Nxera R&D Day

Be Bold, Move Fast.

6 November 2024

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Agenda

01 Business Update

02 Development and Commercial (JP/APAC)

03 Research (UK)

04 FY2024 Q3 Financial Results

05 Appendix

Business Update

Chris Cargill, President and CEO

01

Towards our 2030 vision

Focus on innovative specialty medicines in areas of unmet need

Current portfolio % split

- Neurology 39%
- Metabolism 33%
- Immunology 9%
- Rare 18%

At least 5 products* launched in Japan

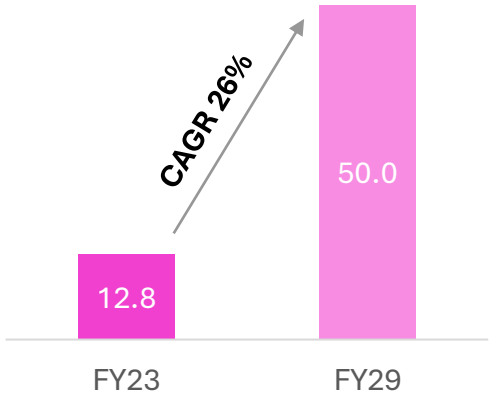
エンドセリン受容体拮抗薬 薬価基準収載
ピヴラッツ® 点滴静注液 150mg

不眠症治療薬 / オレキシン受容体拮抗薬 薬価基準未収載
クービビック® 錠 25mg 50mg

Business development platform actively hunting new product opportunities

At least JPY50 billion in annual revenues

Revenue (JPY billion)



Strengthening management and people

Continuously improving business processes

Implementing technology and leveraging data

Our mission is to accelerate medicine. From Japan, for Japan, and the world.

*Including PIVLAZ® and QUVIVIQ™

Be bold, move fast.

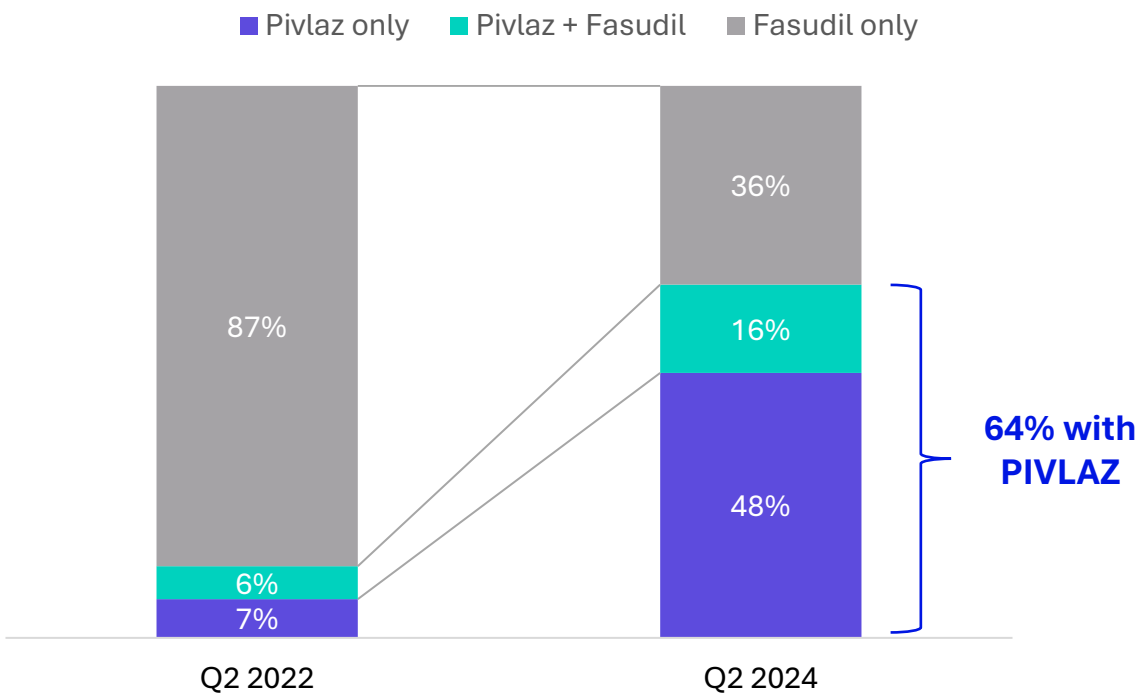
1. **Securing mid-term expansion** by focusing on the growth of key commercial products in Japan and APAC (PIVLAZ® and QUVIVIQ™)
2. **Driving long-term expansion** by transforming medicine across the hottest areas of Neuroscience, Metabolism, Immunology and Rare Diseases
3. **Powering the world's most comprehensive drug discovery platform** for GPCRs and other membrane proteins to fuel new pipeline products
4. **Executing strategic expansion** in Japan with focused licensing and/or acquisitions

Rapidly building Japan's next-generation pharmaceutical company

Mid-term expansion from the stability of PIVLAZ® in Japan

エンドセリン受容体拮抗薬 薬価基準収載
ピヴラッツ® 点滴静注液 150mg

Share evolution – aSAH usage



Strategic roadmap

- **Over 15,000 Japanese patients** have received PIVLAZ®
- Japan Guidelines for Management of Stroke gives neurosurgeons confidence to prescribe PIVLAZ® as a **new standard of care for SAH**
- **Indication expansion** discussions ongoing with Japanese KOLs
- **Territory expansion** ongoing – PIVLAZ® expected to be available to South Korean patients in 2025-2026

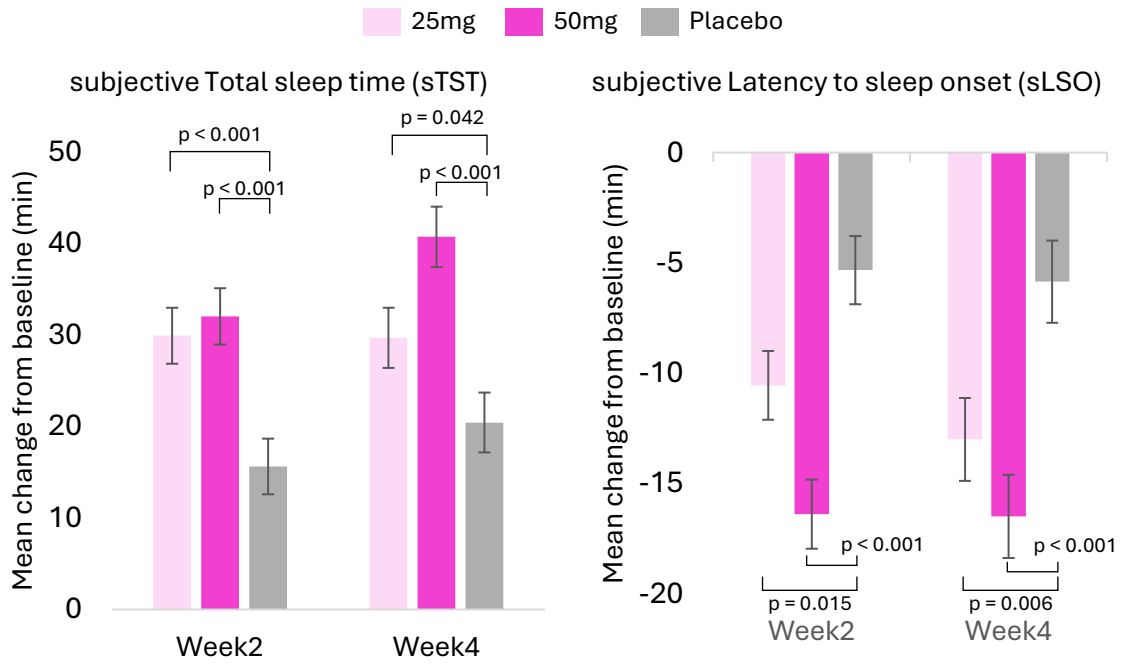
PIVLAZ® is a life-saving treatment and the backbone of our growing Japanese pharma business

Source : MDV (Prescription Data of DPC)

Mid-term expansion with upcoming launch of QUVIVIQ™ in Japan

不眠症治療薬 / オレキシン受容体拮抗薬 クービビック®錠 25mg 50mg 薬価基準未収載

Positive results from Phase 3 trial in Japan



Strategic roadmap

- **MHLW approval** of QUVIVIQ™ 25mg / 50mg for the treatment of insomnia received in September 2024
- New sales scheme with SHIONOGI
  - **Best partner** to market QUVIVIQ™ in Japan
  - **Enhanced economics** receiving double-digit net sales royalties vs. cost of establishing primary care salesforce
- **Indication expansion** being explored with KOLs
- **Territory expansion** – bridging study ongoing in Korea; discussions ongoing with APAC partners

QUVIVIQ™ go-to-market model transformed by new sales scheme with Shionogi for Japan.
Shionogi to exclusively handle sales and distribution activities.

Source: *Sleep Med.* 2024 Oct:122:27-34. doi: 10.1016/j.sleep.2024.07.037.

Long-term expansion by transforming medicine across the hottest areas of Neuroscience…

	PARTNERED WITH NEUROCRINE BIOSCIENCES / DISCOVERED BY Nxera	DISCOVERED BY CENTESSA PHARMACEUTICALS / TECHNOLOGY FROM Nxera	OPTION TO LICENSE WITH Boehringer Ingelheim / DISCOVERED BY Nxera
Compound & Stage	NBI-’568 (Ph 3 ready)	ORX750 (Ph 1/2)	NXE-149 (Ph 1b)
Target Indication	Schizophrenia	Narcolepsy	Schizophrenia
Global Patient Population	**24 million**	**3 million**	**24 million**
Mechanism	Selective M4 receptor agonism	Selective OX-2 receptor agonism	Novel, selective GPR52 receptor agonism
Key Player	BMS/KarXT	Takeda/TAK-861	First-in-Class

Technology, platform and know-how to design convenient, cost effective, easy to manufacture, oral small molecule medicines that could change the treatment paradigm for major diseases

Source : World Health Organization

… and fast-growing areas of Metabolism and Immunology

	DISCOVERED BY Pfizer / TECHNOLOGY FROM Nxera	DISCOVERED BY Pfizer / TECHNOLOGY FROM Nxera	DISCOVERED BY Nxera
Compound & Stage	PF-06954522 (Ph 1)	PF-07054894 (Ph 1)	NXE-744 (Ph 1)
Target Indication	T2D / Obesity	IBD	IBD
Global Patient Population	**483 million / 890 million**	**10 million**	**10 million**
Mechanism	GLP-1 receptor agonist	CCR6 receptor antagonist	Novel, selective EP4 receptor agonist
Key Player	Lilly + Chugai/Orforglipron	First-in-Class	First-in-Class

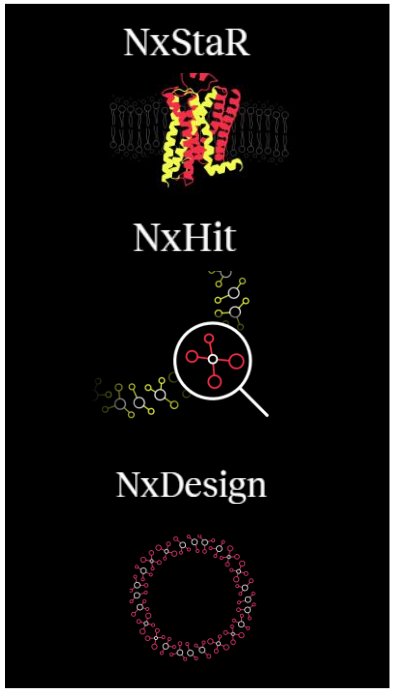
Current clinical programs targeting Neuroscience, Metabolic Disease and Immunology aim to positively impact over 500 million patients worldwide

