



H1 FY2024 Financial Results

Six-month period ended June 30, 2024

9th August, 2024 | Nxera Pharma Co., Ltd. (TSE: 4565)

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- 02 Operational Highlights
- 03 Japan/APAC Commercial Business
- 04 R&D Progress
- 05 FY2024 Objectives
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Financial Results

Hironoshin Nomura, CFO

01



Financial summary for 1H FY2024

Another period of successful business execution with a new collaboration and development milestone events

01

Revenue of ¥12,720m (\$84m) vs. ¥2,146m (\$16m) in the prior comparative period.

Revenue is higher primarily due to (i) the inclusion of PIVLAZ[®] sales in Japan (ii) a new ‘option to license’ transaction with Boehringer Ingelheim signed in March 2024 (iii) \$15m M4 long term tox milestone from Neurocrine (iv) \$4.6m milestone from Centessa and (v) \$10m milestone from AbbVie

02

Core Operating Profit of ¥1,176m (\$8m) vs. Loss of ¥2,720m (\$20m) in the prior comparative period.

The change from Core Operating Loss to Profit is due to the increase in revenue per above, partially offset by an increase in costs, including additional core costs totaling ¥ 4,988m (\$33m) relating to the inclusion of NPJ/NPK* in the scope of consolidation in July 2023.

03

Operating Loss of ¥3,654m (\$24m) vs. ¥4,168m (\$31m) in the prior comparative period.

Amortization charge on intangible assets, PIVLAZ[®] inventory adjustment and integration costs were recorded as non-core costs

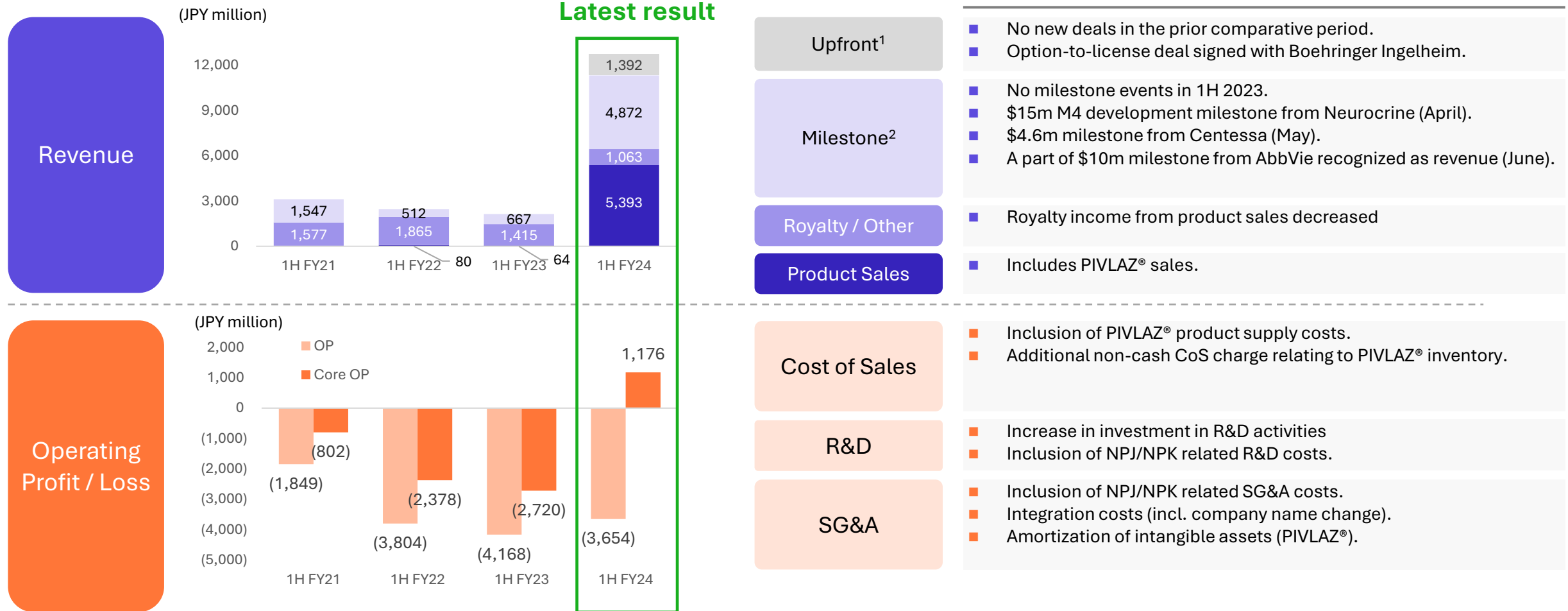
04

¥51bn (\$317m) cash balance as at June 30, 2024.

We have maintained a sufficient cash balance and investment capacity.

Key financial indicators

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



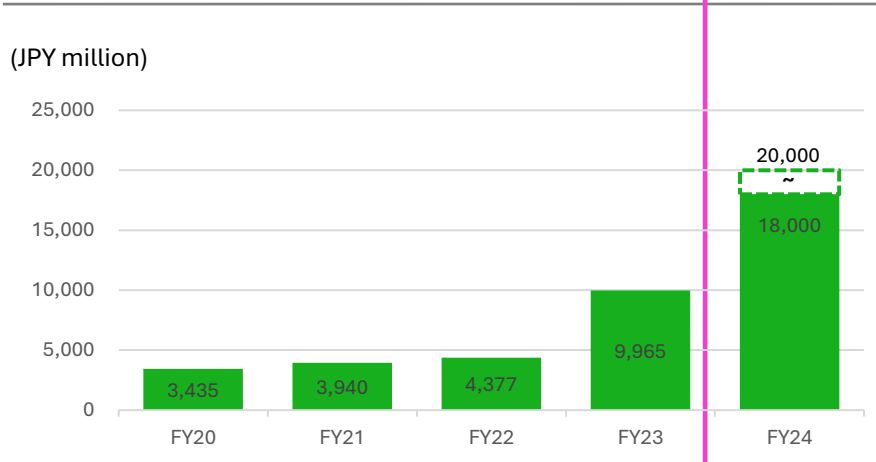
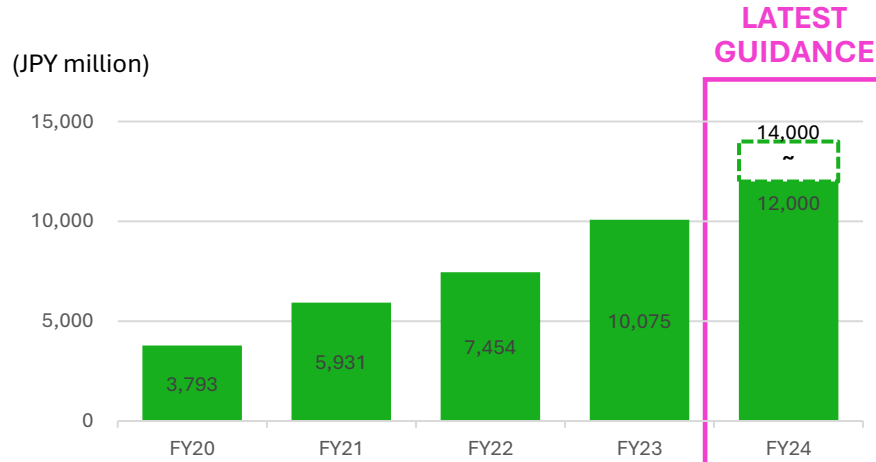
¹ Upfront fee revenue recognised at deal inception

