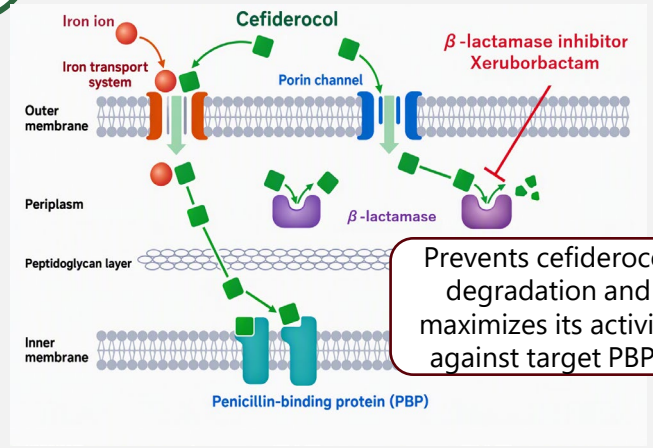
Development Background

① Cefiderocol has expanded treatment options against resistant Gram-negative bacteria

② Concern over future emergence and spread of highly resistant bacteria, driven by the increase in metallo-β-lactamases, etc.

Need for preparedness against further AMR

Mechanism of Action



- Inhibits bacterial cell wall synthesis
- The novel β-lactamase inhibitor xeruborbactam inhibits the degradation of cefiderocol by β-lactamases, enhancing antibacterial activity

Combination with xeruborbactam suppresses the emergence of cefiderocol-resistant strains

Main Milestones

FY26 2H	FY27	FY28	FY29	FY30～
	Phase 2 (FPI)	Topline	Phase 3 (FPI)	Topline

This project has been funded in whole or in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), Administration for Strategic Preparedness and Response (ASPR), U.S. Department of Health and Human Services (HHS), under OTA number HHSO100201600026C.

SHIONOGI

Olorofim | Target Disease: Invasive Aspergillosis

Provides a new treatment option with a novel mechanism of action for invasive aspergillosis, for which challenges remain with existing treatments

- A serious invasive fungal infection that primarily occurs in immuno-compromised patients
- Treatment options are limited, and further improvement in prognosis remains necessary
- Increasing prevalence of fungi resistant to azoles*1, the first-line treatment

Disease Profile

High mortality rate, and the number of fungi resistant to first-line treatment is increasing

-IA*2 patients-

Japan, Europe, Mainland China
More than **200,000** patients annually

-Mortality Rate*3-

Approximately **30**%
Mortality rate with current antifungal therapy

-Treatment Options-

Insufficient
No new drug has been introduced for decades

Unmet Needs

High Safety

Options that can be used more readily in high-risk patients are needed

- **Risk of organ damage**
- **Drugs with fewer DDIs**

Reduced Patient Burden

Expectations for convenient administration methods that support long-term treatment

- **Prolonged intravenous therapy**
- **Transition to outpatient treatment**

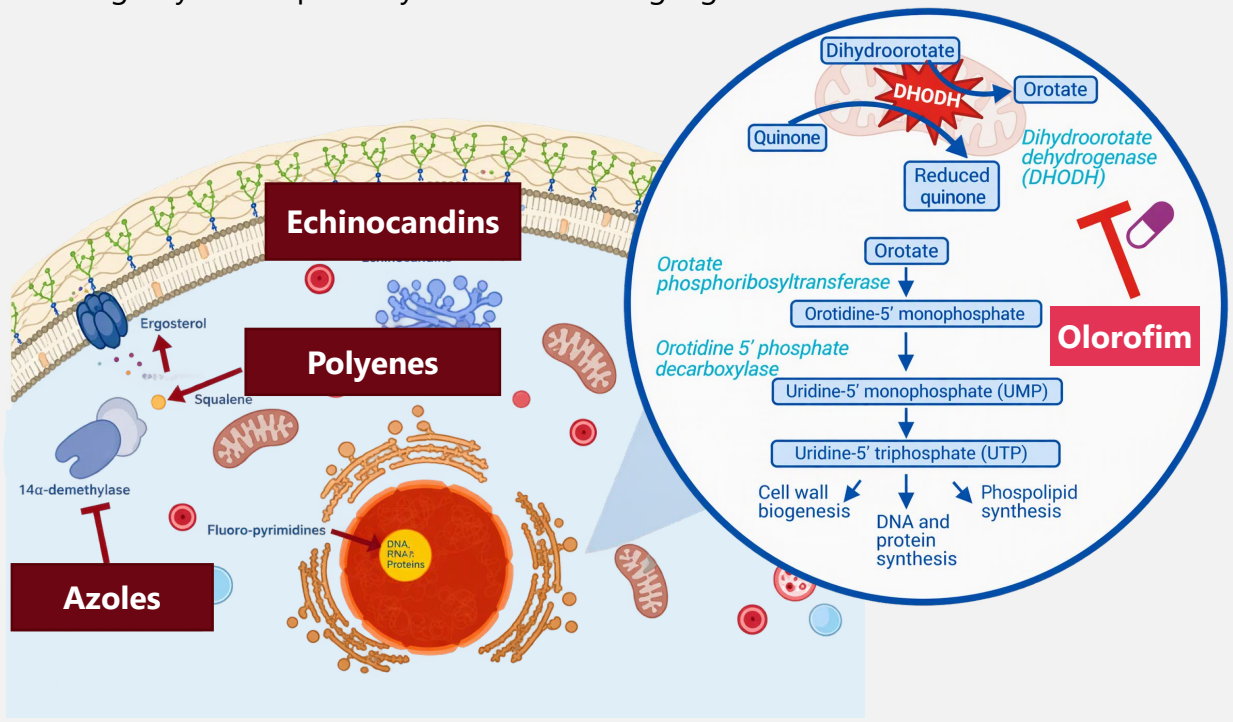
*1 Lestrade PPA, et al. Emerg Infect Dis. 2020;26(7):1447-1455, *2 Invasive Aspergillosis, *3 Walsh TJ et al. J Fungi. 2025, 11(9), 657

Olorofim | Overview

Launch a treatment with high clinical efficacy and a favorable safety profile to address unmet needs

Mechanism of Action of Olorofim

Selectively inhibits fungal dihydroorotate dehydrogenase, blocking a synthetic pathway essential for fungal growth



Product Characteristics and Target Profile

01 | High Antifungal Activity

Active against azole-resistant and rare fungi*1

02 | Favorable Safety

Reduces the burden on patients receiving long-term treatment

03 | Oral Treatment Option

Enables consistent treatment from hospitalization through post-discharge care

Regulatory Submissions

Country/ Region	Responsible Party	FY	Timing
U.S.	F2G	2026	3Q-4Q
Europe	SHIONOGI	2026	4Q
Mainland China	SHIONOGI	2027	1Q

Review of the novel antifungal drug olorofim (F901318) - PMC

*1 *Scedosporium, Lomentospora, Scopulariopsis, Coccidioides*, etc

SHIONOGI

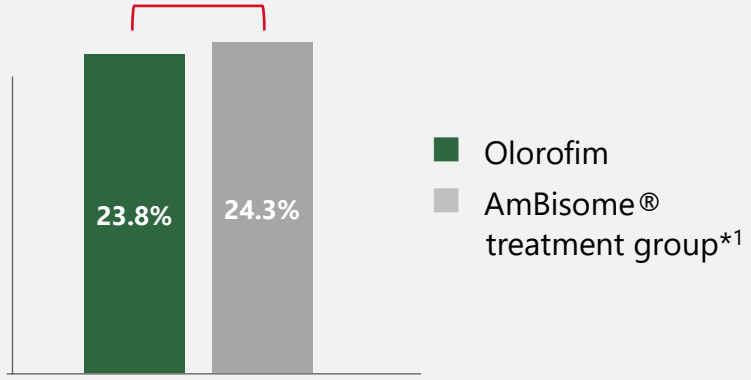
Olorofim | Results of the Phase 3 OASIS Study: Efficacy

Demonstrated non-inferiority to the best alternative by achieving the primary endpoint and showing consistent results in all secondary endpoints

Primary Endpoint: All-Cause Mortality at Day 42

—Primary Endpoint Achieved—

Non-inferiority confirmed



Between-group difference: −0.5%
95% confidence interval: −13.1% to 10.8%

Key Secondary Endpoint: Response Rate at Each Time Point

Overall Response Assessment*2	Olorofim Group (N=151)		AmBisome® treatment group (N=74)	
Response rate at Day 42	40	26.5%	23	31.1%
Response rate at Day 84	46	30.5%	21	28.4%
Response rate at end of study	48	31.8%	24	32.4%

Source: IDWeek 2026 presentation materials

Between-group difference: Day 42: −4.6%, Day 84: +2.1%, End of study: −0.6%

The independent adjudication committee determined **comparable response rates between the two groups** based on MSG-EORTC overall response assessments at each time point

*1 AmBisome® Followed by Standard of Care
*2 Assessed according to MSG-EORTC criteria: Mycoses Study Group Education and Research Consortium / European Organization for Research and Treatment of Cancer

SHIONOGI

Olorofim | Results of the Phase 3 OASIS Study: Safety

Fewer treatment-related adverse events in the olorofim group
Key difference: more frequent renal events in the AmBisome group

Patients with at Least One Adverse Event	Olorofim group (N=151)		AmBisome® treatment group*1 (N=72)	
Adverse events (TEAE*2)	145	96.0%	68	94.4%
Serious TEAEs	104	68.9%	48	66.7%
Treatment-related TEAEs*3	54	**35.8%**	46	**63.9%**
Serious treatment-related TEAEs*3	6	**4.0%**	13	**18.1%**
Renal TEAEs (overall)	29	19.2%	19	26.4%
Treatment-related renal TEAEs	2	**1.3%**	16	**22.2%**
Treatment-related drug-induced liver injury, as adjudicated by the HAC*4	7	4.6%	3	4.2%

Source: IDWeek 2026 presentation materials

Safety analysis population: Olorofim group, N=151; AmBisome® treatment group, N=72 *1 AmBisome® Followed by Standard of Care *2 TEAE: Treatment-Emergent Adverse Event
*3 TEAEs assessed by the investigator as related to the study drug *4 HAC: Hepatic Adjudication Committee

S-910978 | Target Disease: Pulmonary NTM (Nontuberculous Mycobacterial) Disease

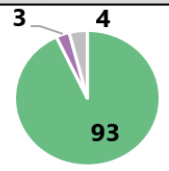
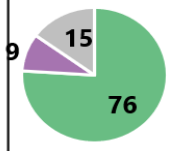
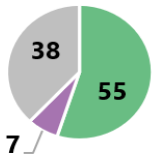
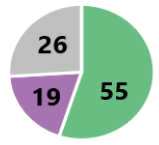
There is an unmet need for new treatment options with high efficacy and good tolerability

Disease Profile

Disease Overview

- Caused by nontuberculous mycobacteria (NTM) **Chronic pulmonary infection**
- **Pulmonary MAC disease***[1] and **Pulmonary MAB disease***[2] are the major disease types

Regional Prevalence by NTM Species

	JP/2017	US/2015	EU*[3]/2016	China/2024
Pulmonary NTM disease	20,000 patients	40,000-95,000 patients	16,000 patients	100,000 patients
Breakdown : MAC : MAB : Others				

Unmet needs

Pulmonary MAC disease

- **Long-term multidrug combination therapy** required
- **Refractory cases** have low response rates

Pulmonary MAB disease

- **Long-term multidrug combination therapy** required
- No established **treatment regimen**
- **Efficacy and tolerability** remain challenging

The pulmonary NTM disease treatment market **has expanded** with the launch of a new MAC treatment

SHIONOGI initiatives for Pulmonary NTM diseases

- Advancing the development of a treatment for pulmonary MAB disease in collaboration with **Qpex**
  - S-910978
- Advancing the discovery of novel treatments for NTM diseases through collaboration with **BioVersys**

*[1] MAC: *Mycobacterium avium complex* *[2] MAB: *Mycobacterium abscessus* *[3] 4EU+UK

S-910978 | Inhaled Formulation Created from Qpex's Technology and Intellectual Property

Leveraging capabilities acquired through the acquisition of Qpex to create a new development product

Process Leading to the Creation of S-910978

Intellectual Property and Development Experience Accumulated by Qpex

Intellectual property related to this project

×

Research and development experience in inhaled antibacterial formulations

Acquired capability

Integration with SHIONOGI

Combining Qpex's technology platform with SHIONOGI's ability to drive projects from research to development

Integrated platform

New Development Asset

Creation of S-910978

Tigecycline inhaled formulation

New asset

S-910978 | Overview

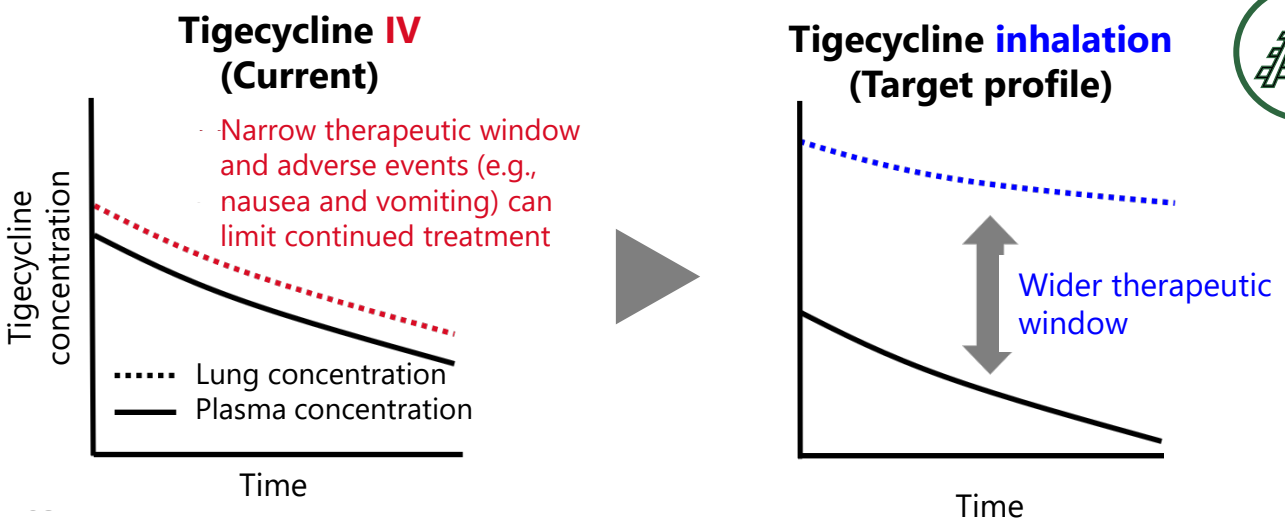
An inhaled formulation designed to balance efficacy and tolerability through direct delivery to the lungs