Source: International Diabetes Federation, World Health Organization, The Lancet Gastroenterology & Hepatology, Volume 5, Issue 1, 17 - 30 , Evaluate Pharma, The European Federation of Crohn's & Ulcerative Colitis Associations (EFCCA)

Leveraging the world's most comprehensive drug discovery platform for GPCRs

UK Research & Early Development

Japanese Clinical Development & Sales



NxWave™ Platform

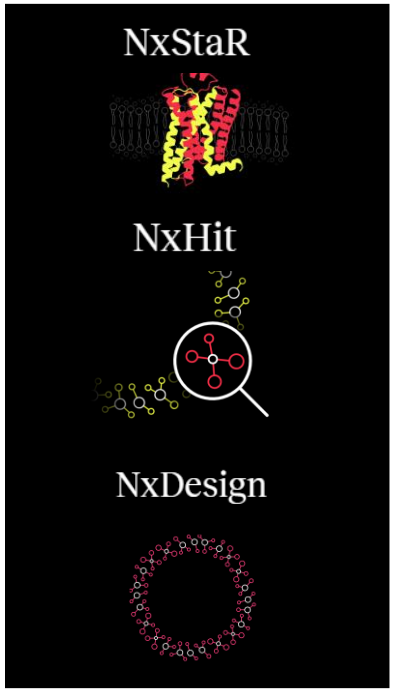
In-license clinical stage product opportunities *for the Japan and APAC markets*

Structure-Based Drug Design	Translational Medicine	Clinical Development	Product Strategy
	Preclinical Development Drug Development Phase I	Safety / PV Regulatory Strategy Phase II Phase III	Medical Affairs Marketing Market Access Sales

Out-license our products *to mega pharma for the global market*

NxWave™ SBDD platform is the backbone that fuels our continuous innovation of new product opportunities.
Our pipeline is bolstered by external innovation and collaboration from partners worldwide.

Leveraging the world's most comprehensive drug discovery platform for GPCRs



NxWave™ Platform

Structure-Based Drug Design

Small Molecules

- Excellent efficacy and safety
- Oral route of administration
- Affordable pricing and cost

+

Antibodies

Antiverse

Peptides & Radiopharma

PeptiDream

Our strength is in small molecules, but expanding to have additional modalities and capabilities that can address the unmet needs that small molecules cannot

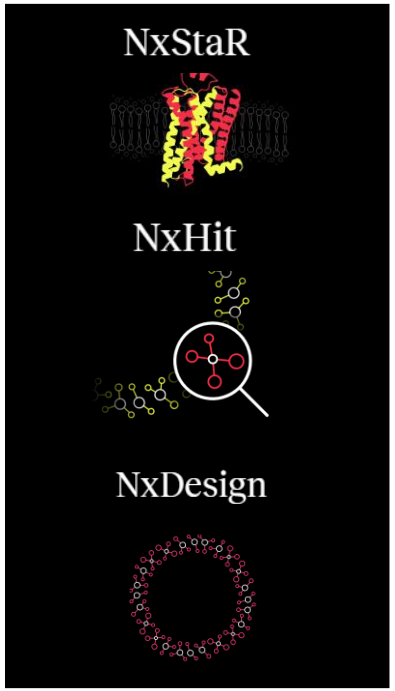
Leveraging the world's most comprehensive drug discovery platform for GPCRs

	Year Founded	# Team Members	IPO / Listing	Value of Business	Modality	# Non-clinical Programs	# Clinical Programs
TECTONIC Therapeutic	2019	44	NASDAQ (2024)	$535M	SME, Biologics	3+	1
septerna	2019	78	NASDAQ (2024)	$745M	SME	3+	1
STRUCTURE THERAPEUTICS	2019	136	NASDAQ (2023)	$2,175M	SME	4	2
Nxera	**2007***	**180****	**TSE PRIME**	$695M	**SME, Peptides, Biologics**	**25+**	**12**

Nxera has 15 years of know-how and technology expertise drugging GPCRs. Across all metrics Nxera has the world's most comprehensive and valuable drug discovery platform for GPCRs

Source: Company Presentations, FactSet as at 25-Oct-2024
*Relates to the founding of Heptares Therapeutics Ltd (now known as Nxera Pharma UK Limited.
** Team members of Nxera Pharma UK Limited.

Leveraging the world's most comprehensive drug discovery platform for GPCRs



NxWave™ Platform

Structure-Based Drug Design

Active Partnerships

Partner	Therapeutic Area(s)	Total Milestones Received to Date	Potential Total Milestones[1]
Boehringer Ingelheim	Schizophrenia	€25m	**€670m**
Lilly	Diabetes and Metabolic	$37m	**$800m**
abbvie	CNS	$50m	**$1.2bn**
NEUROCRINE BIOSCIENCES	CNS	$180m	**$2.6bn**
Genentech A Member of the Roche Group	Multiple	$33m	**$1.0bn**
Pfizer	Multiple	$36m	**$1.8bn**

Terminated Programs

Daiichi-Sankyo

biohaven

Total milestones received ($m)

$17m

$258m

Reverted Programs

teva | abbvie | Takeda | AstraZeneca | Allergan | GSK

The world's leading pharma companies continue to choose Nxera to develop their GPCR products

[1]Potential 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.

Nxera

Executing strategic expansion in Japan & APAC with focused licensing and/or acquisitions

UK Research & Early Development — **Japanese Clinical Development & Sales**

Discovery → Phase I → Phase II → Phase III → Marketed

In-license clinical stage product opportunities for the Japan and APAC

Proactively analyzing opportunities to fill our Phase 2, Phase 3 and commercial stage pipeline. Over US$300m capital available to deploy.

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JAPAN + APAC MARKET

15+ Programs

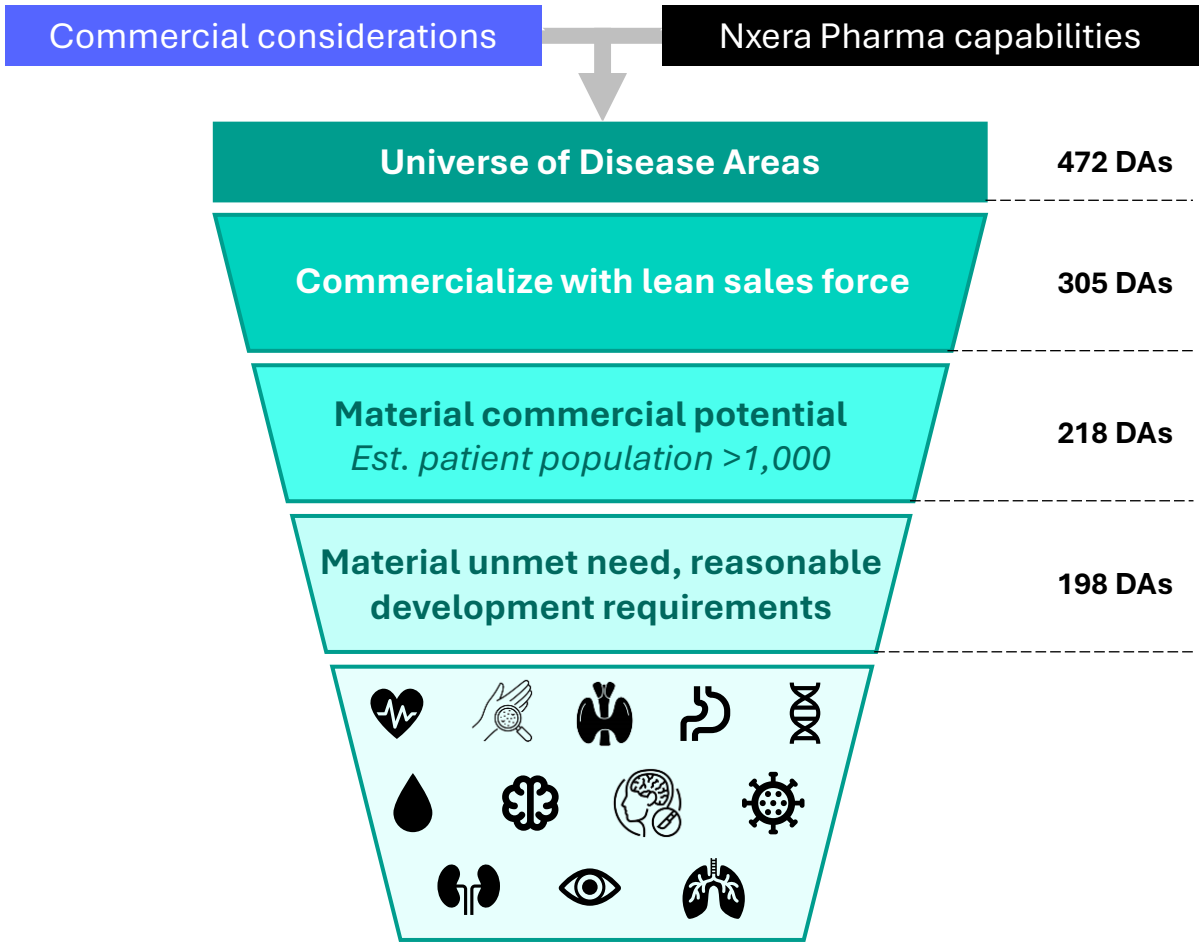
- M1 Ag.
- EP4 Ag.
- GPR52 Ag.
- EP4 Antag.

Progress in-house pipelines and retain Japan and APAC rights

GLOBAL MARKET

Executing strategic expansion in Japan & APAC with focused licensing and/or acquisitions

Approach to prioritizing Disease Areas ("DAs")



Source: Internal Analysis

Active in-licensing discussions targeting 20+ assets

50+ proposals evaluated

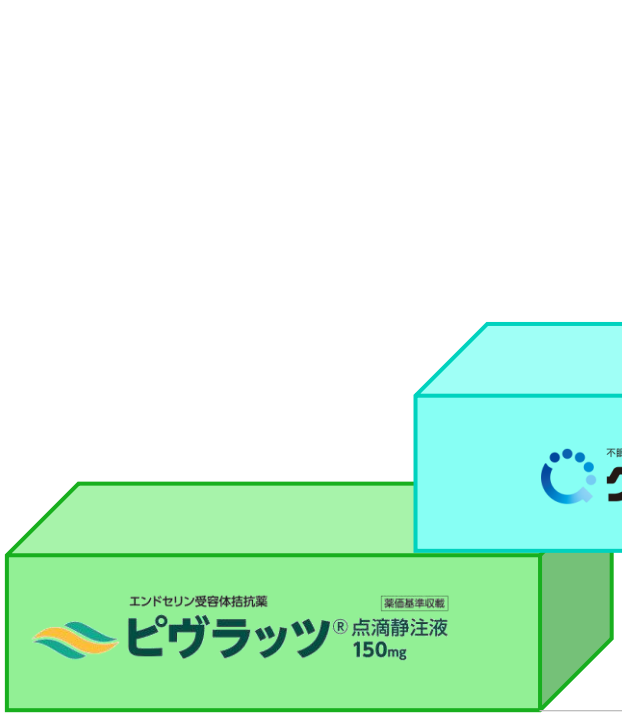
20+ product opportunities prioritized:

- peak sales potential of JPY 15-50bn, or more
- differentiated medicines in compelling indications

- Neurology
- Critical Care (incl. Neurosurgery)
- Rare (Neuro)endocrine
- Immunology & Inflammation
- Rare Genetic
- Rare Respiratory
- Rare Cardiovascular

7 opportunities at term sheet or contracting stage

From a discovery platform towards our 2030 vision



- **At least 3 new launched products** to reach **JPY50 billion in total revenues**
- **Fuelling next 20 years** of **product innovation and partnerships**
- **> JPY 4 billion of peak net sales royalty** potential **+ additional profit from product supply**.
- **JPY16 to JPY20 billion of peak sales** potential.

