

A background image showing a male scientist in a white lab coat and glasses looking through a microscope on the left, and a female scientist in a white lab coat looking down at a document on the right. The image is overlaid with large, semi-transparent circular shapes in orange and blue.

H1 FY2023 Financial Results

Six-month period ended June 30, 2023

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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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Note: This material was created to explain the details of our company and is not intended to be used for investment decisions. In addition, the contents reflect the views of our company at the time of the creation of the material, and the accuracy of the information is not guaranteed. Investments should be made based on the independent views of investors

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Financial Results

Hironoshin Nomura, CFO

Financial Summary for H1 FY2023

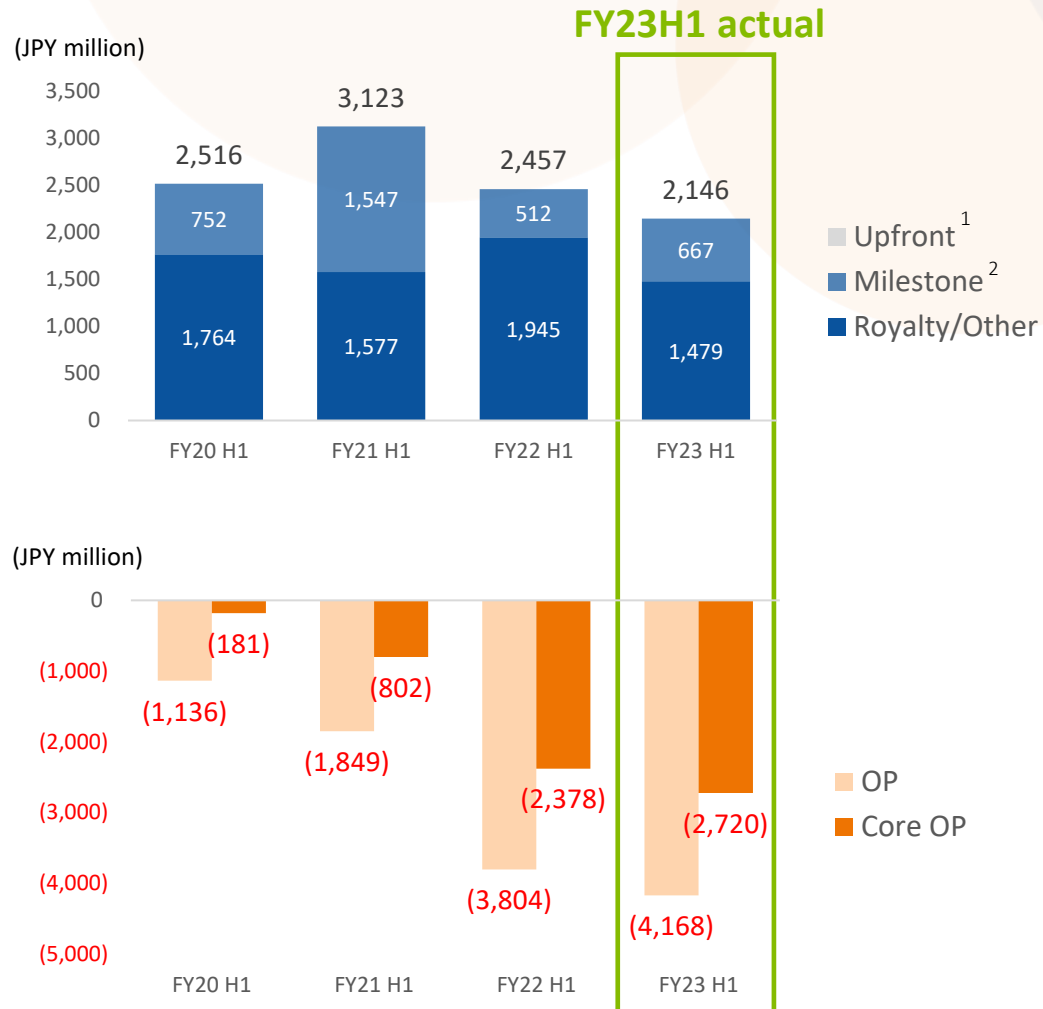
Successful execution of strategy with continuing investment in R&D

- 1 YTD Revenue of ¥2,146m (\$16m) vs. ¥2,457m (\$20m) in the prior comparative period.**
YTD revenue is lower primarily due to a reduction in royalty income in line with expectations, and lower billable R&D as activity has naturally passed over to our partners.
- 2 YTD Core Operating Loss of ¥2,719m (\$20m) vs. ¥2,378m (\$19m) in the prior comparative period.**
The decrease in revenue is matched by a decrease in cost of sales. The planned increase in investment in Core R&D is partially offset by a higher UK RDEC tax credit.
- 3 R&D and G&A expense is in line with guidance beginning of this year.**
Post-closing of Idorsia APAC transaction announced on July 20, the Group is currently evaluating the impact on full-year consolidated costs.
- 4 ¥66bn cash balance (\$453m) as at June 30, 2023.**
Post-closing of Idorsia APAC transaction announced on July 20, the Group will have approximately ¥42 billion cash on hand.

Note: USD:JPY FX rates used: Average rate YTD 2023 = 134.82 / Average rate YTD 2022: 122.83 / Spot rate Jun 30, 2023: 144.78

Key Financial Indicators

2023 Revenue lower due to a reduction in royalty income in line with expectations



Notes:

1. Upfront fee revenue recognised at deal inception

2. Milestone revenue recognised at milestone event + deferred revenue releases

Revenue

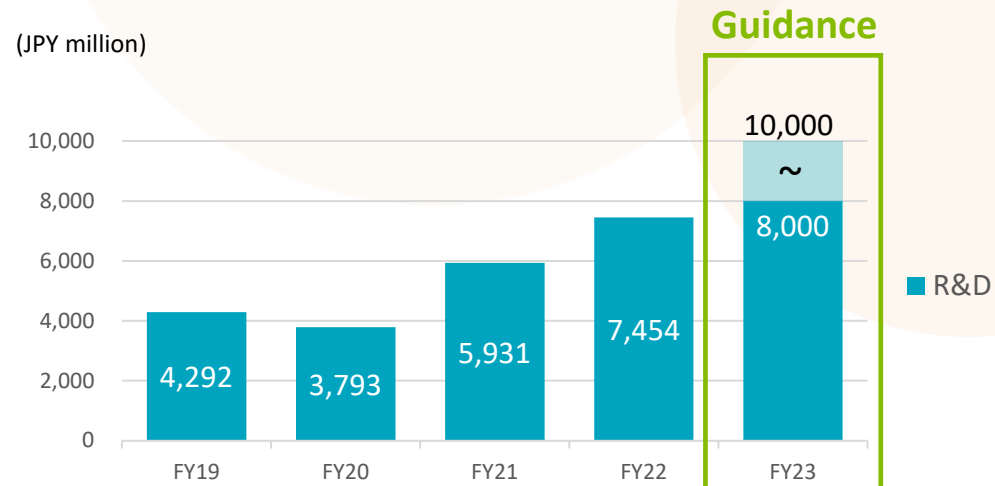
- Revenue can vary significantly quarter on quarter depending on the occurrence of milestone events and the signing of new collaboration agreements with upfront fees.
- Revenue decreased by JPY311m / \$4m in H1 2023 vs. H1 2022.
- Revenue from billable R&D services reduced as activity on some of our more established collaborations has naturally passed over to our partners.
- Royalty Revenue decreased in line with expectations.
- Milestone income from existing partnerships in H1 2023 related to deferred revenue releases on the AbbVie, Genentech and Eli Lilly collaborations, and increased due to there being more active agreements vs. the prior comparative period.
- There were no milestone events in the current YTD vs. two in the prior comparative period.

