



Corporate Presentation

May 2024

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Agenda

- 01** Business Overview
- 02** Strategic Roadmap
- 03** Our Medicines and Pipeline
- 04** Our NxWave™ Platform
- 05** Financial Results
- 06** Appendix

Business Overview

01



Leading the Next Era of Medicine. From Japan, for Japan, and the world

World-leading NxWave™ platform (UK), coupled with Japan's most effective development and commercial organization

Our Mission

To accelerate the development of life-changing medicines, by investing in science and technology.

Our Vision

To lead the next era of medicine.

From Japan, for Japan, and the world.

Our Values

- Patients come first
- Innovation and teamwork
- Focus
- Speed and agility
- Operational excellence



We are Nxera Pharma

A technology-powered biopharma in pursuit of new specialty medicines to improve the lives of patients

Cutting-edge Science

**WORLD-LEADERS IN GPCR
STRUCTURE-BASED DRUG DESIGN**

Strong focus on GPCR targets – solved 375+ molecular structures

Programs by Design


30+ ACTIVE PROGRAMS




Real Human Outcomes


PROTECTING LIVES EVERYDAY

10,300+ patients have received Pivlaz® (Japan and shortly South Korea)
+4 other partnered marketed products

 TSE: 4565
Tokyo Stock Exchange Prime

 350+ FTE Employees

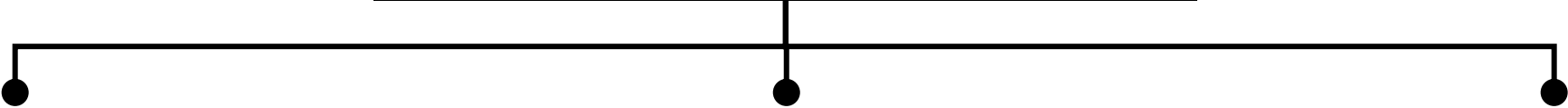
 5 Global Locations
Tokyo, Cambridge, London, Seoul & Basel

 Revenue-Generating
\$350m+ Cash in hand
(Dec-2023)



Global Corporate Structure

Over 350 team members employed across Japan, South Korea, UK and Switzerland



Nxera Pharma UK Limited
(formerly “Heptares Therapeutics”)
Cambridge | ~170 staff



Nxera Pharma Japan Co., Ltd.
(formerly “IPJ” and “Sosei Co.”)
Tokyo | ~130 staff



Nxera Pharma Korea Co., Ltd.
(formerly “IPK”)
Seoul | ~4 staff

Research & Drug Discovery

- NxWave™ – SBDD Platform
- Drug Discovery
- Translational Medicine
- Early Clinical Development
- Business Development

Drug Development & Commercial Operations

- Clinical Development
- Regulatory Affairs
- Marketing Authorisation Holder
- Commercial Sales (direct and via partners)

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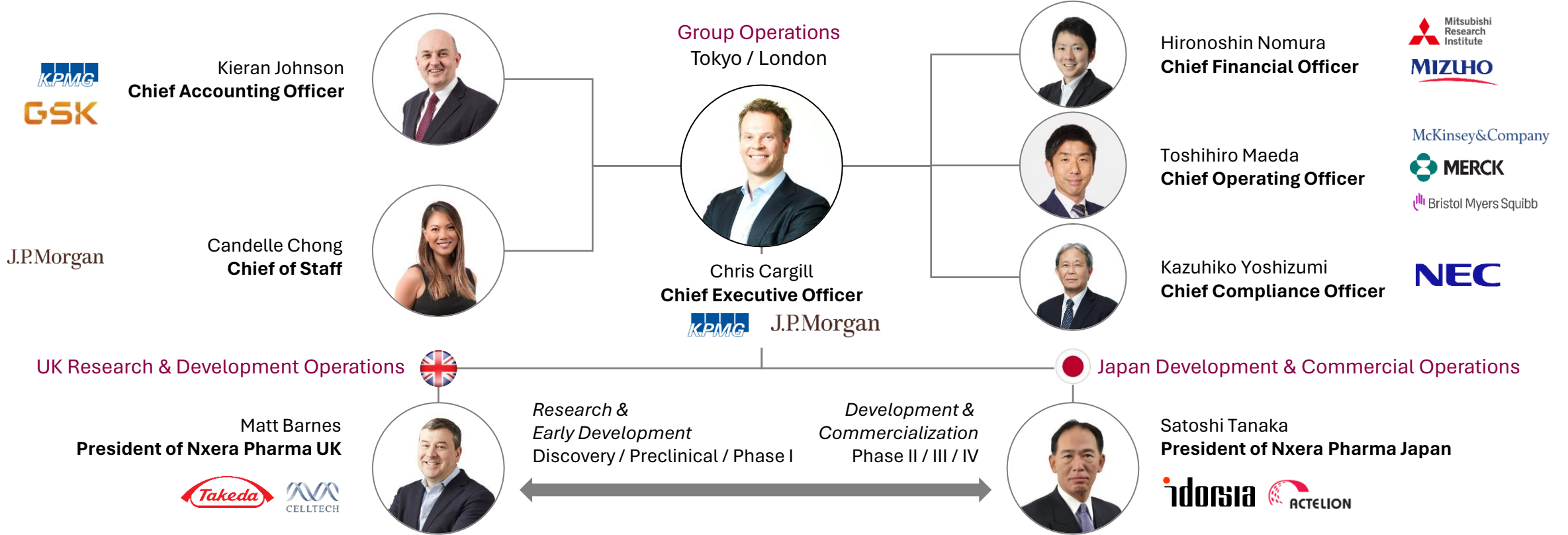


Agile and decisive leadership team

BOARD OF DIRECTORS

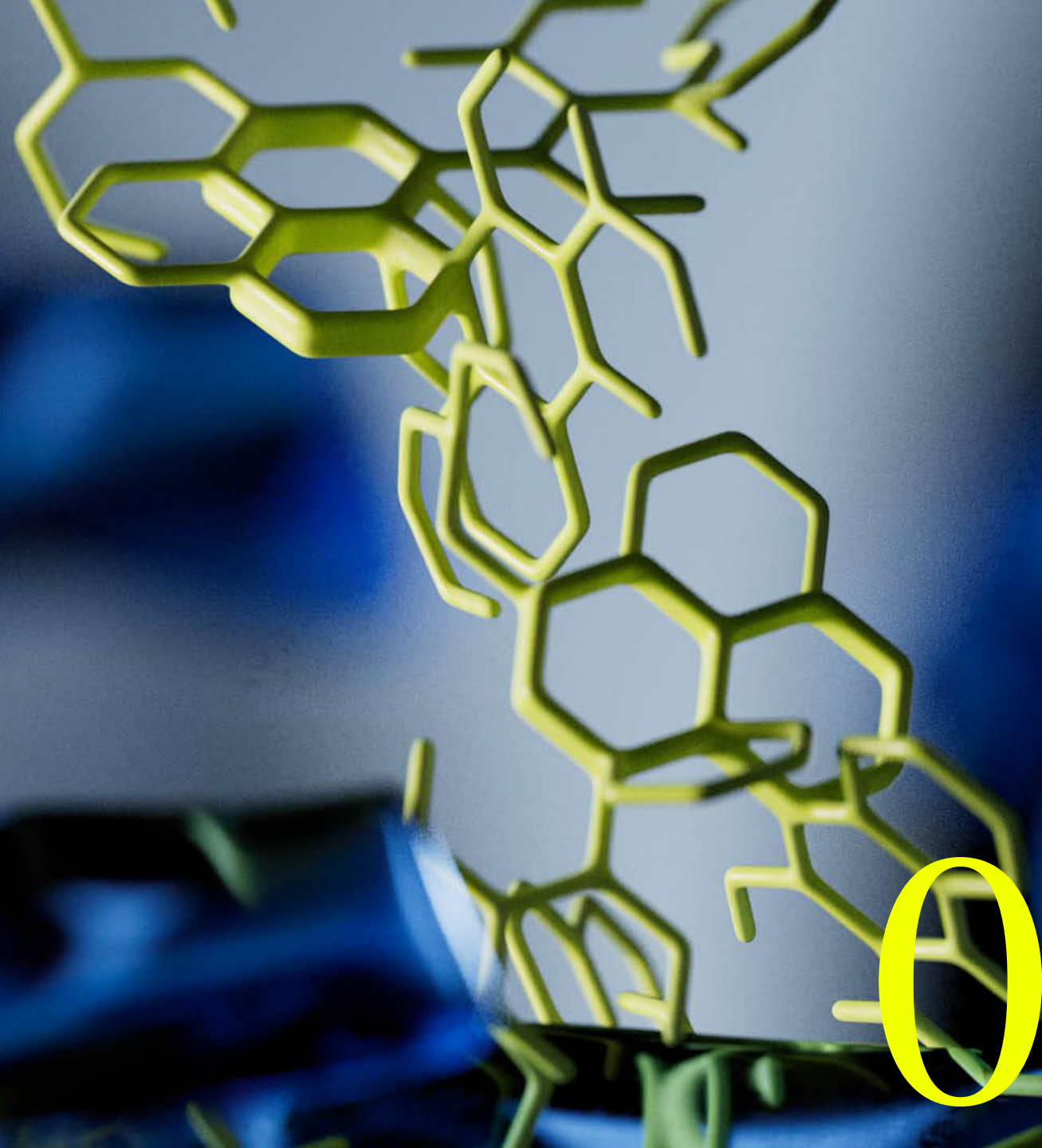
 Shinichi Tamura Chairman	 Chris Cargill CEO	 Tomohiro Toyama Legal	 Rolf Soderstrom Finance	 David Roblin Clin Dev	 Kuniaki Kaga Clin Dev	 Eiko Tomita Reg Affairs	 Noriaki Nagai Compliance	 Miwa Seki Tech/ESG
 	 		  	 		  	 	 

EXECUTIVE MANAGEMENT



Strategic Roadmap

02





Our History

Strategic steps taken to build Nxera over the last two decades

2000s

Launched a public company dedicated to **bringing innovation to Japan**

- ✓ IPO on TSE (MOTHERS) in 2004

Made strategic acquisitions to bring **steady revenue** through groundbreaking medicines

- ✓ \$186m acquisition of Arakis Limited in 2005
- ✓ Royalty revenues from Breezhaler® medicines from 2012 to present

ARAKIS

2015

Out-licensed several programs to global pharma to **generate profit, a cash reserve and a larger market valuation**

- ✓ 15+ partnered programs that generate upfront and milestone revenue (plus future royalties)

Invested in research-focused companies that could **generate a continuous pipeline of new medicines**

- ✓ \$400m acquisition of Heptares Therapeutics Limited in 2015

HEPTARES
therapeutics

2023

Elevated our status in the **Tokyo Stock Exchange**, improving access to institutional investors

- ✓ Promotion to TSE (PRIME) segment in 2023
- ✓ First public healthcare investment by the Japan Investment Corporation in 2023

Acquired a commercial-stage pharmaceutical company which provided an **integrated platform** for even greater sustainable revenue growth

- ✓ \$466m acquisition of Idorsia Pharmaceuticals Japan and Korea
- ✓ Rapidly growing revenues from sales of PIVLAZ®

Idorsia JAPAN
KOREA

2024

NXERA

Launched new corporate branding:

Nxera Pharma Co

With a vision to lead the next era of medicine.