Building a JPY50 billion revenue business by growing sales from new products in Japan and APAC, and global expansion of NxWave™ discovered small molecule, antibody and peptide products

Source: Internal financial analysis

A year of exceptional progress

PROGRAM	PARTNER	TIMING	EVENT
✓ EP4 Ag	Nxera	**Achieved (Mar. 2024)**	Ph.1 start
✓ GPR35 Ag	GSK / Nxera	**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
✓ NBI-568 (M4 Ag)	Neurocrine Biosciences	**Achieved (Aug. 2024)**	Ph.2 topline data
✓ ORX750 (Ox2 Ag)	Centessa Pharmaceuticals	**Achieved (Sep. 2024)**	Ph.1 completion & POC data
Cenerimod	idorsia	4Q 2024	Exclusive opt-in decision
Lucerastat	idorsia	4Q 2024	Exclusive opt-in decision
Daridorexant (Sth Korea)	Nxera	4Q 2024	New Partnership & Ph.3 start
Daridorexant (Japan)	Shionogi	4Q 2024	NDA Approval **(achieved)** & Launch
ORX750 (Ox2 Ag)	Centessa Pharmaceuticals	4Q 2024	Ph.2 start
TMP-301 (mGlu5 NAM)	Tempero Bio	End of 2024	Ph.2 start

Development and Commercial (JP/APAC)

Dr. Makoto Sugita, Executive Officer, Chief Medical Officer (CMO) and President of Nxera Pharma Japan

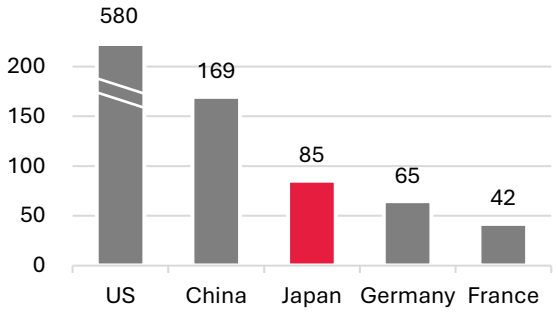
02

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"

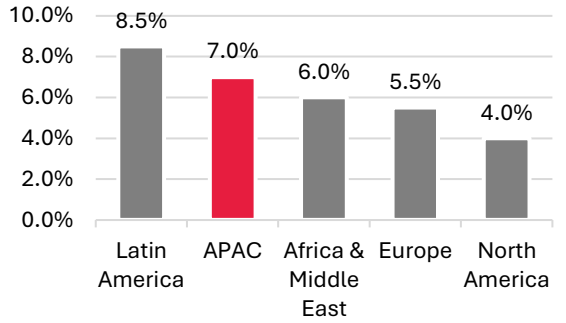
MHLW
Ministry of Health, Labour and Welfare of Japan

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)*



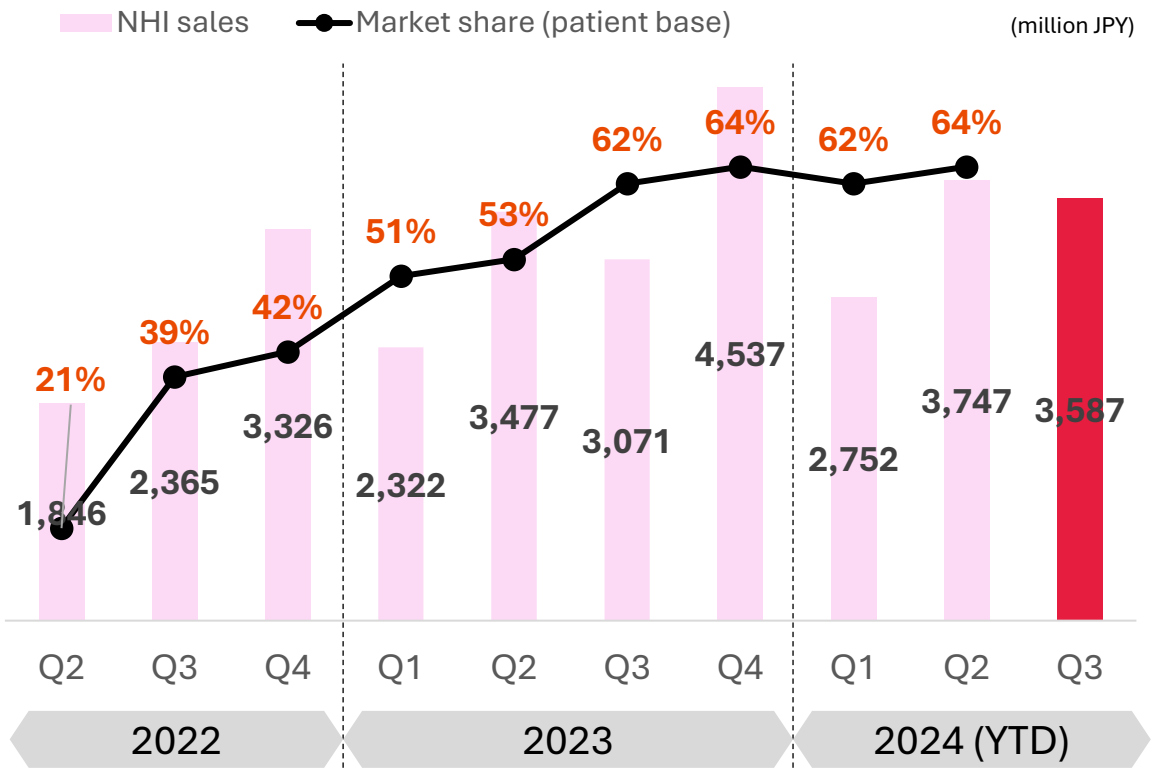
Source: IQVIA Market Prognosis, Sep 2022; IQVIA Institute, Nov 2022.
APAC (ex-China) territory includes South Korea, Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand and Vietnam

Our product: PIVLAZ®

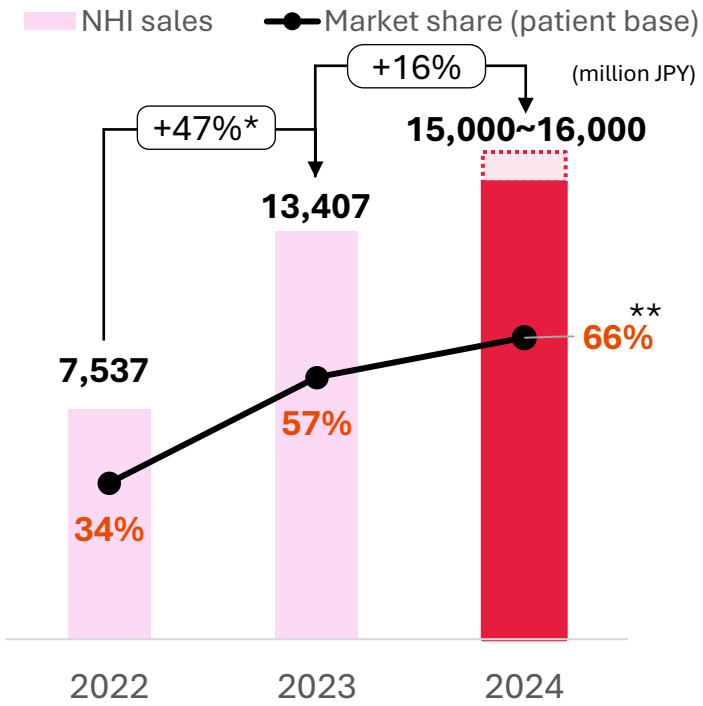
PIVLAZ clazosentan

Our first commercially available medicine is penetrating the market and protecting lives every day.

Quarterly PIVLAZ® Sales (NHI-based)



Yearly PIVLAZ® sales and its growth



- ✓ Target sales changed from previous plan
- ✓ Keeping strong sales growth (2023 - 2024 growth (1Q-3Q): +14%)

PIVLAZ® is rapidly spreading and becoming standard of care in prevention of cerebral vasospasm

Source: MDV DPC hospital data

*: Comparison of 2-4Q of 2022 and 2023, **: Estimation from previous trend

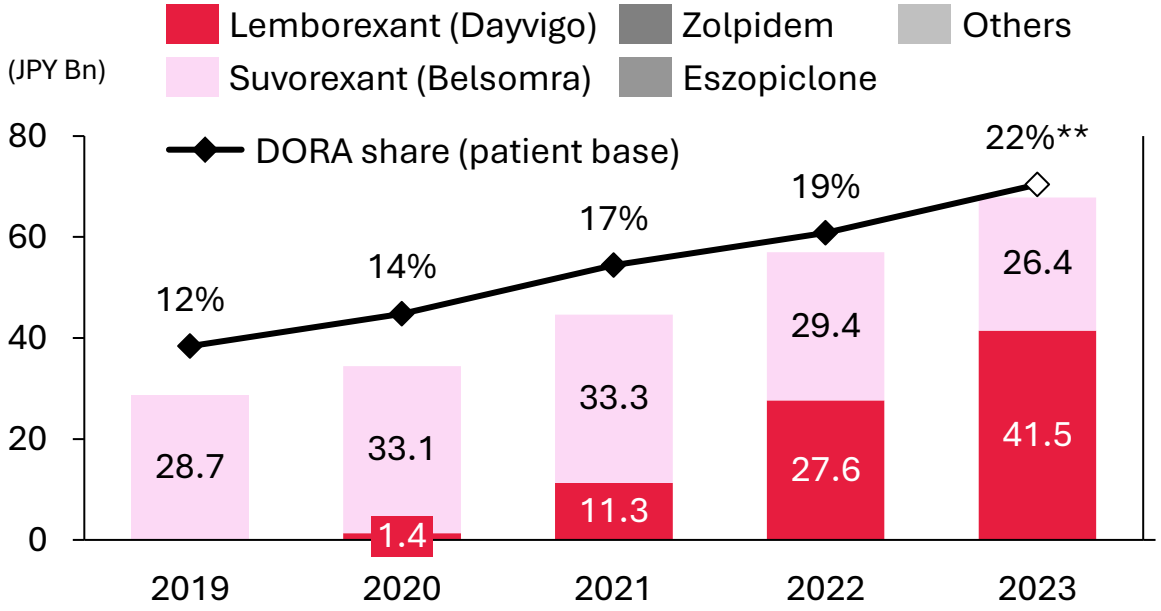
Nxera

QUVIVIQ™ *: A Novel Dual Orexin Receptor Antagonist (DORA)