² Milestone revenue recognised at milestone event + deferred revenue releases



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 NPJ¹/NPK² cost**
 - Inclusion of NPJ/NPK R&D costs for a full year
- Strengthening capability**
 - Investment in discovery and translational medicine capabilities
- Advancing priority programs**
 - At least 1 clinical trial initiation
 - Advancing in-house programs further in the clinic will deliver higher out-licensing revenues

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

¥18,000 to ¥20,000m

- Inclusion of NPJ/NPK cost**
 - Inclusion of NPJ/NPK 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**
 - Costs relating to the acquisition of NPJ/NPK (post-merger integration) are expected in 2024 (c. JPY 1,000m)

1. Nxera Pharma Japan 2. Nxera Pharma Korea





Operational Highlights

Chris Cargill, President and CEO

02

Objectives for 2024

Executing on our objectives to fuel long-term growth

1

JPY 16 billion+
NHI sales for
PIVLAZ[®]

- JPY 6.5bn achieved H1 2024 (+12% yoy)
- Further uptake expected post June KOL symposium (1.4k HCPs)

2

JNDA approval for
daridorexant in
Japan

- On-track for JNDA approval in H2 2024

3

Acquire/in-license
late-stage medicine(s)
for the JAPAC region

- Multiple confidential discussions ongoing

4

Execute new major
partnership(s), and
initiate new in-
house Ph.1 studies

- New option-to-license with Boehringer Ingelheim (GPR52)
- EP4 Agonist Ph 1 start

5

Investment in post-
merger integration
in new branding and
scalable systems

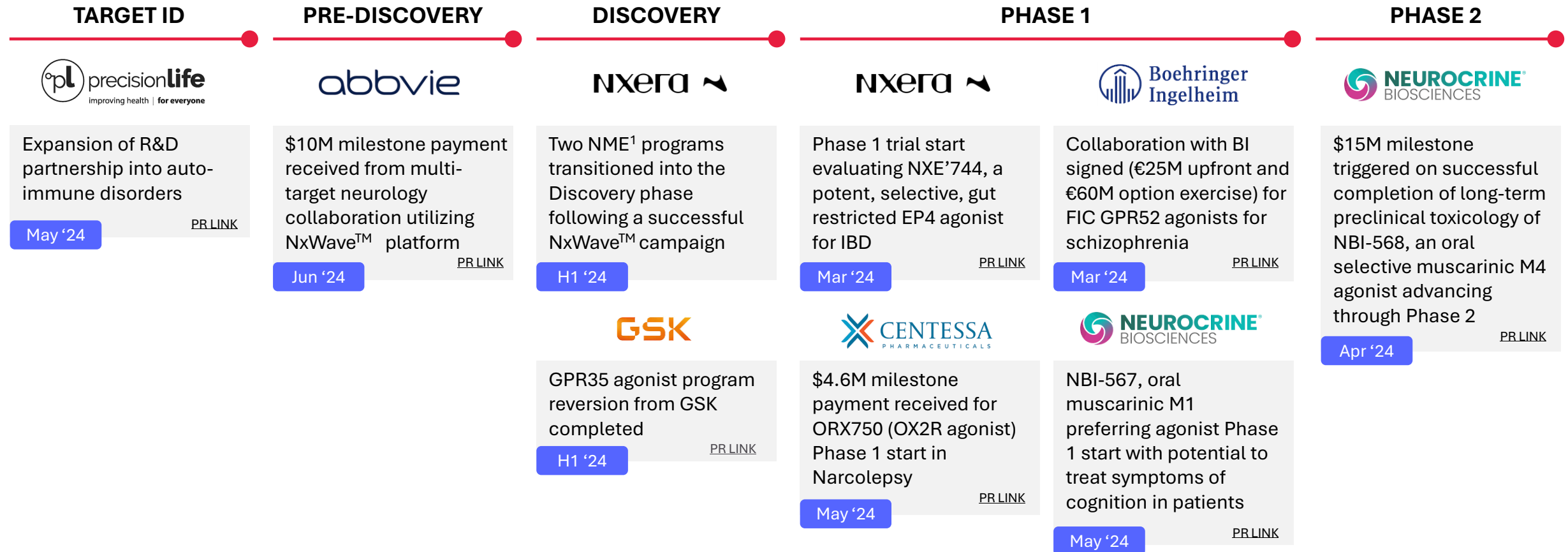
- New brand concept *Nxera Pharma* launched
- Multiple IT system integrations complete/ongoing

Solid first half focused on execution and investment to drive long-term growth



Pipeline progress

Accelerating the development of life-changing medicines, by investing in science and technology



World-leading NxWave™ SBDD platform continues to fuel innovation

1. NME = New Molecular Entity

Exposed to the fastest growing areas of medicine

Advancing with world-leaders in neuropsychiatry, metabolic disease, and sleep disorders

Neuropsychiatry



- Oral, selective muscarinic M4 agonist (NBI-568) for Schizophrenia. **Phase 2 POC¹ data readout expected Q3 2024**

BLOCKBUSTER
OPPORTUNITY

- Most comprehensive portfolio of muscarinic agonists in development globally, sourced from Nxera