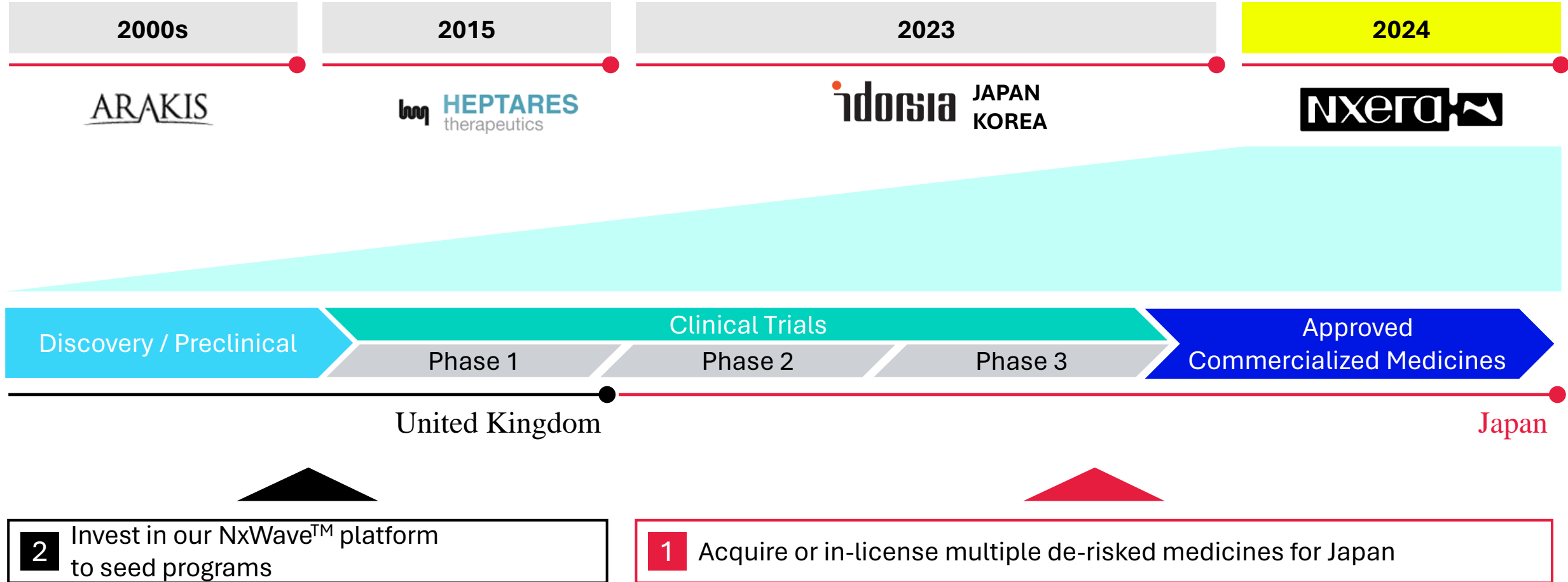
From Japan, for Japan, and the world.

NXERA



Building a fully integrated biopharma from Japan

Accelerating growth to achieve our mission by leveraging business platform in Japan and UK





Our mission is clear

Accelerate the development of life-changing medicines

1

Acquire or in-license multiple de-risked medicines for Japan

2

Invest in our NxWave™ platform to seed programs

3

Build a first-class technology environment

Focusing on these three areas is how we plan to make our mission happen as fast as possible

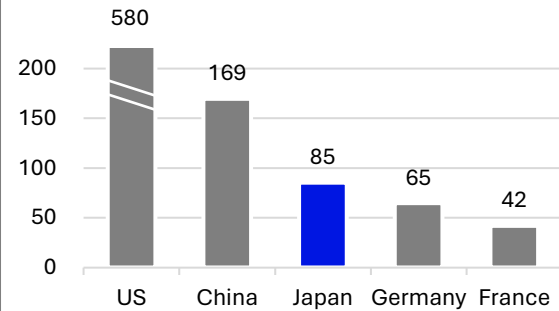


Japan will serve as our base to expand across APAC markets

Japan is an attractive, established market with strong volumes

Japan is the second largest pharma market (ex-China)

Market size (USD bn) (2021)



Tailwinds from near-term regulatory changes

“ Japan Phase 1 Drug Clinical Trials No Longer Needed for Global Clinical Trials ”

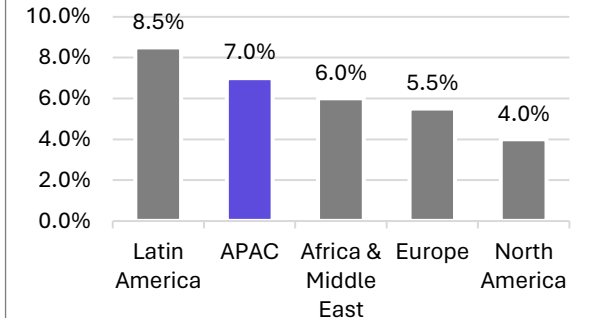


High quality clinical and regulatory environment

- ✓ Excellent access to Doctors/HCPs who evaluate novel drugs
- ✓ Typically achieve strong patient uptake
- ✓ Reduces drug loss and drug lag for Japan patients

APAC is the second highest growth pharma market

Market growth (CAGR %) (2019 - 2027)



Source: IQVIA Market Prognosis, Sep 2022; IQVIA Institute, Nov 2022.

APAC (ex-China) territory includes South Korea, Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand and Vietnam



Priority objectives for FY2024

01

JPY 16 billion+ NHI sales for PIVLAZ®

02

JNDA approval for daridorexant in Japan

03

Acquire/in-license at least one late-stage medicine for the Japan/APAC (ex-China) region

04















Execute at least one new major partnership, and initiate at least one new in-house Ph.1 study

05

PMI investment in new brand concept, plus systems and applications for efficiency and scalability

Several potential catalysts over the next 12 months

(excluding new business development transactions)

	PROGRAM	PARTNER	TIMING	EVENT
	EP4 Ag		Achieved (Mar. 2024)	Ph.1 start
	GPR35 Ag	 	Achieved (Mar. 2024)	Program reversion
	GPR52 Ag		Achieved (Mar. 2024)	Option-to-license agreement
	NBI-567 (M1 pref. Ag)		Achieved (May 2024)	Ph.1 start
	Cenerimod		1H 2024	Exclusive opt-in decision
	Lucerastat		1H 2024	Exclusive opt-in decision
	Daridorexant (Sth Korea)		2H 2024	New Partnership & Ph.3 start
	Daridorexant (Japan)		2H 2024	Potential NDA Approval
	NBI-568 (M4 Ag)		2024 3Q	Ph.2 topline data
	TMP-301 (mGlu5 NAM)		2024	Ph.2 start
	ORX750 (Ox2 Ag)		2024	Ph.1 start
	PIVLAZ® (Sth Korea)		1H 2025	New Partnership & Launch

¹ Co-development and co-promotion agreement with Mochida



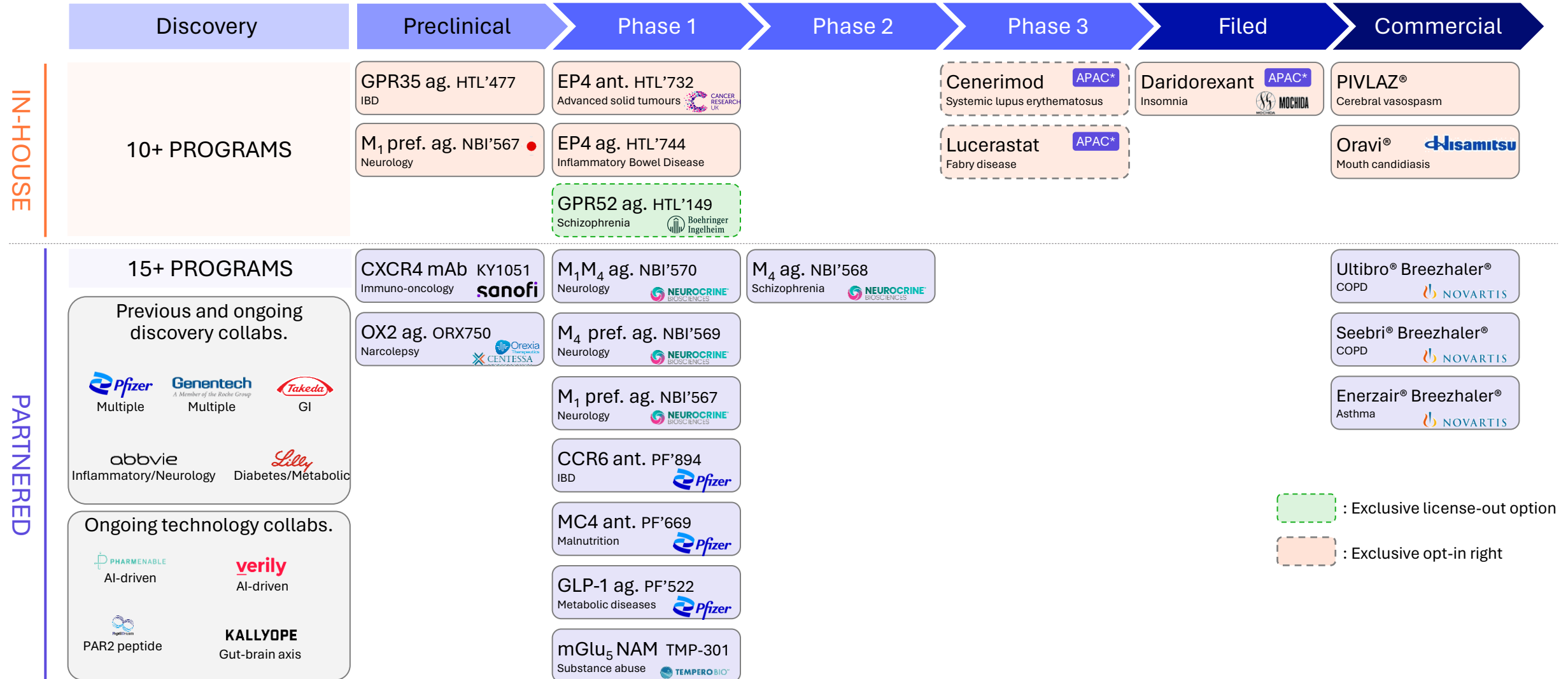
Our Pipeline and Medicines

Programs by Design

03



Active Pipeline Overview



: Exclusive license-out option

: Exclusive opt-in right

Note: Seebri®, Ultibro®, Energair® and Breezhaler® are registered trademarks of Novartis AG.
Pref. ag.: Preferring agonist