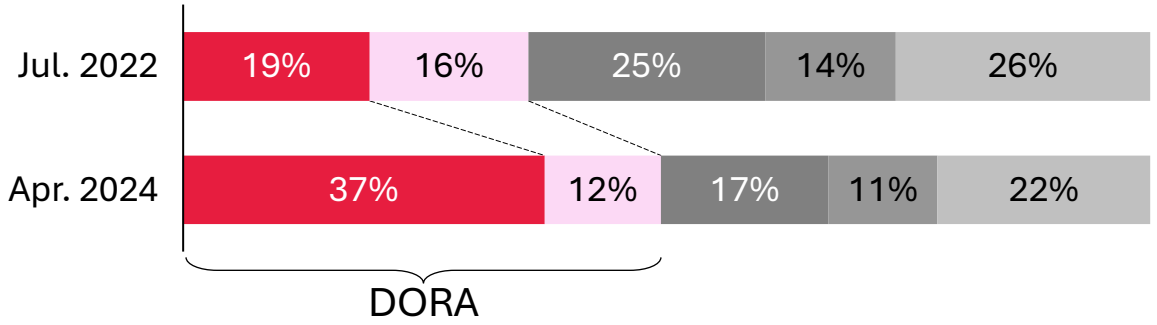
DORA is rapidly establishing its position in insomnia treatment

不眠症治療薬 / オレキシン受容体拮抗薬 薬価基準未収載
クービビック®錠 25mg 50mg

Sales and market share (NHI-base)



Prescription share (Most frequently prescribed sleeping pills)



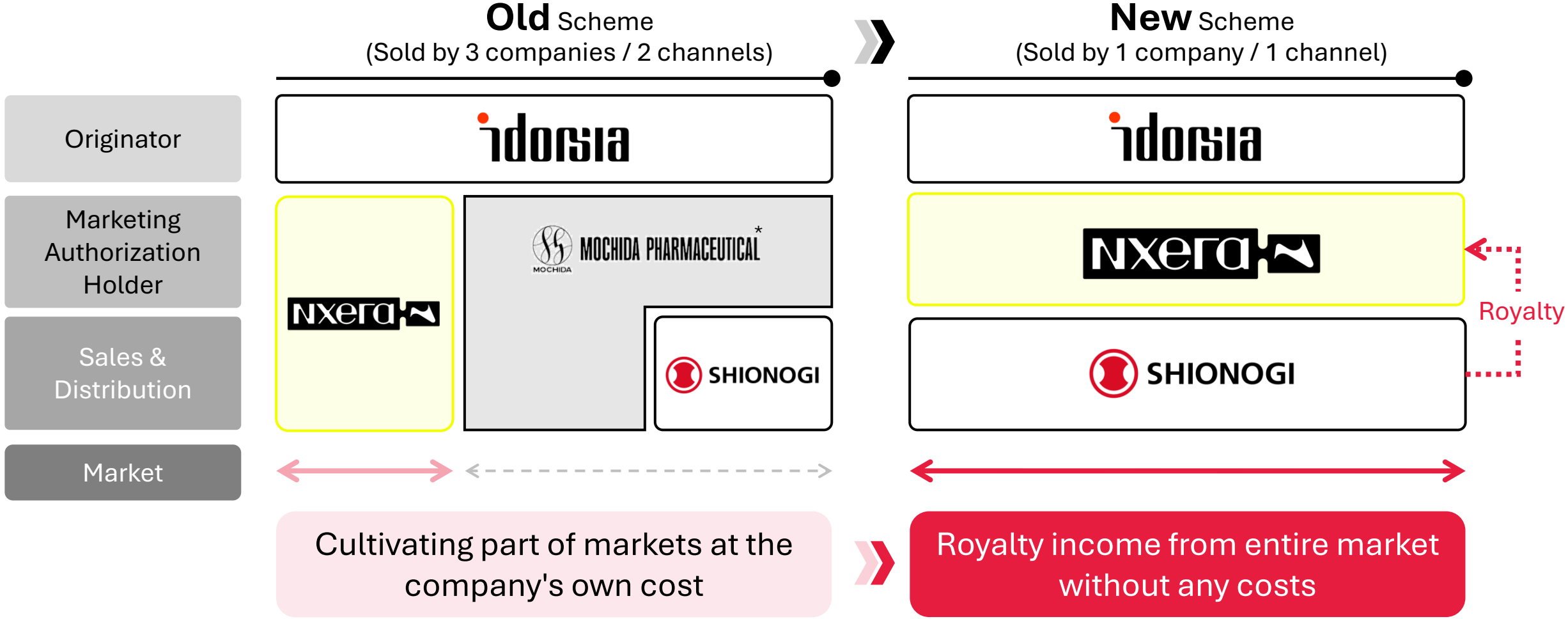
- ✓ DORAs are rapidly penetrating the insomnia treatment market in Japan
- ✓ Japan is one of the largest DORA markets

Source: Nikkei Medical (2022/7/23, 2024/4/13), IQVIA, Encise, Eisai's website
* Discovered by Idorsia ** Estimation

QUVIVIQ™ Business scheme change

SHIONOGI to Exclusively Handle Distribution and Sales Activities in Japan

不眠症治療薬 / オレキシン受容体拮抗薬 クービビック®錠 25mg 50mg 薬価基準未収載



* Mochida will remain exclusively responsible for manufacturing of QUVIVIQ™ in Japan

In-house pipeline: QUVIVIQ™

JNDA approval received in September 2024, and aim to be best-in-class drug

不眠症治療薬 / オレキシン受容体拮抗薬 クービビック®錠 25mg 50mg 薬価基準未収載

Unmet needs in insomnia

- Nocturnal awakenings
- Rapid sleep onset
- Carry-over effects to the next day after medication

About QUVIVIQ™

Dual Orexin Receptor Antagonist	Alleviates excessive wakefulness through strong inhibition of orexin receptors
European Guideline	Recommended in the 2023 European Insomnia Guidelines as **the only orexin receptor antagonist** that can be used [1]
PK profile	T_{max}: about **0.5-1.4 hour** $T_{½}$: about **6-9 hour** Significant improvement in next-day sleepiness and daytime functioning confirmed in global phase 3 trials [2]

Aim to be Best-in-class drug in DORA class

Source: [1] ESRS Home | European Sleep Research Society, [2] Lancet Neurol 2022; 21: 125–39.

Research (UK)

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

03

Key Events 2024

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

TARGET ID

precisionlife — improving health | for everyone

Expansion of R&D partnership into auto-immune disorders

PR LINK

May '24

PRE-DISCOVERY

abbvie

$10M milestone payment received from multi-target neurology collaboration utilizing NxWave™ platform

PR LINK

Jun '24

DISCOVERY

Nxera

Two NME[1] programs transitioned into the Discovery phase following a successful NxWave™ campaign

H1 '24

GSK

GPR35 agonist program reversion from GSK completed

PR LINK

H1 '24

PHASE 1

Nxera

Phase 1 trial start evaluating NXE'744, a potent, selective, gut restricted EP4 agonist for IBD

PR LINK

Mar '24

CENTESSA PHARMACEUTICALS

$4.6M milestone payment received for ORX750 (OX2R agonist) Phase 1 start in Narcolepsy

PR LINK

May '24

Boehringer Ingelheim

Collaboration with BI signed (€25M upfront and €60M option exercise) for FIC GPR52 agonists for schizophrenia

PR LINK

Mar '24

NEUROCRINE BIOSCIENCES

NBI-567, oral muscarinic M1 preferring agonist Phase 1 start with potential to treat symptoms of cognition in patients

PR LINK

May '24

PHASE 2

NEUROCRINE BIOSCIENCES

$15M milestone triggered on successful completion of long-term preclinical toxicology of NBI-568, an oral selective muscarinic M4 agonist advancing through Phase 2

PR LINK

Apr '24

$35M milestone triggered upon successful completion of the Phase 2 trial in adults with schizophrenia

PR LINK

Sep '24

World-leading NxWave™ SBDD platform continues to fuel innovation

[1] NME = New Molecular Entity

Nxera

GPCR targets are our core focus

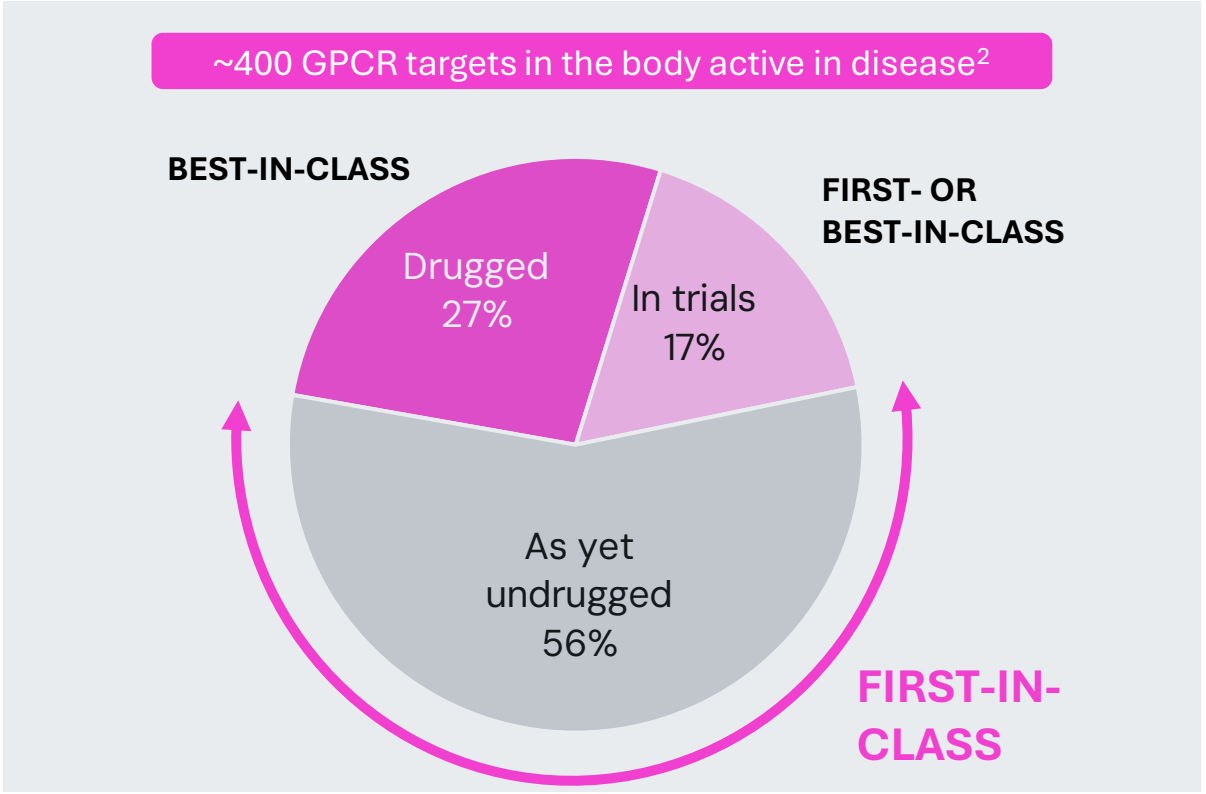
GPCRs are the largest family of drug discovery targets – comprising 1/3 of all FDA approved drugs

~400
GPCR targets active in diseases[2]

~34%
of FDA approvals target GPCRs[1]

27%
of global sales are GPCR drugs[1]

- NEUROLOGICAL DISORDERS
- GASTROINTESTINAL DISEASES
- IMMUNOLOGY/ONCOLOGY
- METABOLIC DISORDERS
- CARDIOVASCULAR
- RESPIRATORY



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: 5-step patient-driven discovery approach

