



# R&D Day

Innovative R&D and Late-stage Development Progress

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References to "FY" in this presentation for periods prior to 1 January 2018 are to the 12-month periods commencing in each case on April 1 of the year indicated and ending on March 31 of the following year, and the 9 month period from April 1 2017 to December 31 2017. From January 1 2018 the Company changed its fiscal year to the 12-month period commencing in each case on January 1. References to "FY" in this presentation should be construed accordingly.

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# Agenda

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Business update

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Supplementary Explanation for Q3FY2023 Results

1

# Business update

Chris Cargill, CEO

# Our mission

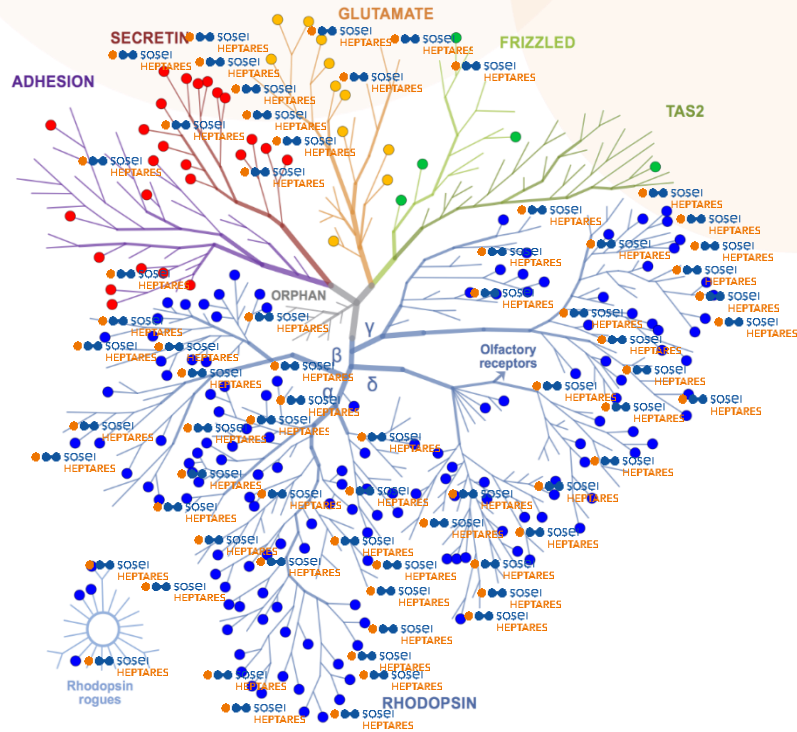


**BUILDING THE NEXT-GENERATION PHARMA COMPANY FOR JAPAN**

# Cutting-edge science

World leaders in structure-based drug design, strong focus on GPCR targets

## GPCRs MOST SUCCESSFUL TARGETS IN MODERN MEDICINE



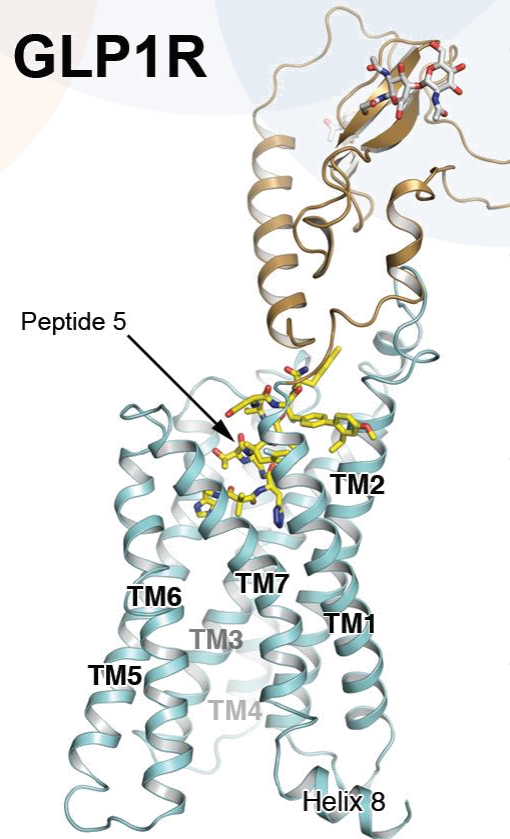
SOLVED **375+** MOLECULAR STRUCTURES  
FROM **50+** DIFFERENT RECEPTORS  
DEVELOPED **80+** StaRs

● Receptors for which a structure has been released in Protein Data Bank (public domain)

●●● Sosei Heptares Receptors for which Sosei Heptares has developed a StaR®

## FIRST TO SOLVE GLP-1R BOUND TO A PEPTIDE AGONIST

### GLP1R



- **Our science** highlights the complexity of receptor interactions
- **Our science** is globally recognized, as published in *Nature* (2017)
- **Our science** offers insights to enable GLP-1 drug discovery and development worldwide
- **Our science** makes a significant contribution to human health

# Cutting-edge science enables medicines by design

Exposed to the fastest growing area in healthcare

## GLP-1

## BEYOND GLP-1

## NEXT-GENERATION

BROAD INCRETIN/ UPSTREAM TARGETS (e.g. GLP-1/GIP/GCG)



PF'522  
Phase 1



Multiple Pre-discovery  
/ Discovery



Multiple Pre-discovery  
/ Discovery

**PFIZER AND LILLY ARE USING OUR SCIENCE TO ENABLE THEIR DRUG DESIGN FOR METABOLIC DISEASES**



# Cutting-edge science enables medicines by design

Exposed to the fastest growing area in healthcare

## Weight-Loss Drugs Bring in Even More Money Than Expected

- Billion-dollar-plus hauls lift Novo and Lilly's earnings
- Both company's revenues shot up nearly 40% this quarter



Sales of Lilly's diabetes drug Mounjaro hit \$1.41 billion in the third quarter, up more than 650% from a year ago. *Photographer: Sandy Huffaker/The Washington Post/Getty Images*

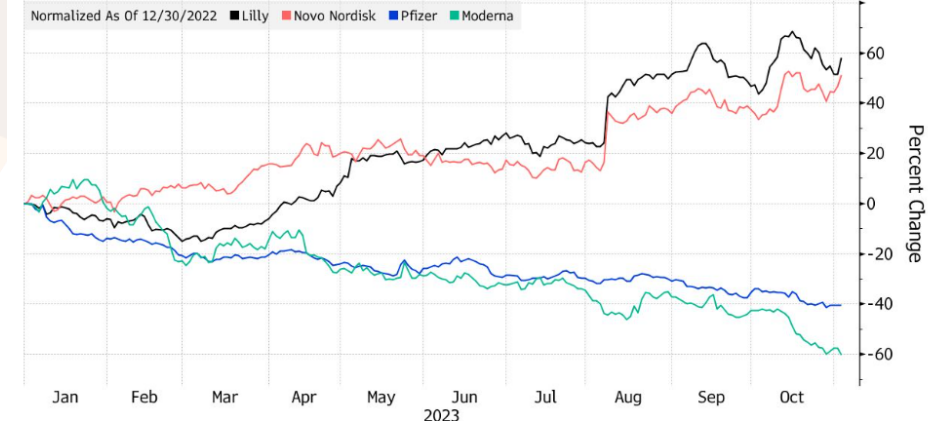
By [Madison Muller](#) and [Tim Loh](#)

3 November 2023 at 00:13 GMT+9

Updated on 3 November 2023 at 00:39 GMT+9

## Obesity Drugs Are the Hottest Thing in Health Care

Weight-loss stocks have soared while Covid shot makers falter



Source: Bloomberg

Bloomberg

And this could be just the beginning. Research is starting to show other potential benefits for heart and kidney disease from these treatments. Meanwhile, Lilly is testing whether a higher dose of Mounjaro will shed even more pounds. Both drugmakers are also testing their treatments in combination with others to see if those get better results and reduce unwanted side effects.