Our product: PIVLAZ®

Our first commercially available medicine protecting Japanese lives every day



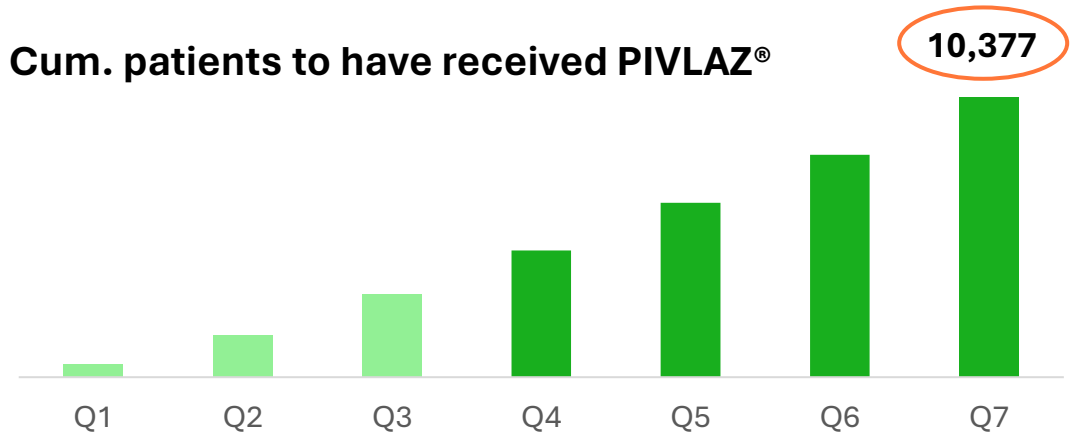
JP GUIDELINES INCLUSION FOR MANAGEMENT OF STROKE¹

- Aug '23: Authorized and recommended by the **Japanese Stroke Society**
- Demonstrated the true endpoints of **Subarachnoid Hemorrhage (SAH)** with higher level of evidence
- Provides confidence to neurosurgeons to **prescribe PIVLAZ® as a new standard of care** for SAH based on strong evidence it can prevent delayed cerebral ischemia and poor outcomes

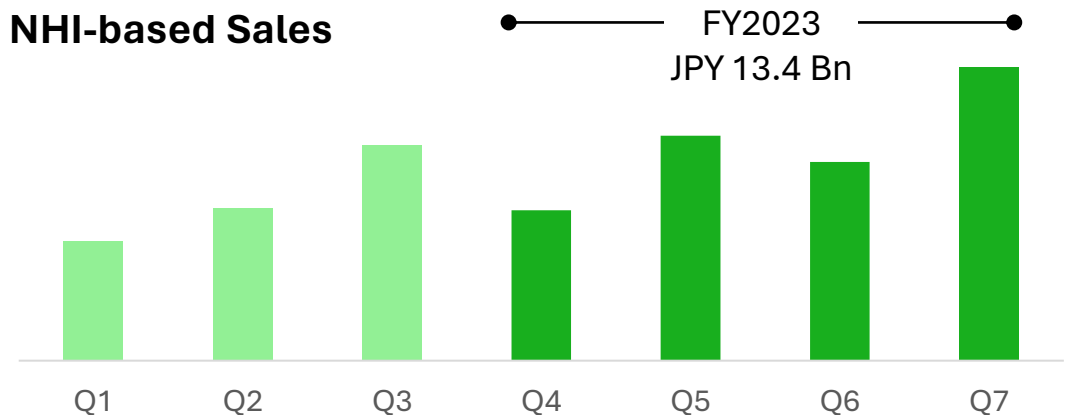
MARKETING APPROVAL FOR SOUTH KOREA

- Dec '23: Received Marketing Approval in South Korea
- Early 2025: Commercially available to patients

Cum. patients to have received PIVLAZ®



NHI-based Sales



PIVLAZ® rapidly building real world evidence mitigating the risk of cerebral vasospasm

¹ Japanese Stroke Society Guideline 2021 for the Management of Stroke (Revised Version 2023)



Our in-house pipeline: Daridorexant

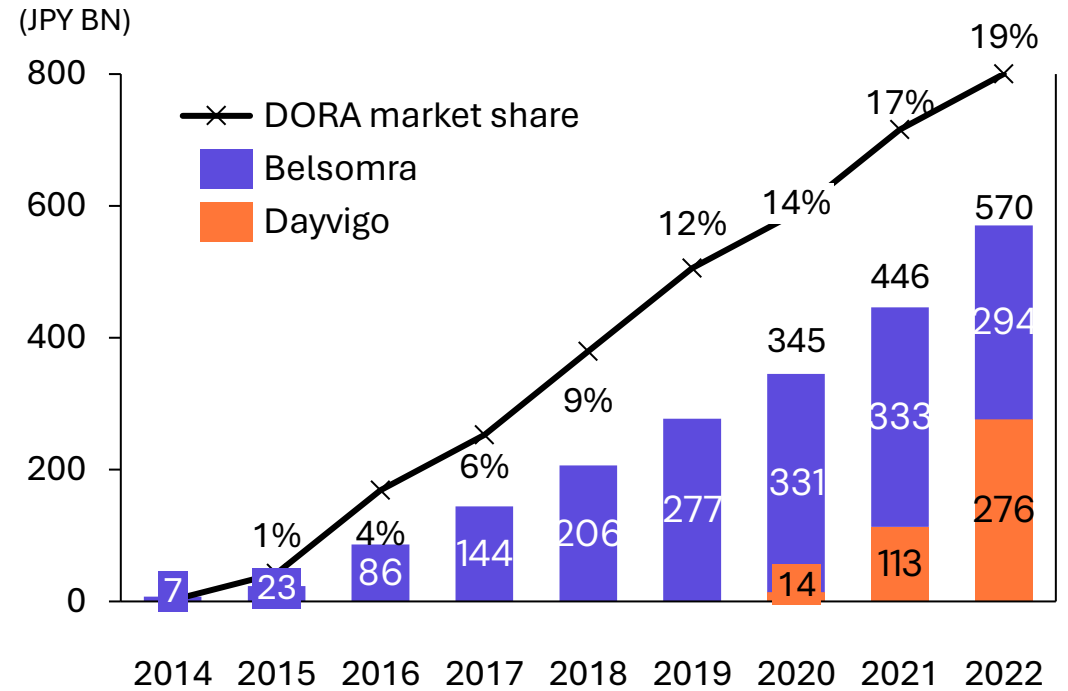
NDA submitted in Oct-2023. Expected to launch 2H 2024



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 submitted in Oct. 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 Nxera

DORA class sales in Japan (NHI basis)



Daridorexant is well positioned to meet the unmet needs of patients with sleep disorders in Japan and APAC (ex-China)