26 Pre-Clinical Candidates; 17 Clinical Starts

Target ID & Validation

Identifying the best targets

- MoA link between biological function and disease
- Tractability aligned with NxWave Platform
- Commercially attractive in core disease/therapeutic areas

→ The Right **Targets**

NxStaR

Stabilising the right targets

- World-leading technology platform
- Protein NxStaR for NxHit
- NxStaR enabling structure determination
- NxStaR supported biophysics and MoA

→ The Right **Structure**

NxHit

Identifying the best hits

- Proprietary screening sets
- NxStaR enabled DEL screening
- NxStaR enabled fragment screening
- Ligand & Structure-based virtual screening

→ The Right **Hits**

NxDesign

Selecting the best Candidate

- SBDD enabled
- CADD focused
- Optimal physchem, pharmacology, DMPK and drug safety
- Confidence in Human PKPD, dose prediction
- Competitor Differentiation

→ The Right **Candidates**

Translational Medicine

Testing the Therapeutic Hypothesis

- Human biology focused translational platform
- Build Translational Pillars to inform biomarker strategy
- Deliver molecules that robustly & safely test therapeutic hypothesis
- Drug manufacture

→ The Right **Drugs**
The Right **Trial**

Major Pipeline Overview

	Discovery – Preclinical	Phase 1	Phase 2	Phase 3	Filed	Commercial
IN-HOUSE	10+ PROGRAMS	EP4 ant. NXE'732 – Advanced solid tumours (Cancer Research UK) EP4 ag. NXE'744 – IBD GPR52 ag. NXE'149 – Schizophrenia (Boehringer Ingelheim)		Cenerimod (A) – Systemic lupus erythematosus Lucerastat (A) – Fabry disease	QUVIVIQ™ (A) – Insomnia (SHIONOGI)	PIVLAZ® (A) – Cerebral vasospasm
PARTNERED	15+ PROGRAMS Previous and ongoing discovery collabs. Pfizer – Multiple Genentech – Multiple Takeda – GI abbvie – Neurology Lilly – Diabetes/Metabolic On-going Technology collabs. PHARMENABLE – AI-driven verily – AI-driven precisionlife – Neurology & Autoimmune PeptiDream – PAR2 peptide KALLYOPE – Gut-brain axis	M_1 pref. ag. NBI'567 (J) – Neurology (NEUROCRINE BIOSCIENCES) M_4 pref. ag. NBI'569 – Neurology (NEUROCRINE BIOSCIENCES) MC4 ant. PF'669 – Malnutrition (Pfizer)	M_1M_4 ag. NBI'570 – Neurology (NEUROCRINE BIOSCIENCES) $mGlu_5$ NAM TMP-301 – Substance abuse (TEMPERO BIO) OX2 ag. ORX750 – Narcolepsy (CENTESSA) GLP-1 ag. PF'522 – Type 2 Diabetes (Pfizer) CCR6 ant. PF'894 – IBD (Pfizer)	M_4 ag. NBI'568 – Schizophrenia (NEUROCRINE BIOSCIENCES)		Respiratory Portfolio – COPD, Asthma (NOVARTIS)

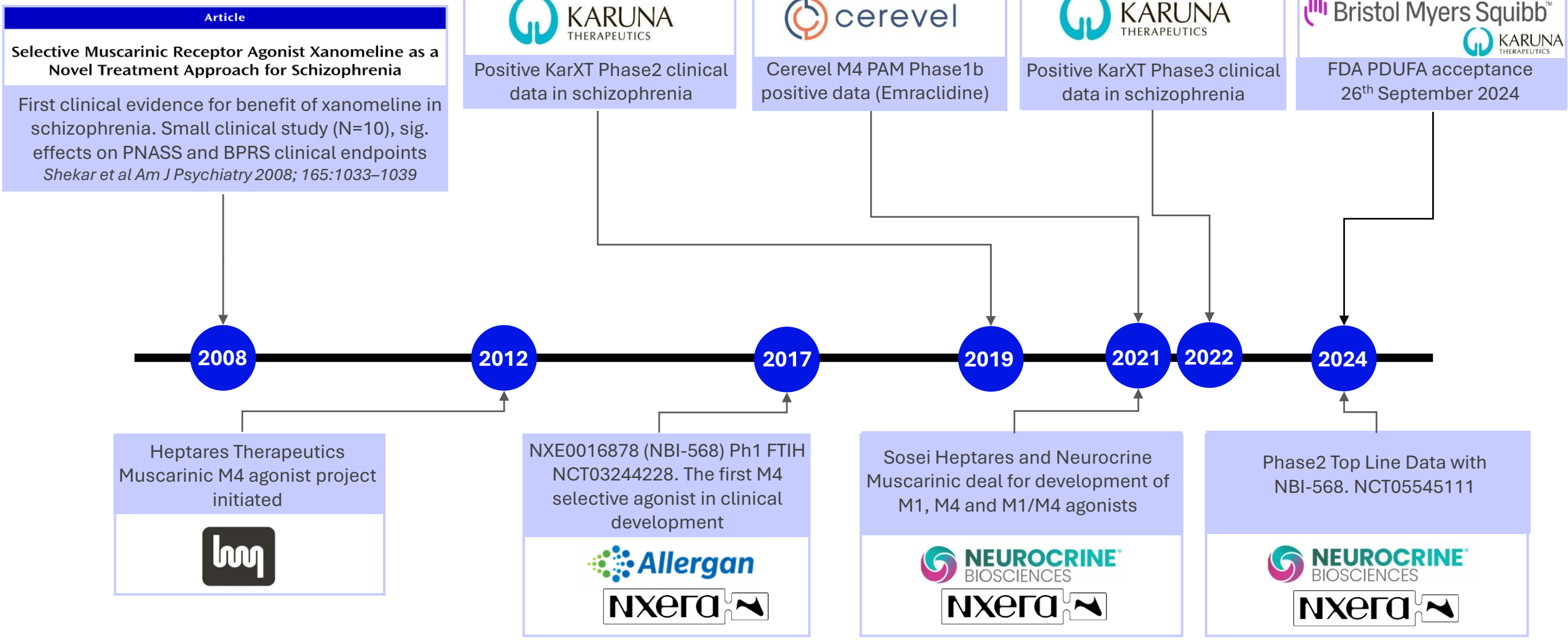
: Exclusive license-out option
: Exclusive opt-in right
(A) : Nxera have APAC* rights
(J) : Nxera have Japan rights

Note: Pref. ag. : Preferring agonist
Respiratory Portfolio = Seebri®, Ultibro®, Enerzair® and Breezhaler® which is registered trademarks of Novartis AG.
*APAC (ex-China) territory includes Japan, South Korea, Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, Taiwan, Thailand and Vietnam

Partnered Program Highlights

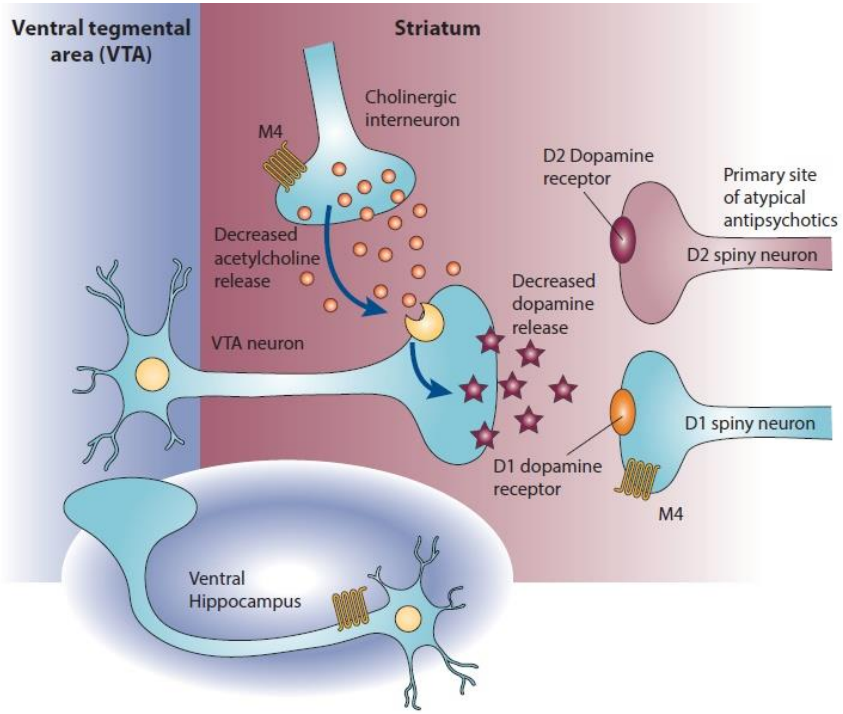
Neurocrine Biosciences
Centessa Pharmaceuticals

Historical Perspective: Muscarinic M4 receptor background and key dates



Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

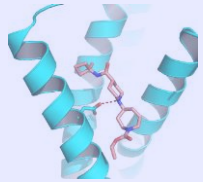
Highly Selective Muscarinic M4 agonists have the potential to revolutionise treatment across multiple disorders



Opportunity

- Preclinical data supports that M_4R agonists modulate VTA and MSN dopamine neuron activity
- This has the potential to modulate dopamine synthesis and/or release and downstream signalling events
- Demonstrates that this **novel mechanism controls excess dopamine** without blockade of D_2 receptor (common drug target for atypical antipsychotics)

Challenge



- Selectivity challenges associated with KarXT due to activity at M2 and M3 receptors and associated cholinergic AE's
- **Broad activity** across a range of CNS indications – including those where acetylcholine is no longer present and PAMs are predicted to be less effective

Solution

- Design of **highly selective orthosteric M4 agonists** using **structure-based design.**
- **NBI-568** Phase 2 trial initiated by Neurocrine Bioscience

Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

NBI-568 Phase2 Design: A dose finding and early efficacy study in schizophrenia

NEUROCRINE BIOSCIENCES

Predicting human efficacious doses

- Consistent dose-related data generated across all pre-clinical models and healthy human subjects
- Pre-Clinical and Phase 1 data including EEG and CSF exposure predicted efficacious doses for Phase 2
- Confident in the human 20mg dose being predicted to be efficacious

Phase 2, 6-week DRF & efficacy study in schizophrenia patients

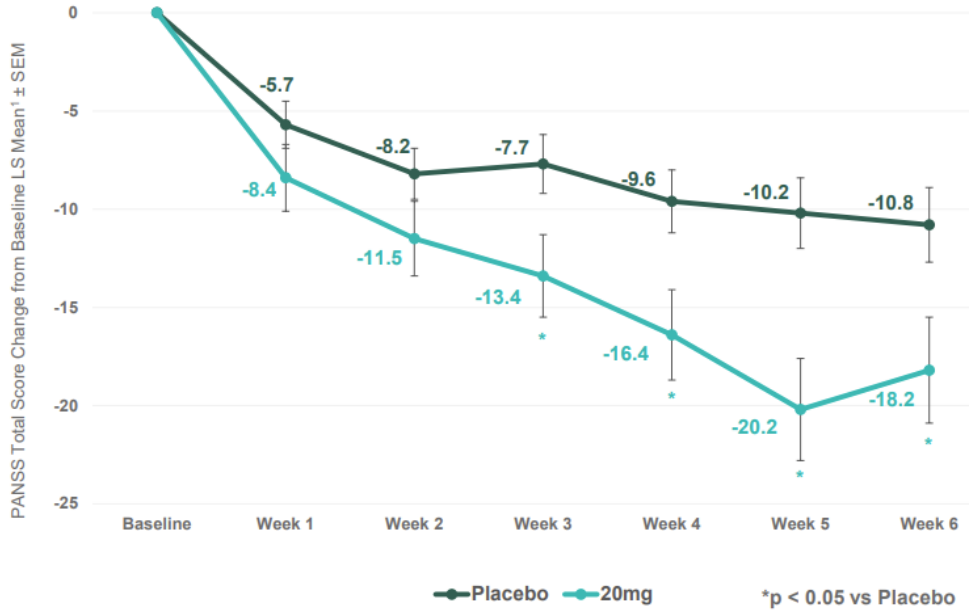
- Objectives:
  - ✓ Explore different doses, different dosing regimens (with and without titration), once a day, twice a day
- Trial Design:
  - ✓ Adults with PANSS ≥80
  - ✓ Ages 18-55 enrolled at
  - ✓ 15 US sites (inpatient)
  - ✓ Initial doses 20mg and 40mg
  - ✓ 2 blinded safety data interim analyses prior to adding pre-specified doses of 60mg QD and 30mg BID
- Good drug-like properties of NBI-568 supported exploring a significantly broader range of doses above the predicted efficacious dose than all previous M4 competitor molecules.