- Option to license collaboration with BI for FIC GPR52 agonists (NXE-149) advancing through Phase 1
- Potential to simultaneously address positive, negative and cognitive symptoms of Schizophrenia

Metabolic disease



- NxWave™ SBDD used by Pfizer (PFE)
- Oral small molecule GLP-1 agonist (PFE-522) for Type 2 Diabetes Mellitus

BLOCKBUSTER
OPPORTUNITY

- NxWave™ SBDD used by Eli Lilly & Co (LLY)
- Multiple next-gen oral small molecule targets ongoing in discovery

BLOCKBUSTER
OPPORTUNITY

Sleep disorders



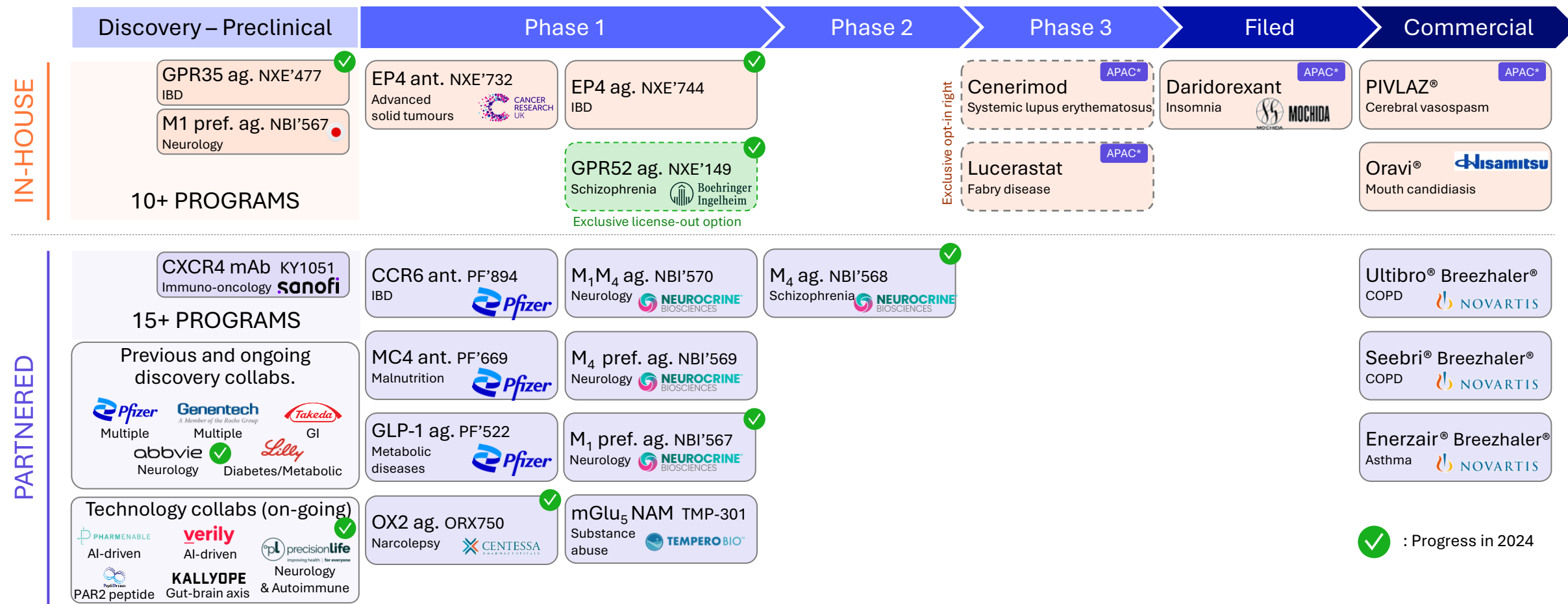
- NxWave™ SBDD used by Centessa Pharmaceuticals (CNTA)
- Oral small molecule orexin 2 agonist (ORX750) for Narcolepsy ongoing in Phase 1

BLOCKBUSTER
OPPORTUNITY

Perfectly positioned with the best partners in the hottest areas of medicine

Pipeline snapshot

A comprehensive clinical development pipeline



Leading the next generation of medicine. From Japan, for Japan, and the world.