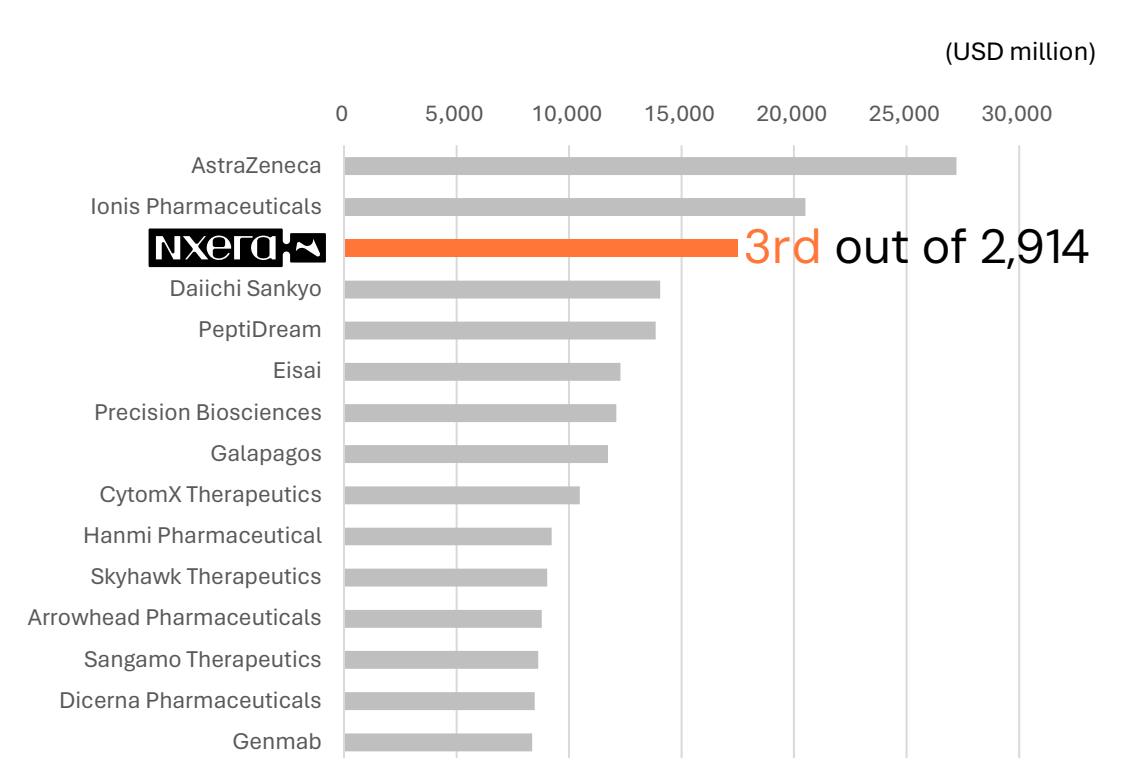
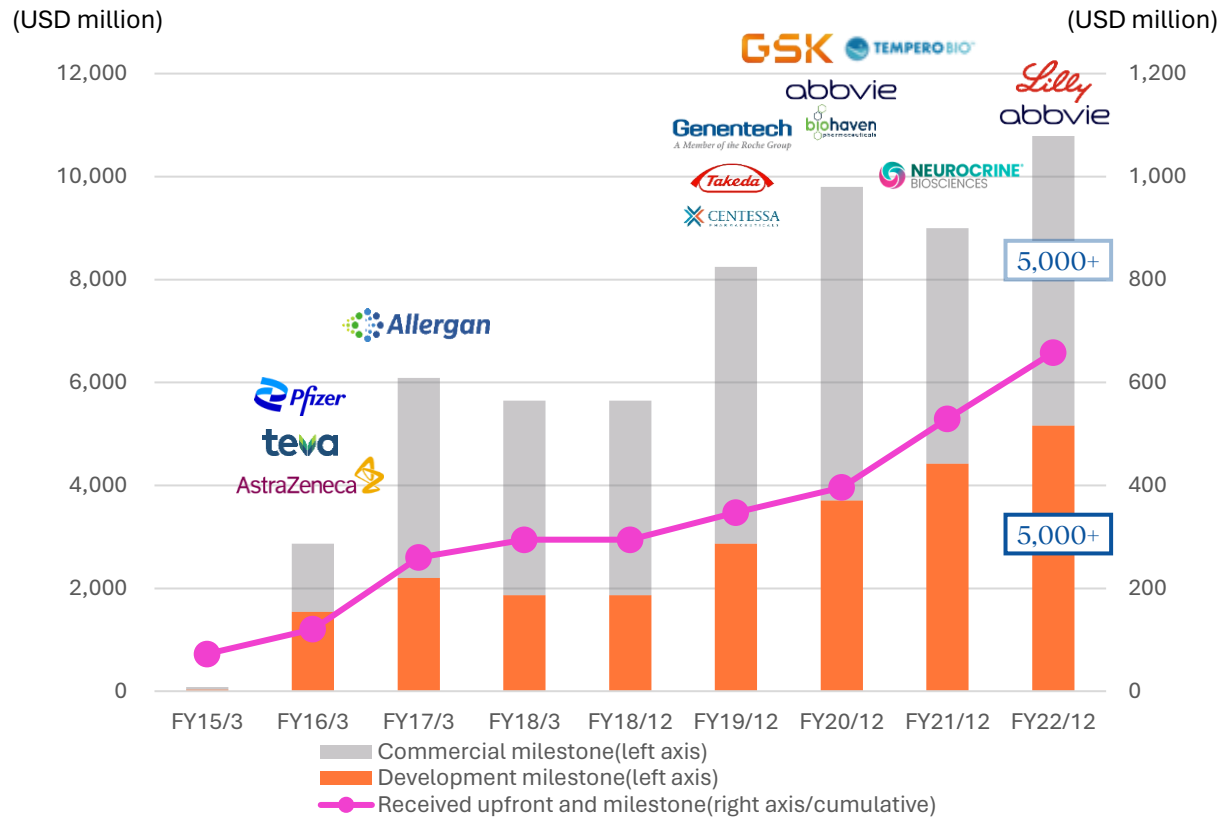


Our track record of major licensing transactions speaks for itself...

Income from licensing provides a great source of non-dilutive financing to support our growth

Balance of potential milestone income from existing license agreements¹

Top 15 pharmaceutical/biotech companies by license value² (cumulative total since 2015)













¹ Balance as of the end of the fiscal year of only those currently under contract. TEVA and Abbvie (formerly Allergan), for which compounds were returned, are excluded from the balances from FY2018 and FY2021, respectively.

² The figures are based on 'Licensing' category on third party's (EvaluatePharma's) proprietary database and therefore do not completely match the amounts shown in the LHS chart.

Source: Company's data (LHS) and EvaluatePharma (as of 2023/2/6) (RHS)

... hundreds of millions of dollars received, billions of dollars in potential milestones to come

New collaboration and exclusive option to license agreement recently executed with Boehringer Ingelheim

Partner	Execution	Program	Therapeutic Area(s)	Upfront and Initial Milestones	Potential Total Milestone ¹
 Boehringer Ingelheim	March 2024	Collaboration and exclusive option-to-license agreement for GPR52 agonist	Schizophrenia	EUR25m	EUR670m
	December 2022	Multi-target Collaboration	Diabetes and Metabolic	\$37m	\$800m
	August 2022	Multi-target Collaboration	Neurological disorders	\$80m	\$1.2bn
	December 2021	Collaboration and license agreement for M ₄ , M ₁ and M ₁ /M ₄ dual agonist	Neurological disorders	\$100m	\$2.6bn
	December 2020	Collaboration and license agreement for GPR 35	Gastrointestinal, immunology	\$44m	\$480m
	December 2020	Collaboration and license agreement for CGRP portfolio	Neurology	\$10m	\$380m
	June 2020	Discovery Collaboration and Option to License ²	Inflammatory and Autoimmune	\$32m	\$400m
	August 2019	Multi-target Collaboration	Multiple; Initial focus on Gastrointestinal	\$26m	\$1.2bn
 <small>A Member of the Roche Group</small>	July 2019	Multi-target Collaboration	Multiple	\$26m	\$1bn
	November 2015	Multi-target Collaboration	Multiple	-	\$1.8bn

¹Potential option fees, development, regulatory and commercial milestone payments agreed at the time of transaction. Nxera is also eligible to receive tiered royalties ranging from high single digit to mid-teen percentage on future net sales of any products developed under the partnership. ² AbbVie has the option to expand the collaboration by an additional three targets