Source: Nair AG et al., 2018; Moehle MS et al., 2017; Foster DJ et al., 2016; Jeon J et al., 2010; Tzavara ET et al., 2004
Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

NXera

Efficacy: Clinically meaningful and statistically significant efficacy at 20mg once daily dose

The placebo effects underpin any differences and are similar to those anticipated in Phase 3 studies



Comparator Efficacy Data at Primary Endpoint

	NBI-568	CVL-231 30mg QD[3]	KarXT EMERGENT-1[4]	KarXT EMERGENT-3[5]
LS Mean[1]	-18.2	-19.5	-17.4	-20.6
LS Mean[1] Diff. vs.Pbo	-7.5	-12.7	-11.6	-8.4
Placebo	-10.8	-6.8	-5.9	-12.2
Effect Size[2]	0.61	0.68	0.75	0.6

- Significant PANSS total efficacy from week 3 at 20mg dose of NBI-'568
- PANSS Total Effect size comparable to known Muscarinic Programs and all leading Antipsychotics
- Statistically Significant Improvement in Additional Endpoints (CGI-S / Marder scores)

[1] Least-squares (LS) means are from a MMRM which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline PANSS total score as a covariate; and subject as a random effect. [2] Effect size (Cohen's D) is based on observed data. [3] Krystal et al (2021) Lancet DOI: 10.1016/S0140-6736(22)01990-0 data at week6. [4] Brannan et al (2021) N Engl J Med 2021;384:717-726 data at week5. [5] Kaul et al (2024) JAMA Psychiatry. 2024;81(8):749–756. doi:10.1001/jamapsychiatry.2024.0785 data at week5

Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

Safety and AE's: Generally safe and well tolerated at all doses tested

Treatment-Emergent Adverse Events Occurring in ≥ 5% of NBI-'568 All Treated Group

Activation of the muscarinic receptors have been clinically associated with a range of dose limiting AE's that has made drug development challenging

Salivation
Lacrimation
Urinary control
Defecation
Gastrointestinal
Emesis

Typically associated With peripheral Cholinergic activity at The M_2 and M_3 receptors

	Placebo N=70	20mg QD N=40	40mg QD N=39	60mg QD N=34	30mg BID N=27	All Treated N=140
Somnolence	2 (2.9)	5 (12.5)	2 (5.1)	7 (20.6)	1 (3.7)	15 (10.7)
Dizziness	1 (1.4)	5 (12.5)	3 (7.7)	4 (11.8)	1 (3.7)	13 (9.3)
Headache	14 (20.0)	1 (2.5)	5 (12.8)	1 (2.9)	5 (18.5)	12 (8.6)
Nausea	2 (2.9)	2 (5.0)	3 (7.7)	3 (8.8)	0	8 (5.7)
Constipation	2 (2.9)	2 (5.0)	3 (7.7)	1 (2.9)	1 (3.7)	7 (5.0)

5.0% Treatment Discontinuation Rate Due to Adverse Events Across All NBI-'568 Arms vs. 4.3% For Placebo

Consistent with EMERGENT-1 Phase2 and the interim pooled analyses from the long-term, open-label EMERGENT-4 and EMERGENT-5 trials for KarXT

The most common treatment-related AEs in the KarXT group were consistent with the known activity of xanomeline and trospium at muscarinic receptors (nausea / vomiting / constipation)

NBI-568 was well tolerated <u>across all dose groups</u>
Consistent with improved muscarinic selectivity profile vs. xanoemline nausea, constipation and other gastrointestinal adverse events were low in frequency and similar to placebo
No weight gain relative to placebo

Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

NEUROCRINE BIOSCIENCES

Summary: NBI-568 is Positioned for Phase3 in schizophrenia in 1H25

This will be the 1st Nxera Pharma UK SBDD compound to progress into Phase3

Clinically Effective
Efficacy at 20mg dose comparable to all competitors

Good Tolerability
Across all doses tested supporting good future compliance

Improved Convenience
Once daily administration with or without food

Broad Utility
Multiple indications where M4 agonists may be effective

NBI-568 Phase 2 was successful and confirmed a safe, well tolerated and efficacious dose to progress into Phase 3 studies in 1H25

Note: *NBI-568 is investigational and not approved for any use by any regulatory body*

Nxera

Strong potential for OX_2R agonists as an improved treatment for Narcolepsy Type 1 and beyond

OX2R Narcolepsy Landscape

Market size

- Approximately $2.0Bn in 2020[1]
- Projected to be $5Bn in US alone by 2026[2]
- OX2R agonist peak sales forecast of $3.8Bn[3]

Pipeline

Discontinued: TAK-994 & TAK-925 (Takeda)
Paused: JZP44DSP-0187 (Jazz/Sumitomo Pharma)

Centessa's recent activities

ORX750

- Positive Interim Phase 1 Clinical Data in Acutely Sleep-Deprived Healthy Volunteers (Sep. 10, 2024)
  - 2.5 mg dose restored normative wakefulness with mean sleep latency of 32 minutes as measured by the Maintenance of Wakefulness Test (MWT)
  - Favorable safety and tolerability profile
  - PK profile supports once-daily dosing

ORX142

- Presents Preclinical Data at Sleep Europe 2024 (Sep. 26, 2024)
  - Non-human primate data support ORX142 as novel drug candidate for the treatment of excessive daytime sleepiness (EDS) in select neurological, neurodegenerative, and psychiatric disorders

Sources: [1]Evaluate Pharma Disease Overview; [2]Jefferies Equity Research; [3]Evaluate Pharma Analyst Consensus Oct 2021

Internal Portfolio Highlights

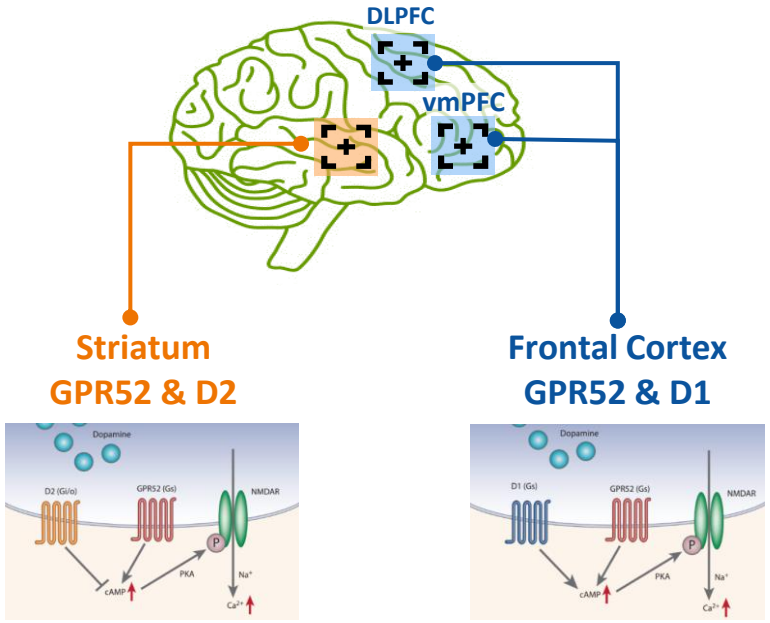
GPR52 ago.

GPR52 Agonist for Schizophrenia

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

Disease Rationale

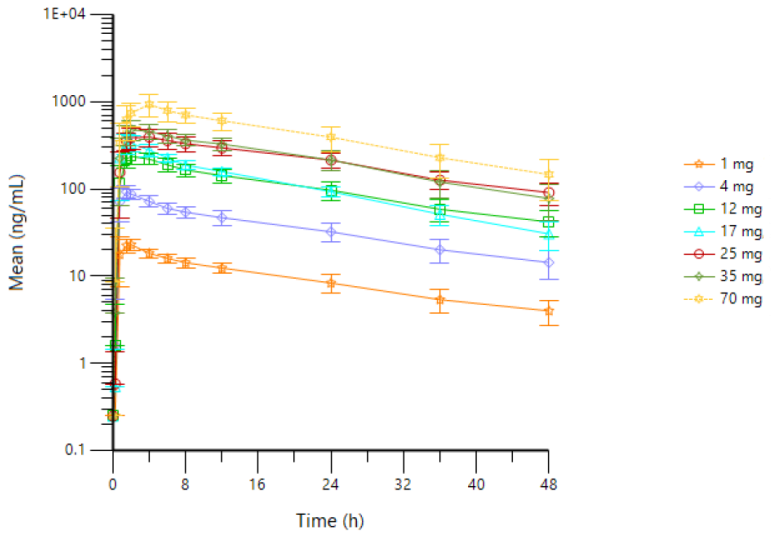
- GPR52 is expressed on D2 dopamine neurons in striatum where activation could lead to D2 antagonist-like effect to treat positive symptoms, e.g. hallucinations
- GPR52 also co-located with D1 dopamine receptor in prefrontal cortex where activation could lead to D1 agonist-like effect to improve cognition,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



Results So Far

- NXE'149, a first-in-class GPR52 agonist identified using SBDD, is being developed for once-daily oral dosing
- Human 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

SAD PK data



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

EP4 ago.

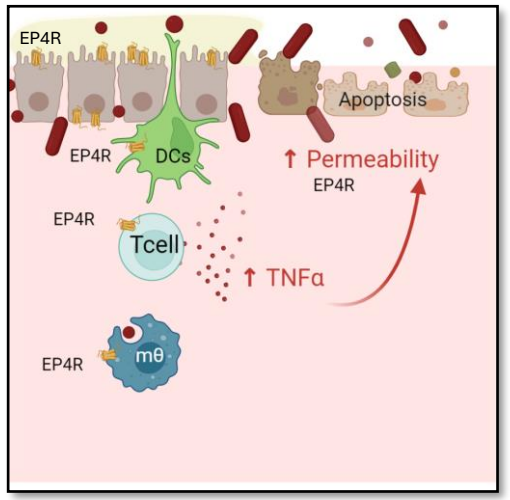
EP4 Agonist for Inflammatory Bowel Disease (IBD)

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 seventh SAD and the third MAD cohorts currently being dosed.
- No concerning adverse events have been noted to date.
- Further activities to support a Ph 1B/II study start are underway including additional cohorts (e.g. sigmoidoscopy) under the FIH umbrella.