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

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



Japan/APAC Commercial Business

Dr. Satoshi Tanaka, President of NPJ

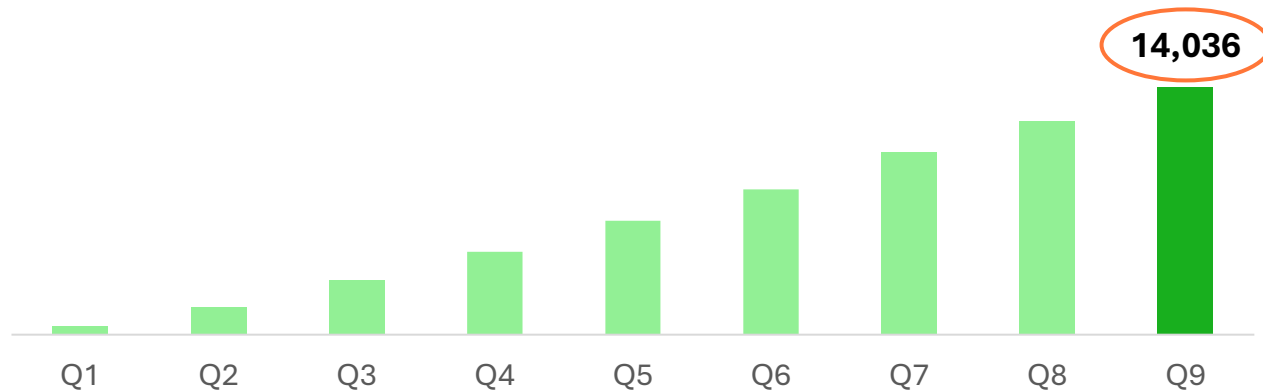
03

Our product: PIVLAZ®

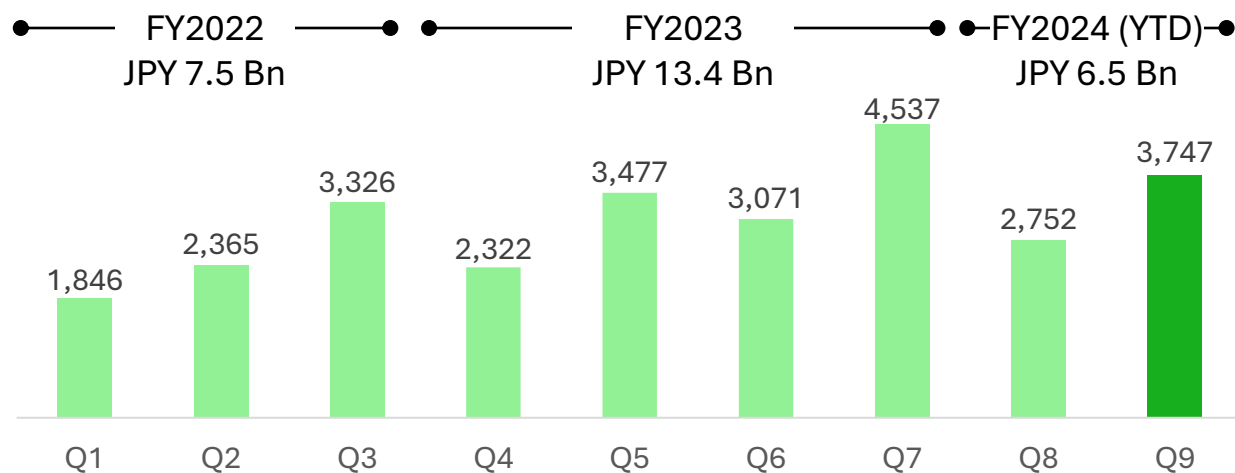
PIVLAZ® sales projected to reach JPY 16+BN* in 2024



Cum. patients to have received PIVLAZ®



NHI-based Sales (JPY Mn)



* NHI price basis which is different to reported net sales basis

- Becoming **the new standard of care** in preventing cerebral vasospasm following Subarachnoid Hemorrhage (SAH)
- Share of market increasing in Japan
 - PIVLAZ® now holds **around 60% market share** as at end 1H 2024 (patient-base), compared to around 40% as at 1H 2023
- Further incremental uptake by neurosurgeons expected (use in SAH operations) following KOL symposium held in June 2024 (1,400 HCPs attended)



In-house pipeline: Daridorexant

On-track for JNDA approval in H2 2024

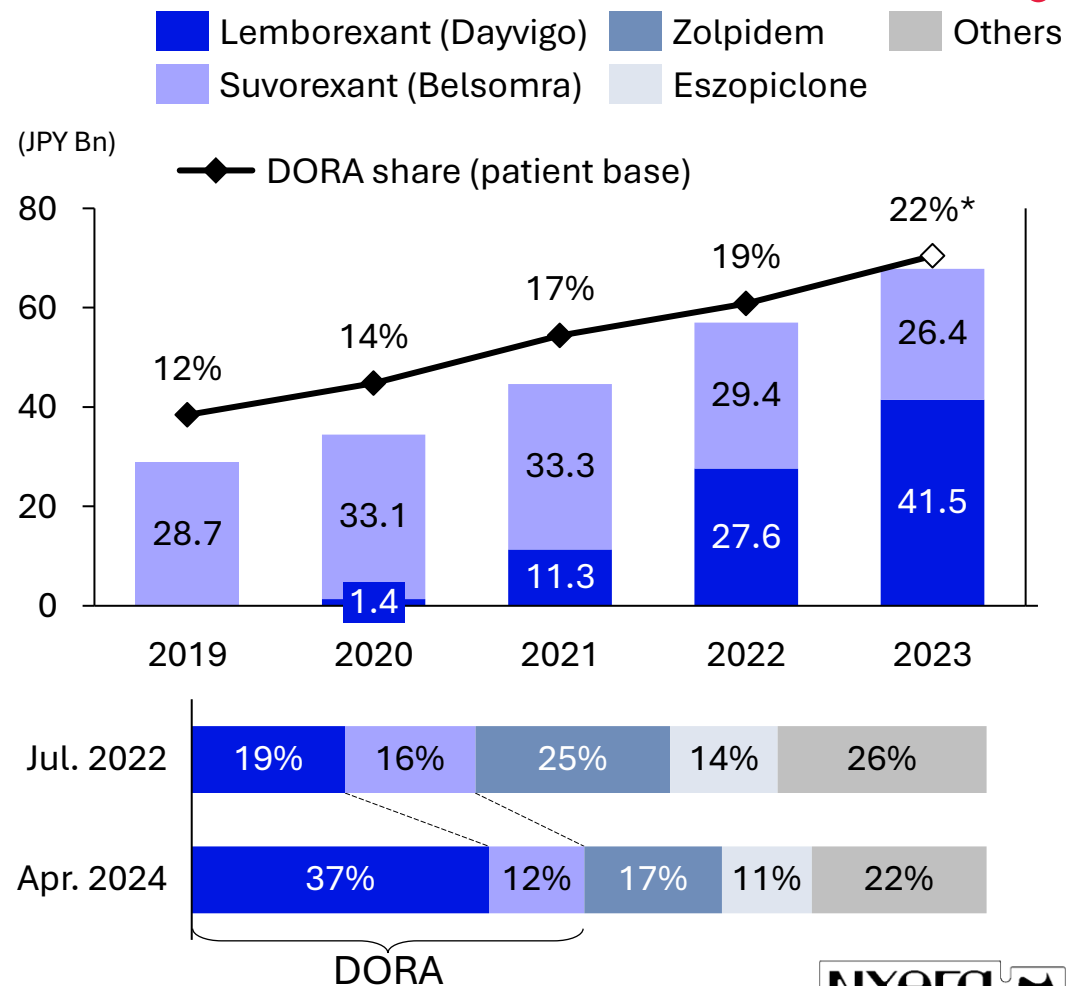
About daridorexant

- Dual orexin receptor antagonist (DORA) 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 JNDA filing submitted in Oct 2023
- Market exclusivity until 2038 (Japan and South Korea)

DORA: rapidly establishing its position in insomnia treatment

Sales (NHI-base) and market share of DORAs

Most frequently prescribed sleeping pills



Source: Nikkei Medical (2022/7/23, 2024/4/13), IQVIA, Encise
* Estimation



Accelerating our Japan/APAC business

Maximizing our Japan APAC business potential by utilizing external partners / alliances



Sales / Marketing

- Announced an exclusive supply and distribution agreement with Handok Inc.
- Handok is exclusively responsible for the promotion, marketing, sales and distribution of PIVLAZ® in South Korea



- Leading innovative pharmaceutical / healthcare company in South Korea
- Proven **track record of introducing new products** to the Korean market through partnerships



In-licensing activity

- Joined the World Orphan Drug Alliance (WODA)
- **Provides access to a pipeline of novel medicines** targeting rare or orphan diseases as potential licensing opportunities
- Nxera to represent WODA in Japan and South Korea



- Global alliance of commercial distributors dedicated to providing access to treatments for **rare diseases and specialty medicines** in complex markets around the world.