Our NxWave™ Platform

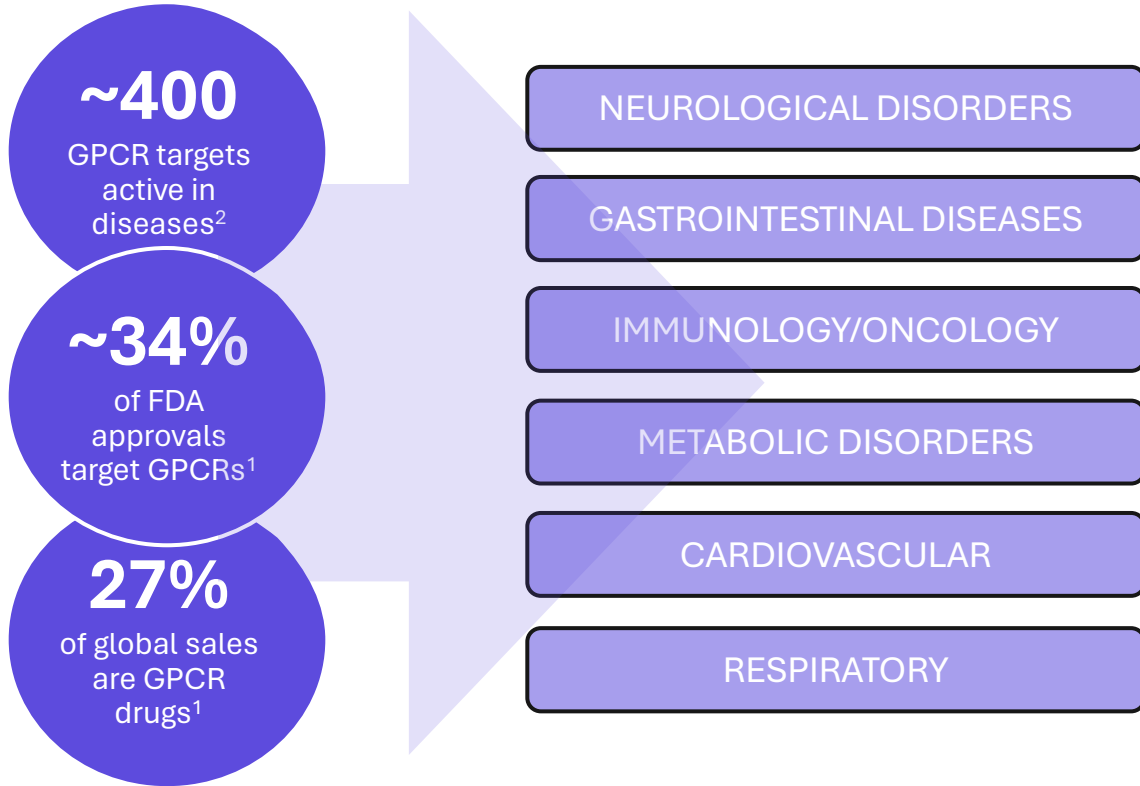
Cutting-edge Science

04

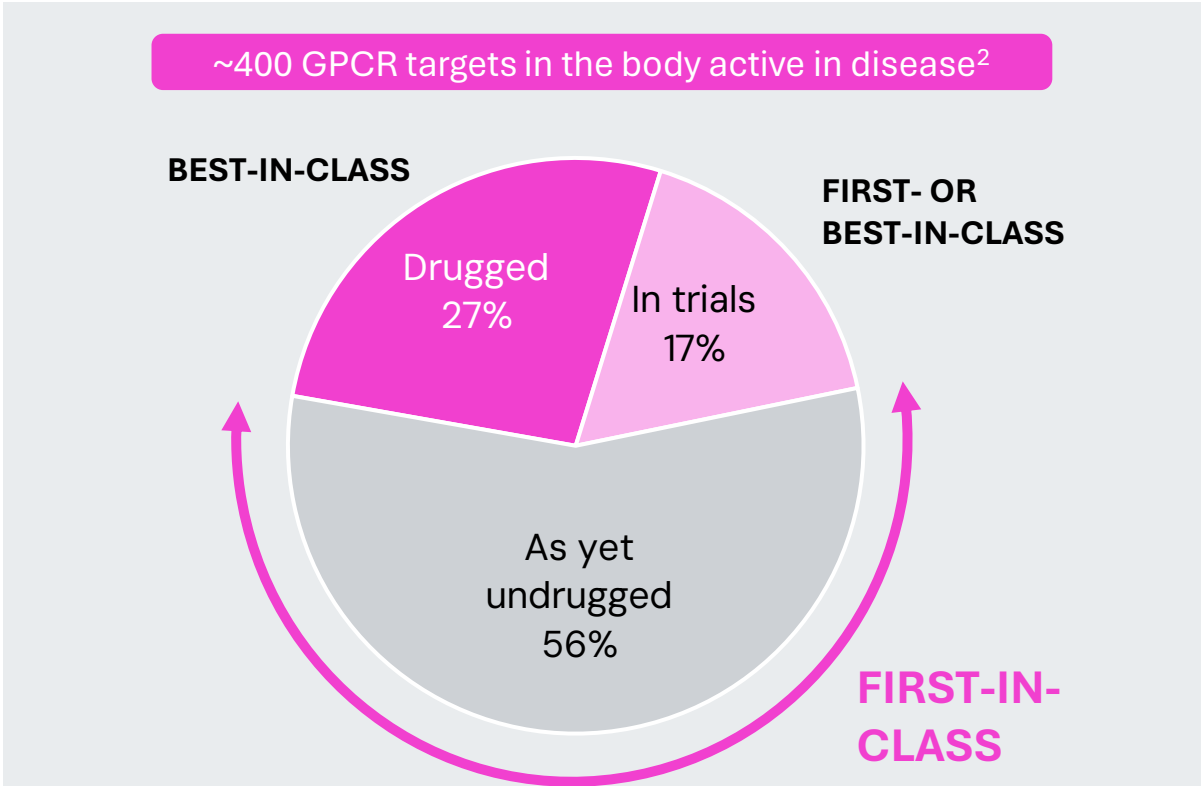


NxWave™ platform is focussed on drugging GPCRs

GPCRs are the largest family of drug discovery targets – comprising 1/3 of all FDA approved drugs



GPCRs are active in a wide range of disease areas, and offer broad therapeutic potential





Significant opportunity to target new first-in-class and/or improved best-in-class GPCR medicines

Sources: ¹ “Unexplored opportunities in the druggable human genome”, Nature Reviews, 2016; ² “Trends in GPCR in Drug Discovery – new agents, targets and indications”, Nature Reviews, 2017



NxWave™ platform enables faster, cheaper and more precise drug discovery

World-leading science and platform enables efficient drug discovery against difficult targets

	 Conventional drug discovery	 Our drug discovery
Approach	Empirical design	Rational design (computer-based)
Method	High Throughput Screening (HTS¹)	Proprietary NxWave™ Platform
Period²	4.5 years on average	3.0 years on average
Costs²	\$15 million	\$5 million
Features³	Difficult to design drugs precisely – high development attrition rate	Execute more precise drug design – lower development attrition rate
Target³	Difficult for GPCRs with unstable structures	Best for GPCRs with unstable structures

¹ HTS/High Throughput Screening is a method to find drug candidates by reacting tens of thousands to millions of compounds with drug targets using large machines and human hands.

² The period from target selection to preclinical testing. For conventional drug discovery, figures are taken from NATURE REVIEWS Drug Discovery (MARCH 2010).

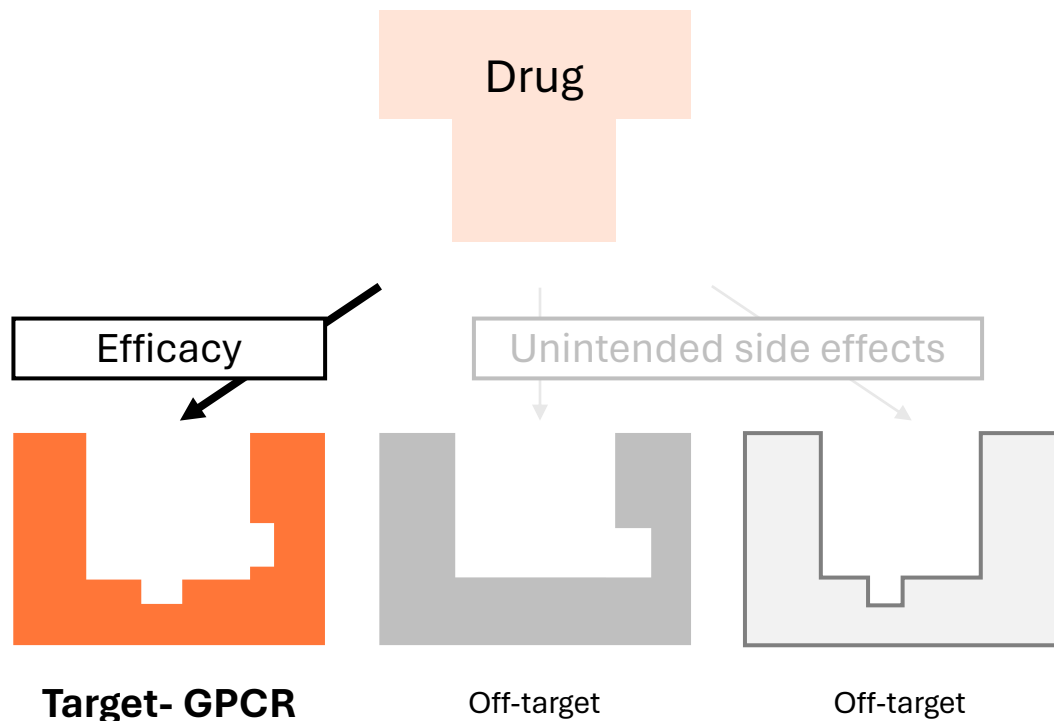
³ Precise drug design make clear the binding site of target, make easier to improve compound, create backups and redo – potentially increase the success rate. GPCR is most popular drug target which account for 30% of current drug target.

Our platform enables to design precise GPCR models

Only by performing detailed structural analysis can we design great drugs.

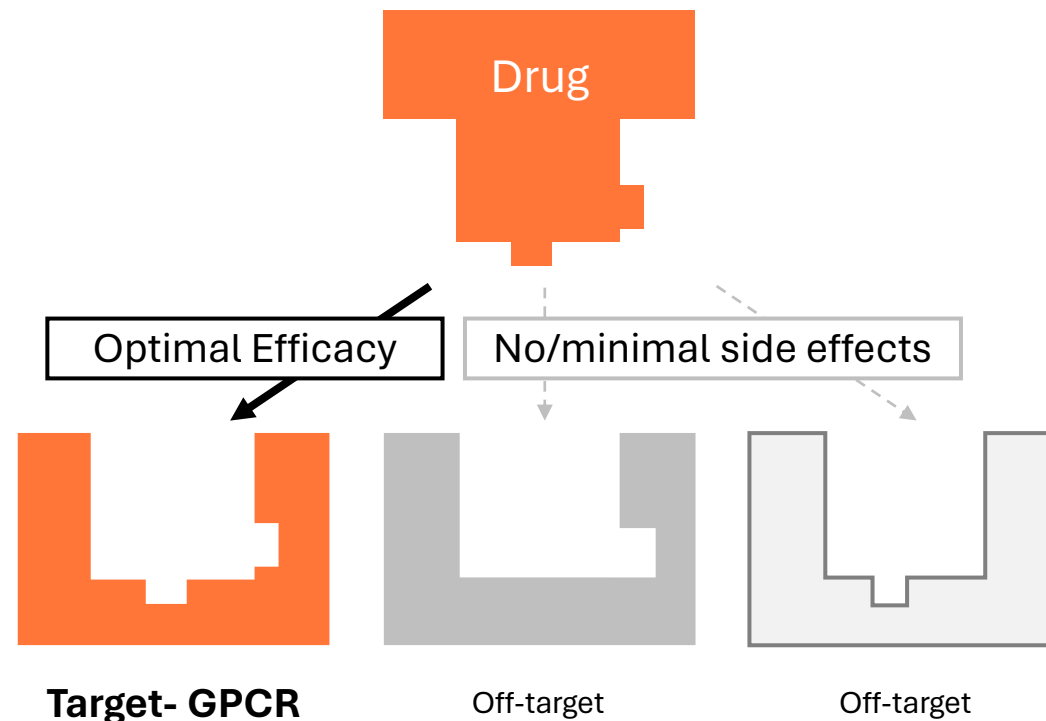
Imprecise GPCR model: **Standard Medicine**

Poorly understood GPCRs (locks) led to suboptimal drugs (keys) being designed



Precise GPCR model: **Optimized Medicine**

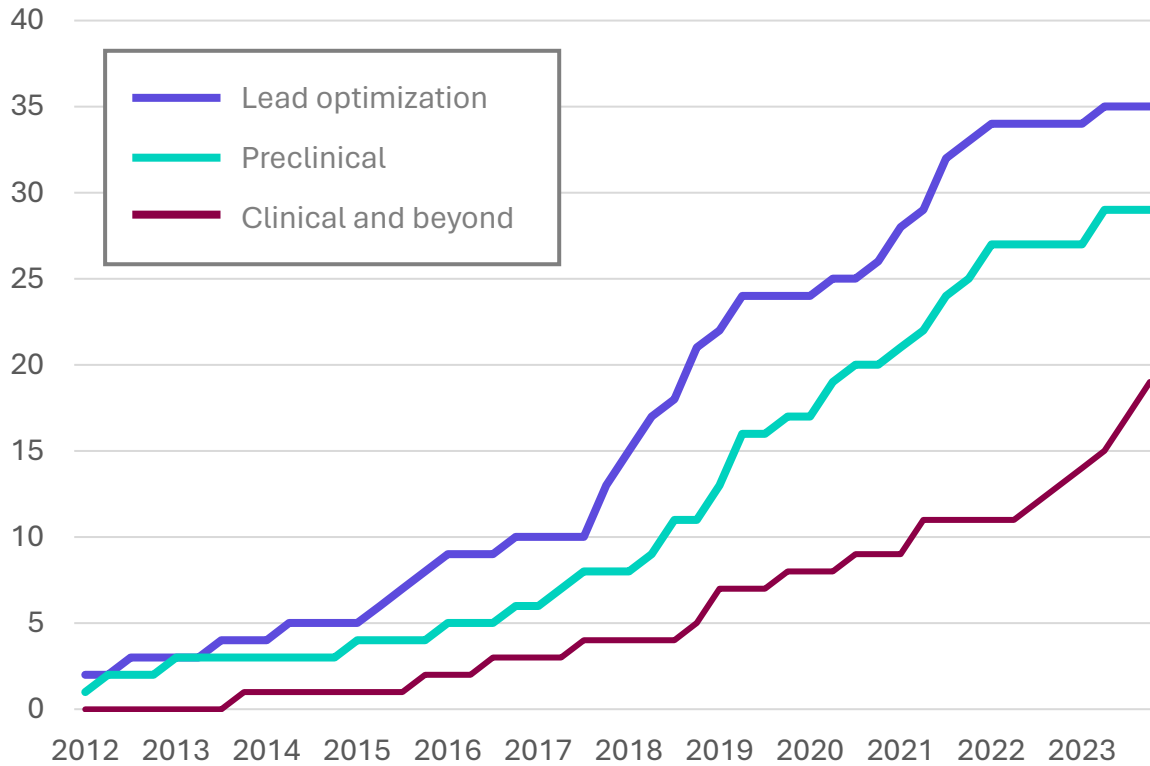
High selectivity enables to **optimize efficacy and minimize side effects**





NxWave™ platform has proven to be more productive than conventional approaches

Trends in the number of programs per stage (cumulative)*



Number of programs* 2022 vs 2023

	2022	2023
Drug discovery	20+	20+
Lead optimization	7	8
Preclinical	9	6
Clinical – Phase 1	7	11
Clinical – Phase 2	3	3
Clinical – Phase 3	0	0
Approval application	0	0
Approved	0	0

* The number of programs here represents the number of all drug candidates generated to date from our NxWave™ drug discovery platform by stage and includes programs that are not currently being actively developed by us or our partners due to lower priority.