Product characteristics

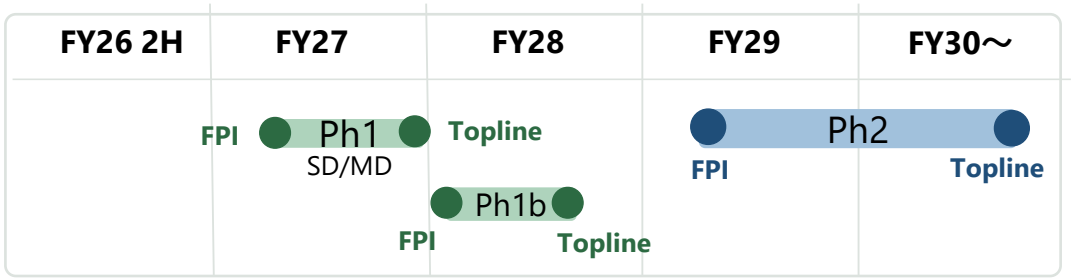
- An inhaled formulation of tigecycline, which shows high antibacterial activity against MAB*[1]
- Reduced patient burden through increased lung exposure and reduced systemic exposure
- Enables at-home treatment reduces the burden of treatment on patients

Mechanism of action

- Tigecycline: Binds to the bacterial 30S ribosome and inhibits protein synthesis
- Inhaled administration ensures high local drug exposure in the lungs



Main milestones



*[1] MAB, *Mycobacterium abscesses*

S-910978 | Pulmonary MAB disease: Treatment potential

Aiming to improve tolerability while maintaining high antibacterial activity and deliver a new treatment option for pulmonary MAB disease

in vitro antibacterial activity*1

MICs of *M. abscessus* (μg/mL)		
	MIC_{50}	MIC_{90}
Tigecycline	**0.5**	**1**
Amikacin	8	16
Imipenem	64	>64
Clarithromycin	>32	>32
Linezolid	32	>32
Clofazimine	1	2

Japanese clinical isolates *M. abscessus* subsp. abscessus (n = 57) antibacterial activity against
MIC: Minimum Inhibitory Concentration
MIC_{50}: MIC that inhibits growth of 50% of tested isolates
MIC_{90}: MIC that inhibits growth of 90% of tested isolates

Potent in vitro antibacterial activity confirmed

Incidence of nausea and vomiting with IV tigecycline*2

cSSSI Ph2 (7-14 days)	After 50 mg LD 25 mg BID (Low-dose group)	After 100 mg LD 50 mg BID (Approved standard dose)
Nausea(treatment-related) overall	13.9%	32.1%
Only moderate	**1.3%** →	**7.4%**
Vomiting(treatment-related) overall	7.6%	17.3%
Only moderate	**1.3%** →	**7.4%**

Nausea and vomiting increase dose-dependently with IV administration

cSSSI, complicated skin and skin structure infections

LD：Loading Dose. Low-dose group: 25 mg twice daily after a 50 mg loading dose，Standard-dose group: 50 mg twice daily after a 100 mg loading dose

At the approved standard dose (100 mg LD → 50 mg BID), nausea and vomiting occur at a certain frequency

*1 Diagn Microbiol Infect Dis. 2025 Mar;111(3):116663. *2 Created based on Phase 2 study data of tigecycline in cSSSI

Total Care for Respiratory Infectious Diseases

Building Solutions Connecting Prevention, Diagnosis, Treatment, and Prevention of severe disease

—Major Target Respiratory Infectious Diseases—

Influenza ***COVID-19*** ***RS virus***

Prevention

Development of Vaccines

Covgoze | COVID-19 (Approved)

S-567123 | Broad-spectrum coronavirus

S-872600 | Influenza (Intranasal)

Diagnosis

Realization of Test to Treat

Collaboration with external partners
Exploration of new diagnostic technologies

Treatment

Expansion of Antiviral Drugs

Xocova | COVID-19 (Launched)

Xofluza | Influenza (Launched)

Secutrelvir | COVID-19 (Phase 3)

S-337395 | RSV (Phase 2)

Prevention of Aggravation

Reduction of Risk of Aggravation

Xocova | COVID-19 (Joint research)

Secutrelvir | COVID-19 (Phase 3)

Secutrelvir | Target Diseases: COVID-19

Needs for treatment and prevention remain, particularly among patients at high risk of severe disease

A respiratory infection caused by SARS-CoV-2
A certain number of infections continue to occur throughout the year, with recurring waves of infection

Disease Profile

The risk of severe disease remains, particularly among elderly people, patients with underlying conditions, and immunocompromised patients

Revenue from oral COVID-19 treatments (CY2025)

Global

Approx.

$ **2.4** B*1

Number of Hospitalized Patients (annually)

U.S.

Approx.

180,000-280,000*2

Japan

Approx.

65,000*3

Unmet Needs

Ease of Use for a Broad Range of Patients
Fewer concerns regarding drug-drug interactions and teratogenicity

Importance of Pre-Exposure Prophylaxis
Prevention of infection in immunocompromised patients

Protection Against Circulating Strains
Treatment and prevention that are less susceptible to changes in circulating strains

*1 Calculated by our company based on Pfizer's financial statements.

*2 Number of COVID-19 hospitalizations in the U.S. from October 1, 2025 through October 3, 2026 (Source: Preliminary Estimates of COVID-19 Burden | COVID-19 | CDC)

*3 Number of COVID-19 hospitalized patients in Japan (Source: Press releases regarding COVID-19)

SHIONOGI

Secutrelvir | SHIONOGI Development Strategy

Building a two-product franchise spanning COVID-19 treatment and long-term prevention

	Ensitrelvir	Secutrelvir*
Treatment	**Approved** | Aged 6 years and older (Japan)	**Develop-ment** | Oral formulation Global Phase 3 studies ongoing
Post-exposure prophylaxis	**Approved** | Aged 12 years and older (Japan, U.S., and Europe) **Filed** | Aged 6 to <12 years (U.S.)	-
Pre-exposure prophylaxis	-	**Develop-ment*** | Long-acting injectable (LAI) Phase 1 ongoing; Phase 2 initiation planned for FY2027
Pediatrics	**Deveop-ment** | Under 6 years of age (Japan)	-

* This project (long acting injectable) has been funded with Federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under OTA Number 75A50123D00005

SHIONOGI

Secutrelvir | Overview

Oral treatment and long-term LAI prophylaxis address remaining needs in high-risk patients

Shared product attributes

- Inhibits the SARS-CoV-2 3CL protease and suppresses viral replication
- Fewer drug-drug interactions and no identified teratogenic risk

Oral formulation | Treatment

For a broad range of patients with COVID-19

- Single oral dose
  - A single 120 mg dose demonstrated strong antiviral activity and symptom improvement in a Phase 2 study
- Evaluating prevention of disease progression in high-risk patients and symptom improvement

Two global Phase 3 studies ongoing

LAI | Long-term pre-exposure prophylaxis*

For immunocompromised patients and others unlikely to mount an adequate immune response to vaccination

- Pre-exposure prophylaxis, with one injection every three months
- A new option for high-risk and immunocompromised patients
- Designed to provide sustained preventive efficacy against all currently circulating and emerging future variants

Safety and favorable drug PK profile in Phase 1
Phase 2 study initiation planned for FY2027

* This project has been funded with Federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under OTA Number 75A50123D00005

Secutrelvir | Two Phase 3 Studies in Treatment

Advancing verification of symptom improvement and prevention of severe disease, aiming to provide an option that meets global treatment needs

All comer Phase 3 study (Verification of symptom improvement)	
Study Design	Multicenter, randomized, double-blind, placebo-controlled
Primary Endpoint	Time to first resolution of 14 COVID-19 symptoms*1
Population	• Moderate or greater COVID-19 signs/symptoms • Within 48 hours of onset
Administration	**Single oral dose on Day 1** (Secutrelvir 120 mg or placebo)
Target Enrollment	1,200 patients
Region	Asia, including Japan
Milestones	July 2027: Enrollment completed **October 2027: Topline results**

High Risk Phase 3 study (Verification of prevention of severe disease)	
Study Design	Multicenter, randomized, double-blind, placebo-controlled
Primary Endpoint	• Proportion of patients with the composite endpoint through Day 28 (Medical visit due to worsening of COVID-19, or hospitalization or death from any cause)
Population	• Patients with an age-dependent number of high-risk factors • Within 72 hours of onset
Administration	**Single oral dose on Day 1** (Secutrelvir 120 mg or placebo)
Target Enrollment	2,000 patients
Region	Multiple countries, including Japan, the US, and Europe
Milestones	June 2028: Enrollment completed **September 2028: Topline results**

*1 Resolution of COVID-19 symptoms is sustained for at least 24 hours

S-337395 | Target Disease: RSV Infection

Aim to provide post-onset treatment options to patients not fully covered by prevention

- Adults: High rates of severe disease among older adults and high-risk adults
- Pediatrics: A major cause of infection-related hospitalization among children under 5 years of age

Disease Profile

No effective and safe treatment
is currently available for use after symptom onset

—Pediatric*1—
(Under 5 years of age, global)

Approx.
33.1 million

—Older Adults*2—
(Aged 60 years and older, developed countries)

Approx.
5.2 million

Unmet Needs

Patients Not Reached by Prophylactic Agents
Infection risk remains for unvaccinated patients and patients who miss opportunities to receive prophylaxis

Infection and Severe Disease After Prophylaxis
Breakthrough infections and cases of severe disease have been reported even after prophylaxis

Reported Resistance Mutations
Resistance mutations to prophylactic agents have been reported

*1 Lancet. 2022;399 (10340):2047-2064. *2 Influenza Other Respir Viruses. 2023;17(1):e13031

S-337395 | Overview

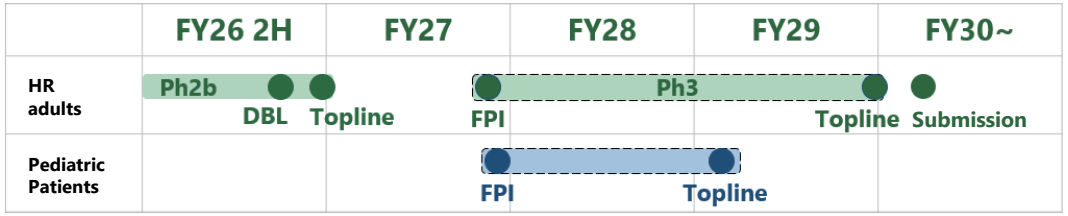
Develop an oral antiviral agent that addresses treatment needs remaining after the widespread adoption of prophylactic agents, contributing to a reduction in the disease burden of RSV infection

Product Characteristics

- Oral antiviral agent targeting the L protein
- Demonstrated strong antiviral efficacy in a human challenge study*1
- Favorable safety profile

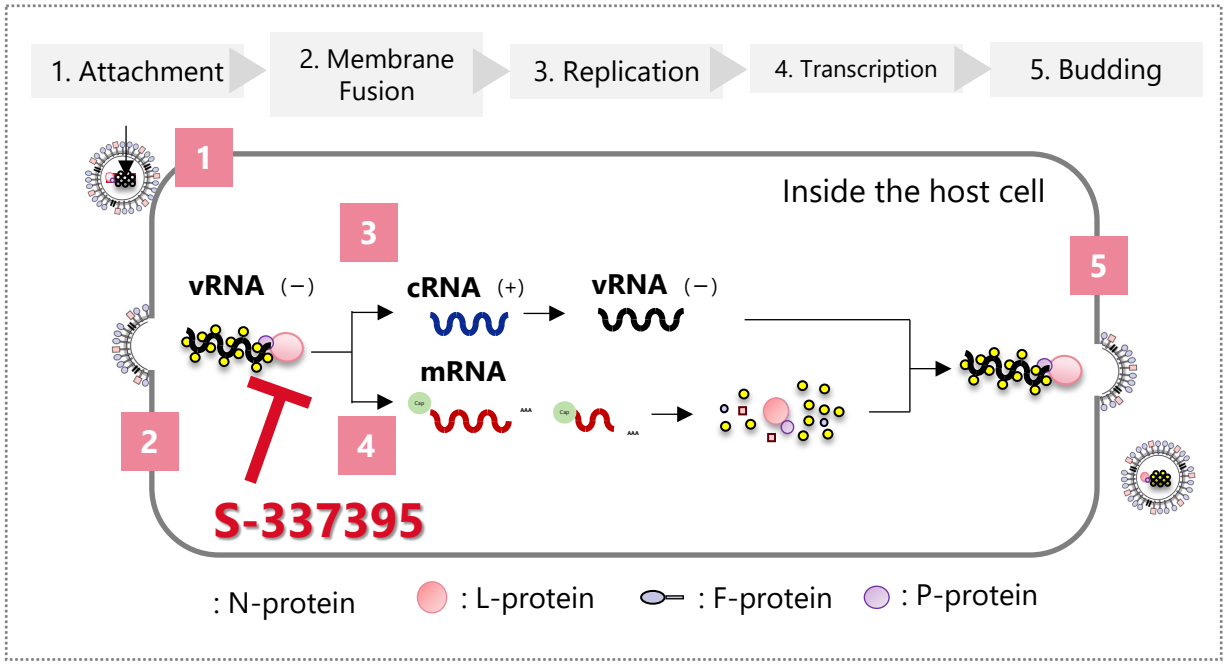
Development plan and key milestones

Prioritize evaluation of prevention of severe disease in high-risk adults, followed by expansion into pediatric patients



Mechanism of Action

Inhibits the RNA-dependent RNA polymerase activity of the L protein, which is essential for viral replication
Inhibits viral genome replication and transcription, thereby suppressing viral proliferation



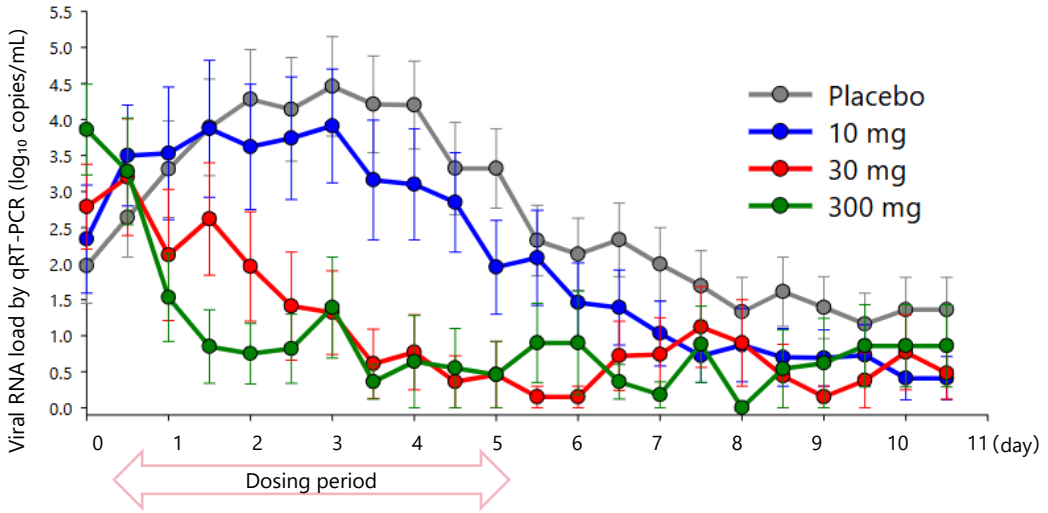
*1 Clinical Infectious Diseases. 2026;83(3):e652-e660