EP4 Ag Study Link:
https://www.isrctn.com/ISRCTN70080074?q=nxera&filters=&sort=&offset=1&totalResults=2&page=1&pageSize=10

Nxera

EP4 ant.

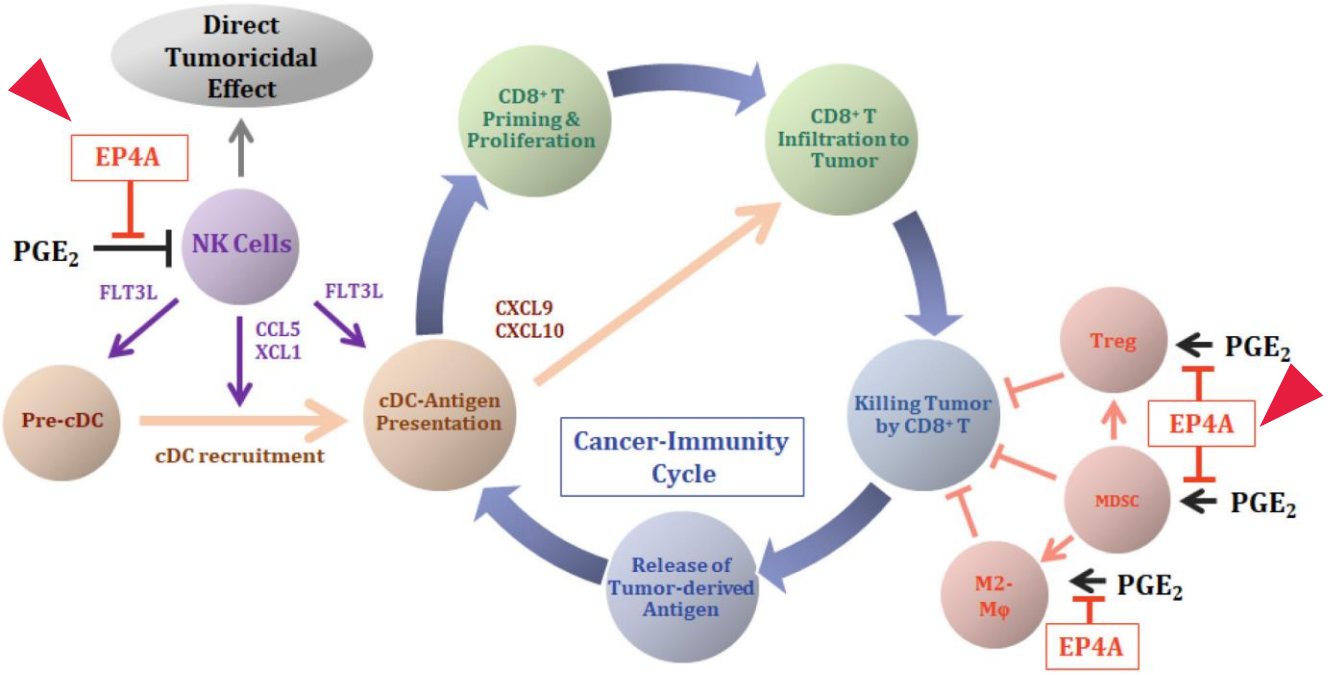
EP4 Antagonism for Advanced Solid Tumours

Alone or in Combination with Checkpoint Inhibitors (CPIs)

CANCER RESEARCH UK

Disease Rationale

- PGE2 binds to EP1-4 GPCR receptors with EP4 the most widely distributed
- Prostaglandin E2 (PGE2) is secreted by tumour and surrounding tissue and signals through EP4 to suppress the immune system promoting tumor development and progression
- 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



Study Link: https://www.isrctn.com/ISRCTN70080074?q=nxera&filters=&sort=&offset=1&totalResults=2&page=1&pageSize=10

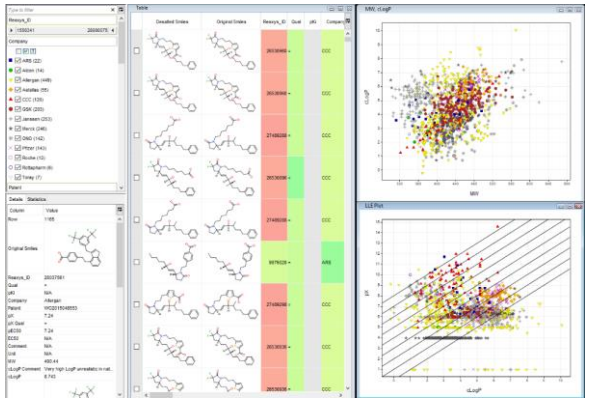
EP4 ant.

GPCR SBDD: EP4 Receptor Antagonist

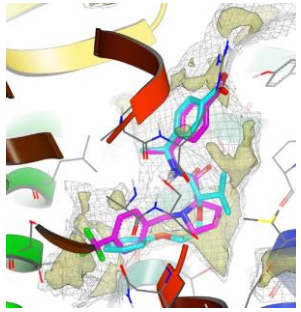
NxWave™ SBDD platform delivering a clinical ready EP4 antagonist

Clinical agents / literature ligands

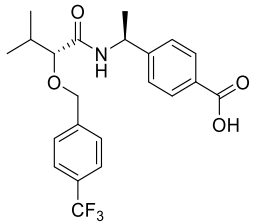
'Big data' patent & literature extraction
Select best ligands to initiate SBDD drug discovery project



SBDD homology-model guided hybrid scaffold hopping (H2L phase)



Lead

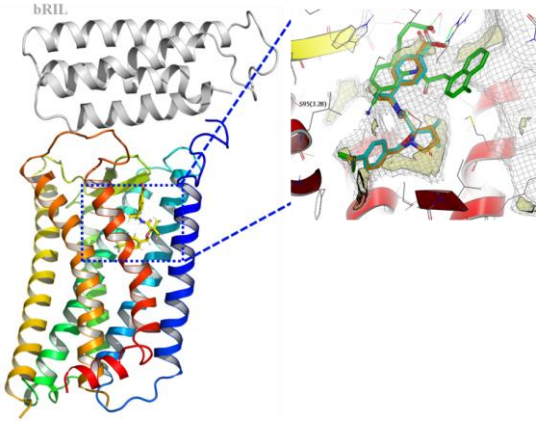


NXE'309

EP4 fpK_B 9.1
EP2 pEC_{50} 6.0
LLE 5.8

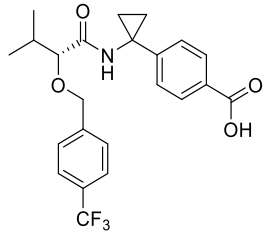
Novel, high efficiency series
Low Cl (rat/dog)
QD human PK prediction
EP2 ago activity

SBDD enabled **selectivity enhancement**



Crystal structure supports binding mode hypothesis and ONO-AE3-208 differentiation

Candidate



NXE0039732

EP4 fpK_B 9.1
EP2 pEC_{50} 5.1
LLE 5.8

Low Cl (rat/dog)
QD human PK prediction
<100 mg dose prediction

Identifying the clinical candidate NXE0039372 with our NxWave™ SBDD platform

EP4 ant.

Human pharmacokinetic and dose predictions for NXE0039732

Candidate Profile

Selected candidate showed excellent profile

High potency

- hEP4 ≈1nM

High selectivity

- >5000-fold hEP1, hEP2, hEP3

Clean in vitro safety profile

- ✓ General Safety Panel
- ✓ Cardiotoxicity
- ✓ Mutagenicity

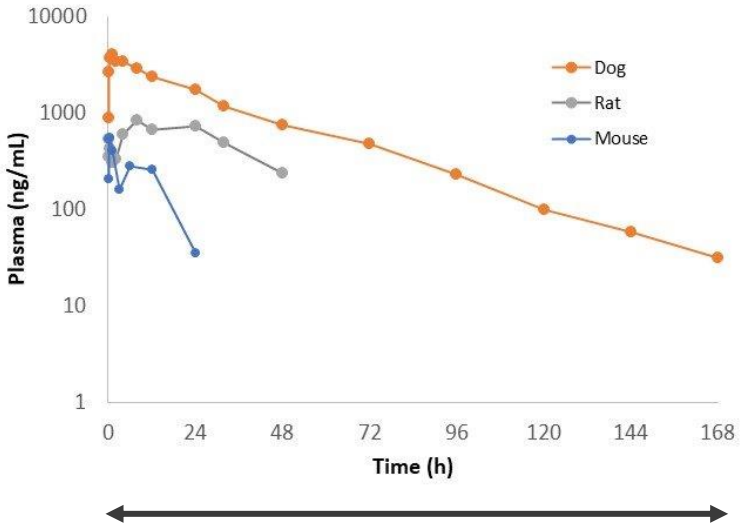
Excellent in vitro ADME properties

Pre-clinical PK

Excellent PK profile across 3 species

- low Cl
- long $T_{1/2}$

(PO, rodent 3mg/kg; dog 1 mg/kg)



7 Days

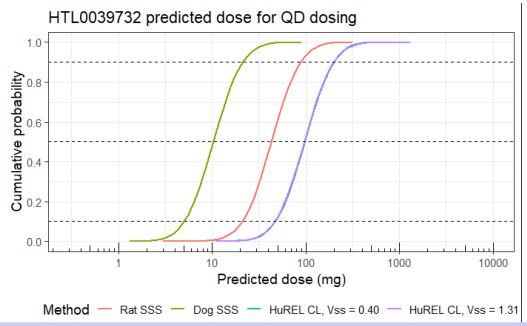
Human Dose Prediction

QD with lower dose is predicted to be sufficient

- Human PK & Dose simulations conducted predicted low Cl & low Vd to meet QD profile
- <100 mg QD predicted to maintain trough IC90 cover
- E7046 (Eisai) prediction - 800 mg QD dose to maintain IC_{90} trough

Predictions to maintain IC_{90} concentration at trough

- Monte Carlo simulations conducted to quantify probability and uncertainty on each prediction



Excellent clinical candidate with high confidence that predicted human PK supports testing the clinical hypothesis

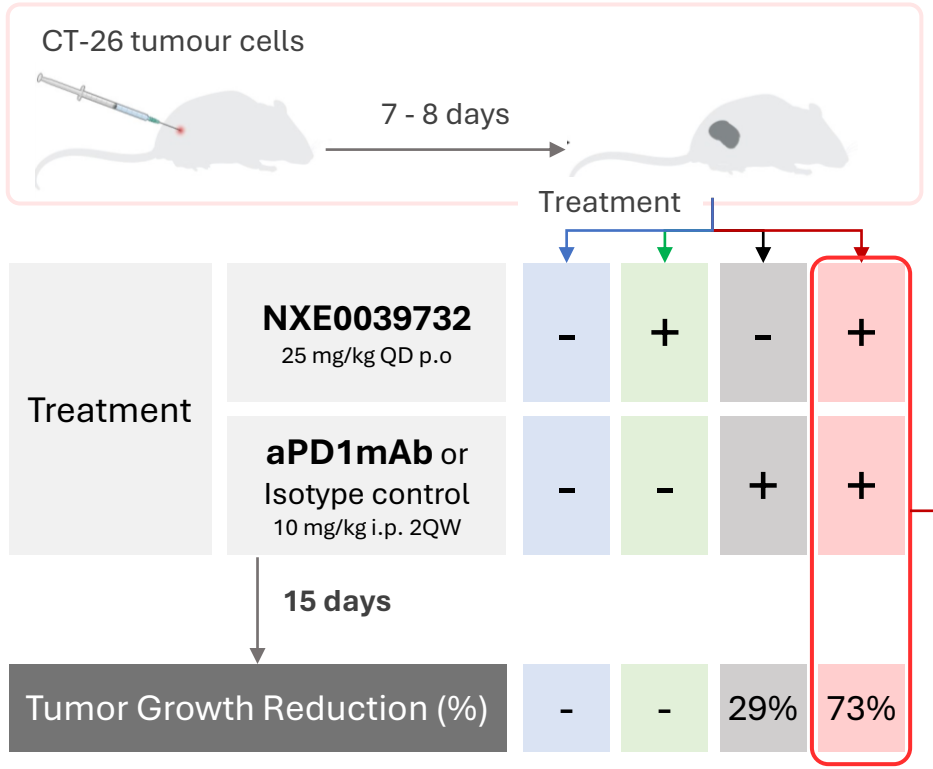
EP4 ant.