Our NxWave™ platform has generated programs in the hottest areas of medicine


Global partners have been drawn to our innovation and productivity in these areas

Neuropsychiatry

Significant market opportunity

- ✓ Karuna: c.US\$14bn (acquisition by BMS – 2023)
- ✓ Cerevel: c.US\$9bn (acquisition by AbbVie – 2023)

Multiple first and best-in-class programs

Muscarinic agonists with  **NEUROCRINE**
BIOSCIENCES


GPR52 agonists with  **Boehringer
Ingelheim**


Metabolic disease

Multi-billion dollar market

- ✓ GLP-1 ag. sales estimated to reach c.US\$50 bn in 2024
- ✓ Over \$100bn market potential by 2030

Obesity and T2D programs

GLP-1 agonist (PF'522) with  **Pfizer**

Multi-target programs with  **Lilly**

In-house programs, upstream of incretins
(a novel oral small molecule appetite suppressor)



Nxera is perfectly positioned to capture economics in the fastest growing areas of medicine



Financial Results

05



Financial summary for Q1 FY2024

Sales increased due to PIVLAZ[®] sales and upfront fee from Boehringer Ingelheim

01

Revenue of ¥4,611m (\$31m) vs. ¥943m (\$7m) in the prior comparative period.

Revenue is higher primarily due to (i) the inclusion of ¥2,283m (\$15m) of PIVLAZ[®] sales in Japan, and (ii) a new ‘option to license’ transaction with Boehringer Ingelheim signed in March 2024 with a EUR 25 million upfront (of which EUR 10 million (¥1,596m / \$11m) has been recognized as revenue in Q1 2024).

02

Core Operating Loss of ¥931m (\$6m) vs. ¥1,465m (\$11m) in the prior comparative period.

The decrease in Core Operating Loss is due to the increase in revenue explained above, partially offset by an increase in costs, including additional core costs totaling ¥ 2,193m (\$15m) relating to the Idorsia businesses acquired in July 2023.

03

Net Loss of ¥3,281m (\$22m) vs. ¥1,402m (\$11m) in the prior comparative period.

The increase reflects (i) the inclusion of higher non-cash costs (incl. PIVLAZ[®] related amortization and an additional non-cash charge in Cost of Sales relating to inventory acquired from Idorsia July 2023) and (ii) an increased tax expense in Q1 2024 due to the reversal of deferred tax assets.

04

¥47bn (\$307m) cash balance as at March 31, 2024.

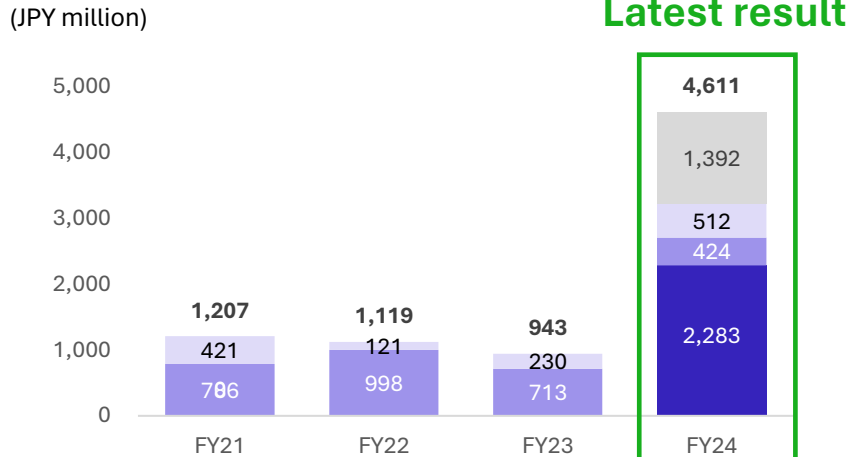
We have maintained a strong cash balance.



Key financial indicators

Quarterly revenues are substantially higher than prior comparative quarters due to the inclusion of PIVLAZ® product sales and revenue from the new Boehringer Ingelheim deal.

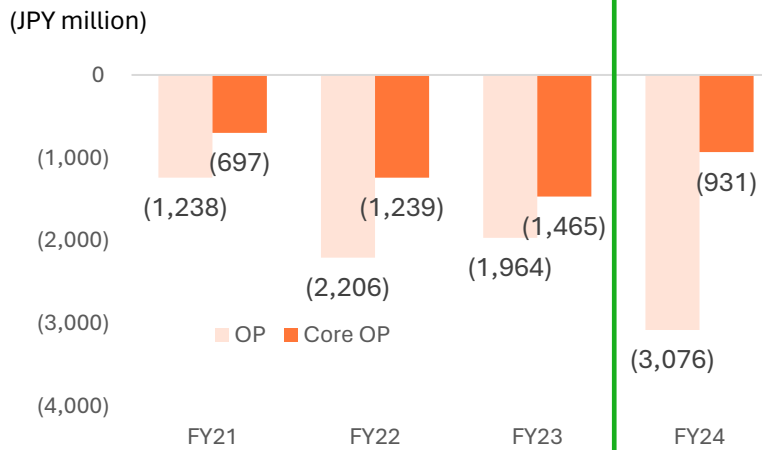
Revenue



EXPLANATION

Upfront ¹	Option-to-license deal signed with Boehringer Ingelheim in Q1 2024 vs. no new deals in the prior comparative period
Milestone ²	No milestone events in Q1 2024 nor in Q1 2023. Increase in deferred revenue releases (which relate to the active collaborations) due to inclusion of new collaboration with Boehringer Ingelheim
Royalty / Other	Royalty income has decreased in line with expectations
Product Sales	Increased due to PIVLAZ® sales

Operating Profit / Loss



Cost of Sales	Inclusion of PIVLAZ® product supply costs Additional non-cash CoS charge relating to PIVLAZ® inventory acquired from Idorsia in July 2023. This will cease when the original balance acquired has been sold.
R&D	Planned increase in investment in discovery activities Inclusion of Idorsia related R&D costs
SG&A	Inclusion of Idorsia related SG&A costs Capability build + Integration costs (incl. rebranding) Amortization of intangible assets (PIVLAZ®)

¹ Upfront fee revenue recognised at deal inception

² Milestone revenue recognised at milestone event + deferred revenue releases

Breakdown of Q1 2024 result

Impact of Non-cash/Non-recurring costs on full-year result is more significant in 2024 due to the inclusion of Idorsia businesses

(JPY million)	Legacy Business ^{*1}	+ NPJ / NPK ^{*2}	= Consolidated P&L (Core)	+ Non-cash costs	+ Non-recurring Costs	= Consolidated P&L (IFRS)
Revenue	2,328	2,283	4,611			4,611
Cost of Sales + SG&A	(1,164)	(1,821)	(2,985)	A (686) B (341) D (615)	C (214) Integration Other	(4,841)
R&D	(2,503)	(371)	(2,874)	D (289)		(3,163)
Other income	317	-	317			317
OP/Core OP	(1,022)	91	Core OP (931)			OP (3,076)
Idorsia & Integration related Costs	<p>A Additional CoS charge for PIVLAZ® inventory acquired from Idorsia in July 2023 and sold in the period. Impact will continue until mid 2024.</p> <p>B Amortization of intangible assets (currently relates to PIVLAZ®). Annual charge to increase to c. JPY 1,800m per year from 2025.</p> <p>C Integration costs including IT system integration and Corporate rebranding.</p>					
Other	<p>D Amortization of other intangible assets (e.g. IP), depreciation (e.g. laboratory equipment), share-based payments and other restructuring costs.</p>					