SHIONOGI

S-337395 | Results of Phase 2a Human Challenge Study

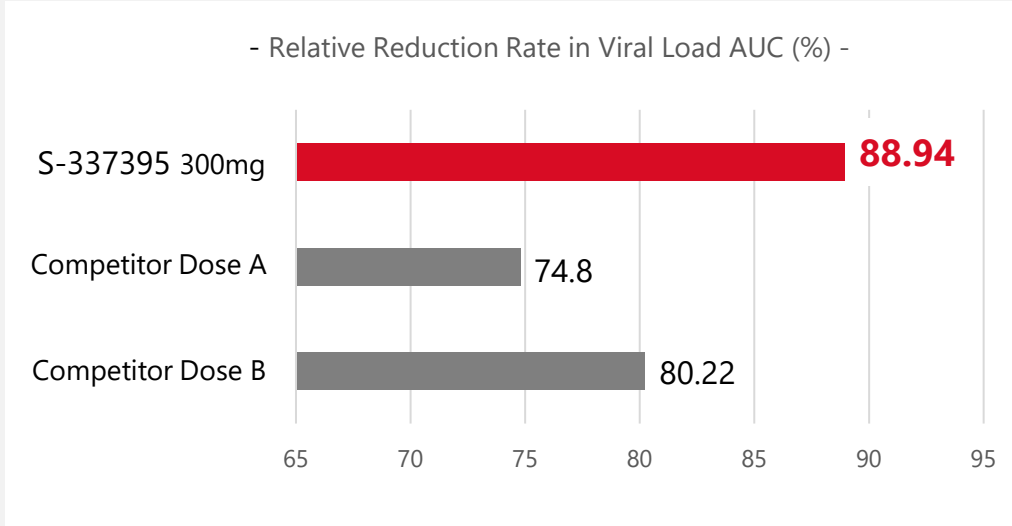
Statistically significant antiviral effect and clinical symptom improvement confirmed

- Change in Viral RNA Load -



- **88.94% reduction in viral load in the highest dose group** (P<0.0001)
- Dose-dependent reduction in viral load confirmed
- Statistically **significant improvement in clinical symptom score**
- No concerns regarding tolerability or safety

【Reference: Comparison of Antiviral Effect with Competitor Product】*1



Strongest antiviral effect confirmed in the challenge study

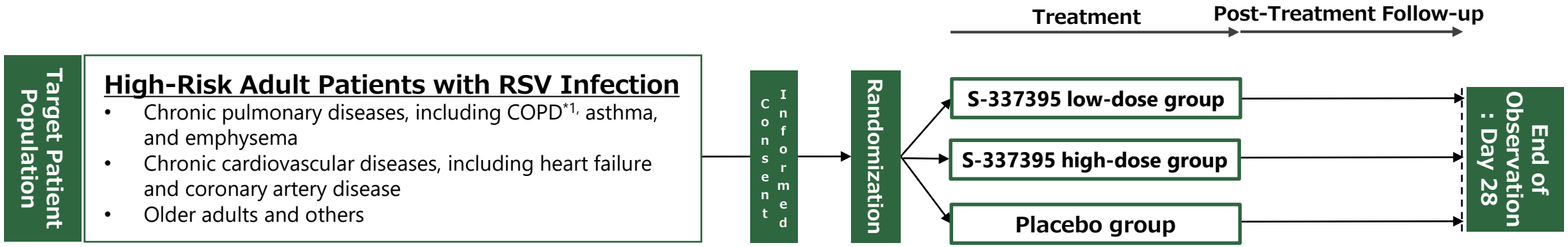
*1 N Engl J Med.2021;385(24):2250-2259

SHIONOGI

S-337395 | Overview of the Phase 2b Study

Aim to provide new treatment options and rapidly transition to Phase 3 based on the Phase 2b results

Primary Endpoint	**Change from baseline in viral RNA load, measured by qRT-PCR**
Secondary Endpoints	**Efficacy: Change From Baseline in Severity of RSV Systemic Symptoms Score and other endpoints**
Study Design	Multicenter, randomized, double-blind, placebo-controlled, parallel-group study
Dosage and Administration / Number of Patients	• Placebo: 64 patients • S-337395 low-dose group: 64 patients • S-337395 high-dose group: 64 patients



* Joint devlopment with UBE Corporation *1 COPD: Chronic Obstructive Pulmonary Disease

SHIONOGI

S-048133 | Target Diseases: Malaria

Taking on the global threat of malaria with SHIONOGI's drug discovery capabilities, delivering new prevention and treatment options to the world

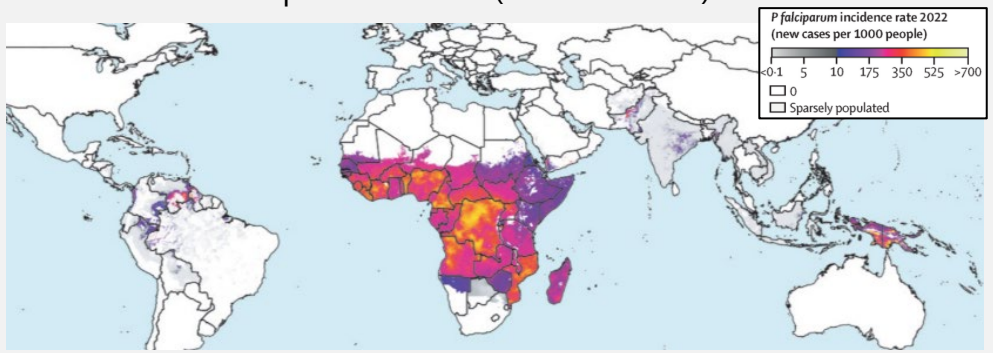
Malaria remains one of the world's three major infectious diseases yet to be overcome

HIV/AIDS | Tuberculosis | **Malaria**

Number of cases **282 million** per year (2024 estimate*[1])

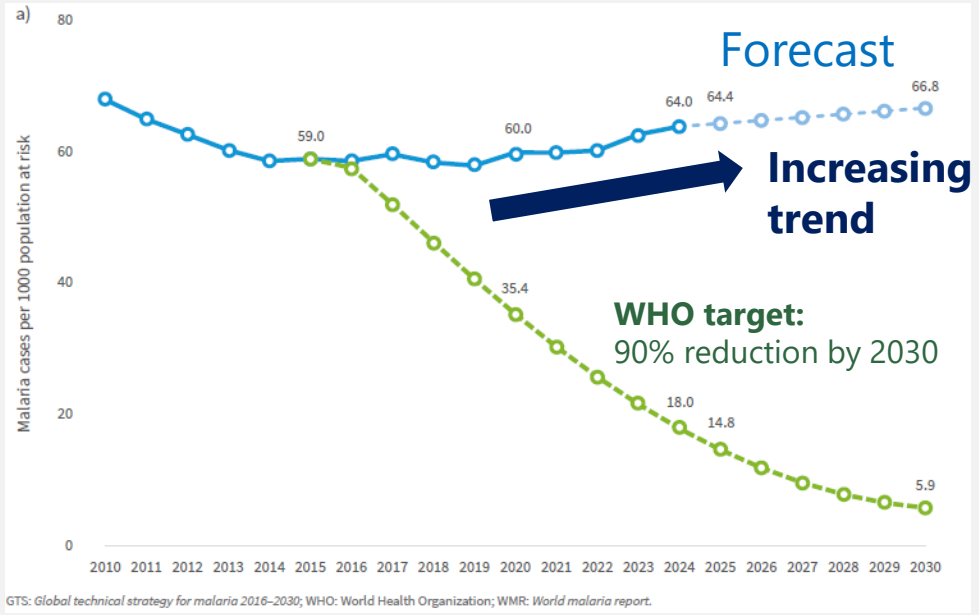
Number of deaths **610,000** per year (2024 estimate*[1])

Incidence of P. falciparum malaria (2022 estimate)*[2]



New innovation is needed to curb the increase

Malaria incidence per 1,000 population at risk



*[1] World malaria report 2025 *[2] Weiss D. J. et al., The Lancet, 2025

SHIONOGI

S-048133 | Overview

Starting with initial clinical evaluation of the oral formulation, we aim to explore the potential of long-acting injectable formulations for long-term prevention and oral formulations for treatment

- As an oral medication, it has a proven clinical mechanism for treatment and prevention.
- Expected to provide three months or longer of durability with a single administration (Existing oral therapy requires three consecutive days of dosing each month for several months*1)
- Effective across broad stages of the malaria parasite life cycle in its two hosts, Anopheles mosquitoes and humans

Development plan and key milestones

— Oral formulation —

Consider the possibility of treatment

October 2027 | Planned Phase 1 initiation

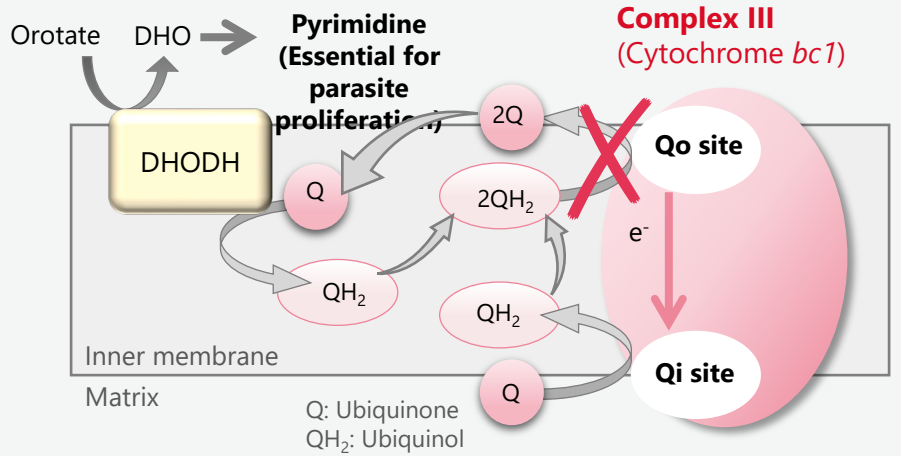
— Long-acting injectable formulation —

Expand to long-term prevention

November 2028 | Planned Phase 1 initiation

Mechanism of action

Inhibition of Complex III in the malaria parasite mitochondrial electron transport chain blocks ubiquinone regeneration and de novo pyrimidine synthesis essential for parasite proliferation*2



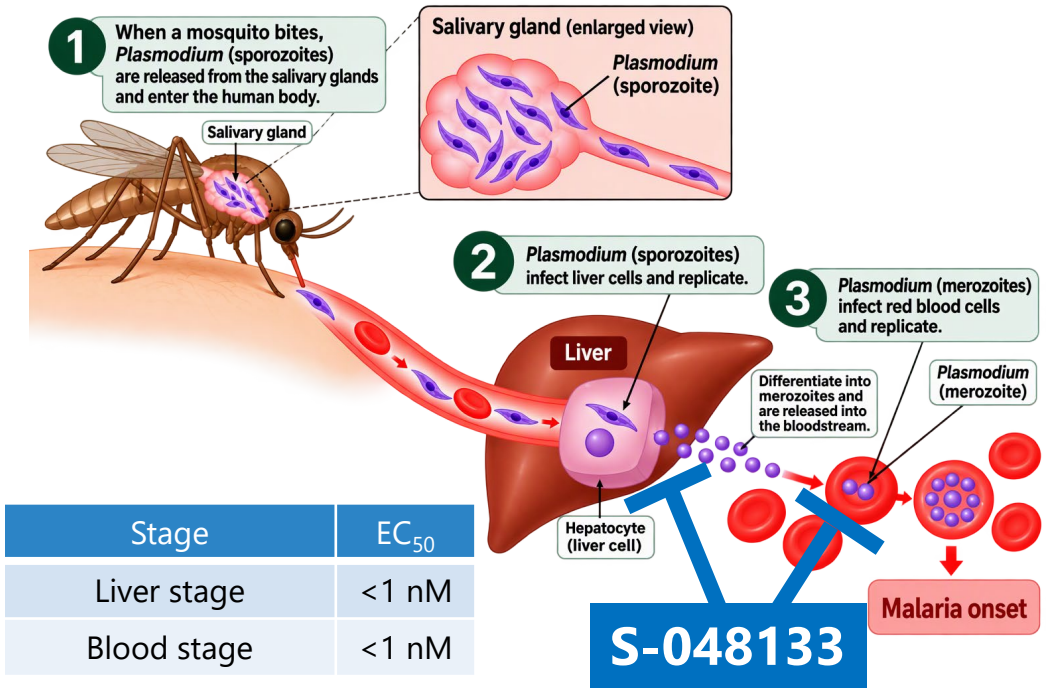
*1 For Seasonal Malaria Chemoprevention (SMC)
*2 Blood Stage

SHIONOGI

S-048133 | Profile Suited for Malaria Prevention

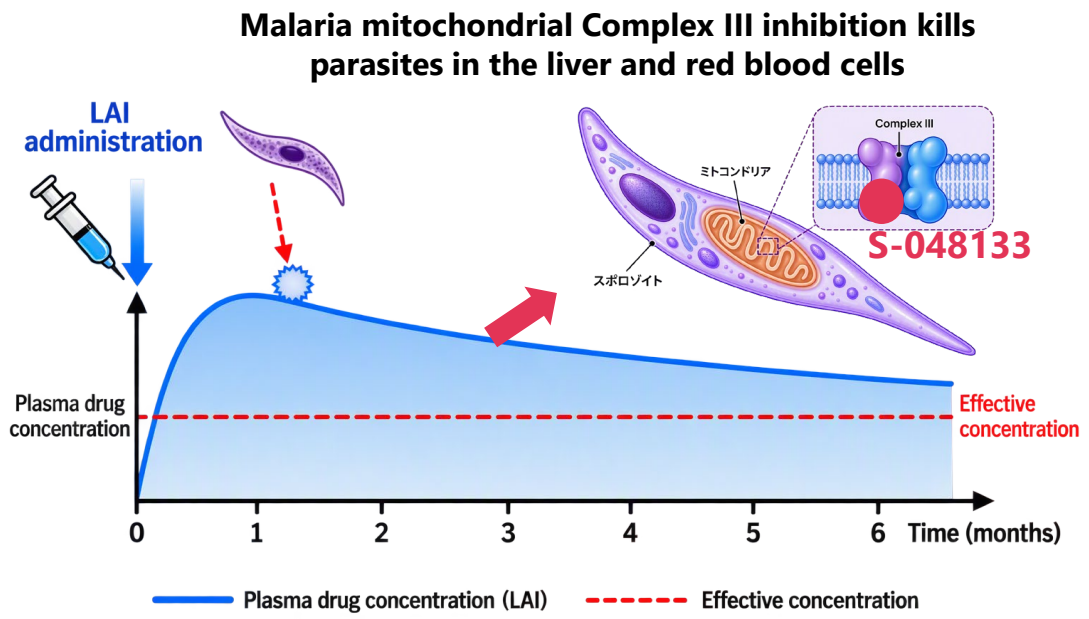
Selected S-048133, which has efficacy across a broad range of life cycle stages and long-lasting activity, and advancing preclinical development with MMV*1 and Nagasaki University*2

−Antimalarial Activity Throughout the Life Cycle of the Malaria Parasite−



Stage	EC_{50}
Liver stage	<1 nM
Blood stage	<1 nM

−Sustained Preventive Effect Through Long-Acting Activity−



Suppresses the onset of malaria over a long period at the pre-symptomatic liver and blood stages, providing an optimal solution for prevention

*1 Medicines for Malaria Venture *2 Funded by GHIT Fund and MMV.