Operating Profit

- Core COS costs decreased by ¥274m vs. H1 2022 reflecting the decrease in FTE revenue.
- Core R&D costs increased by ¥507m vs. H1 2022 primarily due to increased investment in discovery activities, as planned.
- UK RDEC tax credits included under Other income increased by ¥328m vs. H1 2022 as a result of an increase in tax credit rates.

Full year cost guidance

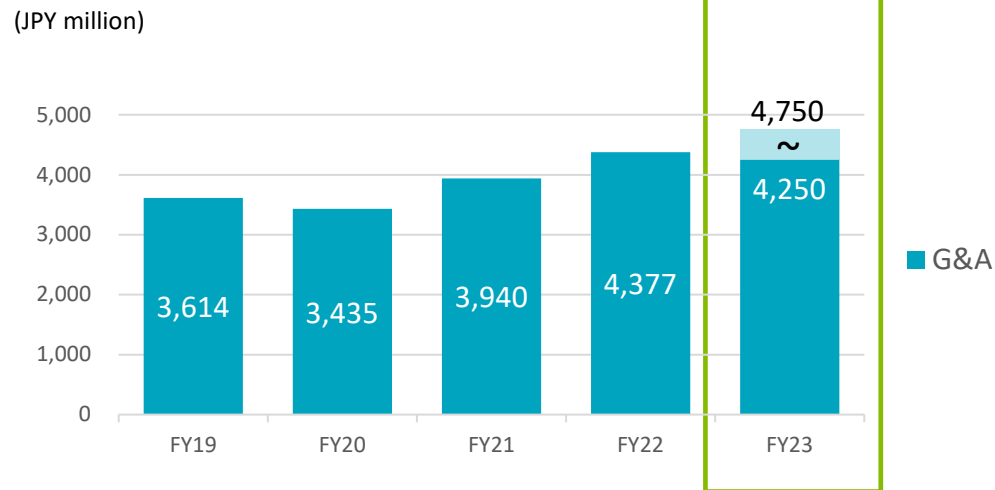
Incremental investment designed to deliver greater returns over the medium to long term



R&D expenses (IFRS basis)

¥8,000 to ¥10,000m

- Expand platform and grow discovery capacity
- Build a program-centric clinical development focus, and invest in new translational medicine capabilities
- Move priority programs into Phase 1b clinical studies to deliver greater value
- This guidance does not include any impact of the Idorsia APAC acquisition



G&A expenses (IFRS basis)

¥4,250 to ¥4,750m

- Invest in functional teams to support great science
- Continue to enhance corporate governance
- Costs associated with TSE Prime listing project
- This guidance does not include any impact of the Idorsia APAC acquisition

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Operational Highlights

Chris Cargill, CEO

Accelerating Our Mission

Now delivering life-changing medicines to patients



Combining our **leading GPCR drug discovery platform** with one of **Japan's world-class clinical development and profitable commercial operations**

Accelerating our transformation into a fully integrated biopharma company committed to helping patients in Japan and across the APAC region.

Four strategic pillars to increase corporate value








2023

On track to meet our key FY2023 objectives by year's end

FY2023 OBJECTIVES

ACHIEVEMENT

<p>1 WORLD-LEADING DRUG DISCOVERY</p>	<p>1 Invest to enhance GPCR SBDD platform capability</p>	<p> Expected H2 2023</p>
<p>2 MAJOR CASH FLOW GENERATING PARTNERSHIPS</p>	<p>2 Execute <u>at least one</u> new high value collaboration, and progress existing partnerships</p>	<p> Expected H2 2023</p>
<p>3 EVOLVE IN-HOUSE R&D</p>	<p>3 Advance <u>at least two</u> new in-house programs into first-in-human clinical trials</p>	<p> GPR52 Ph1 start EP4 Ant expected H2 2023</p>
<p>4 JAPAN COMMERCIAL PHARMA UNIT</p>	<p>4 Take <u>clear steps to build</u> a Japan Commercial Pharma Unit</p>	<p> </p>

Japan Pharma Business Unit

Acquired two companies and up to nine product/pipeline rights

TRANSACTION FUNDING

Purchase Price ~JPY 65 BN ¹	New Long-Term Corporate Loan (Mizuho Bank) JPY 40 BN
	Existing Cash JPY 25 BN

ACQUIRED LEGAL ENTITIES²

Idorsia Pharmaceuticals Japan (IPJ)

Established: 26 March 2018
 Number of Employees: 130
 Office Locations: Tokyo, Osaka
 Acquired Shareholding: 100%

Idorsia Pharmaceuticals Korea (IPK)

Established: 7 July 2022
 Number of Employees: 5
 Office Location: Seoul
 Acquired Shareholding: 100%

PORTFOLIO OF CATALYST RICH PRODUCTS

| Cerebral vasospasm associated with aSAH³

- Commercially available in Japan; launched (Apr-22)
- NHI Sales: JPY 7.5 BN (FY22A); JPY 13.3 BN (FY23E)
- Included in stroke treatment guidelines (Q3 23)
- ~6,500 patients treated to date and growing

| Insomnia

- FDA & EMA approved; Positive Ph 3 Japan data (Oct-22)
- J-NDA filing (Q4 23) and NHI Pricing/Launch (Q4 24)
- Co-promotion with Mochida
- Right to receive all future milestones from Mochida

Plus, up to 7 other clinical programs from Idorsia's global development pipeline via exclusive opt-ins⁴ & ROFN/ROFR⁵

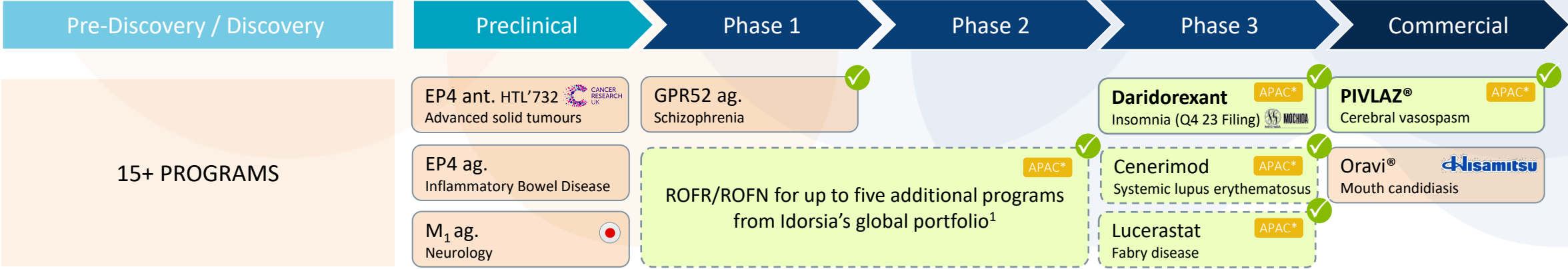
Cash Flow positive transaction brings a portfolio of life-changing medicines and late-stage clinical programs. Synergistic development and profitable commercial operations in Japan to serve as platform for APAC expansion.