DIABETES AND OBESITY ARE JUST THE BEGINNING.  
EMERGING RESEARCH SUGGESTS BENEFITS IN HEART, LIVER AND KIDNEY DISEASES

Source: <https://www.bloomberg.com/news/articles/2023-11-02/weight-loss-drugs-are-bringing-in-even-more-money-than-expected>



# Medicines by design

Advancing through early clinical development

## IN-HOUSE PROGRAMS

GPR52 ag



**Neurology**  
Phase 1

EP4 ant



**Solid tumours**  
Phase 1

EP4 ag

**IBD**  
Phase 1 (H1 24)

## PARTNERED PROGRAMS

M<sub>4</sub> ag



**Schizophrenia**  
Phase 2

M<sub>1</sub>M<sub>4</sub> ag



**Neurology**  
Phase 1

mGlu<sub>5</sub> NAM



**Substance abuse**  
Phase 1

CCR6 ant



**IBD**  
Phase 1

MC4 ant



**Malnutrition**  
Phase 1

GLP-1 ag



**Metabolic diseases**  
Phase 1

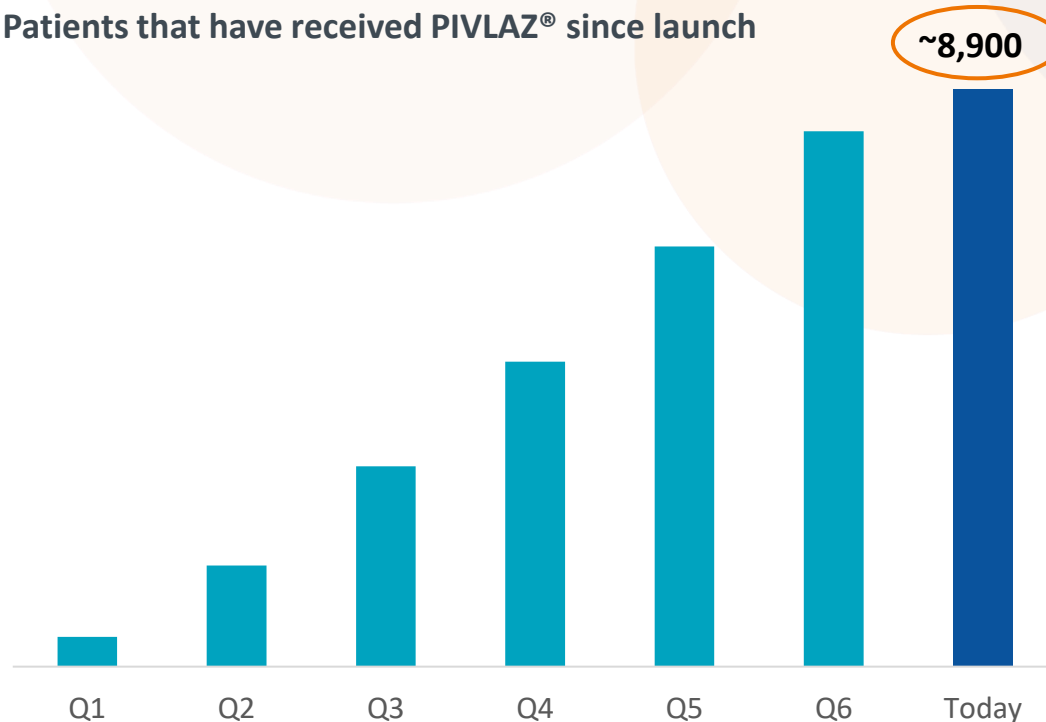
Clinical start in 2023

**FIVE CLINICAL STARTS** THIS YEAR BY US AND OUR PARTNERS

# Real human outcomes

First commercially available medicine (PIVLAZ<sup>®</sup>) protecting lives in Japan every day

Patients that have received PIVLAZ<sup>®</sup> since launch



*“The mechanism of action targets the root cause of cerebral vasospasm, which other drugs could not show”*  
– Neurosurgeon 1, University Hospital

*“PIVLAZ<sup>®</sup> was the first drug with a well-defined pathomechanism that I can prescribe confidently”*  
– Neurosurgeon 2, General Hospital

*“PIVLAZ<sup>®</sup> has a success rate of 30 out of 30 for me, not a single patient developed cerebral vasospasm”*  
– Neurosurgeon 3, University Hospital

*“The efficacy of PIVLAZ<sup>®</sup> is incomparable to other treatment options, I will not prescribe anything else”*  
– Neurosurgeon 4, General Hospital

**PIVLAZ<sup>®</sup> RAPIDLY BUILDING REAL WORLD EVIDENCE MITIGATING THE RISK OF CEREBRAL VASOSPASM**

# Real human outcomes

Daridorexant to contribute significantly to Japanese health (Q4 2024 potential launch)



**15 TRILLION YEN (3% GDP)**  
ECONOMIC LOSS

Due to decreased productivity



**604,000**  
LOST WORKING DAYS / YEAR

Due to absences and sick leave



**10%**  
HIGHER MORTALITY RISK

If average <6 hrs sleep per night

THE IMPACT OF SLEEP DISORDERS ON JAPANESE SOCIETY IS SIGNIFICANT.  
**DARIDOREXANT IS A BEST-IN-CLASS SOLUTION FOR INSOMNIA**

Source: "Why sleep matters – the economic costs of insufficient sleep" (2016) RAND Research Reports

# Our mission, in progress

## CUTTING-EDGE SCIENCE



World-leader in SBDD, using AI/ML tools, **accelerating** new drug discovery



Exposure to fastest growing area of healthcare, **revolutionizing** treatments for metabolic diseases

## MEDICINES BY DESIGN



Exclusive opt-ins for Phase 3-ready products, **building** our commitment to healthcare in Japan



Additional pipeline of 30+ medicines by design, **adding** new programs and partners every year

## REAL HUMAN OUTCOMES



PIVLAZ® launch ongoing, **protecting** patients daily



Daridorexant NDA filing submitted to PMDA, **transforming** the management of sleep disorders