R&D Progress

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

04


Clinical Partnered Programs

9 Clinical Programs in Neuroscience, Autoimmune and Metabolic Diseases

 **M4 Agonist**
Schizophrenia - Phase 2



Oral M4 agonist for the potential treatment of adults with schizophrenia. **\$15M Milestone received following the long-term toxicology assessment. Phase 2 top-line data Q3 2024.**

 **M1 Agonist**
Neuropsychiatry - Phase 1



Oral M1-preferring agonist studied for the treatment of neurological and neuropsychiatric conditions **progressed into Phase 1** clinical trials

M₁M₄ Agonist
Neuropsychiatry - Phase 1



Oral selective M1/M4 dual agonist for potential treatment of neurological and neuropsychiatric conditions. **Phase 1 study ongoing**

GLP-1 Agonist
Metabolic - Phase 1



Oral small molecule GLP-1 receptor agonist has **started Phase 1 clinical trials.**

MC4 Antagonist
Malnutrition - Phase 1



The MAD study is **listed as completed** on clinicaltrials.gov

CCR6 Antagonist
IBD - Phase 1




Ongoing **Phase 1b study is progressing** as planned and expected to be completed within 2024.

mGlu₅ NAM
Substance Use Disorder - Phase 1




Phase 1 trials ongoing for the treatment of substance use disorders

 **OX2R Agonist**
Narcolepsy - Phase 1



Phase 1 clinical trials initiated for narcolepsy

- Centessa PR: <https://ssl4.eir-parts.net/doc/4565/tdnet/2452048/00.pdf>
- NBI-1117568: <https://clinicaltrials.gov/study/NCT05545111>
- Neurocrine NBI'567 PR: https://ssl4.eir-parts.net/doc/4565/ir_material14/228619/00.pdf
- Neurocrine NBI'568 PR: <https://ssl4.eir-parts.net/doc/4565/tdnet/2422333/00.pdf>

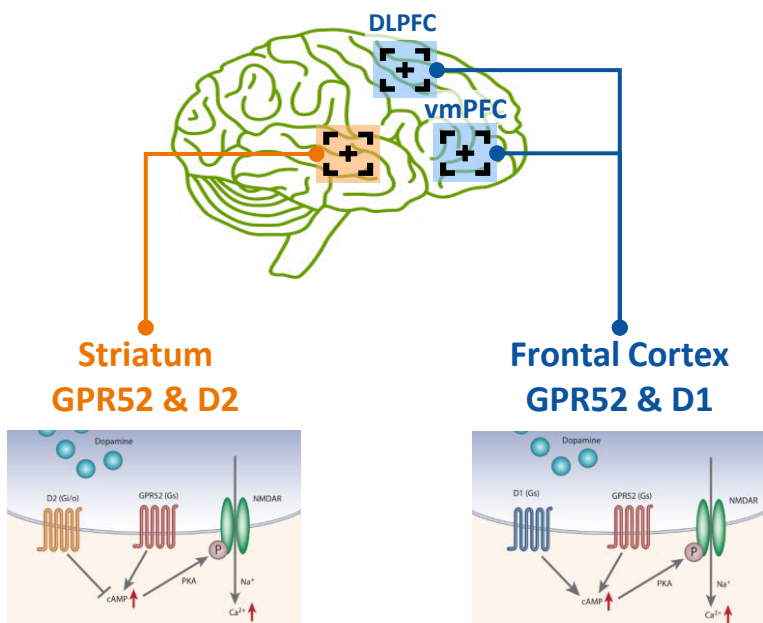
 : Progress in 2024

GPR52 Agonist for Schizophrenia

A Novel First-In-Class Mechanism to Treat Positive, Negative & Cognitive Domains of Schizophrenia

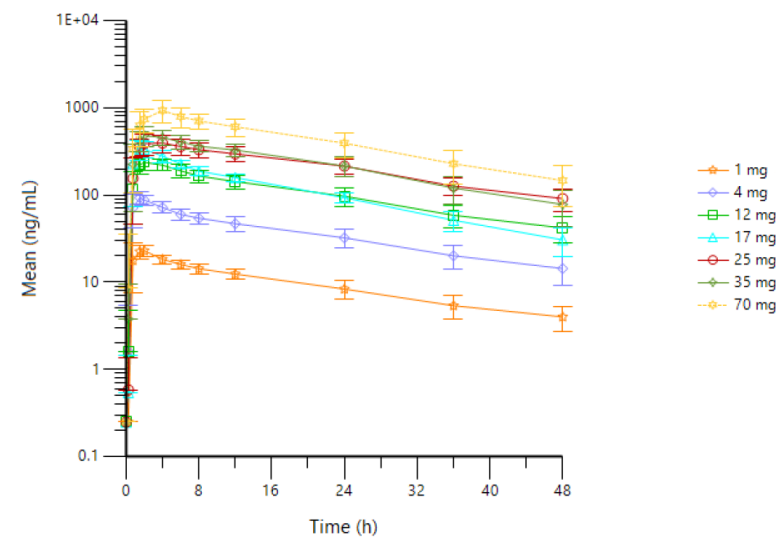
Disease Rationale

- GPR52 is expressed on D2 dopamine neurons in striatum where activation could lead to D2 antagonist-like effect to treat positive symptoms, e.g. hallucinations
- GPR52 also co-located with D1 dopamine receptor in prefrontal cortex where activation could lead to D1 agonist-like effect to improve cognition, e.g. attention



Results So Far

- In June 2023 we were the first company to initiate a Phase 1 study against this novel GPR52 target identified using Nxera's NxWave™ platform
- NXE'149 developed using SBDD for once-daily oral dosing
- Phase 1 on track. SAD PK data in line with preclinical predictions, linear across full dose range with low variability and consistent with once daily dosing
- Phase 1 MAD study including pharmacodynamic measures now ongoing