¹ Based on FX rate 1 CHF = 163 JPY as at 19 July 2023. ² As of 1 July 2023. ³ Aneurysmal Subarachnoid Hemorrhage ⁴ Exclusive opt-in rights for Cenerimod (Ph 3) and Lucerastat (Ph 3); ⁵ Right of First Negotiation / Right of First Refusal for Selatogrel, ACT-1004-1239, ACT-1014-6470, IDOR-1117-2520, ACT-777991

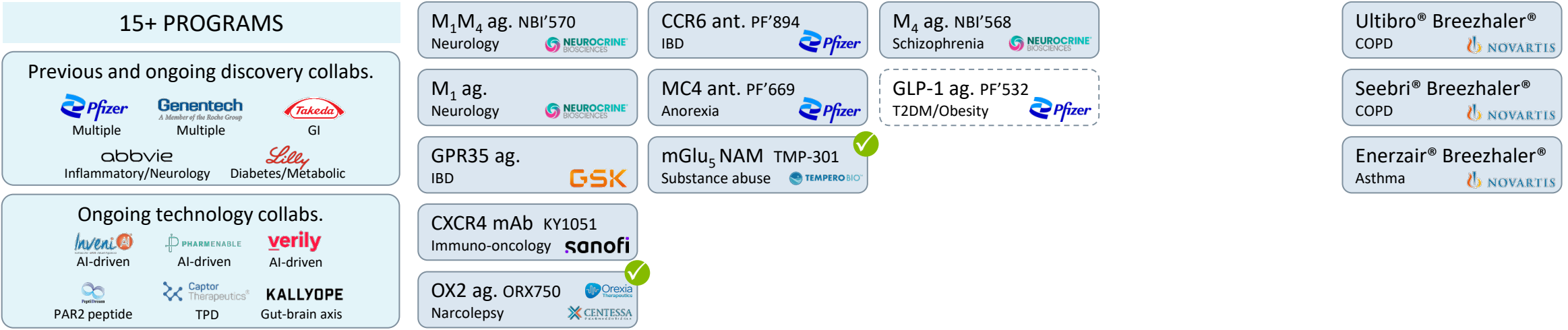
Broad, Diversified and Balanced Pipeline

Pioneering novel and differentiated therapies across multiple therapeutic areas

IN-HOUSE



PARTNERED



✓ Updates since the beginning of FY23

Note: Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG.
¹ROFR = Right of First Refusal / ROFN = Right of First Negotiation in the APAC (ex-China) territory for Selatogrel, ACT-1004-1239, ACT-1014-6470, IDOR-1117-2520, ACT-777991

3

R&D Progress

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

Technology collaboration landscape

Adding complementary approaches to increase discovery opportunities



Choosing the right target

verily

KALLYOPE

Inveni AI
Innovate with Intelligence

Our Core Technologies

StaR®	SBDD
CryoEM	DEL Screening
Protein Binder Toolkit	Chemogenomic Library Screening

Discovering a therapeutic agent

PHARMENABLE **Captor Therapeutics** **PeptiDream** **sanofi**

Clinical stage partnerships (Muscarinic Programs)

Developing novel muscarinic receptor agonists for schizophrenia and other neuropsychiatric disorders

NBI'568: Phase II initiated '22

NBI'570: Phase I to be initiated Q3 '23

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
- **Clinical Trial Application Accepted for NBI-1117570*, a dual M1 / M4 agonist**
 - ✓ Initiating Phase 1 study in Q3 2023
- **Anticipate advancing additional muscarinic compounds into clinic over time**

Sosei Heptares received
\$100m upfront, +\$30m @ Ph 2

Sosei Heptares to receive **ongoing R&D funding** and **up to \$2.6bn** in potential development, regulatory and commercial milestones, plus **tiered double digit percentage royalties** on net sales

Sosei Heptares **retains rights to develop all M1 agonists in Japan in all indications**, with NBIX receiving co-development and profit share options



*In-licensed from Sosei Heptares. NBI-1117568 and NBI-1117570 are investigational and not approved in any country

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Source: Neurocrine Biosciences Announces Conference Call and Webcast of Second Quarter 2023 Financial Results
https://www.neurocrine.com/assets/2023/08/Final-NBIX-Q2-2023-Earnings-Presentation_08.01.23.pdf



Clinical Trial Starting for in-house programs

GPR52 Ag and EP4 Ant is now starting clinical trials



GPR52 Ag (HTL0048149)

Indication	Schizophrenia
MoA	GPR52 receptor agonist
Stage	Phase1 (FSFD completed at the end of June)
Target number of participants	104
Participant type	Healthy volunteer
Start date	06/2023
End date (ESTIMATED)	11/2024

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

EP4 Ant (HTL0039732)

Indication	Advanced solid tumours
MoA	EP4 receptor antagonist
Stage	Phase1/2a (FSFD is expected very shortly)
Target number of participants	150
Participant type	Patient
Start date	07/2023
End date (ESTIMATED)	09/2026

Partner 

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

4

Japan/APAC Commercial Business

Dr. Satoshi Tanaka, President of IPJ/IPK

PIVLAZ[®] – Commercially Available (Launched Japan in 2022)

Strong uptake since launch and growing number of patients treated



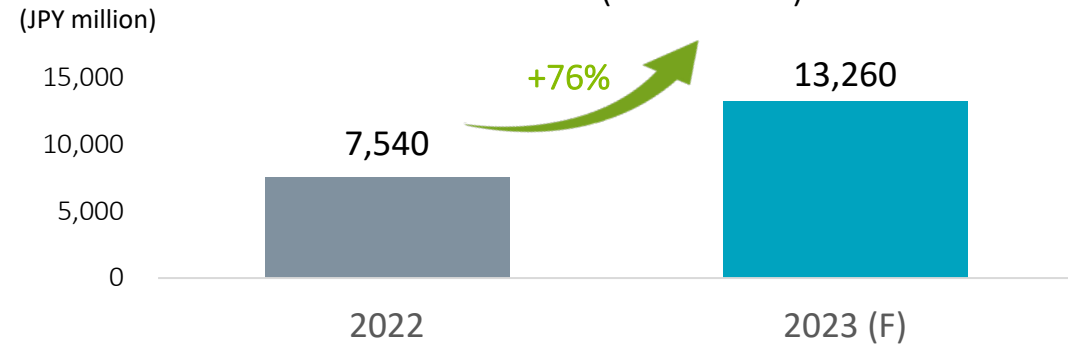
PIVLAZ[®] (clazosentan) is a fast-acting, selective endothelin A (ETA) receptor antagonist for the prevention of cerebral vasospasm (CV) after aneurysmal subarachnoid hemorrhage (aSAH)

- aSAH is a condition involving sudden life-threatening bleeding in the brain, and requires rapid medical treatment
- **Japan and South Korea have two of the highest incidence rates of aSAH in the world**, at least twice as high as in many countries in the world
- Market exclusivity until 2030 (Japan) and 2029 (South Korea)

Cumulative Patients Treated Since Launch



PIVLAZ[®] Sales (NHI basis)



Inclusion of PIVLAZ[®] in Japanese treatment guidelines was confirmed in Q3 2023. Further increases in uptake are expected to strengthen the already successful launch.