# 2

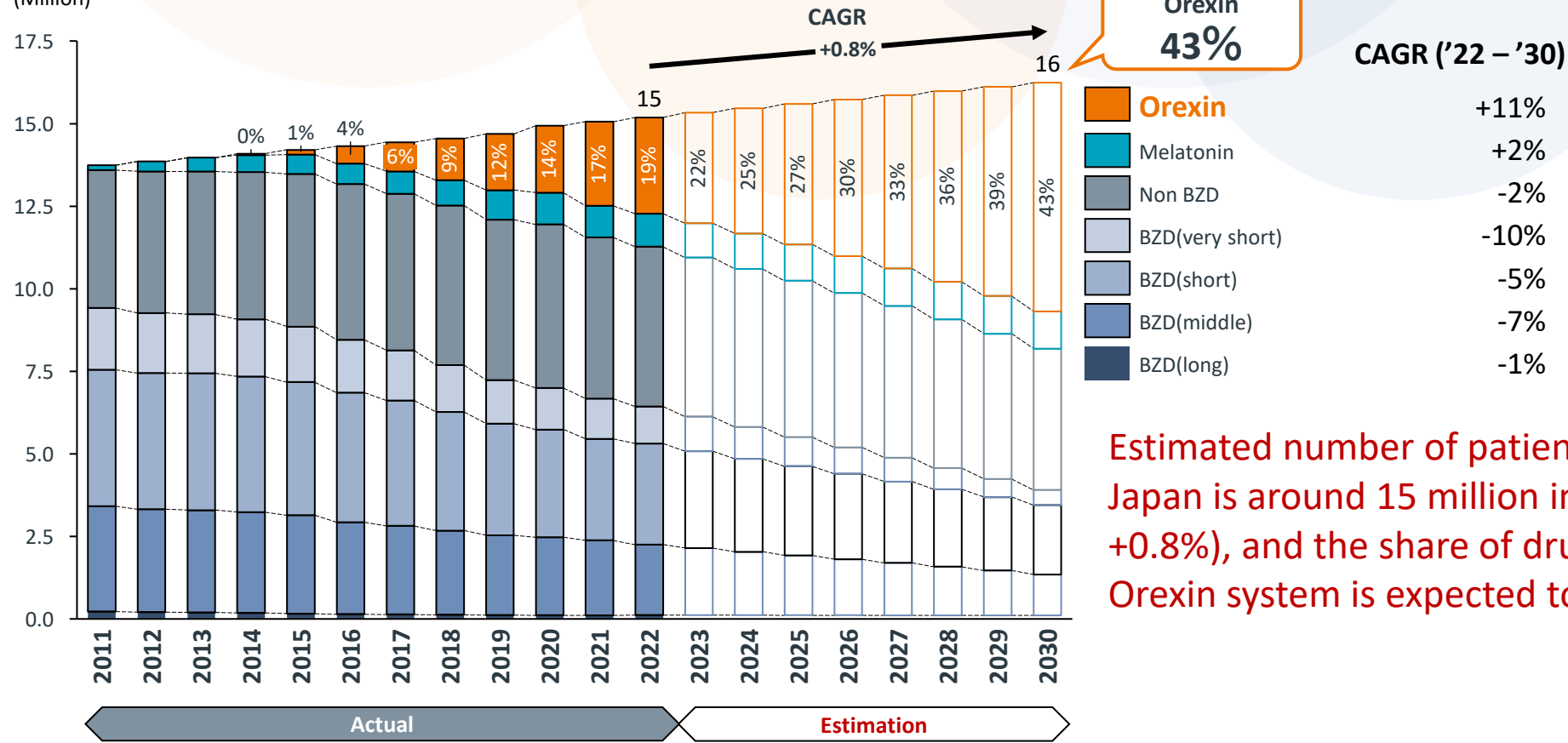
## Development and Sales in Japan and APAC

Dr. Satoshi Tanaka, President of IPJ/IPK

# Insomnia: potential in Japan of drugs targeting the Orexin system

Market size of orexin system is expected to grow rapidly

Number of Patients (Million)



Source: IQVIA JPM (2011-2022/07MAT)

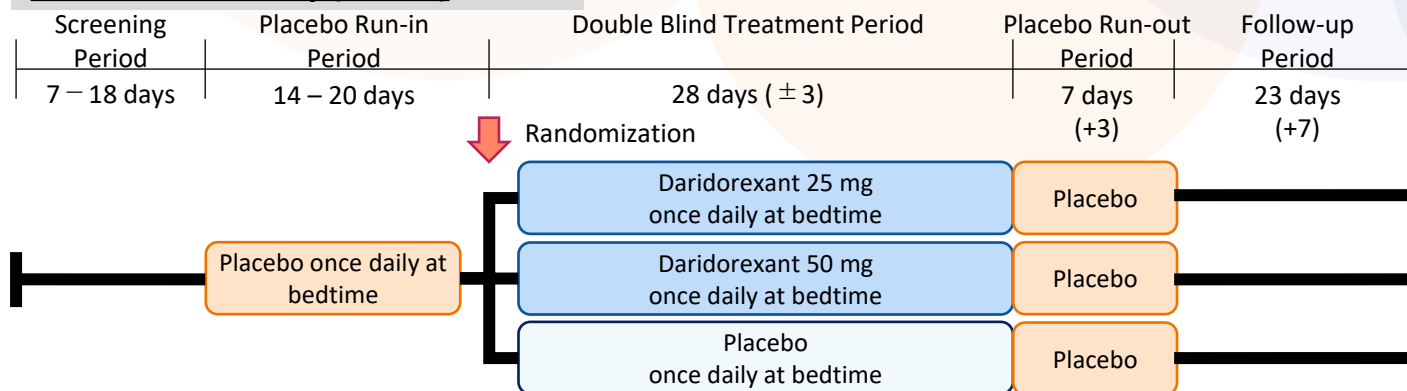
# NDA submission of daridorexant

NDA submission on 31 Oct 2023 based on the excellent results of Japanese Phase 3 studies

## Japanese Phase 3 study design

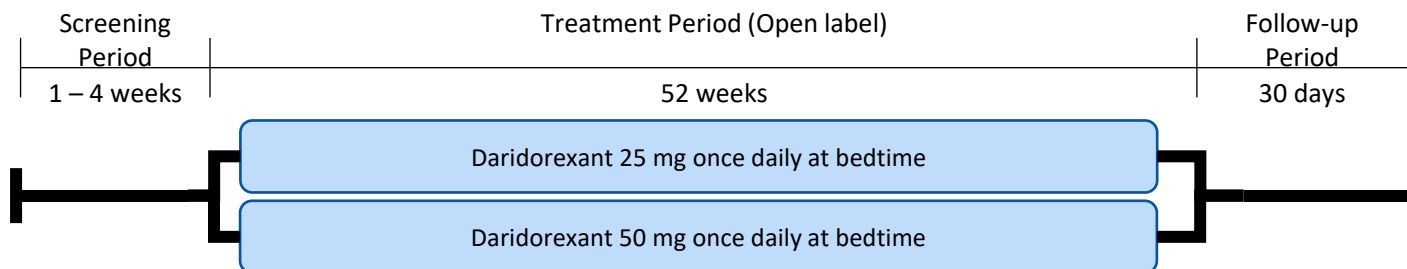
## Double blind study results

### Double blind study (n=490)



- Efficacy endpoint: sTST and sLSO at Week 4
- Other endpoints : other sleep parameters (sWASO, etc.), safety

### Long-term study (n=154)



- Endpoints: safety, sleep parameters (sTST, sLSO, sWASO, etc.)