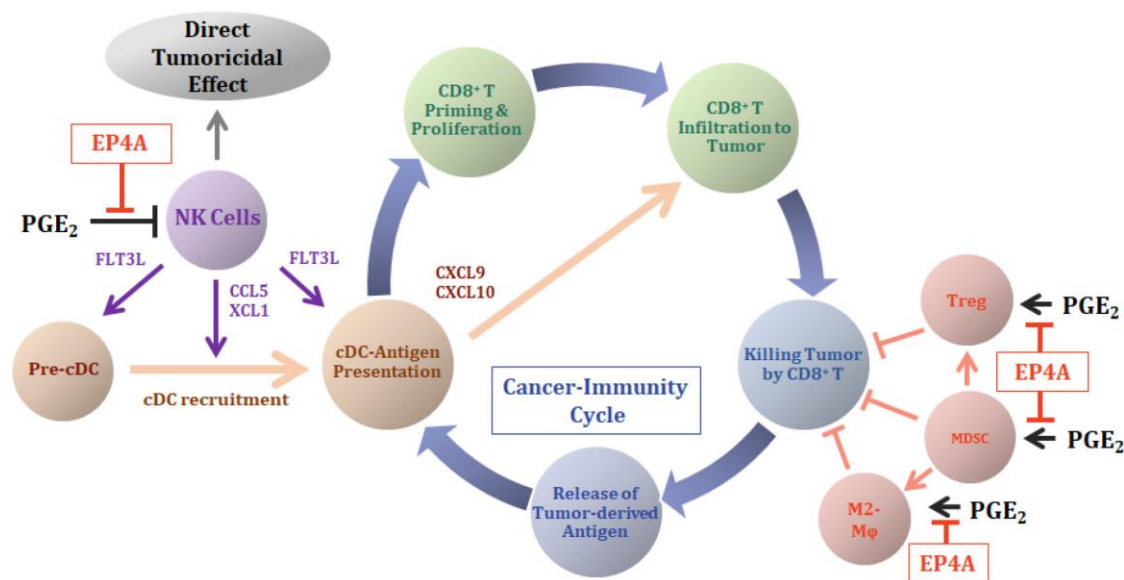


EP4 Antagonism for Advanced Solid Tumours

Alone or in Combination with Checkpoint Inhibitors (CPIs)

Disease Rationale

- Prostaglandin E2 (PGE₂) is secreted by tumour and surrounding tissue and signals through EP4 to suppress the immune system
- EP4 antagonism is expected to restore immunosurveillance and enhance the effect of CPIs
- Less than 20% of eligible patients derive benefit from CPIs, meaning there is a great unmet need



Results So Far

- Selective, potent EP4 antagonist identified using Nxera's NxWave™ platform
- PK in line with predictions
- Trials in progress and update to be presented at ESMO; https://cslide.ctimeetingtech.com/esmo2024/attendee/confcal_2/presentation/list?q=679TiP
- First public chemical disclosure: abstract to be presented at the 9th RSC-BMCS/RSC-SCI Symposium on GPCRs in Medicinal Chemistry in October

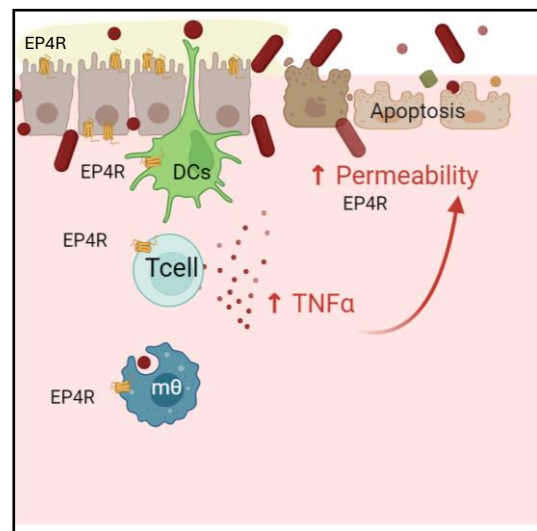
EP4 Agonist for Inflammatory Bowel Disease (IBD)

A First-In-Class GI Targeted Agent to Promote Mucosal Healing in IBD

Disease Rationale

- IBD is an immunological disorder in which current standard-of-care agents have treatment "ceilings" of about 40% response rates.
- All approved IBD agents are immunomodulatory in nature and do not directly target disease-induced mucosal barrier defects.
- Through combined anti-inflammatory and barrier repair effects, EP4 agonists are expected to bring benefits in IBD by promoting mucosal healing.
- Previous attempts to agonise the EP4 receptor have demonstrated early signals of clinical efficacy but have been limited by systemic safety.

Improved barrier repair & homeostasis
↓ Permeability



Created with BioRender.com

Results So Far

- Novel, potent GI targeted EP4 selective agonist (NXE'744) identified through Nxera's NxWave™ platform
- Preclinical discovery activities generated a novel gut-restricted agent with rodent efficacy in IBD models and demonstrated specific mechanistic effects in mucosal healing.
- A First-in-Human Phase 1 study, in healthy volunteers, commenced in March 2024, with single ascending dose (SAD) and multiple ascending dose (MAD) cohorts to be undertaken in an overlapping design.
- Dosing has proceeded well with the sixth SAD cohort currently being dosed and the second MAD cohort due to start imminently.
- No concerning adverse events have been noted to date.
- A Scientific Advisory Board was held in June 2024 with significant interest in the molecule from worldwide key opinion leaders.
- Further Ph 1B and II studies are currently being designed with the intent to commence the first of these in 2025.



FY2024 Objectives

Chris Cargill, CEO

05



Priority objectives for FY2024

01 JPY 16 billion+ NHI sales for PIVLAZ® ON-TRACK

02 JNDA approval for daridorexant in Japan ON-TRACK

03 Acquire/in-license at least one late-stage medicine for Japan/APAC (ex-China) ON-TRACK

04 Execute at least one new major partnership, and initiate at least one new in-house Ph.1 study ✓  **Boehringer Ingelheim**
✓ EP4 ag.