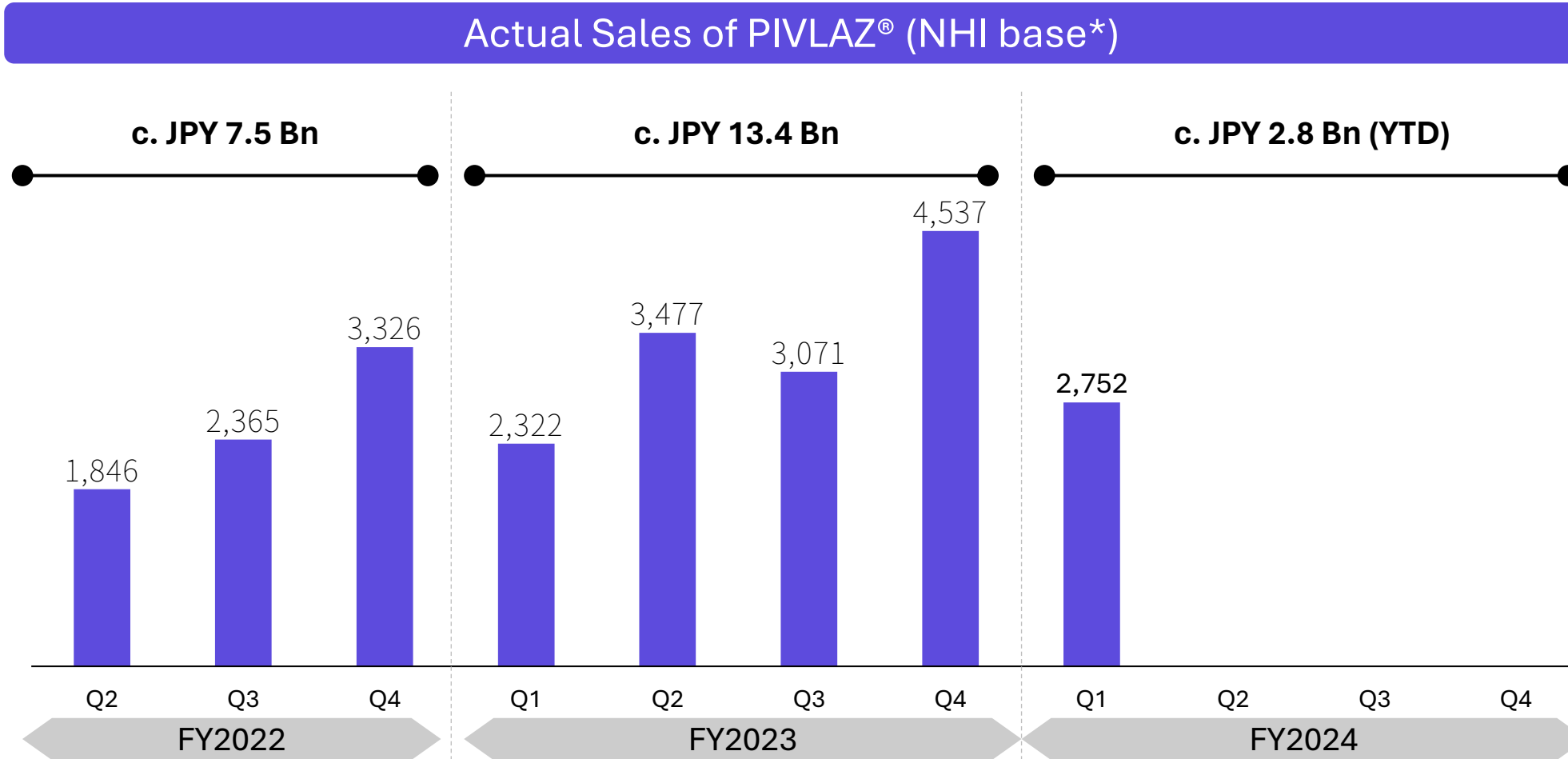
*1 = Nxera Pharma Co. Ltd. (formerly Sosei Group Corporation) + Nxera Pharma UK Ltd (formerly Heptares Therapeutics Ltd.) + Sosei K.K

*2 = Nxera Pharma Japan (formerly Idorsia Pharmaceuticals Japan) + Nxera Pharma Korea (formerly Idorsia Pharmaceuticals Korea)



Product sales

PIVLAZ® sales are projected to reach JPY 16+ billion* (c. 114+ million USD) in 2024



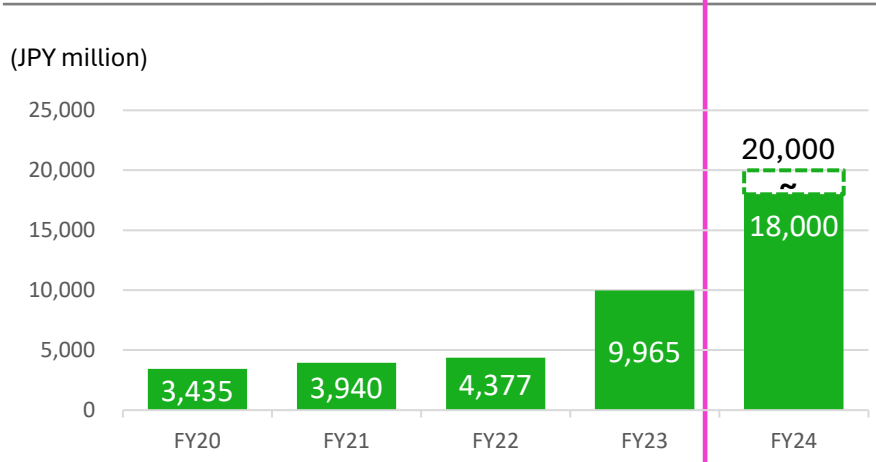
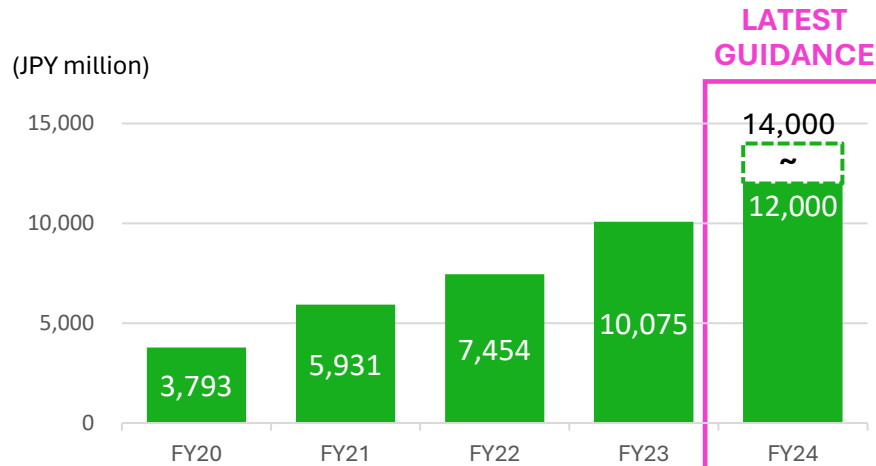
- Q1 2024 PIVLAZ® sales are up 19% vs prior comparative quarter.

* NHI price basis which is different to reported net sales basis
 The assumed USD:JPY FX rate in 2024 is 140



Full year cost guidance

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



R&D expenses (IFRS basis)

¥12,000 to ¥14,000m

Inclusion of IPJ/IPK cost	<ul style="list-style-type: none"> Inclusion of IPJ/IPK R&D costs for a full year
Strengthening capability	<ul style="list-style-type: none"> Investment in discovery and translational medicine capabilities
Advancing priority programs	<ul style="list-style-type: none"> Maturity of several priority programs, incl. at least 1 clinical trial initiation Advancing priority programs further in the clinic will deliver greater value through higher out-licensing revenues

S&M + G&A expenses (IFRS basis)

¥18,000 to ¥20,000m

Inclusion of IPJ/IPK cost	<ul style="list-style-type: none"> Inclusion of IPJ/IPK SG&A costs for a full year Increase in amortization charge (c. JPY 700 mil.) Increase in support for PIVLAZ® to drive growth, commercialization of Daridorexant in Japan and preparation for launch of PIVLAZ® in South Korea (c. JPY 2,000m)
Post-merger integration	<ul style="list-style-type: none"> Costs relating to the acquisition of IPJ/IPK (post-merger integration) are expected in 2024 (c. JPY 1,000m)

Appendix

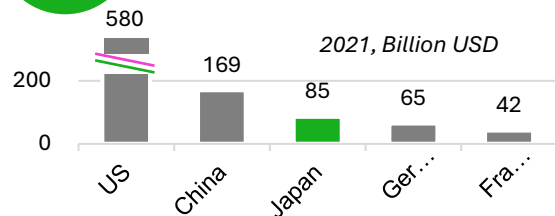
Japan will serve as our base to expand across APAC markets

APAC is one of the most rapidly growing markets in the world

Established market with strong volumes



Second largest pharma market (excl. China)

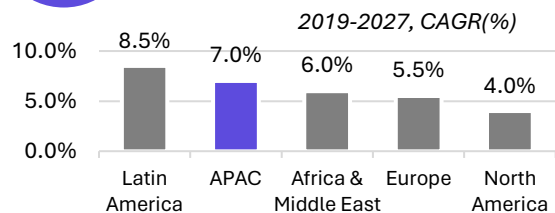


- Universal health care system
- Relatively weak incumbents
- Attractive market for newcomers
- Large, ageing population
- Stable, pro-innovation market

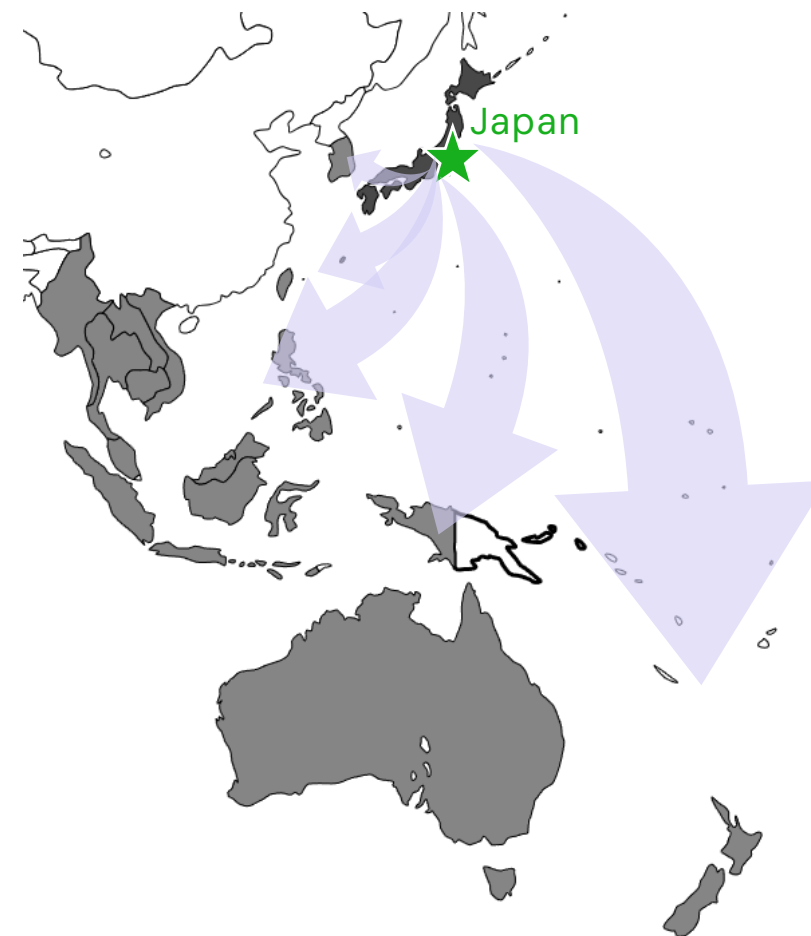
APAC* One of the fastest growing pharma regions globally



Second highest growth pharma market



- Significant population growth
- Developing GDP/economies
- Attractive market for newcomers
- Large, ageing population
- Accessible via other regulatory approvals



Source: IQVIA Market Prognosis, Sep 2022; IQVIA Institute, Nov 2022.