Milestones for Priority Pipeline Programs

Development Compound	Preclinical	Phase1	Phase2	Phase3	Milestone Through FY2027	Expected Stage in FY2030
Olorofim Invasive Aspergillosis					Submission and Approval (US*1, EU*2) Submission (Mainland China, Japan)	Launch
Secutrelvir COVID-19 treatment (Oral)					RYZON AC study: Completion, NDA (Japan)	Launch
S-337395 RSV infection					Initiation of Phase 3 for adults Initiation of the clinical study for pediatric	Filling for adult Late-stage clinical trial for pediatric
S-649228 Gram-negative bacterial infection /AMR					Initiation of Phase 2 (cUTI)	Phase 3 completed
Secutrelvir COVID-19 pre-exposure prophylaxis （LAI）					Initiation of Phase 2	Phase 3
S-910978 Pulmonary MAB					Initiation of Phase 1	Phase 2 completed
S-048133 Malaria					Initiation of Phase 1	Phase 2 in preparation

*1 To be Conducted by F2G *2 Approval: FY2027 to FY2028 1Q

Next Growth Area

SHIONOGI

Next Growth Areas | Three Selected Disease Areas

Advancing research and development to address significant unmet needs, leveraging our established expertise

1

Sleep Disorders



—Impact on Life Expectancy—

Patients with obstructive sleep apnea worldwide*1

approx. **0.9** B*2

R&D Focus

Developing new treatment options for sleep disorders, including obstructive sleep apnea

S-054502 / S-213951 etc.

2

Psychiatric Disorders



—Treatment Options Remain Limited—

Patients with mental disorders worldwide

Approx. **1.2** B*3

R&D Focus

Advancing multiple research programs by leveraging SHIONOGI's drug discovery expertise and know-how

3

Hearing Loss



—Growing Concern over Headphone-Induced Hearing Loss—

People at potential risk

Approx. **1.1** B*4

R&D Focus

Advancing multiple research programs to preserve and restore hearing

*1 Total patients with mild to severe disease *2 Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis - The Lancet Respiratory Medicine *3 Updated trends in the global prevalence and burden of mental disorders, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023
*4 World Health Organization, 2015. Available: https://www.who.int/news-room/events/detail/2015/03/03/default-calendar/world-hearing-day-2015-make-listening-safe

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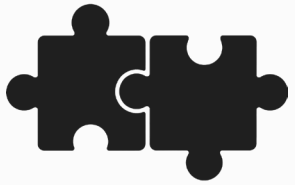
Sleep Disorders | Vision and Unmet Needs to Be Addressed

Improve nighttime apnea and daytime impairment, and restore time to "sleep, wake, work, and enjoy"

Our Vision

01 Choice suited to each patient's condition



Sleep apnea syndrome has diverse causes, requiring treatment options tailored to each individual patient

02 Continuous treatment



Current treatments often cannot be continued, creating a need for treatment that is easy to continue

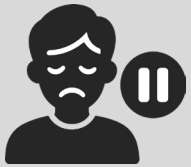
Unmet Needs

Symptoms and treatment effects are difficult to see



Because it occurs during sleep, patients find it difficult to perceive severity or improvement

Continuation of existing treatment is difficult



Due to the burden of wearing CPAP or intolerance, patients cannot continue treatment even when needed

Causes differ by patient



Even within SAS, pathophysiological endotypes differ, making a uniform treatment approach not possible

Nighttime abnormalities take away daytime life



Sleep fragmentation, sleepiness, and fatigue interfere with work, driving, and social participation

Sleep Disorders | Therapeutic Approach

Taking a multifaceted approach to provide treatment options suited to each patient

1 Anatomical upper airway obstruction



Treatment options that open the upper airway and improve obstruction

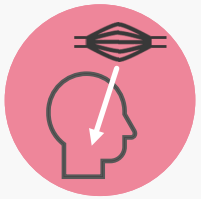
3 High loop gain



Treatment options that reduce ventilatory control instability and stabilize breathing

OSA pathophysiology is formed by a complex interplay of four factors
– The impact of each factor on OSA differs by patient, presenting with various symptoms –

2 Reduced pharyngeal dilator muscle responsiveness



Treatment options that enhance upper airway muscle response during sleep

4 Low arousal threshold



Treatment options that regulate excessive arousability and maintain sleep

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S-054502 (Sulthiame) | Overview

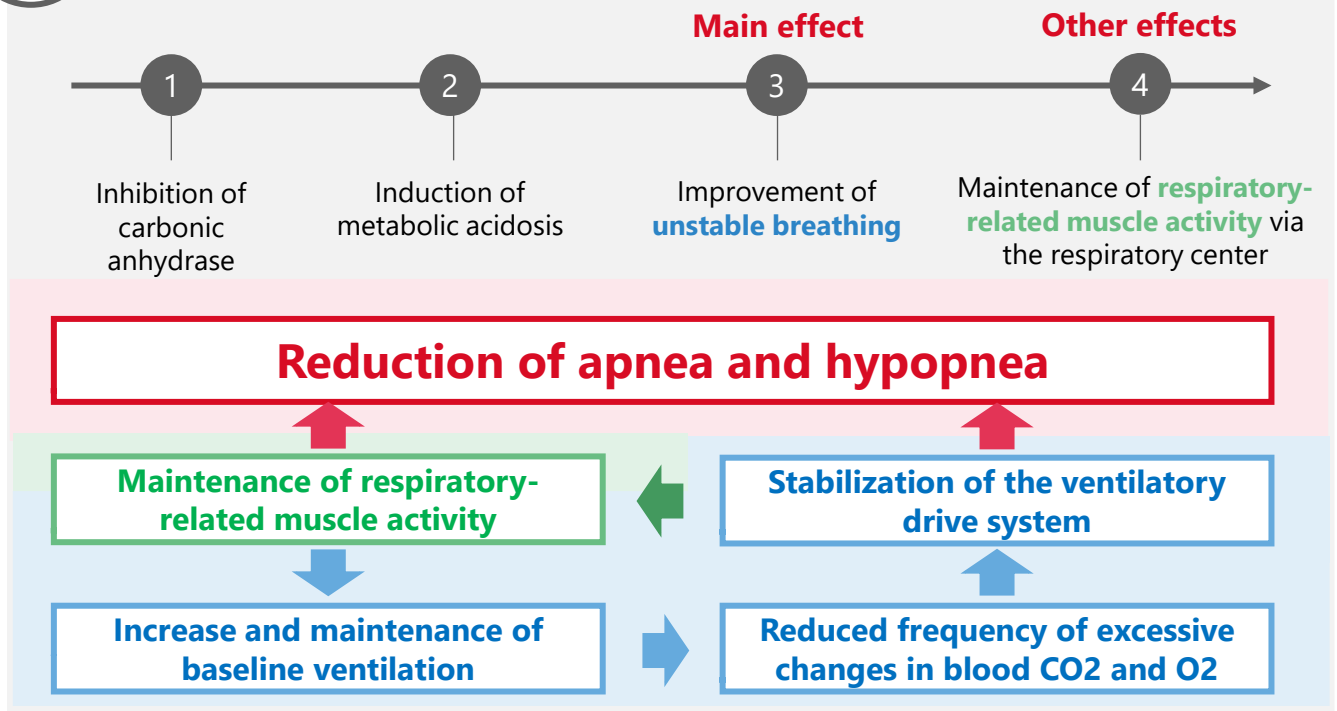
Disease Overview: Obstructive Sleep Apnea (OSA)

- Main type, accounting for approx. 90% of SAS patients
- In addition to daytime sleepiness and fatigue, CV risk increases
- CPAP is highly effective, but adherence remains a challenge
- Target patient population of approx. **170** million*1

Product Profile

- Once-daily oral treatment administered before bedtime
- Applicable to a broad patient population, including OSA/CSA
- Treatment option regardless of severity

Hypothesized Mechanism of Action



Development compound	Preclinical	Phase1	Phase2	Phase3	Milestones through FY2027	Expected stage in FY2030
S-054502 Sleep apnea					Phase 2b/3: completion of participant enrollment	Phase 3

*1 Estimate for Europe (France, Germany, Italy, Spain, UK), US, and JP

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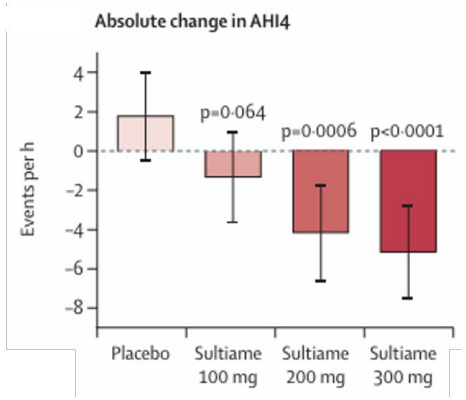
S-054502 | Clinical Results and Phase 2b/3 Study Plan

Verify globally the efficacy demonstrated in the Phase 2 study, toward a new oral treatment option for OSA

Phase 2 Study

- Efficacy confirmed in a study in Europe -

Study Design	Double-blind, placebo-controlled study 298 patients (N=74–75/group)
Primary Endpoint	Change from baseline in Apnea-Hypopnea Index (AHI*[1])
Treatment Period	15 weeks
Dosage and Administration	Placebo group, 3 active groups (100, 200, 300 mg) Once daily before bedtime



Primary Endpoint

- Dose-dependent improvement in AHI

Secondary Endpoints

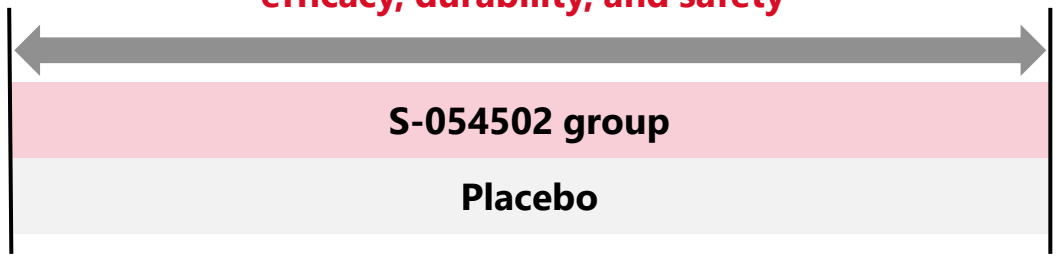
- ignificant improvement in oxygen desaturation index and mean oxygen saturation vs. placebo group

Ph2b/3 Study Overview

- Clinical study planned in Japan, Europe, and the U.S. -

Study Design	Double-blind, placebo-controlled study 400 patients, 200 per group
Primary Endpoint	Change from baseline in AHI
Treatment Period	52 weeks
Dosage and Administration	Placebo group, active group (dose titration) Once daily before bedtime

Determine clinical value based on evaluation of efficacy, durability, and safety



*[1] AHI4: Apnea-hypopnea index based on oxygen desaturation of ≥4%*Lancet*. 2025 Oct 25;406(10514):1983-1992.

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New SHIONOGI's Research Capabilities

Toshiyuki Asaki, PhD
Corporate Officer, Senior Vice President, Drug Discovery Research Division

SHIONOGI

The Vision for Research at New SHIONOGI

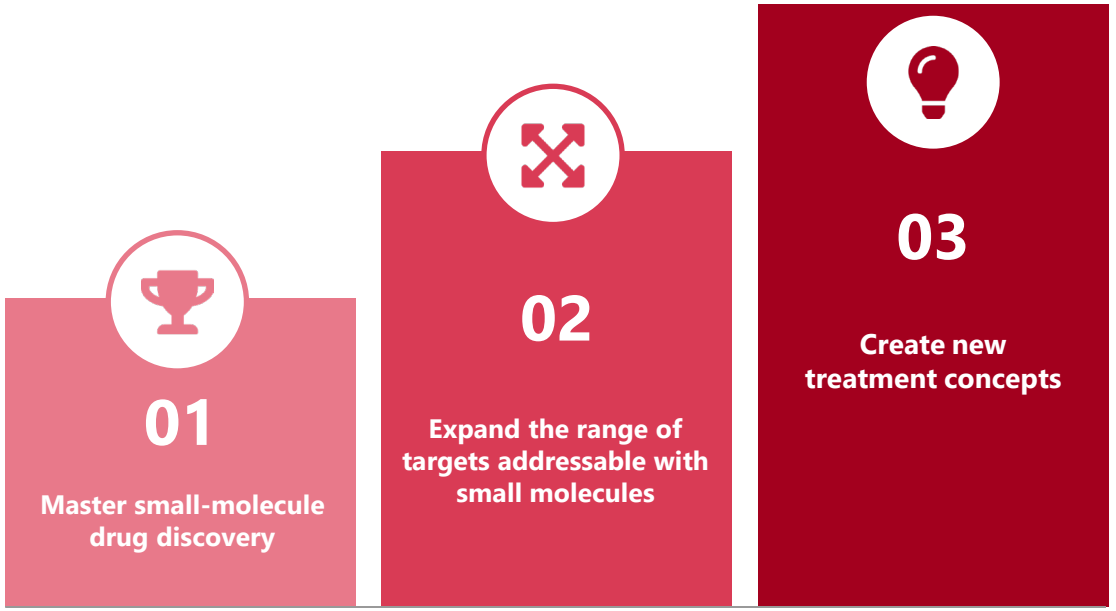
OUR VISION

A research organization that rapidly and continuously creates the world's most valuable drug candidates

Small Molecule

Achieve world-class capabilities, speed, and compound quality in small-molecule drug candidate generation

Strategically incorporate SHIONOGI's proprietary AI technology platform to expand target space and applicability with small molecules