05 PMI investment in new brand concept, plus systems and applications for efficiency and scalability ON-TRACK

Several potential catalysts remain for 2024

(excluding new business development transactions)



PROGRAM	PARTNER	TIMING	EVENT
EP4 Ag	NXERO	Achieved (Mar. 2024)	Ph.1 start
GPR35 Ag	GSK NXERO	Achieved (Mar. 2024)	Program reversion
GPR52 Ag	Boehringer Ingelheim	Achieved (Mar. 2024)	Option-to-license agreement
NBI-568 (M4 Ag)	NEUROCRINE BIOSCIENCES	Achieved (Apr. 2024)	Long-term TOX study completed
NBI-567 (M1 pref. Ag)	NEUROCRINE BIOSCIENCES	Achieved (May 2024)	Ph.1 start
ORX750 (OX2 Ag)	CENTESSA PHARMACEUTICALS	Achieved (May 2024)	Ph.1 start
Cenerimod	idorsia	Mid 2024	Exclusive opt-in decision
Lucerastat	idorsia	Mid 2024	Exclusive opt-in decision
NBI-568 (M4 Ag)	NEUROCRINE BIOSCIENCES	3Q 2024	Ph.2 topline data
Daridorexant (Sth Korea)	NXERO	2H 2024	New Partnership & Ph.3 start
Daridorexant (Japan)	MOCHIDA PHARMACEUTICAL ¹	2H 2024	Potential NDA Approval
ORX750 (Ox2 Ag)	CENTESSA PHARMACEUTICALS	2H 2024	Ph.1 completion
TMP-301 (mGlu5 NAM)	TEMPERO BIO	2024	Ph.2 start
PIVLAZ® (Sth Korea)	HANDOK 한독 NXERO	1H 2025	New partnership (achieved) & Launch

¹ Co-development and co-promotion agreement with Mochida



Thank you

Appendix

Breakdown of 1H 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	7,327	5,393	12,720			12,720
Cost of Sales + SG&A	(3,039)	(4,290)	(7,329)	A (1,619) B (681) D	C (563) Integration (1,323) Other	(11,514)
R&D	(4,143)	(699)	(4,842)	D	(645)	(5,487)
Other income	626	1	627			627
OP/Core OP	771	405	Core OP 1,176			OP (3,654)
Idorsia & Integration related Costs	<p>A Additional CoS charge for current PIVLAZ[®] stock. This impact will continue until around 3Q 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)

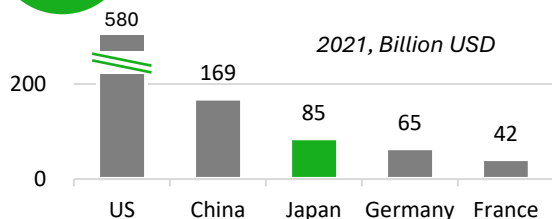
Japan will serve as our base to expand across APAC markets

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

Established market with strong volumes



Second largest pharma market (excl. China)

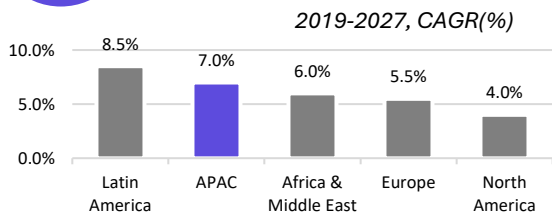


- Universal health care system
- Relatively weak incumbents
- Attractive market for newcomers
- Large, ageing population
- Stable, pro-innovation market

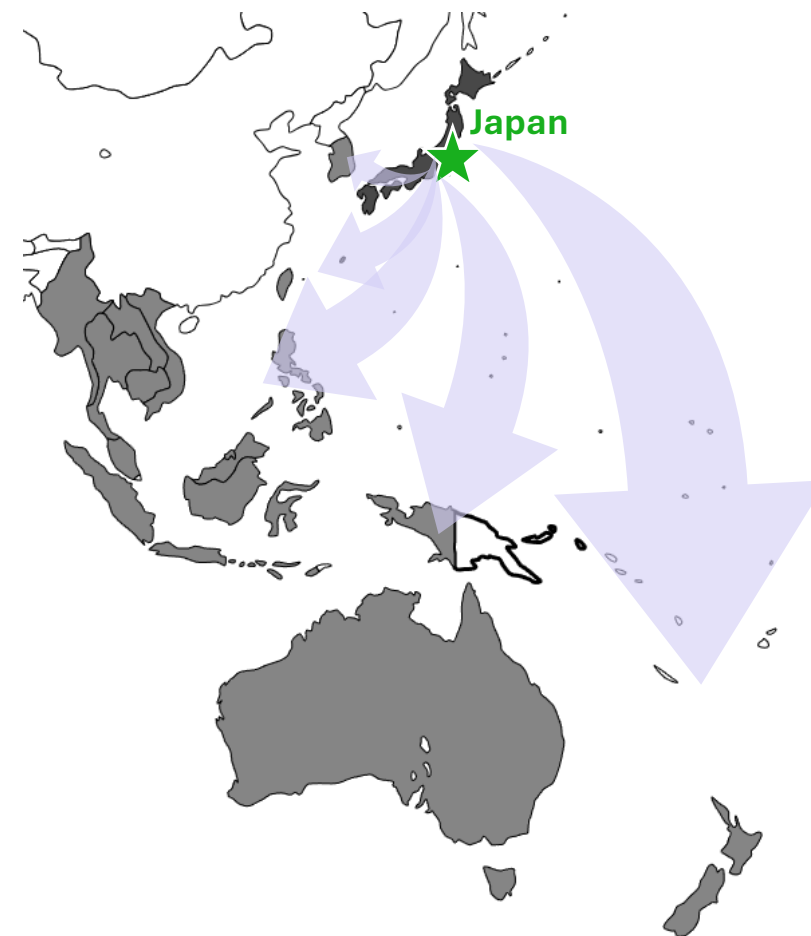
APAC* One of the fastest growing pharma regions globally