### Efficacy

sTST (compared to placebo at 28 days)

- 25 mg:  $p = 0.042$
- 50 mg:  $p < 0.001$

sLSO (compared to placebo at 28 days)

- 25 mg:  $p = 0.006$
- 50 mg:  $p < 0.001$

### Safety

Treatment-emergent adverse events

- Placebo: 24.4%
- 25 mg: 22.7%
- 50 mg: 23.5%

# Cenerimod (S1P<sub>1</sub> receptor modulator)

S1P<sub>1</sub> receptor modulator proven to be effective for treating multiple immune-related diseases



## S1P<sub>1</sub> receptor

- Sphingosine-1-phosphate receptor 1 (S1P<sub>1</sub>) is a GPCR receptor that regulates a wide range of biological processes, especially **immune responses (both T cell and B cell)**
- Modulation of S1P receptors regulates immune responses by inhibiting the egress of lymphocytes into the circulation
- Mechanism being targeted multiple disease as follows;



## Inflammatory Bowel Diseases

- Ulcerative Colitis
  - Ozanimod (BMS)
  - Etrasimod (Pfizer, approved)
- Crohn's disease
  - Ozanimod (BMS)



## Autoimmune Diseases

- Multiple Sclerosis
  - Ozanimod (BMS)
  - Ponesimod (J&J)
  - Siponimod (Novartis)
  - Fingolimod (Novartis /Mitsubishi Tanabe, approved)



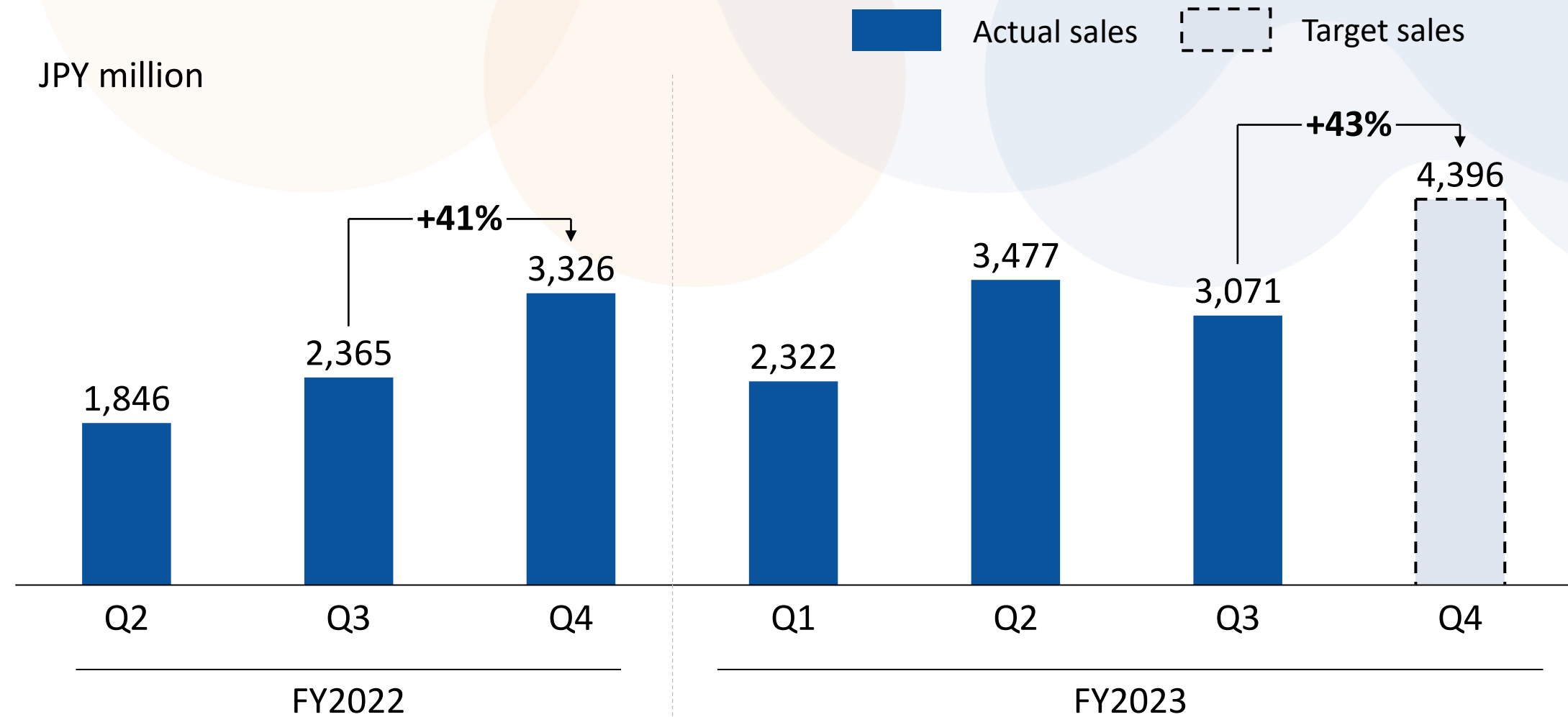
## Cenerimod

- Orally available selective S1P<sub>1</sub> modulator
- Idorsia Ltd. is developing cenerimod in Phase 3 trials as a therapy for SLE
- As cenerimod has potential to treat a wide range of immune-related disease, Sosei Heptares will initiate a rapid development program in an indication where it can be positioned and launched as a first-in-class therapy



# Sales trend and target of PIVLAZ<sup>®</sup> (NHI based sales)

Sales Target in 2023 : JPY 13,266 million



# PIVLAZ<sup>®</sup> included in Japanese Guidelines for the management of STROKE

PIVLAZ<sup>®</sup> demonstrated the true endpoints of SAH with higher level of evidence



## Japanese Guidelines for the management of STROKE



## The impact of inclusion in the guideline

PIVLAZ<sup>®</sup> (clazosentan) was officially authorized and recommended by the Japanese Stroke Society in Aug '23 owing to quality of evidence demonstrated by pivotal Phase 3 studies conducted in Japan.