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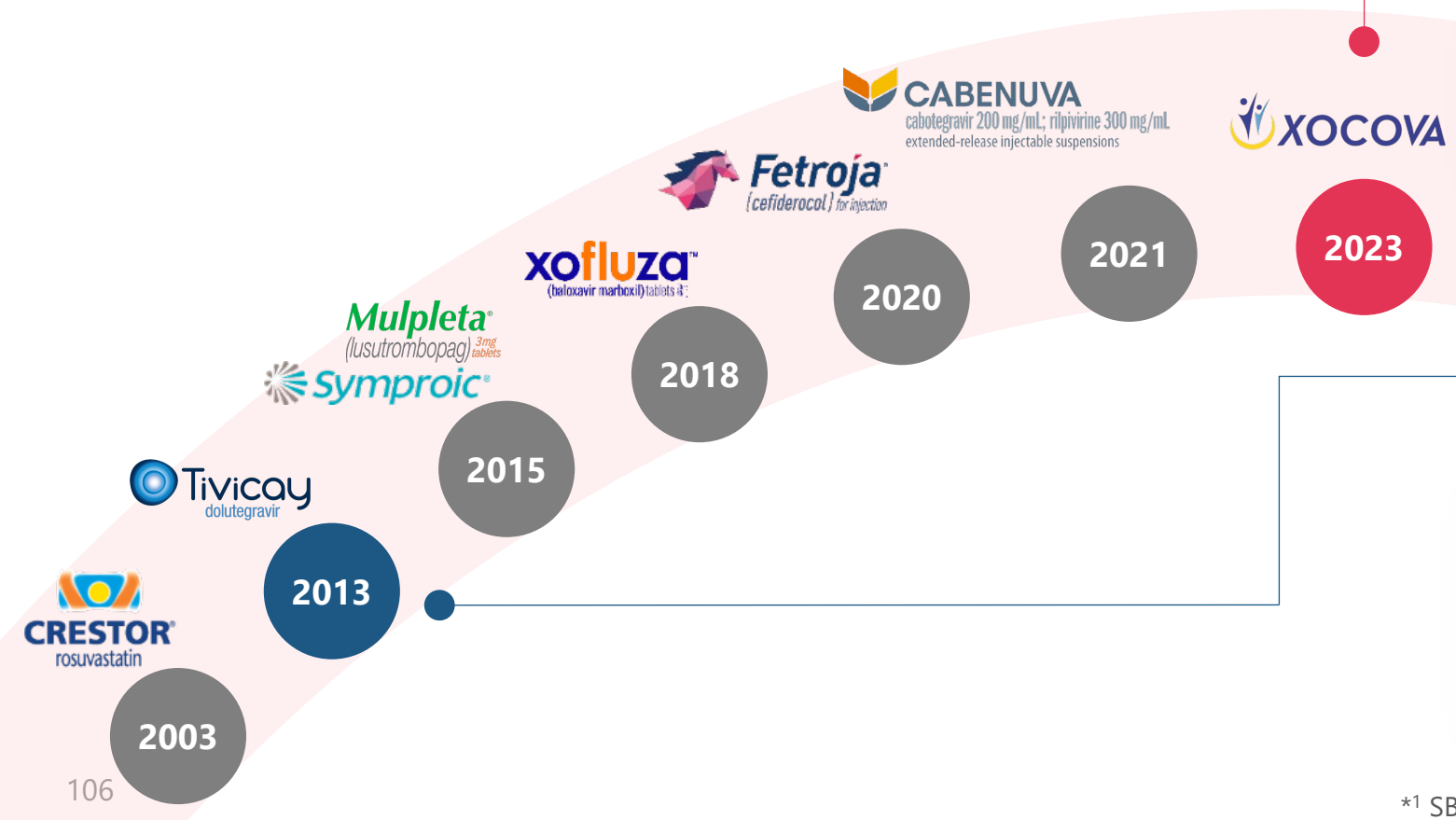
SHIONOGI's Two Successful Models | Ensitrelvir & Dolutegravir

Establishing a drug discovery framework that reproduces the "speed" and "PoC generation capabilities" of these two representative drug discovery models

– History of major new drugs discovered by SHIONOGI –



01 | Rapid Drug Discovery

– Rapid, high-quality drug discovery through SBDD*1 –

Rapid acquisition of high-quality hit compounds × **Rapid optimization by in-house medicinal chemistry**

Time from drug discovery to preclinical development **80** % Reduction

02 | Pioneering Drug Discovery

– FIC*2 drug discovery based on strong scientific capabilities –

Pharmacological evaluation capabilities × **Medicinal chemistry capabilities**

Assess the validity of drug discovery targets and identify genuine hit compounds

Create novel structures

*1 SBDD : Structure-Based Drug Design *2 FIC: First in class

SHIONOGI

Evolution of the Drug Discovery Model through Integration with the Former JT Pharmaceuticals Business

Enhancing our research platform to increase both the “speed” and “probability of success” in drug discovery

Strengthening Capabilities to Create Compounds

Candidate compound acquisition technologies

- Expansion of compound library diversity
- Screening expertise accumulated by the former JT Pharmaceuticals business
- Large-scale virtual library × high-precision virtual screening × AI
- Acquisition of structural analysis talent and introduction of cryo-EMMedicinal Chemistry Capabilities

Medicinal Chemistry Capabilities

- Diversification of design hypotheses
- Enhanced compound optimization capabilities

Number of medicinal chemistry researchers **×1.7**

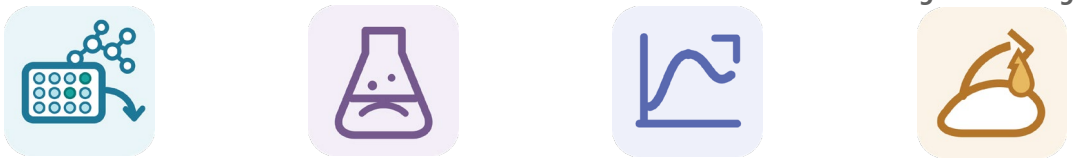
AI Drug Discovery Capabilities

- Data-driven DMTA*1 utilizing AI Agents
- Generative AI × quantum computing
- Leverage SHIONOGI’s information assets to establish a framework for efficient AI-driven drug discovery

Advancing Drug Discovery Evaluation Capabilities

In addition to computational science and medicinal chemistry, functions from the former JT Pharmaceuticals business that support the process from candidate generation through clinical prediction and product development have been integrated

Pharmacology Research | Safety | Pharmacokinetics | Topical Formulation Design Technologies



01 Improving Confidence in Drug Discovery Targets

Identify targets with a strong causal relationship to disease based on RWD*2 and clinical data

02 Faster, More Accurate Compound Evaluation

Fully leverage AI prediction × in vitro × proprietary data

03 Improving the Probability of Achieving Early Clinical PoC

Appropriate disease selection and patient segmentation based on AI prediction × TR*3 × proprietary data

*1 DMTA：Design–Make–Test–Analyze *2 RWD：Real World Data *3 TR：Translational Research

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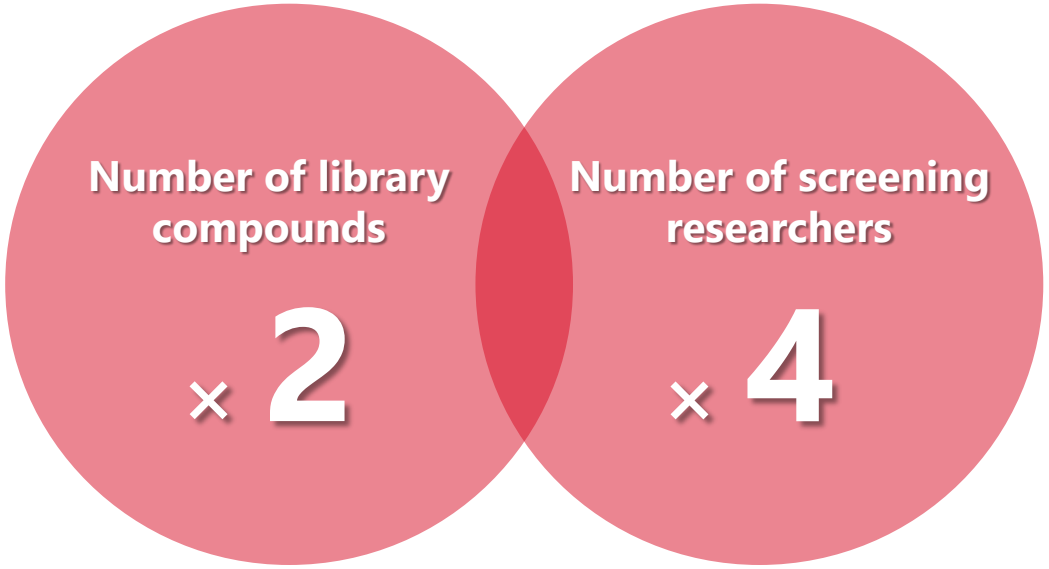
Strengthening Capabilities to Create Compounds | Candidate Compound Acquisition Technologies

02
Expand the range of targets addressable with small molecules

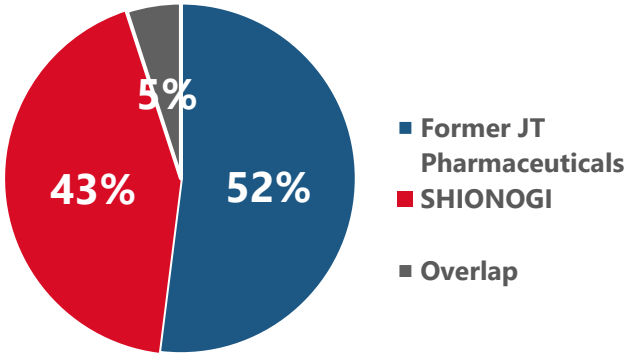
Enhance the probability of selecting "high-quality hit compounds" by strengthening the compound library and screening capabilities

Significant Expansion through Integration with the Former JT Pharmaceuticals Business



01 Expansion of Compound Library Diversity

- Limited overlap, doubling the size of the compound library



02 Screening Expertise

- Expand the chemical space explored by integrating the compound libraries of both companies
- Addition of competitive HTS technologies, including AS-MS*1
- Achieve more than 2× throughput at 1/7 the previous cost

*1 AS-MS, Affinity Selection–Mass Spectrometry

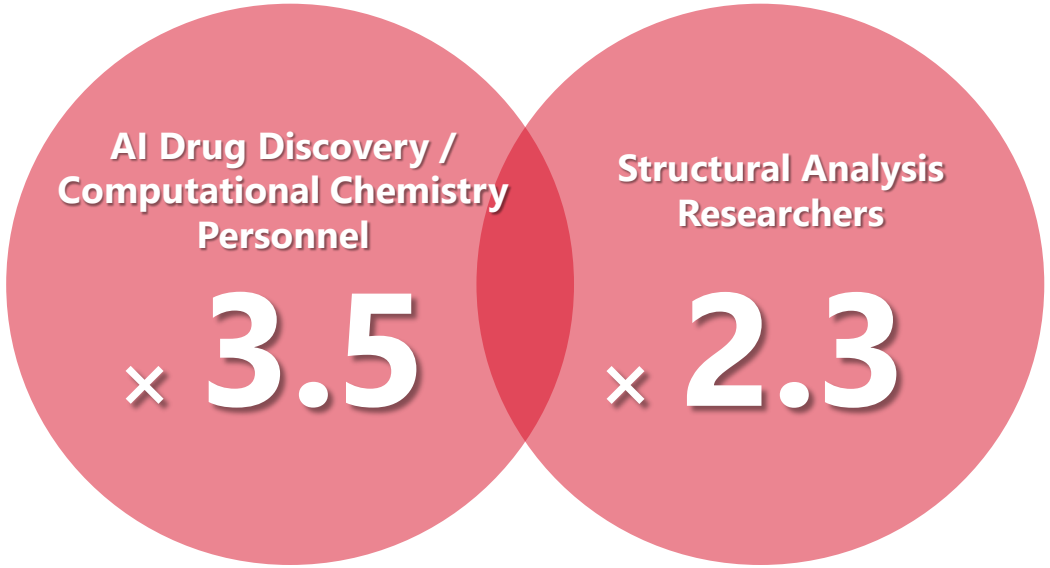
SHIONOGI

Strengthening Capabilities to Create Compounds | Lead Compound Acquisition Technologies

02
Expand the range of targets addressable with small molecules

Rapidly and efficiently identify candidate compounds from hits by utilizing protein structural analysis data, computational chemistry, and AI

Significant Expansion through Integration with the Former JT Pharmaceuticals Business



01 Large-scale Virtual Library/Screening × AI

- Environment enabling the use of AI/computational chemistry talent and one of Japan's leading large-scale computing systems
- Improve virtual screening accuracy and efficiency through AI/AI Agents



HPC System
(Takatsuki Research Center)

02 Acquisition of Structural Analysis Talent and Introduction of Cryo-EM

- Structural information utilization rate across all drug discovery programs has reached >80%
- Significant increase in protein engineering researchers, a key bottleneck



Introduction of cryo-electron microscopy (June 2026)

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Strengthening Capabilities to Create Compounds | Enhancing Drug Discovery through Data-Driven DMTA

Expand the drug discovery processes used in the Ensitrelvir and Dolutegravir models to other research programs

Before

– DMTA driven primarily by the experience of highly skilled researchers –



Difficult to leverage successful know-how across research programs

- Reliance on individual researchers' experience and tacit knowledge
- Data and knowledge of success dispersed across individual programs

After

– DMTA based on an integrated drug discovery platform –



Structural Information
Cryo-EM×SSIMS*1

Measured and Predicted Data
DRIVE



Integrated Drug Discovery Platform
– People make decisions based on data –



Analysis and Design
Generative AI / AI Agent

Hypothesis Testing
Chemistry Capabilities



HPC × Quantum Computing
– Computing infrastructure supporting large-scale analysis and prediction –

*1 SSIMS：**S**HI**O**NOGI **S**tructure **I**nformation **M**anagement **S**ystem, HPC: High Performance Computing

Strengthening Capabilities to Create Compounds | Compound Exploration Using SHIONOGI's Proprietary AI Technology Platform

Aim to expand chemical space using generative AI × quantum computing and create compounds that could not be reached through conventional exploration

INPUT

– Input the desired compound properties –

– Efficacy –
Target / Mechanism of action

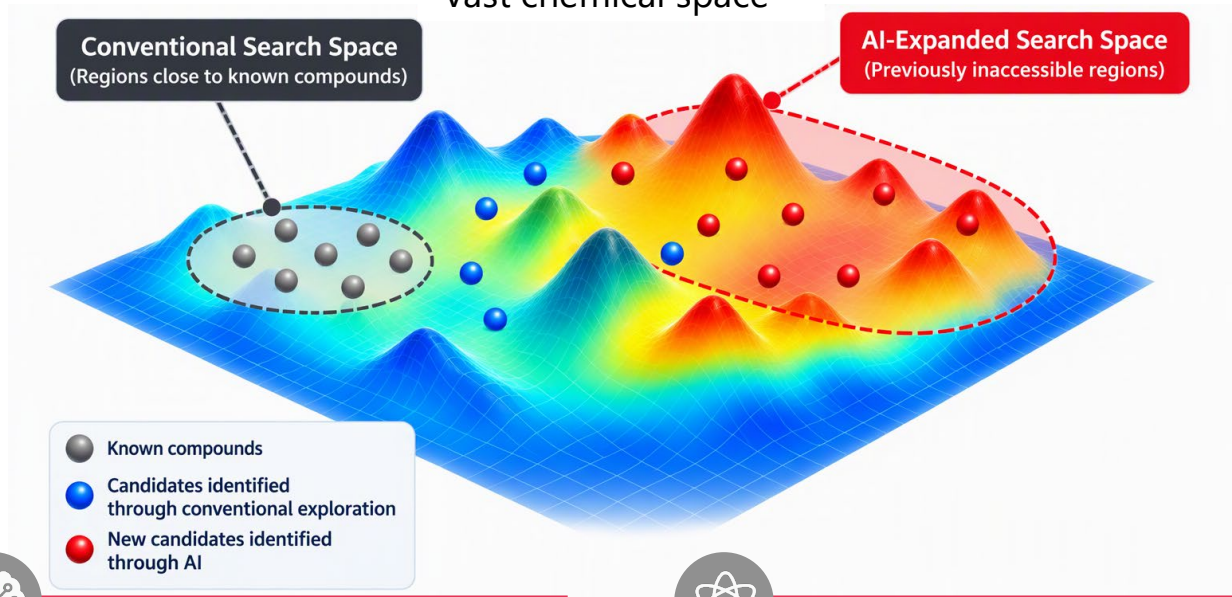
–ADMET–
Safety / Pharmacokinetics

– Physicochemical Properties –
Solubility / Lipophilicity, etc.