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

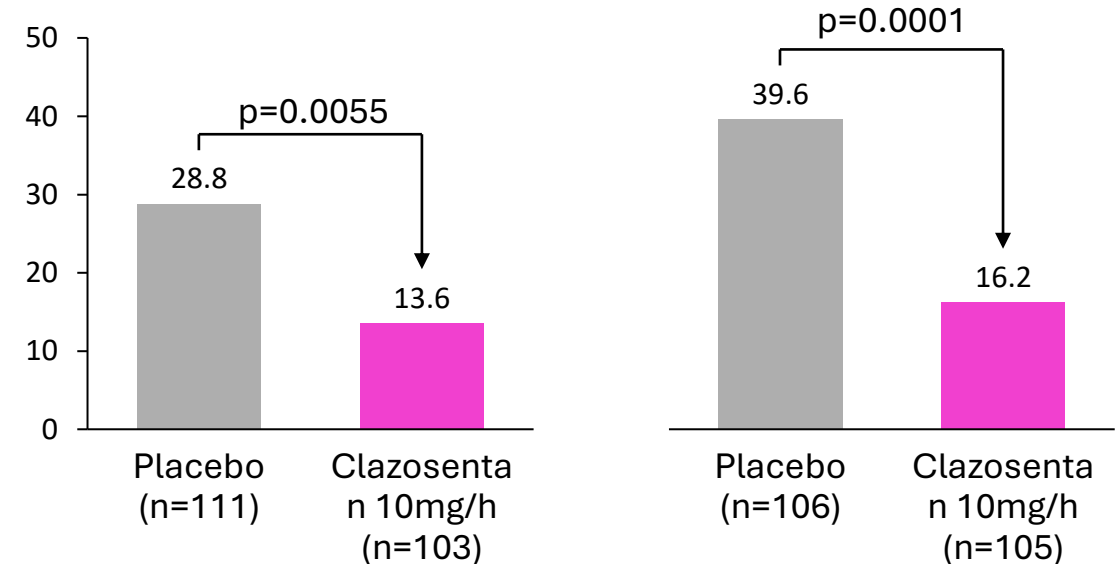
RESULTS OF TWO PIVOTAL PHASE 3 STUDIES IN JAPAN¹

- 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

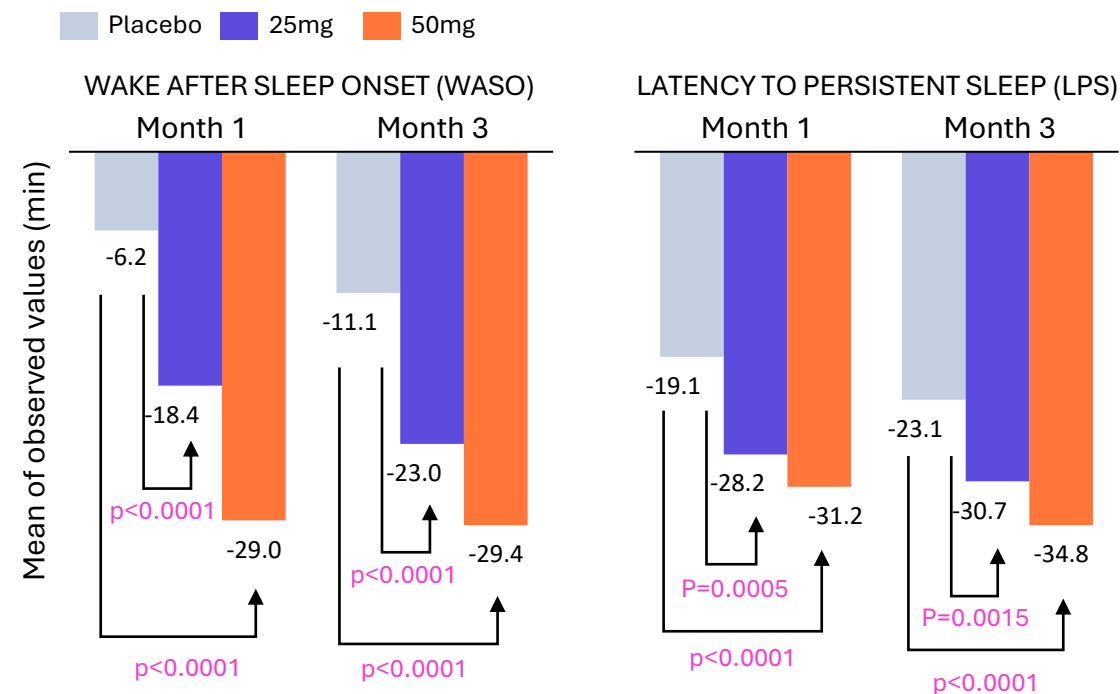


RESULTS OF GLOBAL AND JAPANESE PIVOTAL TRIALS¹

- 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
- NDA was completed in Oct. 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% \geq 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.



Partnered pipeline (1/2)

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 ¹	Adenosine A2a ant. combo	SME	mCRPC	AstraZeneca							
NBI-1117568	Muscarinic M4 agonist	SME	Schizophrenia	NEUROCRINE BIOSCIENCES							
NBI-1117569	Muscarinic M4 preferring agonist	SME	Neurology diseases	NEUROCRINE BIOSCIENCES							
NBI-1117570	Muscarinic M1/M4 agonist	SME	Neurology diseases	NEUROCRINE BIOSCIENCES							
NBI-1117567	Muscarinic M1 preferring 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)	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	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 2: Pfizer decided not to continue develop lotiglitprion (PF-07081532) in Q2 2023.



Partnered pipeline (2/2)

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

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								
Daridorexant	Dual Orexin antagonist	SME	Insomnia								
NXE'149	GPR52 agonist	SME	Neurology diseases								
NXE'732	EP4 antagonist	SME	Immuno-oncology								
NXE'744	EP4 agonist	SME	Inflammatory bowel disease								
NXE'477 ²	GPR35 agonist	SME	Inflammatory bowel disease								
(Not disclosed)	Muscarinic M1 agonist (JP)	SME	Neurology diseases								
(Not disclosed) ¹	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								
In-house Programs (No longer internally funded. Targeting academic / industrial partnership)											
NXE'310	SSTR5 agonist	Peptide	Hypoglycaemic disorders								
NXE'097	GLP-1 antagonist	Peptide	Hypoglycaemic disorders								
NXE'023	Dual GLP-2/GLP-1 agonist	Peptide	Intestinal failure/NASH								
(Not disclosed)	Apelin agonist	Peptide	Pulmonary Arterial Hypertension								
NXE'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. 1 Due to changes of strategy, we deprioritized until we will find another indication opportunity 2 : Exclusive license-out option



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.



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