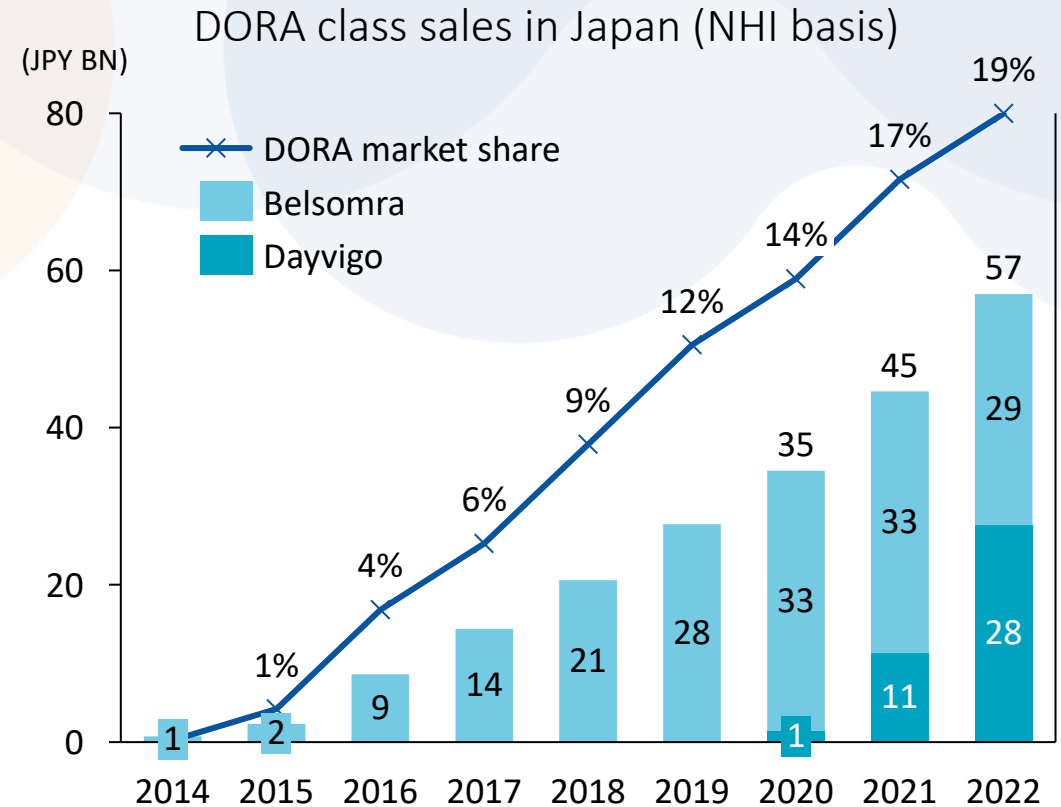
Daridorexant – Best-In-Class Drug With 2H 2023 J-NDA Filing

Expected to launch 2H 2024



Daridorexant is a dual orexin receptor antagonist (DORA) that selectively blocks the binding of the wake-promoting neuropeptides for the treatment of chronic insomnia

- Approved in the US, Europe, Canada (2022) – marketed as QUVIVIQ®; Positive results in Japan Phase 3 trial reported in Oct 2022, and NDA filing expected 2H 2023
- **Insomnia is highly prevalent in Japan and South Korea and most diagnosed patients are receiving pharmacological treatment**
- DORA class is growing rapidly as safer alternatives to benzodiazepines and the “Z-drugs” (e.g., zolpidem) are highly sought
- Market exclusivity until 2038 (Japan and South Korea)
- Co-Promotion with Mochida; all milestones after transaction from Mochida are payable to Sosei Heptares



Daridorexant is a best-in-class medicine for insomnia, and well positioned to meet the unmet needs of patients with sleep disorders in Japan and APAC (ex-China).

Cenerimod and Lucerastat

Exclusive opt-in rights for two potentially exciting product opportunities

Cenerimod

Indication	Systemic Lupus Erythematosus (SLE)
MoA	Selective S1P ₁ receptor modulator
Stage	Global Ph3 studies ongoing
Number of Patients	~120,000 in Japan
Major therapies* (Japan)	<p>Total Market Size : c.300 Oku JPY</p> <ul style="list-style-type: none"> • Benlysta (GSK, 50~100 Oku JPY est. peak sales) • Saphnelo (AZ, 50~100 Oku JPY est. peak sales) • Plaquenil (Sanofi, ~50 Oku JPY)
Value proposition	<ul style="list-style-type: none"> • Potential to be the first oral, disease-modifying SLE therapy that acts by reducing circulating T and B cells early in the immune cascade • S1P₁ modulation is a well-established mechanism in other diseases, such as MS (Gilenya, Zeposia) • Broadly-applicable mechanism means potential to expand to other autoimmune diseases

Lucerastat

Indication	Fabry Disease
MoA	Glucosylceramide synthase inhibitor
Stage	<ul style="list-style-type: none"> • Phase 3 (MODIFY) study primary endpoint (neuropathic pain) not met, however, renal function and echocardiography secondary endpoints were positive • Open Label Extension (OLE) study ongoing
Number of Patients	~1,000 in Japan
Major therapies* (Japan)	<p>Total Market Size : c.300 Oku JPY</p> <ul style="list-style-type: none"> • Replagal (ERT, Takeda, ~140 Oku JPY) • Fabrazyme (ERT, Sanofi, ~100 Oku JPY) • Galafold (PCT, Amicus, ~46 Oku JPY)
Value proposition	<ul style="list-style-type: none"> • Potential to provide a broadly-applicable oral monotherapy option as an alternative to IV enzyme replacement therapy (Galafold is currently the only available oral therapy, and applicable to patients with certain rare mutations)

Small opt-in fee to license each program, with Sosei responsible for all development plans and future costs in the territory. If successfully commercialized, Sosei is obligated to pay tiered single digit royalties to Idorsia for each product.