– Binding Affinity –
How to bind each other

EXPLORE

– Vast chemical space –



Multimodal Generative AI
Integrated learning of structures, sequences, physicochemical properties, etc.

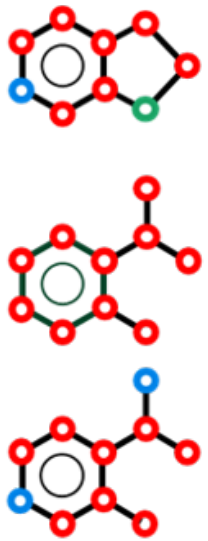
×

Quantum Computing
Enables simultaneous exploration for optimal solutions

SHIONOGI's Proprietary AI Technology Platform

OUTPUT

– Generate new candidate compounds –



Validate potential through synthesis and experimental evaluation

SHIONOGI

Advancing Drug Discovery Evaluation Capabilities | Faster, More Accurate Compound Evaluation

03 Create new treatment concepts

From “make and measure many compounds” to “predict and select the compounds to make”

Data

Accumulate Proprietary BMC Data

physicochemical and ADME parameters

17

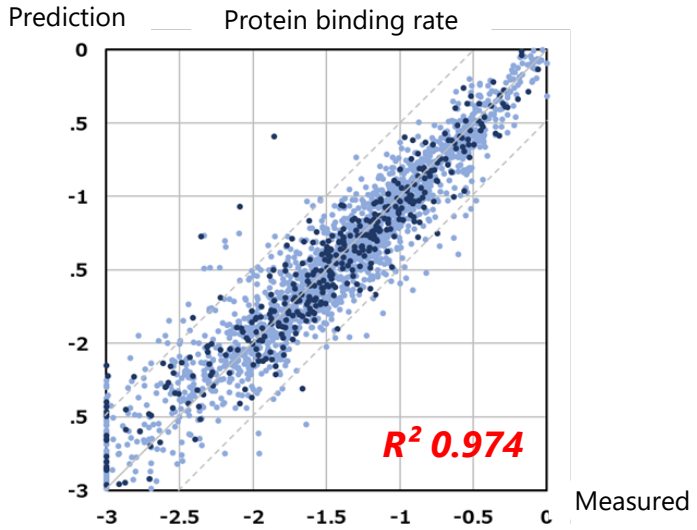
Continuously accumulate measured data

Aim to Reduce the Number of Compounds Evaluated

Develop SHIONOGI’s proprietary prediction technology using BMC*1

PREDICT

Build Highly Accurate AI Models from Measured Data



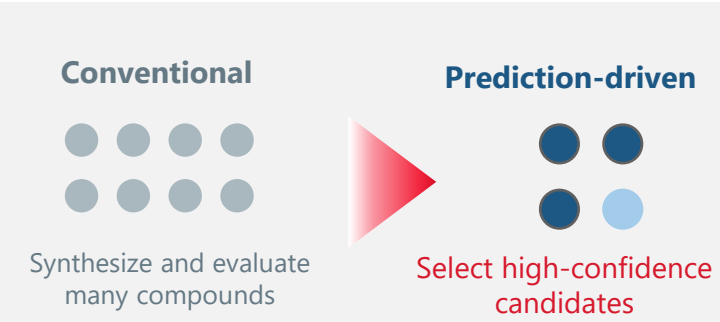
Predict physicochemical and ADME parameters with high accuracy

96 → **47** compounds/week

Reduce the Number of Compounds Evaluated

SELECT

Select High-Confidence Candidates through Prediction-Driven Evaluation



Number of Compounds Synthesized

*Current*2*	*By 2030*
Approx. **1/2**	Approx. **75** % Redcution

*1 Biomimetic Chromatography K.L. Valko, Analytical Science Advances, 3 (2022), pp. 146-153 *2 Comparison of results at the former JT Pharmaceuticals business between 2019 and 2024

Advancing Drug Discovery Evaluation Capabilities | Improving the Probability of Achieving Early Clinical PoC (1)

Validate causal relationships using human genetic and clinical data to assess the "therapeutic hypothesis" before clinical trials

Steps for the Therapeutic Hypothesis

01 Formulate the Hypothesis
– Proprietary MR Analysis –

Does increased glucose uptake lead to improved cognitive function?

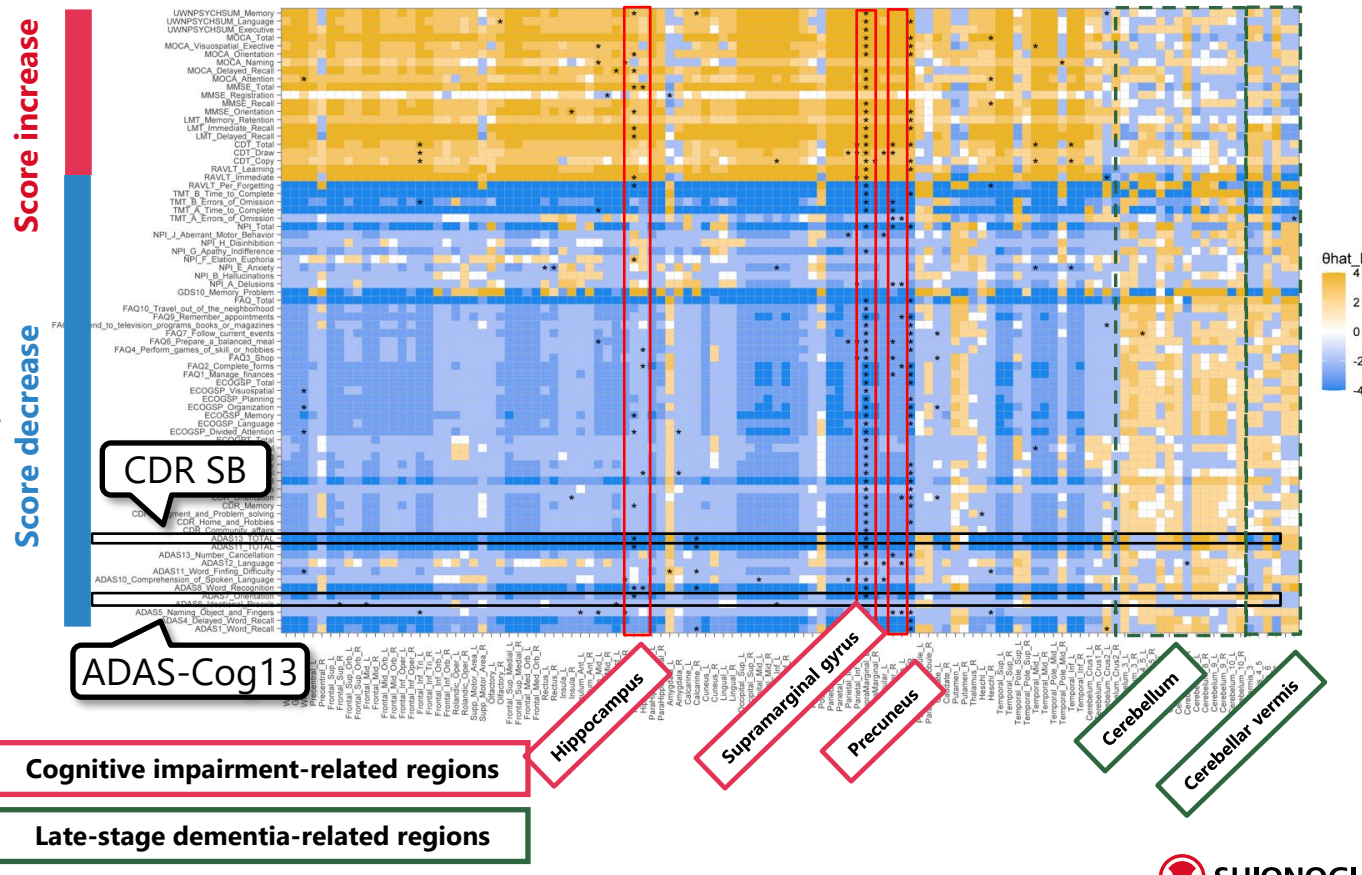
02 Establish Causality

Confirm increased glucose uptake in relevant brain regions
→ Supports a causal relationship with improved cognitive function

03 Increase the Probability of Drug Discovery Success

Increase confidence in the therapeutic hypothesis before clinical trials

(Ex) Validate the causal relationship between glucose uptake and improvement in cognitive function using MR analysis*1,2



*1 MR; Mendelian randomization *2 Results from this study have been published Alzheimers Dis. 2026 Mar;110(2):895-908.

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Advancing Drug Discovery Evaluation Capabilities | Improving the Probability of Achieving Early Clinical PoC (2)

Identify patient populations in which changes can be more readily detected and determine the "appropriate patients" before clinical trials

Steps for the Therapeutic Hypothesis

01 Formulate the Hypothesis
– Proprietary MR Analysis –

Classify patients according to the rate of decline in glucose uptake and compare changes in cognitive function over time

02 Establish Causality

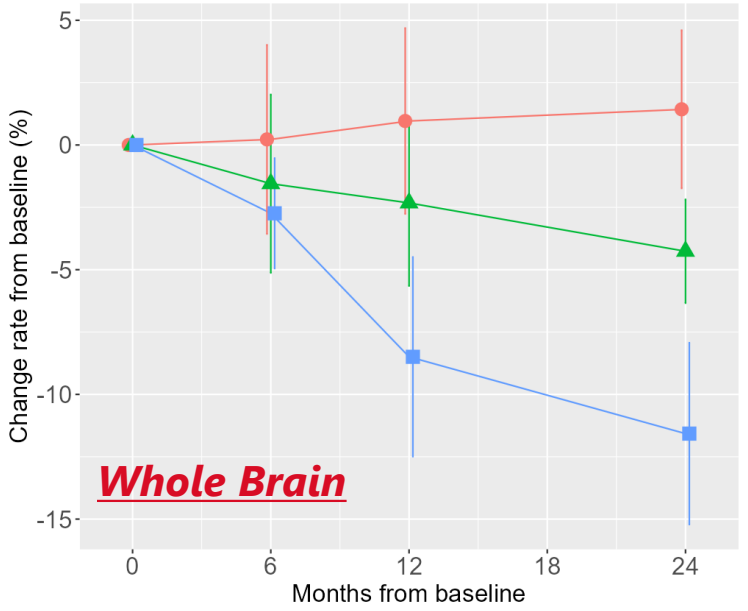
Patients with a faster decline in glucose uptake also experience faster deterioration in cognitive function

03 Increase the Probability of Drug Discovery Success

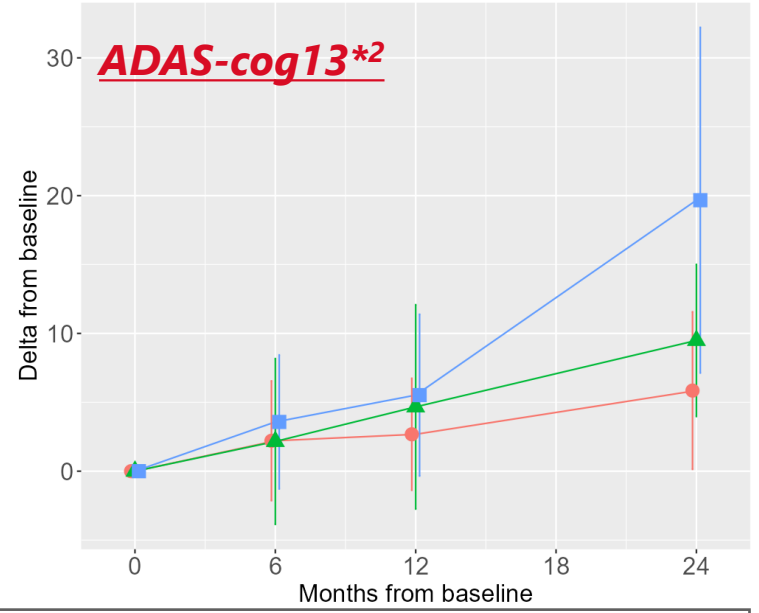
Increase confidence in appropriate patient selection before clinical trials

(Ex) Establish the causal relationship between the rate of glucose uptake decline and deterioration in cognitive function*1

– Stratify patients by the rate of decline in glucose uptake –



– Faster decline is associated with greater deterioration in cognitive function –



Glucose Uptake Decline Patient Subtypes

- **Slow rate of decline (n=41, 32%)**
- **Moderate rate of decline (n=74, 58%)**
- **Fast rate of decline (n=13, 10%)**

*1 In house data *2 ADAS-cog13: One of the major endpoints used in clinical trials for cognitive impairment

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New SHIONOGI Moves into New Frontiers

Evolve the strengths cultivated in infectious diseases through integration with the former JT Pharmaceuticals business and expand them into priority disease areas

Infectious Diseases

– Foundation cultivated in HIV and AMR –

Vast Proprietary Data

B-lactam drug discovery	Compound structure × Activity	Genome × Drug resistance
60Years	120,000strains	6,000Strains

Integration with the Former JT Pharmaceuticals

– Greater speed and higher-quality drug discovery –

Strengthening Capabilities to Create Compounds

Advancing Drug Discovery Evaluation Capabilities

- Hit generation / Medicinal chemistry capabilities
- Accelerating drug discovery through AI
- More accurate target and compound evaluation
- Improving the probability of achieving clinical PoC

Further evolve drug discovery evaluation capabilities according to disease characteristics

Neuromuscular Diseases



Allergy / Immunological Diseases



SHIONOGI

Neuromuscular Diseases |
Creating an In-House Drug Discovery Pipeline

Toward a future where previously inaccessible treatments reach patients and restore freedom in their daily lives

1

Research Platform Built through Drug Discovery and Development Targeting Cellular Function



Supplement deficiencies | Reduce burden | Restore regulatory systems

In-house discovery programs targeting cellular function

Brain- and Muscle-Penetrating Modalities

Maintain and restore cellular function

2

Research Platform Built through Drug Discovery and Development Targeting Neural Function



Suppress neuroinflammation | Modulate neural circuits

In-house discovery programs targeting neuroinflammation and glia

In-house discovery programs targeting BU/LCM of development products

Protect and regulate neural function

Immunological / Allergic Diseases |
Creating an In-House Drug Discovery Pipeline

Toward a future where patients regain daily lives free from allergies and no longer suffer from recurrence

1



Immunotherapy Research Built through AIT Development × Research Platform for Long-Acting Therapies

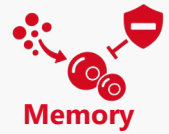
Novel antigens | Next-generation AIT

Novel-antigen SLIT
(Plants → Foods)

Next-generation SCIT
Subcutaneous immunotherapy

Control of allergies

2



Research on Recurrence Mechanisms Built through AD Development × Immunoregulatory Research through Treg Development

Suppress recurrence | Regulate immunity

In-house discovery programs targeting suppression of recurrence / disease modification

In-house discovery programs targeting BU/LCM of development products

Control recurrence and immunity

SHIONOGI

Infectious Diseases |
Creating an In-House Drug Discovery Pipeline

Continue to rapidly and continuously provide
"valuable options" to address societal challenges related to infectious diseases

1

Capabilities to Understand Pathogens and Evaluation Platform

Novel mechanisms of action |
Ideas for targets and combination regimens

- **Next-generation AMR drugs IV | Oral**
- **Neglected tropical diseases**

Never let treatment options run out

2

Capabilities to Turn Difficult Molecules into Products

Formulation design (long-acting)

- **Long-acting prophylactic agents for various infectious diseases**
- **Therapeutics for respiratory viral infections**

Prevent infection, disease onset, and severe disease

3

Molecular Design to Create New Concepts

Broad-spectrum targets, etc.