### IV. Subarachnoid Hemorrhage

#### 7-1 Treatment of Delayed Cerebral Vasospasm

2023 Guideline Recommendation			
	PRODUCT	RECOMMENDATION LEVEL	EVIDENCE LEVEL
1	Clazosentan	B	MEDIUM
2	Fasudil	B	LOW
3	Ozagrel Sodium	B	LOW

Included from 2023

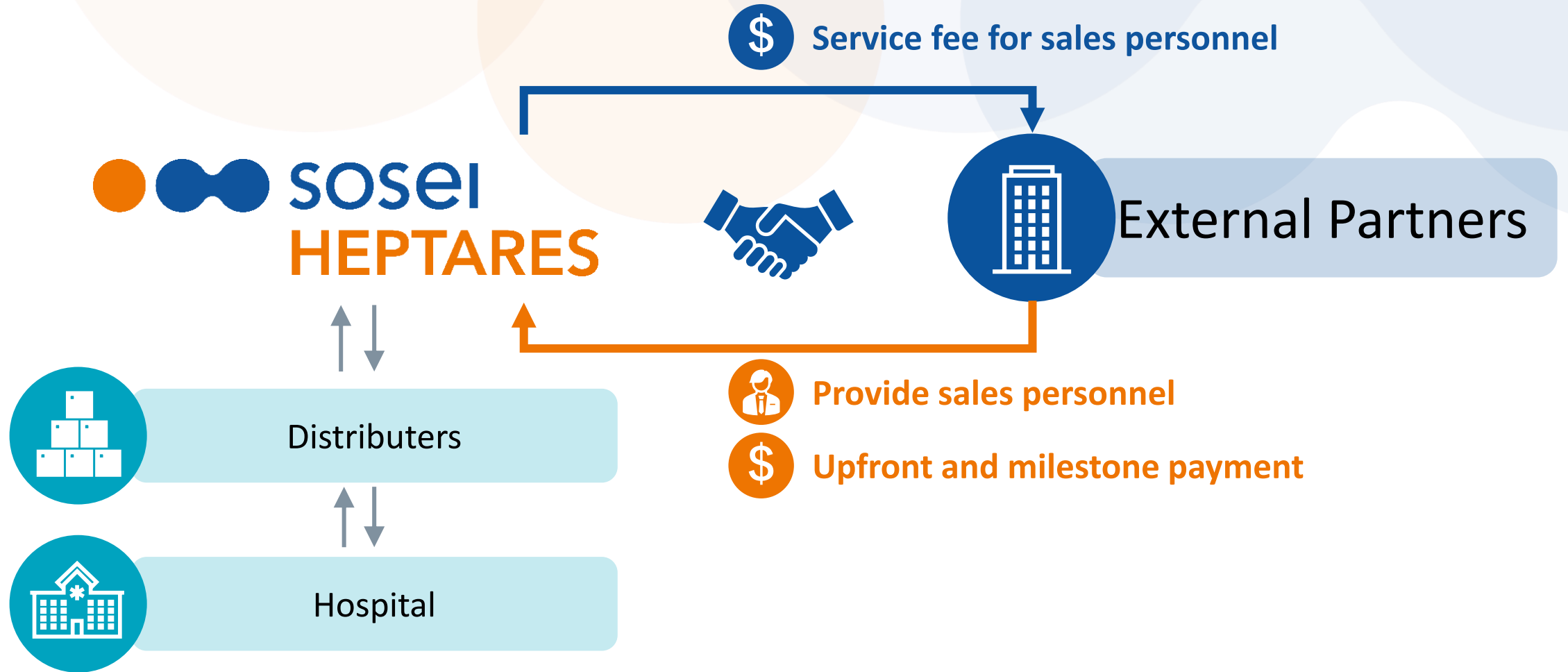
- Provides confidence to neurosurgeons to prescribe PIVLAZ<sup>®</sup> as a new standard of care for SAH based on strong evidence it can prevent delayed cerebral ischemia (DCI) and poor outcomes
- The Guidelines for recommending the treatment of vasospasm have not been revised for over several years, so most neurosurgeons have been paying close attention to that revision
- Inclusion in the Guidelines is expected to be a trigger for neurosurgeons to switch from prescribing conventional treatments to new evidence-based medicines such as PIVLAZ<sup>®</sup>

DCI: delayed cerebral ischemia, SAH: Subarachnoid hemorrhage

Source: Japanese Stroke Society Guideline 2021 for the Management of Stroke (Revised Version 2023)

# Leverage commercial capability by using external resource

Creating commercial synergies to optimize sales and distribution



3

## Progress in UK R&D

Dr. Matt Barnes, President of Heptares  
and Head of UK R&D

# Partnered Programs (1)

## Neurocrine Biosciences Collaboration

### Neurocrine Biosciences Advancing Muscarinic Portfolio

Clinical studies, include:

- **Initiated Phase 2 placebo-controlled study of NBI-1117568\*, a selective M4 agonist, as a potential treatment for schizophrenia**
  - ✓ NBI-1117568 offers the potential for an improved safety profile:
    - ❑ Without the need of combination therapy to minimize side effects
    - ❑ Avoids the need of cooperativity with acetylcholine when compared to non-selective muscarinic agonists and positive allosteric modulators in development
- **Initiated Phase 1 Study for NBI-1117570\*, a dual M1 / M4 agonist**
- **Anticipate advancing additional muscarinic compounds into clinic over the coming months**

# Partnered Programs (2)

## Highlights

### Clinical & Pre-clinical Programs



Oct. '23

#### Clinical Program

- **PF-06954522**, a new oral small molecule **GLP-1 receptor agonist** progressed into Phase 1 clinical trials targeting the treatment of metabolic diseases.



Sep. '23

#### Clinical Program

- **NBI-1117570**, a selective **M1/M4 dual agonist** progressed into Phase 1 clinical trials for potential treatment of neurological and neuropsychiatric conditions.



TEMPERO BIO™

Jan. '23

#### Clinical Program

- **TMP-301**, a selective **mGluR5 NAM** progressed into clinical trials for alcohol and substance use disorder
- CEO of Aditum Bio commented this program is expected to move into Phase 2 in 2024 <sup>1)</sup>



Oct. '23

#### Pre-Clinical Program

- Preclinical data supporting best-in-class potential of **OX750**, an oral **OX2R agonist** for treatment of narcolepsy and other sleep-wake disorders presented at the World Sleep Congress (Oct '23)

### Discovery & Technology Collaborations

Genentech

A Member of the Roche Group

Oct. '23

#### Discovery Program

- **\$3.75M** payment for the progression of a potential first-in-class project targeting an undisclosed GPCR

<sup>1)</sup> Endpoints news (October 20, 2023)



Oct. '23

#### AI drug design

- Drug discovery collaboration expanded to a second neurological target
- SBDD + chemUNIVERSE

verily

Oct. '23

#### Target ID/ Validation

- Nomination and validation of first GPCR target for drug discovery in IBD
- Immune Profiler platform

KALLYOPE

Nov. '23

#### Gut-brain axis platform

- Nomination of first GPCR target for therapeutic development in Gastrointestinal Diseases
- Gut-brain axis platform



# Wholly-owned clinical & peri-clinical programs

Advancing priority programs into early clinical studies



Immunosuppression  
in solid tumors

EP4 antagonist

- Once daily oral small molecule
- Combination with checkpoint inhibitors
- Collaboration with Cancer Research UK

Ph1 initiated: Aug 2023



- Participants: 150 patients
- Estimated duration: 8/2023 - 9/2026

- Patients dosed with no DLTs or SUSARs reported
- Two clinical sites currently open with a third anticipated to open imminently



Schizophrenia  
and Psychosis

GPR52 agonist

- Once daily oral small molecule
- 24hr target engagement

Ph1 initiated: June 2023

- Participant: 104 healthy volunteers
- Estimated duration: 6/2023 - 11/2024

- Clinical trial is proceeding as planned with good progress through dose escalation