Source: *Estimate from Evaluate Pharma; JMDC; Datamonitor
ERT: Enzyme replacement therapy; PCT: Pharmacological chaperone therapy

Japan Is A Leading Market for Clinical Innovation And Quality

APAC countries respect Japan for its high data quality

Quality Clinical Development



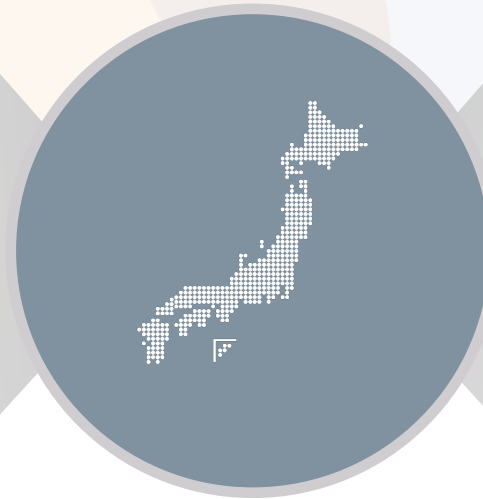
Deep understanding of disease and treatment by Doctors/HCPs



High quality data from clinical studies through to Post Marketing Surveillance



High penetration in of patient population during commercial phase



Quality excellent access to Doctors/HCPs who evaluate novel drugs

Achieve strong patient uptake

Contribute to reduce drug loss/lag for Japan patients

Quality Regulatory Environment



Reasonable NHI price for reimbursement supported by high quality clinical trial and PMS data



Prolongation of patents via extended clinical development



Regional optimization makes clinical trials cheaper and faster to execute

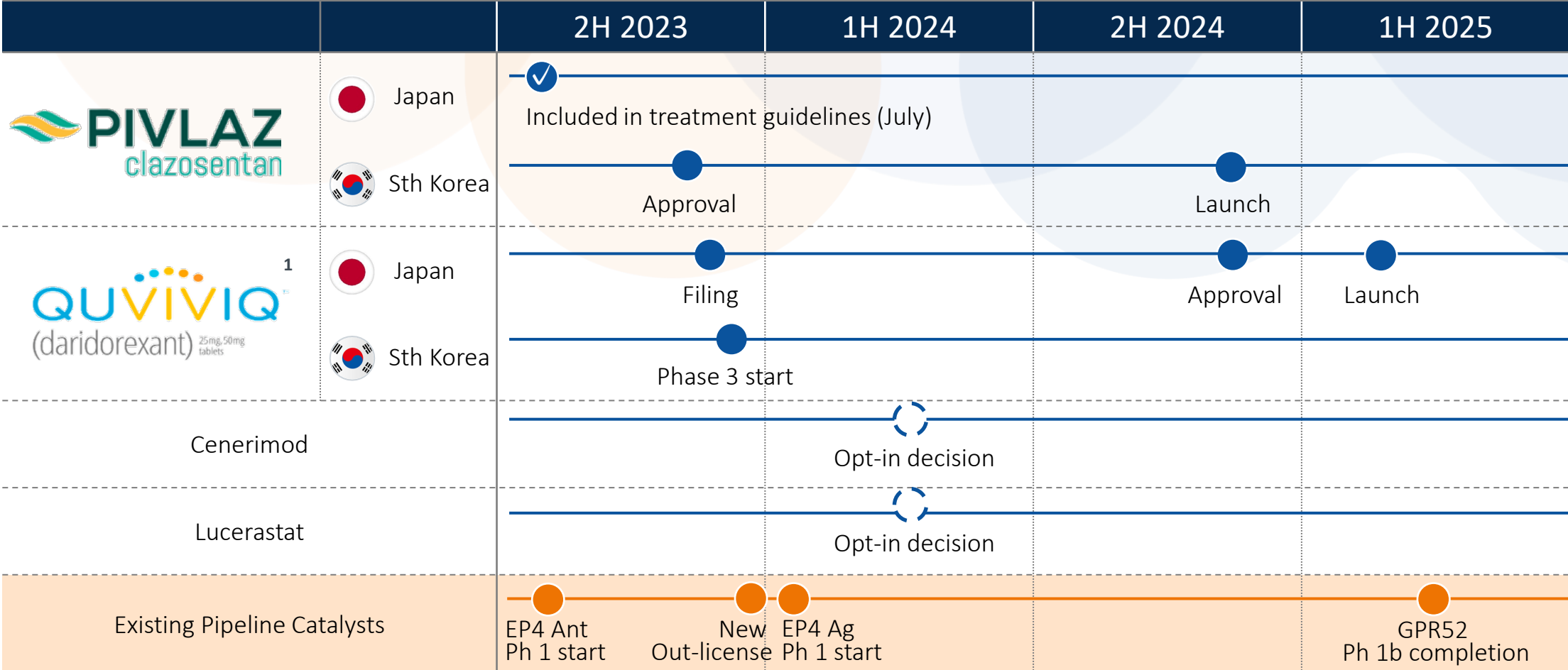
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Objectives for FY2023 and beyond

Chris Cargill, CEO

Expected News Flow

Several catalysts on-track to be achieved over the next 18 months



¹ Milestone payment expected to be received from Mochida Pharmaceutical upon achievement of development progression

Our 2030 vision



Novel medicines on the market globally, through our collaborations with partners

Commercial business in Japan, based on in-licensed and in time, own products

Broad, deep and sustainable pipeline of programs with significant potential

Rapidly growing sales, cash flow and profits

Leading biopharma company in Japan driving innovative medicines to patients

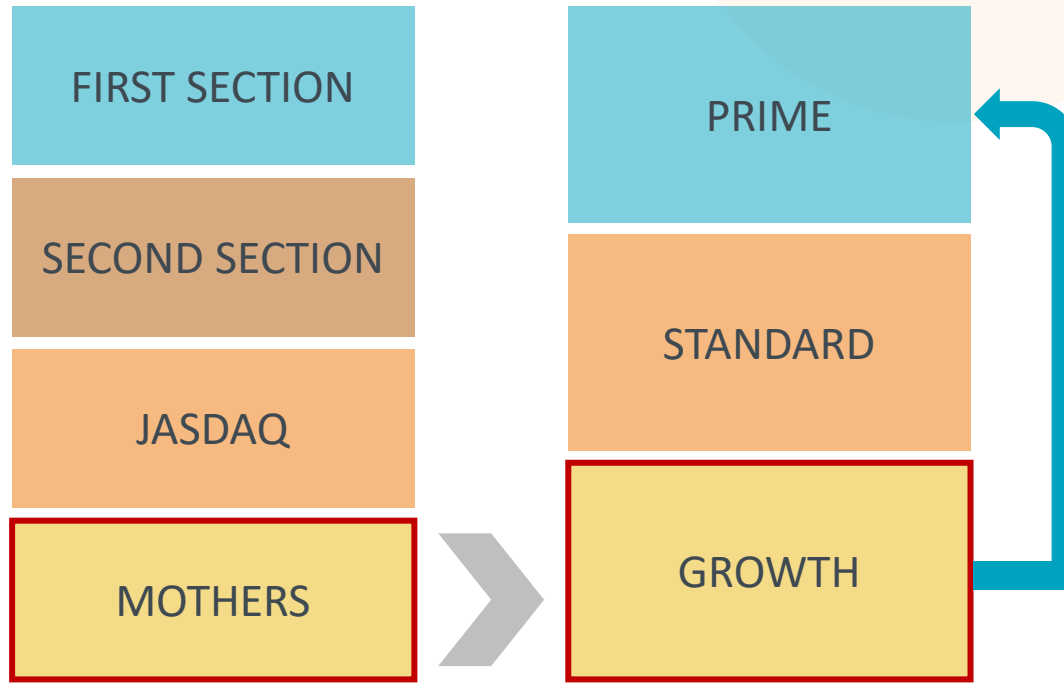
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Appendix