*APAC (ex-China) territory includes South Korea, Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand and Vietnam



Utilizing Japan's high quality clinical data in development and marketing

Expanding into APAC by leveraging clinical innovations based on Japan's high-quality data

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



Excellent access to Doctors/HCPs who evaluate novel drugs
Typically achieve strong patient uptake
Reduces 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



PIVLAZ®

Positive top-line results from Japan specific registration program

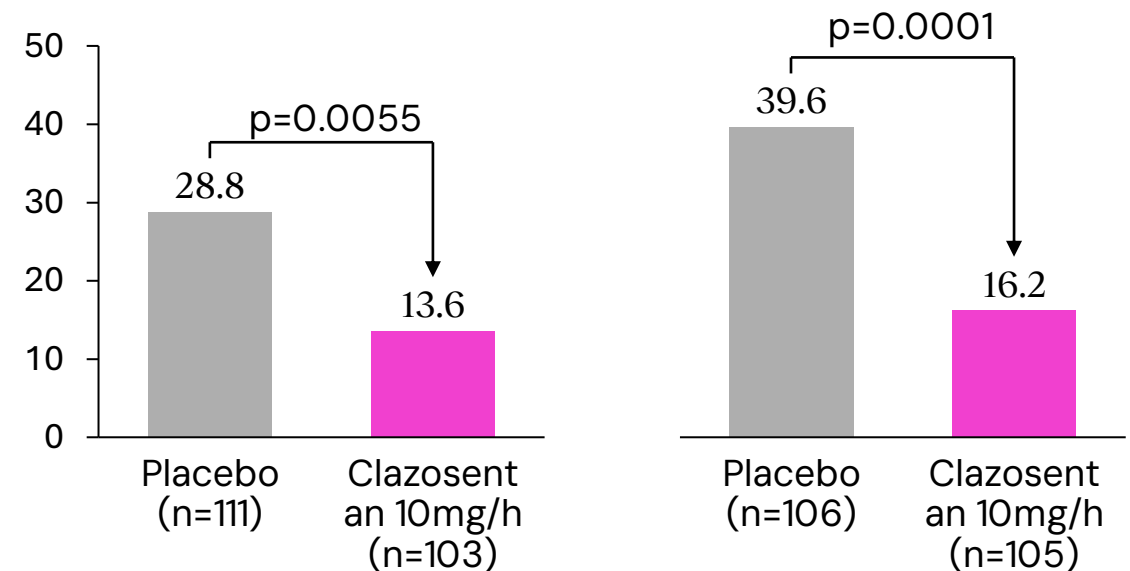
RESULTS OF TWO PIVOTAL PHASE 3 STUDIES IN JAPAN¹

- PIVLAZ® (clazosentan) demonstrated significant reduction of vasospasm-related morbidity and all-cause mortality in patients following aSAH (primary endpoint)
- Clazosentan showed a numerical reduction of all-cause morbidity and mortality in both studies. The effect of clazosentan on this endpoint was significant ($p < 0.05$) in a pre-planned pooled analysis
- Encouraging positive trends were observed on long-term measures of clinical outcome (GOSE and mRS) at week 12
- There were no unexpected safety findings
- Results published in the Journal of Neurosurgery: Endo H, et al. April 01, 2022; DOI: 10.3171/2022.2.JNS212914

COILING STUDY

CLIPPING STUDY

Event rate (%)



PIVLAZ® significantly reduced vasospasm-related morbidity and all-cause morbidity and mortality in domestic Phase 3 trials. It is a highly impactful medicine used to prevent death and disability after aSAH.

¹ Two prospective, multicenter, double-blind, randomized, placebo-controlled, pivotal Phase 3 studies assessing the efficacy and safety of clazosentan in reducing vasospasm-related morbidity and all-cause mortality events in adult Japanese patients post-aSAH, were conducted in parallel in 57 neuro surgical centers in Japan. Patients were randomized 1:1 to receive continuous infusion of either 10 mg/hr of clazosentan or placebo within 48 hours of the onset of aSAH for up to a cumulative maximum of 15 days after aSAH. Protocols were identical, each study enrolling 221 patients, except for the securing intervention, which was either endovascular coiling (JapicCTI-163369; the “coiling study”) or surgical clipping (JapicCTI-163368; the “clipping study”)



Daridorexant – Global And Japan-Specific Program

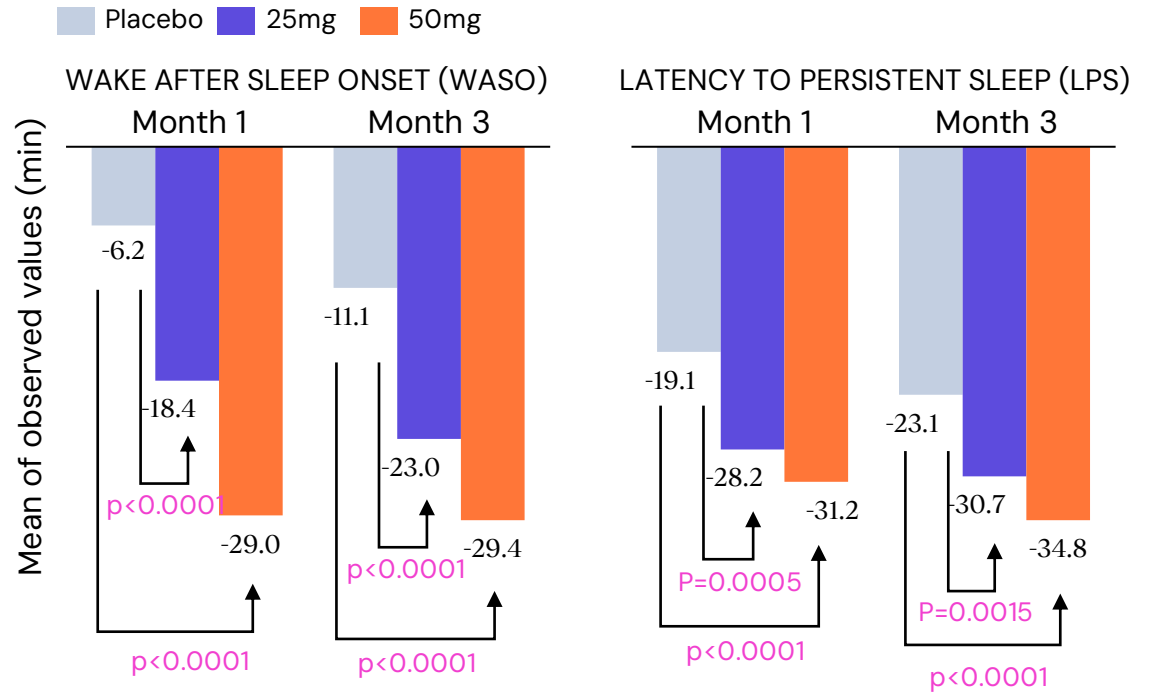
Positive Japanese Phase 3 study; in-line with US study as published in The Lancet¹

RESULTS OF GLOBAL AND JAPANESE PIVOTAL TRIALS¹

- A Japanese Phase 3 trial¹ in 490 adult and elderly patients met both primary and secondary efficacy endpoints, with similar results to the global study published in Lancet Neurology
- Daridorexant significantly improved total sleep time (sTST, $p < 0.001$ for 50 mg dose) and significantly improved latency to sleep onset (sLSO, $p < 0.001$ for 50 mg) v placebo at 28 days
- The rate of adverse events was comparable between placebo and daridorexant
- In the global trial, daridorexant also demonstrated significant improvement in daytime sleepiness, which means patients reported feeling less mentally and physically tired, less sleepy and more energetic during the day
- Submission to the PMDA based on the global and Japanese data is planned for 2H 2023

¹The global study published in the Lancet Neurology is Mignot E, et al. Lancet Neurol 2022; 21: 125–39. The Japanese study (JRCT2031200452) was a randomized, double-blind, placebo-controlled, Phase 3 study to investigate the efficacy and safety of daridorexant. 490 randomized adult and elderly patients (30.1% ≥ 65 years) with insomnia disorder received 50 or 25 mg doses of daridorexant or placebo once daily for 28 days.

TWO PRIMARY ENDPOINTS FULLY MET IN GLOBAL PHASE 3 TRIAL



Daridorexant significantly improves wake after sleep onset, latency to persistent sleep, subjective total sleep time, and next-day sleepiness/daytime functioning (as measured by IDSIQ sleepiness domain) compared to placebo



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 Nxera responsible for all development plans and future costs in the territory. If successfully commercialized, Nxera 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

Exclusive Opt-in Rights And ROFN/ROFR¹

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	S1P1 receptor modulator	Systemic lupus erythematosus	Phase 3	APAC (ex-China) ²
	Lucerastat	Glucosylceramide synthase inhibitor	Fabry disease	Phase 3	
ROFR /ROFN ¹	Selatogrel	P2Y12 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*	

¹ ROFN/ROFR - Right of first negotiation / Right of first refusal

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

* Global Phase



Core Operating Profit - Definition

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

Operating Profit

“Core”

- Core Operating Profit/ Loss is a key financial indicator that highlights the underlying recurring cash generating capability of our business.
- Core Operating Profit/Loss 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, M&A related professional fees and other material one-off items.

+ Material Non-cash Costs

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

+ Material Non-recurring Costs

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

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

Operating Profit

“IFRS”

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



Estimation of potential market size

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

Category	Indication ²	Number of Patients	Market Size		Individual Products	Our Candidates
Neurological disorders	Dementia	~55 million	\$7.3 billion (2010)		\$3.9 billion (2009/Aricept)	M1 agonist, M1/M4 agonist
	Schizophrenia	~20 million	\$20.7 billion (2011)		\$5.7 billion (2013/Abilify)	M4 agonist, M1/M4 agonist, GPR52 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 ¹ The number of patients with drug addiction

Source (Peak Sales): Sales of each indications are extracted from Evaluate Pharma's data of sales by disease and sales by individual products (as of 30 June, 2022). ² Nxera 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.



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	Nxera' 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.



Locations



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Japan



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Steinmetz Building
Granta Park,
Cambridge
CB21 6DG

United Kingdom



Spaces Grosspeter
Tower,
Grosspeteranlage
29,
4052 Basel

Switzerland



Thank you