Inflammatory  
Bowel Disease

EP4 agonist

- Oral GI restricted
- Good potency and selectivity
- Minimal GI systemic exposure

Ph1 initiation target: H1 2024

- Regulatory submission to commence trial planned for Q4 2023

- Preclinical evaluation is ongoing and on track
- H1 2024 Phase 1 start

DLT: Dose Limiting Toxicities, SUSAR: Suspected Unexpected Serious Adverse Reactions

EP4 Ant study link: <https://clinicaltrials.gov/study/NCT05944237?term=Heptares&viewType=Table&page=2&rank=15>

GPR52 Ag study link: <https://www.isrctn.com/ISRCTN17231793?q=&filters=&sort=&offset=58&totalResults=23608&page=6&pageSize=10>

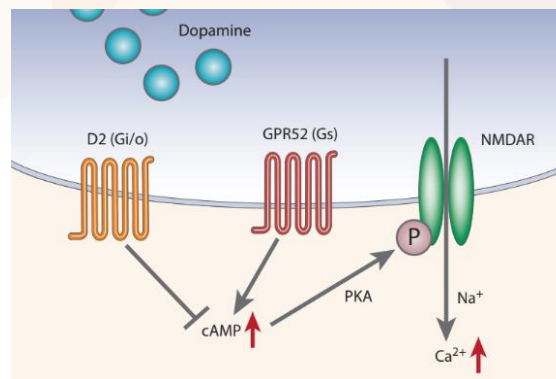


# GPR52 agonist – a novel approach to treat schizophrenia

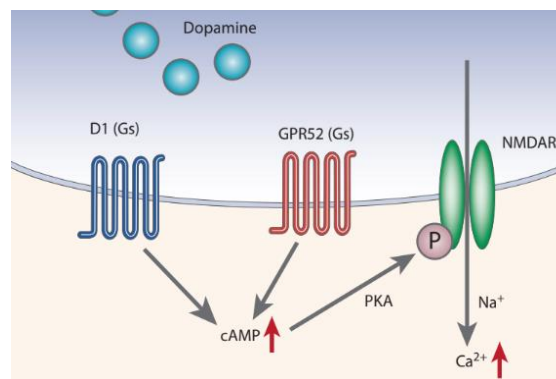
## Mechanism

## Preclinical results

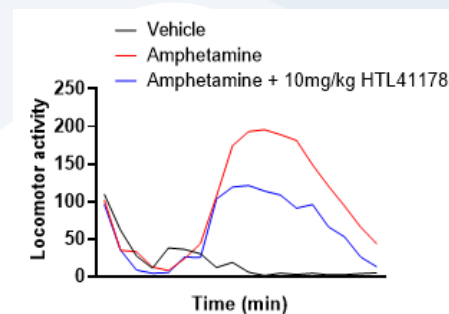
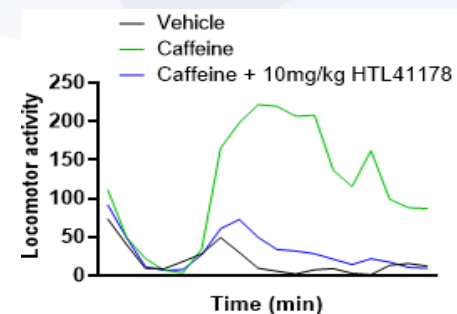
**Striatum**  
– GPR52 & D2



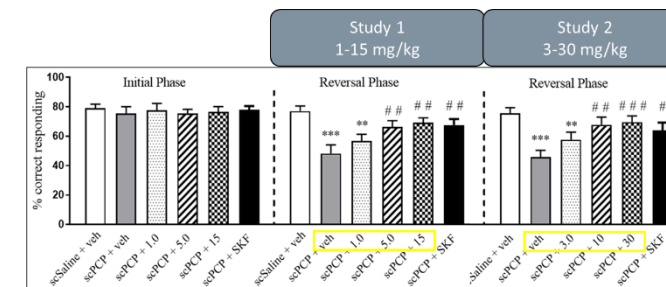
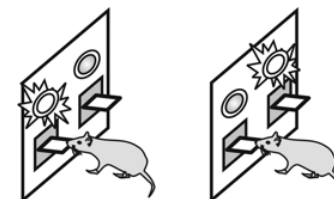
**Frontal Cortex**  
– GPR52 & D1



- HTL0041178 **blocks psychostimulant-hyperlocomotion** in rodents



- HTL0041178 **improves cognitive flexibility** in subchronic PCP rat



PCP: phencyclidine

Poulter et al. ACS Med Chem Lett. 2023;14(4):499-505; MacSweeney et al. SOBP 2020 (poster); MacSweeney et al. SIRS 2022 (poster)



# In House Portfolio – Future Programs

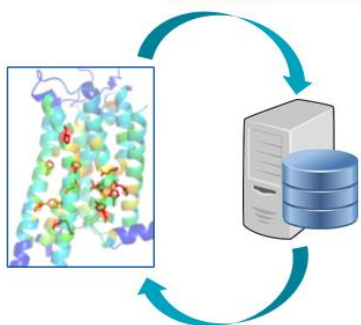
Several internal targets

	1	2	3
	<b>Inflammatory bowel disease</b>	<b>Major Depressive Disorder</b>	<b>Metabolic Disorders</b>
<b>Stage</b>	Pre-clinical	Discovery	Pre-discovery
<b>Target Product Profile</b>	Once daily, first-in-class oral small molecule	Once daily, best-in-class oral small molecule	Once daily, first-in-class oral small molecule
<b>Next Milestone</b>	Phase 1 start	Pre-clinical development	Discovery
<b>Mechanism of Action</b>	Mucosal healing concept - targeting gut epithelial cells axis aimed at promoting barrier repair	Modulation of dopaminergic transmission in reward circuits	Modulation of broad incretin release (inc. GLP-1; GIP; GCG) and appetite suppression. Upstream of current GLP-1 small molecule agonists

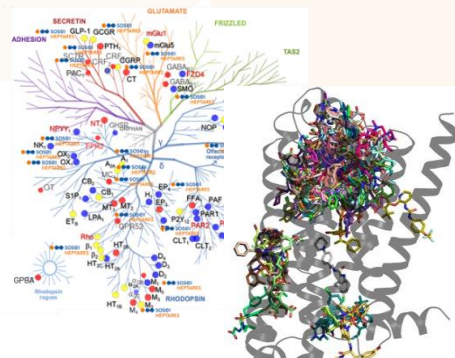
# R&D Artificial Intelligence (AI)/Machine Learning (ML) Approaches