TSE Prime Listing

A significant milestone achieved to truly become a global biotech company

TSE Market Segments



OLD STRUCTURE

NEW STRUCTURE

- ✓ **Business Performance and Financial Status**
 - Revenue > JPY 10bn and Market Cap > JPY 100bn
- ✓ **Liquidity thresholds** – sufficient number of tradable shares and shareholders, and trading value
- ✓ **Governance** – tradable share ratio maintained

8-MAR-23 TSE approved change of market listing segment from Growth Market to the Prime Market ✓

15-MAR-23 Effective date of move to Prime Market ✓

APR-23 > Included in TOPIX index ✓

✓ Updates since the beginning of FY23

Introduction of 'Core Operating Profit'

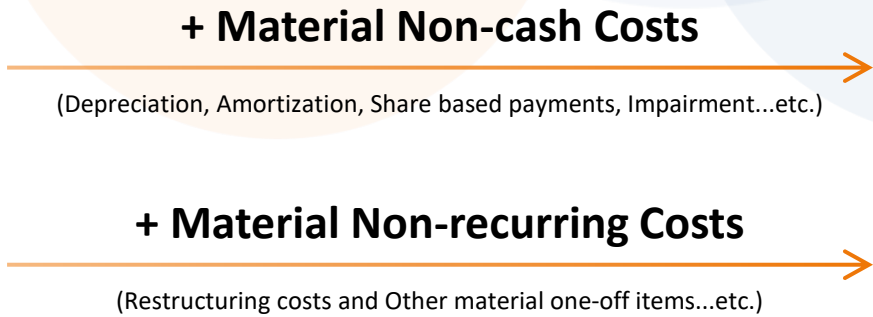
Core Operating Profit – the financial indicator closer to the reality of our business

Operating Profit "IFRS"

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

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"

Financial Impact of IPJ/IPK transaction

Transaction expected to be cash flow positive in the first full calendar year

Purchase Price	~JPY65 Bn ¹ (CHF400 Mn)		Transaction Funding	Long-term corporate loan: <ul style="list-style-type: none"> ● JPY40 Bn ● 7 year, low-rate loan from Mizuho Bank 	From existing cash: <ul style="list-style-type: none"> ● JPY25 Bn
Key Dates	Closing Date 20 July 2023 (JST)	Purchase Price Payment Date within a week post-closing	Impact on FY23 Financials	Post-closing, financial results of the acquired entities will be reflected in the Group's consolidated financial results	
Impact on Consolidated Financial Results	<ul style="list-style-type: none"> ● The amounts of intangible assets and goodwill arising in the consolidated balance sheet are currently under review by Management / Auditors. ● Goodwill will not be amortized in accordance with IFRS standards, whilst intangible assets will be amortized over the expected sales period. ● SGC's carried forward tax losses will be utilized against future taxable profits. ● Post-closing, the Group will have approximately JPY42 billion cash on balance sheet. 				
Mid- to Long-Term Impact (Guidance)	Peak Sales (E)	JPY 35 Bn+	<ul style="list-style-type: none"> ● Peak forecasts based on PIVLAZ[®] and Daridorexant performance in Japan, Korea and Taiwan only ● Potential upsides to forecasts include: <ul style="list-style-type: none"> ✓ Launch of PIVLAZ[®] and Daridorexant in additional APAC (ex-China) regions ✓ Exercise of opt-in right and launch of Cenerimod and Lucerastat ✓ Exercise of ROFR/ROFN rights and launch of up to additional five products ✓ Launch of existing in-house programs, incl. GPR52 agonist and M1 agonist ✓ Launch of potential other in-licensed products in the future 		
	Peak EBITDA (E)	JPY 10 Bn+			

¹ Based on FX rate 1 CHF = 163 JPY as at 19 July 2023

Estimation of potential market size

Multi-billion USD annual peak sales potential for our post-pre-clinical pipeline

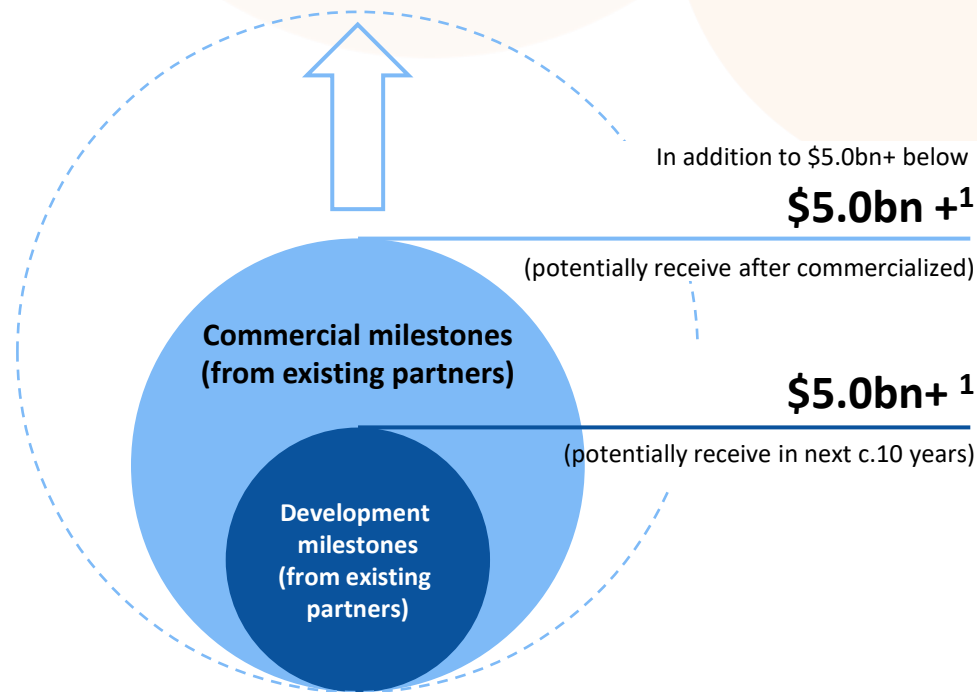
Category	Indication ²	Number of Patients	Peak Sales(USD million)		Our Candidates	
			Market Size	Individual Products		
Neurological disorders	Dementia	~55 million	\$7.3 billion (2010)		M1 agonist, M1/M4 agonist	
	Schizophrenia	~20 million	\$20.7 billion (2011)		M4 agonist, M1/M4 agonist	
	Substance use disorders	~10.4 million ¹	-	-	-	mGlu5 NAM
	Narcolepsy	~3 million	\$2.3 billion (2022)		\$1.7 billion (2020/Xyrem)	OX2 agonist
	Other	-	-	-	-	CGRP antagonist, GPR52 agonist
Immunological disorders	Cancer	~42 million	\$178.9 billion (2022)		\$21.0 billion (2022/Keytruda)	A2a antagonist, EP4 antagonist, CXCR4 mAb
	IBD	~10 million	\$23.5 billion (2022)		\$7.5 billion (2022/Humira)	CCR6 antagonist, GPR35 agonist, EP4 agonist
	Atopic Dermatitis	~13.3 million	\$8.1 billion ³ (2022)		\$7.0 billion (2022/Dupixent)	H4 antagonist, PAR2 mAb
Other	T2DM/Obesity	~420 million	\$58.3 billion (2022)		\$8.8 billion (2022/Ozempic)	GLP1 agonist
	Anorexia	~10 million	-	-	-	MC4 antagonist
Total			~\$299 billion/year		~\$56 billion/year	

Source (Number of patients): World Health Organization, Evaluate Pharma, The European Federation of Crohn's & Ulcerative Colitis Associations (EFCCA), Narcolepsy Network, Inc., GBD 2015 Disease and Injury Incidence and Prevalence Collaborators (October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet. 388 (10053): 1545-1602 ¹The number of patients with drug addiction
Source (Peak Sales):Sales of each indications are extracted form Evaluate Pharma's data of sales by disease and sales by individual products (as of 30 June. 2022). ²Sosei Heptares may target one segment in the market for specific diseases. ³ Since there is no applicable indication category, the market size of "Eczema" is stated. Current market size for Atopic Dermatitis may be larger than stated above.