- **Broad-spectrum antivirals MCM-ready*1**
- **Vaccines for infectious diseases**

Prepare for unknown infectious diseases

*1 MCM: Medical Countermeasures

Our Vision for 2030

Build an organization capable of consistently delivering rapid drug discovery, and continue to deliver new drugs in priority disease areas through world-class small-molecule drug discovery capabilities and a high probability of success

SPEED	*PIPELINE*	SUCCESS RATE
– Speed of Exploratory Drug Discovery –	**– In-House Discovery Pipeline –**	**– Early Clinical PoC Achievement Rate –**
As fast as 2 years	**20 +programs**	**>50%**
Hit compound → Entry into preclinical development	Entering preclinical development during FY2026–2030 In-house discovery ratio: >**60**%	World-class level

Rapidly create → **Generate in-house** → **Advance into the clinic with high confidence**

SHIONOGI

CMC Research Capabilities of the New SHIONOGI

Tatsumori Yoshida
Corporate Officer, Senior Vice President, Pharmaceutical Technology Research Division

SHIONOGI

Strengthening Pharmaceutical Technology Research

Delivering the value of patient convenience by transforming compounds (active ingredients) into pharmaceutical products through manufacturing

Core Capabilities



Small Molecules

—Formulation・Drug Delivery Technology—

- Oral
- Injectable
- Topical (Strengthen)
- LAO/LAI -Long-acting-

Expansion of Capabilities



Diverse Modalities

—From Nucleic Acids and Peptides to Antigens and Antibodies—

- Allergen (New)
- Vaccine
- Antibody
- Nucleic Acid
- Peptide

Formulation Design Capabilities for Topicals

- Track record with poorly soluble and water/light-unstable compounds
- Sensory evaluation know-how, including texture on application

Capabilities Strengthened through Acquisition of JT's Pharmaceutical Business

- Formulation and manufacturing know-how, including antigen extractionInsights into AIT gained through the SLIT business

Formulation Know-how from the SLIT Business

Rationale for Reintegrating Manufacturing

Managing cost of goods, one of the key elements supporting the foundation of our management, on our own

1

Risks of Being Fabless



—Unable to manage our business on our own—

- Flexible supply response is essential, as demand for infectious disease drugs changes rapidly with outbreaks
- Supply chain management has become increasingly complex
  - ✓ Geopolitical risks, stricter regulations, and competition for talent
- Research and production are separated, making it difficult to circulate knowledge, talent, and investment

2

Connecting Research and Production

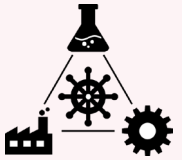


—Rebuilding the value creation loop in-house—

- Seamless technology collaboration with production, from research to industrialization, commercial production, and LCM
- End-to-end responsibility through post-launch product evolution and cost of goods reduction
- Controlling cost of goods and expenses to deliver rapid, high-quality, and stable supply

3

Our Aims through the Reintegration



—Expanding the scope, we can control in-house—

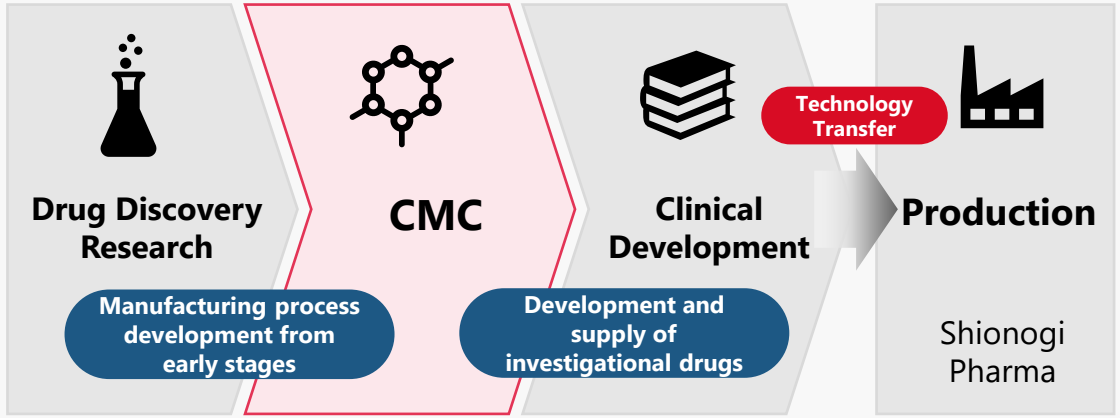
- Establishing manufacturing processes at our own plants and expanding to 2nd and 3rd sites in line with sales scale
- Implementing advanced product and manufacturing process design and quality management systems in pursuit of patient QOL (e.g., LAI)
- Domestic manufacturing site capable of supplying vaccines and therapeutics in times of emergency

Evolving the Role of CMC

Connecting R&D and production, and circulating on-site insights and technological innovation to continuously enhance product value

Current

Structure in which production and R&D are separated



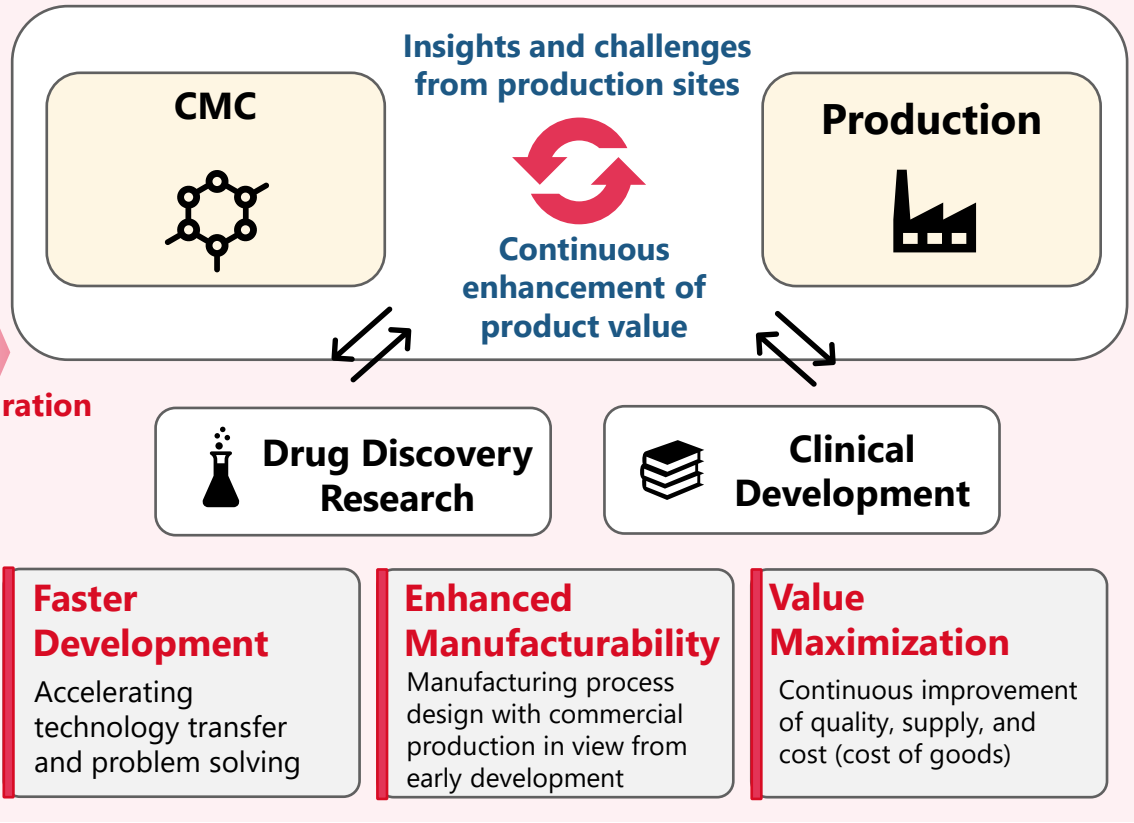
Challenges

- It takes time for insights from production sites to reach R&D
- Improvement cycles after technology transfer tend to become separated

Reintegration

Our Vision

Structure in which production and R&D are operated as one



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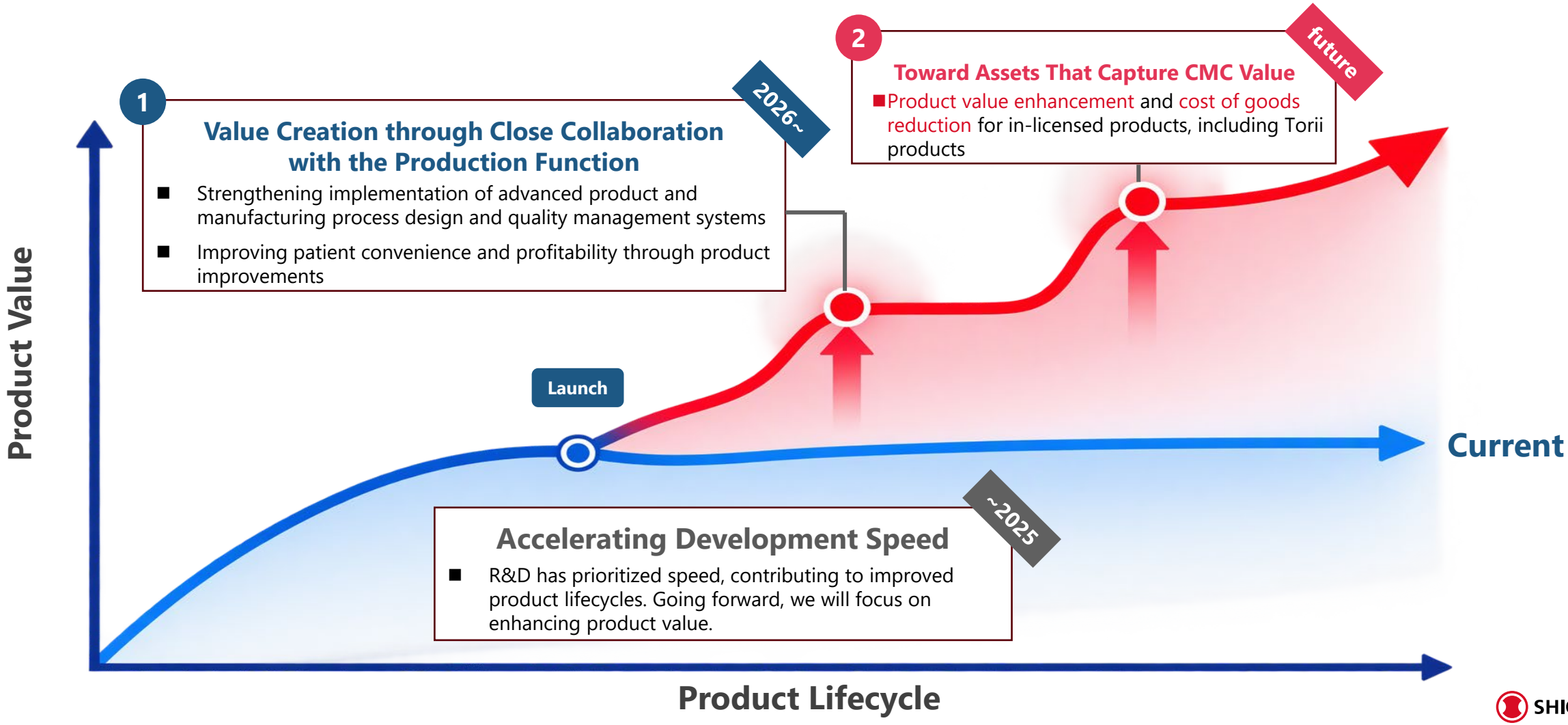
Continuous Enhancement of Product Value

Expanding the scope of value creation not only by accelerating development, but also through advanced manufacturing processes and post-launch value enhancement



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Closing

John Keller, PhD
Director of the Board, Senior Vice President, R&D Supervisory Unit

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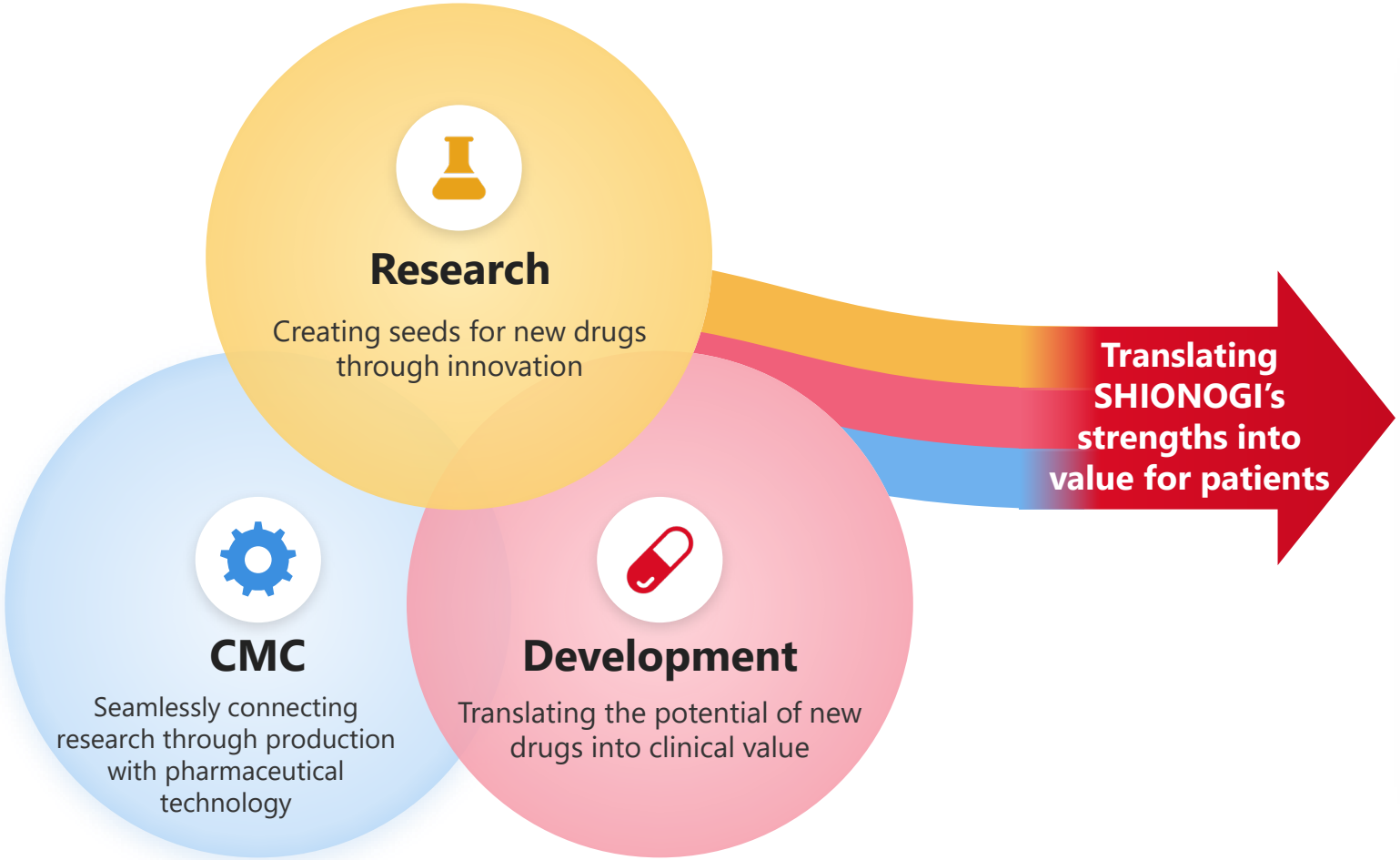
SHIONOGI's In-House Drug Discovery Capabilities