Broad application of AI techniques across multiple functions

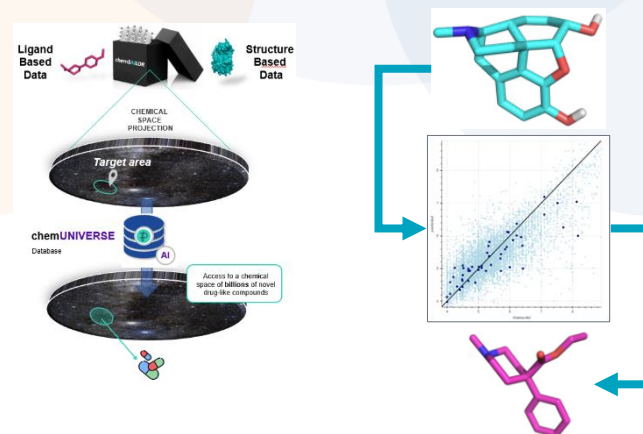
## StaR®



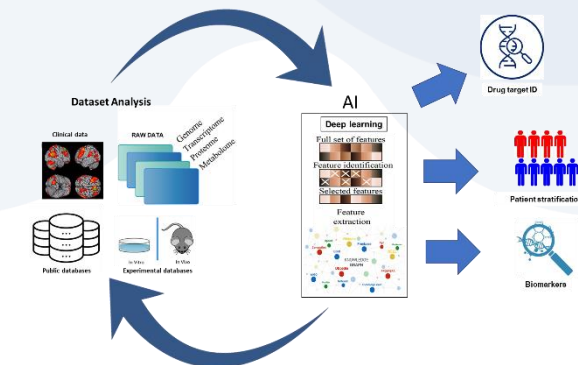
## Structure



## Molecule Design



## Translational Medicine



Approach

- GPCR rich mutagenesis datasets are mined using ML algorithms to predict future StaR® enabling mutations
- AI used to predict GPCR binding site/mode using database of proprietary internal/external structures
- Hit ID through AI-assisted medicinal chemistry expertise
- ML based QSAR models based on proprietary internal and public datasets
- AI led analysis of large patient datasets to identify biomarkers and stratify patients



Impact

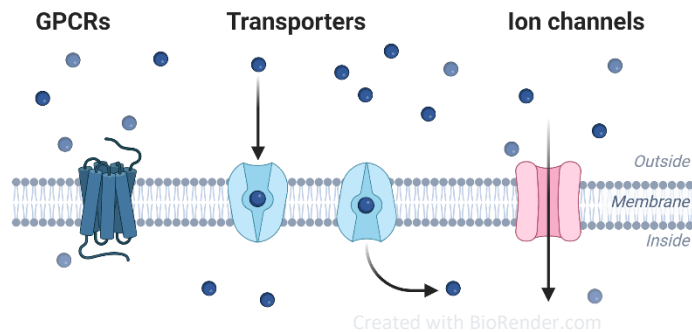
- Accelerates StaR® generation
- Improves breadth and depth of GPCR homology models to support molecule optimization and virtual screening.
- Supports identification of novel chemical series
- Supports optimization of chemical series to improve drug like properties
- Enables the design of the 'right' clinical studies

# Future Innovation & Platform Growth

Investing in non-GPCR membrane drug targets and laboratory expansion

## Non-GPCRs

- Utilizing know-how to explore other membrane protein target classes.
- Ion channels and transporters projects initiated
- Drug targets with strong validation selected where SBDD approach offers differentiation
- Opportunity to demonstrate technical feasibility & generate best-in-class medicines in our therapeutic areas of interest

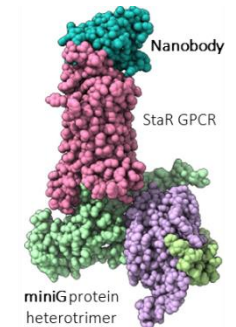


## Laboratory Expansion

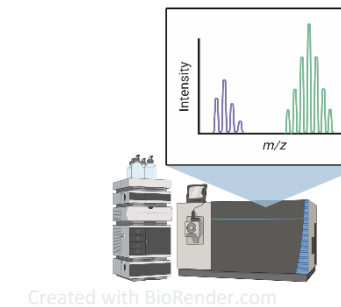
- Completion of additional laboratory space – October 2023



- New Phage Display lab created to utilize naïve nanobody libraries to screen against purified GPCR StaR® targets – identify Protein Binders to support cryo-EM and SBDD platform



- New Mass Spectrometry (MS) facility created & state-of-the-art mass spectrometer purchased to drive advanced GPCR MS methodologies.



4

# Supplementary Explanation for Q3FY2023 Results

Hironoshin Nomura, CFO

# Breakdown of Q3 FY2023 result

Because of M&A, Non-cash/Non-recurring cost impacted 3rd quarter results

(JPY million)	Sosei Heptares* (1Q-3Q : 9month)	+	IPJ/IPK* (7/20-9/30 : c.2.4month)	=	Consolidated P/L (Core)	+	Non-cash cost	+	Non-recurring Costs	=	Consolidated P/L (IFRS)
Revenue	3,130		2,344		5,474						5,474
CoS + SG&A	(2,501)		(1,379)		(3,880)		(226)	(684)	(1,272)		(7,364)
								Amortization of products	Current PIVLAZ® stock		
									M&A-related fee		
									Others		
R&D	(6,112)		(313)		(6,425)				(588)		(7,013)
Other income	906		6		912						912
OP/Core OP	(4,577)		658		Core OP (3,920)						OP (7,992)

M&A related Adjustments  
(total. JPY 2,182 mil.)

- A** Additional CoS charge only for current PIVLAZ® stock. This impact will continue until around Apr 2024.
- B** Amortization of intangible assets (relating to PIVLAZ® and Daridorexant). Plan to be c. JPY 1,800 million / year from 2025.
- C** One time M&A related fee covering the IPJ/IPK transaction and evaluation of other potential opportunities was basically fully charged in Q3 2023.

\* Sosei Group, Sosei Co. Ltd. and Heptares Therapeutics Ltd., IPJ: Idorsia Pharmaceuticals Japan, IPK: Idorsia Pharmaceuticals Korea



# Appendix

# Exclusive Opt-in Rights And ROFN/ROFR<sup>1</sup>

Option to develop up to seven clinical programs for Japan and APAC (ex-China) from Idorsia

	Program	Mechanism of Action	Indication**	Stage	Region
Exclusive Opt-in Right	Cenerimod	S1P <sub>1</sub> receptor modulator	Systemic lupus erythematosus	Phase 3	APAC (ex-China) <sup>2</sup>
	Lucerastat	Glucosylceramide synthase inhibitor	Fabry disease	Phase 3	
ROFR /ROFN <sup>1</sup>	Selatogrel	P2Y <sub>12</sub> antagonist	Suspected acute myocardial infarction	Phase 3*	
	ACT-1004-1239	ACKR3 / CXCR7 antagonist	Multiple sclerosis and other demyelinating diseases	Phase 2*	
	ACT-1014-6470	C5aR1 antagonist	Immune-mediated disorders	Phase 1*	
	IDOR-1117-2520	Undisclosed	Immune-mediated disorders	Phase 1*	
	ACT-777991	CXCR3 antagonist	Recent-onset Type 1 diabetes	Phase 1*	

<sup>1</sup> ROFN/ROFR - Right of first negotiation / Right of first refusal

<sup>2</sup> Territories include Japan, South Korea, Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand and Vietnam

\* Global Phase

\*\* This is an indication currently under development, but does not necessarily mean that Sosei will develop for this indication

# Introduction of ‘Core Operating Profit’

Core Operating Profit – the financial indicator closer to the reality of our business

## Operating Profit “IFRS”

- Financial results recorded and prepared in accordance with International Financial Reporting Standards (IFRS)

### + Material Non-cash Costs

(Depreciation, Amortization, Share based payments, Impairment...etc.)