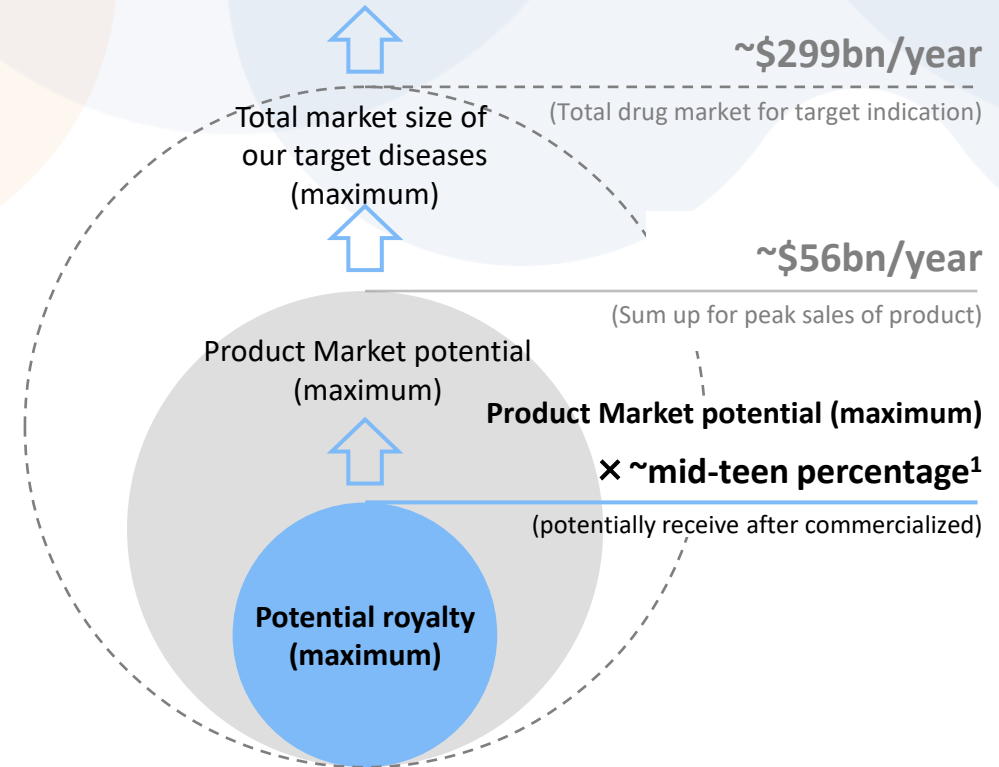
Potential revenues from existing partnerships




Securing stable revenues in the short to medium term from existing partnerships

Potential milestones from existing partners



Potential royalties from existing partners



 Short to medium term revenue potentially received in next 10 years	 Mid to long term revenue potentially received after commercialization	 Expand by executing new collaborations
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¹ All of these are the maximum values if all existing programs are successful. Note that the probability of success in drug discovery is not relatively high, and realistically not all programs will be successful.
Source: Total market size of our target diseases and Product Market potential is stated in the previous page

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	Mitsubisu	█	█	█	█	█	█	█
Imaradenant ¹	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	Anorexia	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. ¹ 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
Co-development											
KY1051	CXCR4 mAb	mAb	Immuno-oncology		██████████						
(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		██████████						
(Not disclosed)	Gut-brain axis drug discovery	SME	Gastrointestinal disorders		██████████						
Co-owned companies											
TMP301	mGlu5 NAM	SME	Substance use disorders		██████████						
(Not disclosed)	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
In-house Programs											
PIVLAZ®	ETA antagonist	SME	Cerebral vasospasm	SOSEI HEPTARES							
Daridorexant	Dual Orexin antagonist	SME	Insomnia	SOSEI HEPTARES							
HTL'149	GPR52 agonist	SME	Neurology diseases	SOSEI HEPTARES							
HTL'732	EP4 antagonist	SME	Immuno-oncology	SOSEI HEPTARES							
(Not disclosed)	EP4 agonist	SME	Inflammatory bowel disease	SOSEI HEPTARES							
(Not disclosed)	Muscarinic M1 agonist (JP)	SME	Neurology diseases	SOSEI HEPTARES							
(Not disclosed) ¹	H4 antagonist	SME	Atopic Dermatitis	SOSEI HEPTARES							
(Not disclosed)	SARS CoV-2 Mpro	SME	Coronaviruses	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	Neurology diseases	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	GI and Inflammatory diseases	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	Immunology diseases	SOSEI HEPTARES							
In-house Programs (No longer internally funded. Targeting academic / industrial partnership)											
HTL'310	SSTR5 agonist	Peptide	Hypoglycaemic disorders	SOSEI HEPTARES							
HTL'097	GLP-1 antagonist	Peptide	Hypoglycaemic disorders	SOSEI HEPTARES							
HTL'023	Dual GLP-2/GLP-1 agonist	Peptide	Intestinal failure/NASH	SOSEI HEPTARES							
(Not disclosed)	Apelin agonist	Peptide	Pulmonary Arterial Hypertension	SOSEI HEPTARES							
HTL'641	Dual orexin antagonist	SME	Insomnia and sleep disorders	SOSEI HEPTARES							
(Not disclosed)	PAR-2 mAb	mAb	Atopic Dermatitis/Pain	SOSEI HEPTARES							