Leveraging our strength of having all essential drug discovery capabilities in-house to deliver the best medicines needed to protect people's health



In-house drug discovery products that meet the needs of patients and society

New Therapeutic Value

Treatment options not previously available

Reliable Quality and Safety

Medicines that patients can use with confidence

Better Treatment Experience

Medicines that fit patients' lives

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APPENDIX

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Overall Pipeline

Priority pipeline: 21 products

Neuromuscular Disease Area

- **Levacetylleucine** CACNA1A-related disorders
- **Zatolmilast** Fragile X syndrome
- **Zatolmilast** Jordan's syndrome
- **S-051051** Interstitial cystitis / bladder pain syndrome
- **S-606001** Pompe disease
- **S-262262** Neurodegenerative diseases

Infectious Disease Area

- **Secutrelvir** COVID-19 (oral, treatment)
- **Secutrelvir** COVID-19 (LAI, PrEP)
- **Olorofim** Invasive aspergillosis
- **S-337395** RSV infection
- **S-649228** Gram-negative bacterial infection
- **S-048133** Malaria
- **S-910978** Pulmonary MAB disease

Immune / Allergic Disease Area

- **TO-210** Acne vulgaris
- **TO-209** Grass pollen-induced allergic rhinitis
- **Cantharidin** Common warts
- **S-531011** MSS colorectal cancer (3L+)
- **S-531011** Postoperative MRD-positive MSS colorectal cancer
- **Redasemtide** Epidermolysis bullosa
- **S-462462** Atopic dermatitis

Next Growth Area

- **S-054502** Sleep apnea syndrome

Additional indications / formulations: 5 products

- **Ensitrelvir Fumaric Acid** Treatment of COVID-19 (Pediatric, 0 to 5 years)
- **Tapinarof** Atopic dermatitis in infant patients
- **Delgocitinib** Atopic dermatitis in pediatric patients
- **Naldemedine tosilate** Parkinson's disease with constipation
- **Naldemedine tosilate** Opioid-induced constipation (pediatric)

Other pipeline: 20 products

- **SR-0379** Cutaneous ulcer (Pressure ulcer, Diabetic ulcer)
- **SDS-881** Cognitive impairment in dementia
- **S-588410** Esophageal cancer
- **S-588410** Bladder cancer
- **S-488210** Head and neck squamous cell carcinoma
- **Redasemtide** Stroke
- **S-861861** Chronic heart failure
- **S-054501** Sleep Apnea with a Central Component
- **S-064064** Neurodegenerative diseases
- **S-162162** Autoinflammatory/Autoimmune diseases
- **S-461461** Chronic spontaneous urticaria
- **S-588210** Solid tumor
- **S-567123** Broad-spectrum coronavirus vaccine
- **S-263263** Peripheral artery disease
- **S-161161** Pulmonary arterial hypertension
- **S-229531** Autoimmune diseases
- **S-109802** Post-stroke upper- and lower-limb spasticity
- **S-540956** Nucleic acid adjuvant
- **S-872600** Influenza virus vaccine (intranasal)
- **S-213951** Obstructive sleep apnea (OSA)

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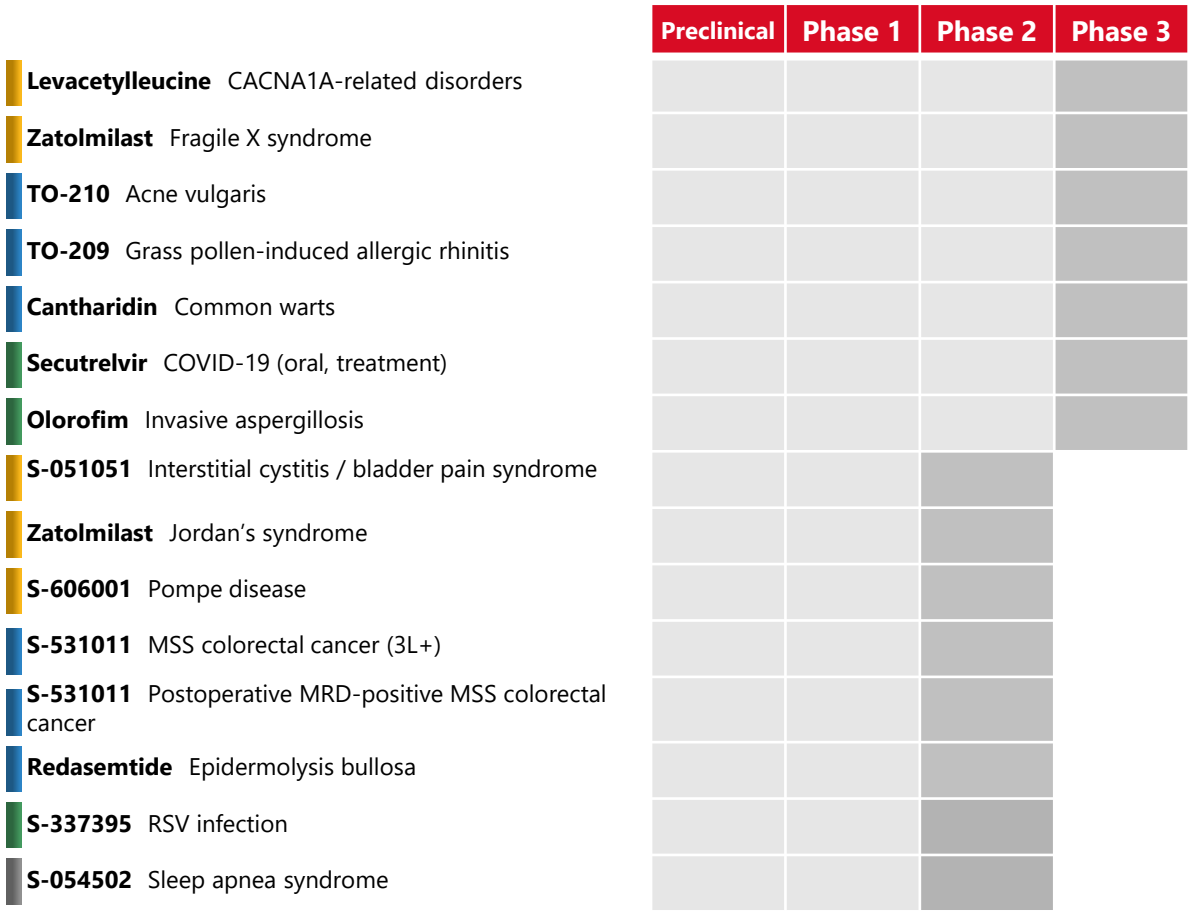
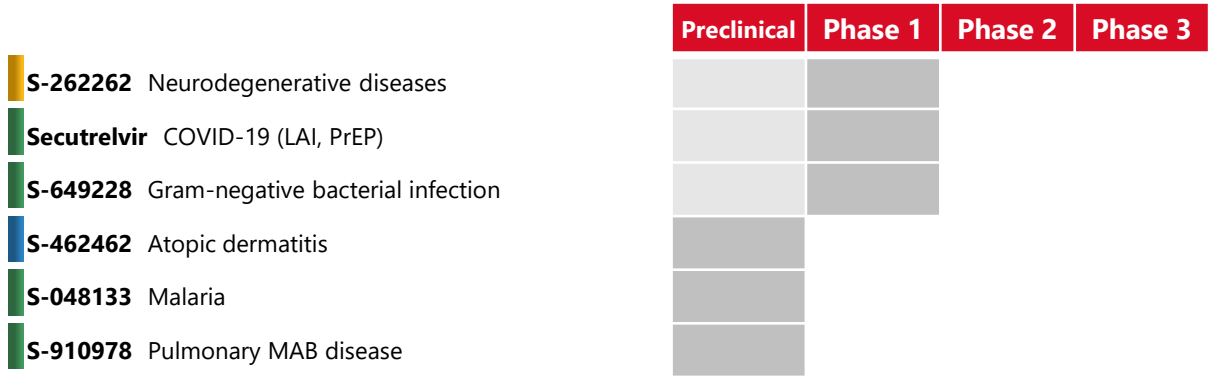
Priority Pipeline





Neuromuscular Disease Area | Immune / Allergic Disease Area | Infectious Disease Area | Next Growth Area

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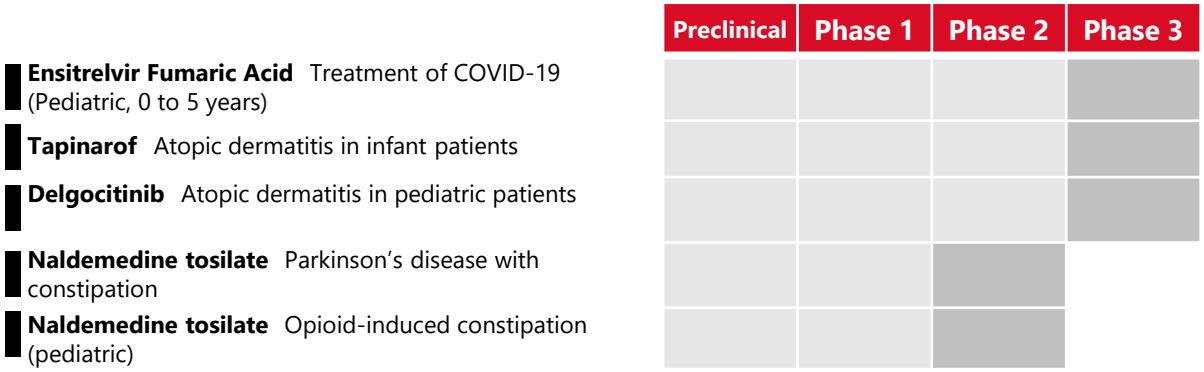
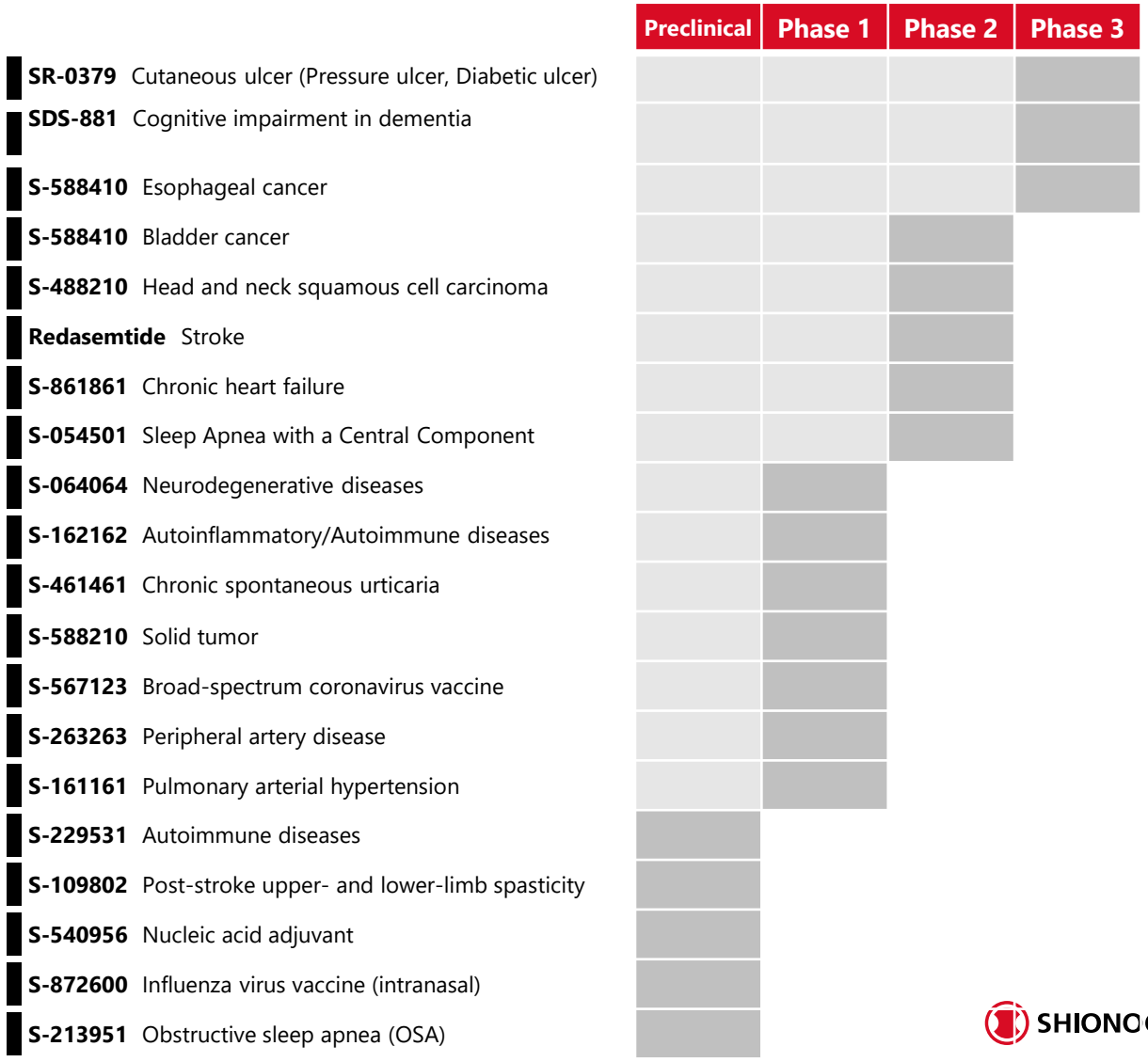
Pipeline - Additional Indications / Formulations, Others -





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