### + Material Non-recurring Costs

(Restructuring costs and Other material one-off items...etc.)



















## Operating Profit “Core”

- Core Operating Profit is a new key financial indicator that highlights the underlying recurring cash generating capability of the business.
- Core Operating Profit is defined as IFRS Operating Profit + material Non-cash costs + material non-recurring costs
- Material Non-cash Costs include depreciation, amortization, share based payments and impairment.
- Material Non-recurring Costs include restructuring costs and other material one-off items.
- Core Operating Profit = Cash Earnings + material Non-recurring Costs

	Cash	Non-cash (Material)
Recurring	Costs under “Core”	
Non-recurring (Material)		Costs under “IFRS”










# Partnered pipeline

Compound	Target / Mechanism of Action	Modality	Indication	Partner	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
Partnered											
Seebri® Breezhaler®	LAMA	SME	COPD	 NOVARTIS	█	█	█	█	█	█	█
Ultibro® Breezhaler®	LAMA+LABA	SME	COPD	 NOVARTIS	█	█	█	█	█	█	█
Energair® Breezhaler®	LAMA+LABA+ICS	SME	Asthma	 NOVARTIS	█	█	█	█	█	█	█
ORAVI®	Antifungal agent miconazole	SME	Oropharyngeal candidiasis	 Hisamitsu	█	█	█	█	█	█	█
Imaradenant <sup>1</sup>	Adenosine A2a ant. combo	SME	mCRPC	 AstraZeneca	█	█	█	█	█	█	█
NBI-1117568	Muscarinic M4 agonist	SME	Schizophrenia	 NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
(Not disclosed)	Muscarinic M1 agonist	SME	Neurology diseases	 NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
NBI-1117570	Muscarinic M1/M4 agonist	SME	Neurology diseases	 NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
PF-07081532	GLP-1 agonist	SME	T2DM/Obesity	 Pfizer	█	█	█	█	█	█	█
PF-07054894	CCR6 antagonist	SME	Inflammatory bowel disease	 Pfizer	█	█	█	█	█	█	█
PF-07258669	MC4 antagonist	SME	Malnutrition	 Pfizer	█	█	█	█	█	█	█
PF-06954522	GLP-1 agonist	SME	Metabolic diseases	 Pfizer	█	█	█	█	█	█	█
(Not disclosed)	CGRP antagonist	SME	Neurology diseases	 Pfizer	█	█	█	█	█	█	█
(Not disclosed)	GPR35 agonist	SME	Inflammatory bowel disease	 GSK	█	█	█	█	█	█	█
(Not disclosed)	Multi target	SME/LME	Multiple indications	 Genentech <small>A Member of the Roche Group</small>	█	█	█	█	█	█	█
(Not disclosed)	Multi target	SME/LME	Gastrointestinal and other	 Takeda	█	█	█	█	█	█	█
(Not disclosed)	Multi target	SME	Inflammatory/Neurology	 abbvie	█	█	█	█	█	█	█
(Not disclosed)	Multi target	SME	Diabetes/Metabolic	 Lilly	█	█	█	█	█	█	█



































Note: SME = small molecule. LME = large molecule. Seebri®, Ultibro®, Energair® and Breezhaler® are registered trademarks of Novartis AG. <sup>1</sup> AstraZeneca have removed the A2a program from their clinical pipeline as at Q3 2021

# Partnered pipeline (cont'd)

Compound	Target / Mechanism of Action	Modality	Indication	Partner	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
<b>Co-development</b>											
KY1051	CXCR4 mAb	mAb	Immuno-oncology	<b>sanofi</b>	██████████						
(Not disclosed)	PAR-2	Peptide	Inflammatory diseases		██████████						
(Not disclosed)	Targeted Protein Degradation	SME	Gastrointestinal disorders		██████████						
(Not disclosed)	AI-Augmented Drug Discovery	SME	Neurology diseases		██████████						
(Not disclosed)	Multi target AI-powered	SME/LME	Immune diseases		██████████						
(Not disclosed)	Multi target AI-powered	SME/LME	Immune diseases	<b>verily</b>	██████████						
(Not disclosed)	Gut-brain axis drug discovery	SME	Gastrointestinal disorders	<b>KALLYOPE</b>	██████████						
<b>Co-owned companies</b>											
TMP301	mGlu5 NAM	SME	Substance use disorders		██████████						
ORX750	OX2 agonist (Oral)	SME	Narcolepsy	 	██████████						

Note: SME = small molecule. LME = large molecule

# In-house pipeline

Compound	Target / Mechanism	Modality	Indication	Originator	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
<b>In-house Programs</b>											
PIVLAZ®	ETA antagonist	SME	Cerebral vasospasm								
Daridorexant	Dual Orexin antagonist	SME	Insomnia								
HTL'149	GPR52 agonist	SME	Neurology diseases								
HTL'732	EP4 antagonist	SME	Immuno-oncology								
(Not disclosed)	EP4 agonist	SME	Inflammatory bowel disease								
(Not disclosed)	Muscarinic M1 agonist (JP)	SME	Neurology diseases								
(Not disclosed) <sup>1</sup>	H4 antagonist	SME	Atopic Dermatitis								
(Not disclosed)	SARS CoV-2 Mpro	SME	Coronaviruses								
Multiple programs	Not disclosed	SME/LME	Neurology diseases								
Multiple programs	Not disclosed	SME/LME	GI and Inflammatory diseases								
Multiple programs	Not disclosed	SME/LME	Immunology diseases								
<b>In-house Programs (No longer internally funded. Targeting academic / industrial partnership)</b>											
HTL'310	SSTR5 agonist	Peptide	Hypoglycaemic disorders								
HTL'097	GLP-1 antagonist	Peptide	Hypoglycaemic disorders								
HTL'023	Dual GLP-2/GLP-1 agonist	Peptide	Intestinal failure/NASH								
(Not disclosed)	Apelin agonist	Peptide	Pulmonary Arterial Hypertension								
HTL'641	Dual orexin antagonist	SME	Insomnia and sleep disorders								
(Not disclosed)	PAR-2 mAb	mAb	Atopic Dermatitis/Pain								

Note: SME = small molecule. LME = large molecule. <sup>1</sup>Due to changes of strategy, we deprioritized until we will find another indication opportunity

# (For Reference) IPJ\* Standalone Operating Results

(JPY million)

	FY2022	FY2023 2Q
<b>Revenue</b>	<b>11,709</b>	<b>5,950</b>
Product sales	6,254	4,812
Contract revenue (from related parties)	5,455	1,138
CoS	1,959	1,692
R&D	4,485	1,034
SG&A	4,475	2,876
<b>Operating profit</b>	<b>790</b>	<b>348</b>
<b>Net income</b>	<b>468</b>	<b>158</b>

\* IPJ: Idorsia Pharmaceuticals Japan

# Locations

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