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

Glossary

Basic Terminology/Technology		
GPCR	G Protein-Coupled Receptor	There are about 800 types of GPCRs in the human body. While 400 of them are known to be potential drug targets, about 300 of them are not yet drugged
StaR	Stabilized Receptor	Sosei Heptares' proprietary technology to stabilize a GPCR by engineering a small number of single point mutations outside of the ligand-binding site. It enables to identify the structure of GPCRs to be used for SBDD drug discovery as well as antibody drug discovery as antigens
SBDD	Structure-Based Drug Design	A method to design drugs on a computer base based on the analysis of the three-dimensional structure of the drug target (e.g., protein receptor)
TPD	Targeted Protein Degradation	Drugs that promote the degradation of target proteins (e.g., receptors) in cells and aim for therapeutic effects by reducing disease-causing proteins
PAM	Positive Allosteric Modulator	A regulator that binds to unusual active sites (allosteric sites) on the receptor to increase the affinity and effect of the agonist
NAM	Negative Allosteric Modulator	A regulator that binds to an unusual active site on the receptor (allosteric site) and reduces the affinity and effectiveness of the agonist
Ag	Agonist	A therapeutic drug that binds to a receptor and activates an intracellular signaling system similar to biological substances
Ant	Antagonist	A therapeutic drug that suppresses biological reactions by binding to receptors and preventing them from binding to biological substances
PK	Pharmacokinetics	Research and testing on the relationship between drug dosage and blood concentration. Mainly describes the rate process of ADME
PD	Pharmacodynamics	Research and testing on the relationship between drug concentration and pharmacological effects
ADME	Absorption, Distribution, Metabolism and Excretion	A series of process in the absorption of drugs into the body, distribution within the body, metabolism in the liver and other organs, and excretion in the kidneys and other organs
POM	Proof of Mechanism	Proof of mechanism of action, mainly through biomarkers. It can suggest the possibility of efficacy in fewer cases than POC
POC	Proof of Concept	Proof of a therapeutic concept, primarily through clinical efficacy and safety
Ach	Acetylcholine	A neurotransmitter released from the peripheral parasympathetic and motor nerves to transmit nerve stimuli
IND	Investigational New Drug	Information packages for development candidates to be submitted to the U.S. Food and Drug Administration (FDA) at the time of initiation of clinical trials
Ph1	Phase1	A study in humans. The main purpose is to confirm the safety of the drug candidate mainly by healthy volunteers.
Ph2	Phase2	A study in humans. The main purpose is to confirm the efficacy of the drug candidates on a small scale (however, the number of patients varies greatly depending on the disease)
Ph3	Phase3	A study in humans. The main purpose is to determine the efficacy of the drug candidates on a large scale (however, the number of patients varies greatly depending on the disease)
NDA	New Drug Application	An application to the U.S. Food and Drug Administration (FDA) for approval to market a new drug
Disease/Drug		
LAMA	Long Acting Muscarinic Antagonist	An inhalant that dilates bronchial tubes and improves respiratory function by inhibiting the action of acetylcholine receptors (M3), which increase parasympathetic nerves.
LABA	Long Acting Beta2-Agonist	An inhalant that improves respiratory function by stimulating sympathetic beta2 receptors to dilate the bronchi.
ICS	Inhaled Corticosteroid	An inhalant that suppresses airway inflammation to prevent coughing attacks and other symptoms caused by asthma, also promotes the action of beta 2 stimulants and improve airway hyperresponsiveness.
mCRPC	Metastatic Castration-Resistant Prostate Cancer	Cancer that has spread (metastasized) beyond your prostate gland and for which hormone therapy is no longer effective in stopping or slowing the disease.
COPD	Chronic Obstructive Pulmonary Disease	A group of diseases that causes damage to the bronchi and lung due to smoking or inhalation of toxic substances, resulting in breathing problems.
AD	Alzheimer's Disease	Alzheimer's disease is a progressive neurologic disorder that causes the brain to shrink (atrophy) and brain cells to die, the most common cause of dementia .
DLB	Dementia with Lewy Bodies	Protein deposits, called Lewy bodies, develop in nerve cells in the brain regions involved in thinking, memory and movement (motor control), the second most common type of dementia.

Glossary (cont'd)

Drug discovery target		
M1	Muscarinic M1 Receptor	One of the five subtypes M1 to M5 of muscarinic acetylcholine receptors, known to be involved in learning and memory.
M4	Muscarinic M4 Receptor	One of the five subtypes M1 to M5 of muscarinic acetylcholine receptors, known to be involved in behavior and dopamine release.
CGRP	Calcitonin Gene-Related Peptide	CGRP is thought to be involved in vasodilation, decreased heart rate, and increased myocardial contractility via receptors.
A2A	Adenosine A2A receptor	One of the four subtypes of adenosine receptors, A1, A2A, A2B, and A3. It is expressed in many tissues and has multiple functions such as neural activity, vasodilation, and immune regulation.
GLP-1	Glucagon-like Peptide 1	GLP-1 is secreted by gastrointestinal cells when we eat, and is involved in insulin secretion from the pancreas and appetite regulation in the central nervous system.
CCR6	Chemokine Receptors 6	A type of B chemokine receptor that responds to chemokines generated during inflammation. It is believed to be involved in inflammation and immunity mainly by it's regulating the migration activity of leukocytes into inflamed tissues.
MC4	Melanocortin 4 Receptor	MC4 is expressed in the central nervous system and is the main receptor that mediates the appetite suppressing effect of alpha-melanocyte stimulating hormone.
GPR35	G Protein-Coupled Receptor 35	Orphan receptors - expressed mainly in immune and gastrointestinal tissues and is thought to be involved in areas of gastrointestinal tract, cardiovascular, inflammation, and central nervous system.
CXCR4	CXC Motif Chemokine Receptor 4	CXR4 induces migration of cancer cells and is known to be important in metastasis process.
mGlu5	Metabotropic Glutamate Receptor 5	One of the metabolic glutamate receptors expressed in the central nervous system. Glutamate is known to be the most abundant excitatory neurotransmitter in the human nervous system.
OX1, OX2	Orexin 1 Receptor, Orexin 2 Receptor	Orexins are a class of neuropeptides that are known to play a role in stabilizing wakefulness and inhibiting sleep.
GPR52	G Protein-Coupled Receptor 52	An orphan receptor that is highly expressed in the striatum- may play a role in the regulation of frontal lobe-striatal and limbic dopamine in psychiatric and neurological disorders.
H4	Histamine H4 Receptor	H4 is particularly expressed in immune system cells and is known to be involved in inflammation and allergy.
EP4	Prostaglandin EP4 Receptor	EP4 suppresses innate and acquired immunity and is known to induce tumor progression
PAR2	Protease-Activated Receptor 2	PAR2 is known to be associated with many physiological and pathophysiological processes such as inflammation, tumor metastasis, gastrointestinal motility, pain, and itching
SSTR5	Somatostatin Receptor 5	SSTR is expressed mainly on small intestinal endocrine cells and pancreatic beta cells, inhibits the secretion of gastrointestinal hormones such as GLP-1 and PYY by binding somatostatin.
GLP-2	Glucagon-like Peptide 2	Intestinal GLP-2 is secreted together with GLP-1 during nutrient intake, and repairs and protects the intestinal tract.
Mpro	SARS-CoV-2 Main Protease	An enzyme essential for the replication of Sars-CoV-2(COVID-19 cause virus). One of the target proteins for the development of antiviral drugs.
D2	Dopamine Receptor D2	Dopamine is a neurotransmitter in the brain involved in motor control, motivation, and learning - known to be associated with Parkinson's disease and schizophrenia.
5-HT	5-Hydroxytryptamine Receptor	5-hydroxytryptamine (serotonin), as a transmitter in the central nervous system, is thought to play an important role in the regulation of brain function.
	Orphan receptor	A receptor whose existence is known based on genetic analysis, but for whom no ligand has been identified.
	Ligand	A ligand is a molecule that binds to a specific receptor in vivo, such as hormones, neurotransmitters. For example, the ligand for muscarinic receptors is acetylcholine.

Locations

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