Synergistic effect of EP4 antagonist in CT-26 syngeneic model of colorectal carcinoma

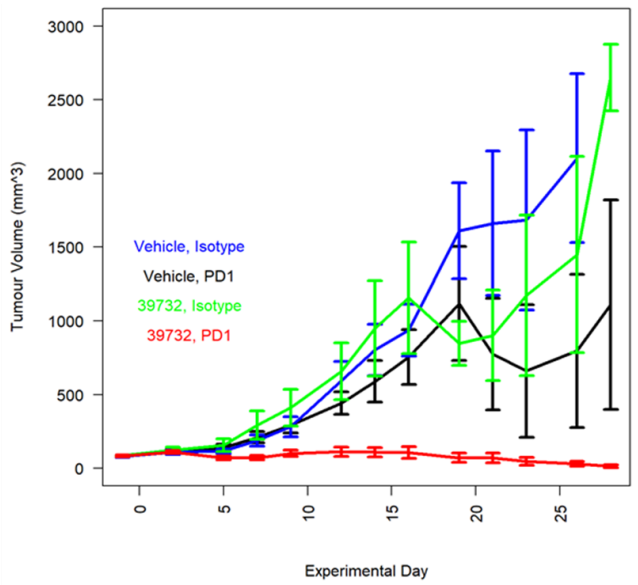
Synergistic activity of PD-1 checkpoint inhibitor and EP4 antagonist provides long lasting anti-tumour immunological memory

Combination efficacy to CT-26 (Colorectal Tumour model) in Mouse

Strong evidence for **combination benefits** of EP4 ant + aPD1 mAb treatments on control of tumour growth

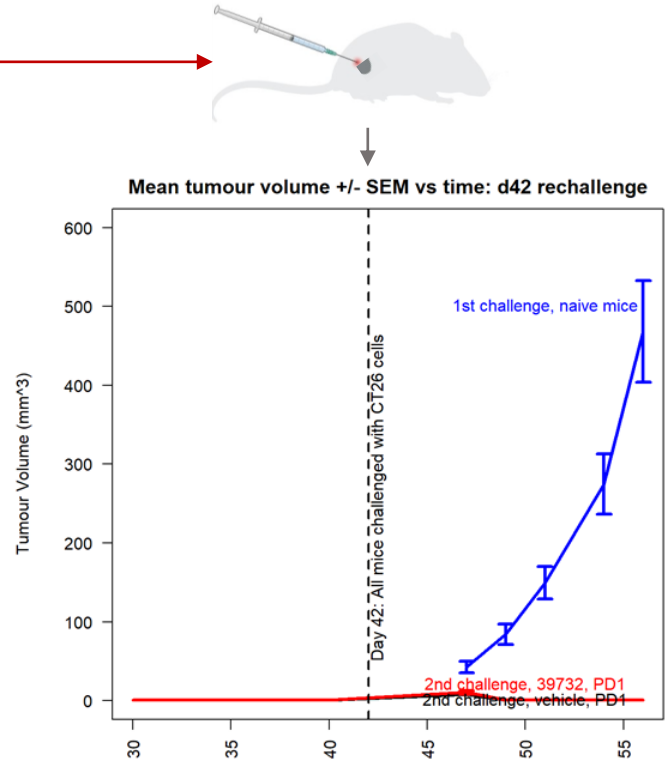


aPD1 / EP4 ant treatment group survivors re-challenged with CT-26 tumour cells



CT-26 Tumour Challenge

Clear long-lasting **anti-tumour memory response** following treatment with EP4 antagonist



EP4 ant.

Progressing through Ph1/2a in collaboration with CRUK

Evaluating anti-tumour activity of NXE0039732 as a monotherapy and in combination with CPI, Atezolizumab

CANCER RESEARCH UK

Cancer Research UK presented the study design at ESMO

Nxera's Partner Cancer Research UK to Present on Phase 1/2a Clinical Trial with Cancer Immunotherapy Drug HTL0039732 at ESMO

- HTL0039732 (also known as NXE0039732) is Nxera's novel oral EP4 antagonist with the potential to treat a wide range of cancers in combination with other immunotherapies
- Cancer Research UK's Centre for Drug Development is sponsoring and managing the ongoing Phase 1/2a clinical trial of HTL0039732

Tokyo, Japan and Cambridge and London, UK, 13 September 2024 – Nxera Pharma (TSE: 4565, "Nxera") and Cancer Research UK announce an upcoming presentation on the ongoing Phase 1/2a clinical trial (NCT05944237) of Nxera's immunotherapy drug HTL0039732 (also known as NXE0039732) at the European Society for Medical Oncology Congress (ESMO) 2024, taking place on 13–17 September in Barcelona, Spain.

The trial's co-chief investigator, Dr. Debashis Sarker from Guy's and St Thomas' NHS Foundation Trust, will present a "Trial in Progress[1]" poster at ESMO 2024 on Saturday 14 September (presentation 679TiP, available on the ESMO website here).

The first-in-human trial is evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and anti-tumor activity of HTL0039732 as a monotherapy and in combination with the checkpoint inhibitor atezolizumab, in patients with advanced solid tumors.

HTL0039732 is an oral small molecule drug candidate that was rationally designed using Nxera's NxWave™ platform and evaluated through rigorous translational and preclinical studies. HTL0039732 works by blocking signaling through a specific type of prostaglandin receptor, the prostaglandin E2 (PGE2)-type prostanoid receptor 4 (EP4). PGE2 acts in the tumor microenvironment to trigger cancer cells to evade the immune system. Targeting EP4 to block the effects of PGE2 increases the ability of the immune system to detect and control cancer cells and makes HTL0039732 a potential candidate to treat patients with cancers that generally do not respond well to current immunotherapies.

Cancer Research UK's Centre for Drug Development is sponsoring and managing the trial, which is led by chief investigator Dr Bristi Basu, University of Cambridge, and Dr Sarker. The first patient was dosed in August 2023 and the trial is currently open for recruitment at Addenbrooke's Hospital in Cambridge, Guy's Hospital in London, and the Christie Hospital in Manchester.

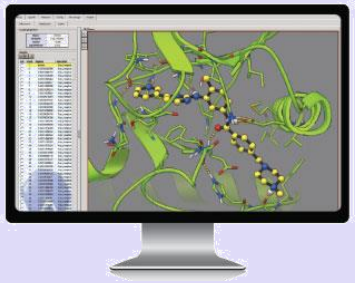
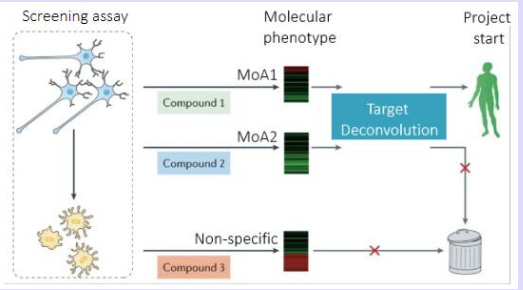
Results So Far (presented at ESMO)

- Clinical trial enrolment began 2023 and is ongoing in the UK
- Monotherapy escalation (Part A) has completed without DLTs
- Combination escalation (Part B) has now completed recruitment
- PK is in line with predictions and exhibits general dose proportionality across all dose level
- Target engagement has been observed at all dose levels tested. Additional PD analysis, including evaluation of paired biopsies for infiltration, is underway
- Toxicities, where these have occurred, have generally been mild (Grade 1-2) and resolved without dose interruption
- Preparation for Phase 2a is ongoing

Nxera


Innovation Growth

Repeatable approach to mining for next generation targets

	In Silico	Phenotypic Screening
		
Why?	• To identify new GPCR drug targets across multiple disease types	• To identify new GPCR drug targets through use of disease specific assay systems
How?	• Using 'big-data' and precision medicine to identify molecular signatures of disease and potential patient stratification opportunities • Use ML to identify influential drivers of disease, finding patterns to model non-linear biology	• Testing a curated compound library covering 270 GPCRs in various disease relevant phenotypic screening assay systems (ideally human)
What?	• Approach can be applied to multiple disease indications: scalable methodology	• Demonstrate disease relevant functional responses • Approach already used to identify tractable GPCR targets in IBD and currently under investigation in neurological disease
Partner	precisionlife improving health | for everyone; Intelligent OMICS	KALLYOPE

Scalable AI-Genetics approach to mining for next generation targets

Nxera Pharma and PrecisionLife expand strategic partnership in auto-immune disorders to identify new drug targets and patient stratification biomarkers for complex, chronic conditions

Why?

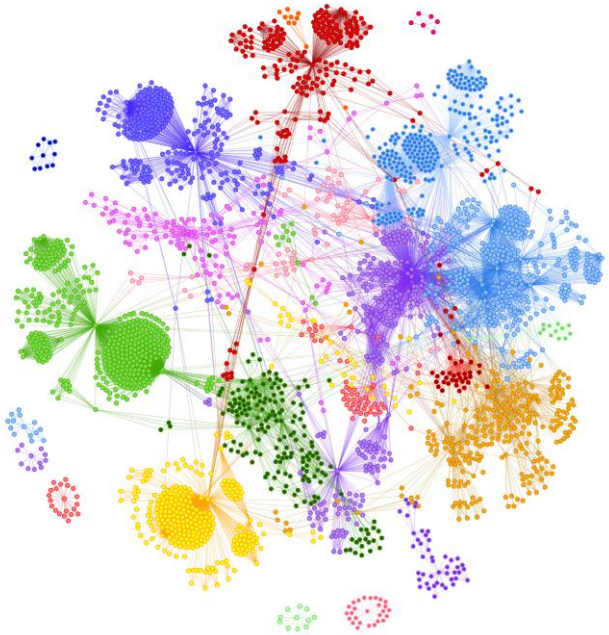
- Identifies novel GPCR drug targets, strongly associated with patient subgroups in heterogeneous populations across and between genes
- Autoimmune diseases are enormously complex, caused by genetic and environmental factors

How?

- PrecisionLife uses combinatorial analytics to find non-linear interactions between genes that drive disease biology
- PrecisionLife focuses on mechanism – providing uniquely actionable insights across the value chain:
  - ✓ **Target Identification** – allows selection of innovative novel drug targets that are drivers of disease biology with supporting genetic evidence
  - ✓ **Development** – patient stratification biomarkers to refine clinical trial design
  - ✓ **Healthcare** – identification of responders supports payer discussion, launch and prescriptions

What?

- 1st indication under review is Rheumatoid Arthritis with potential to expand to additional auto-immune indications
- Highly scalable – novel insights into 50+ diseases including CNS and auto-immune conditions



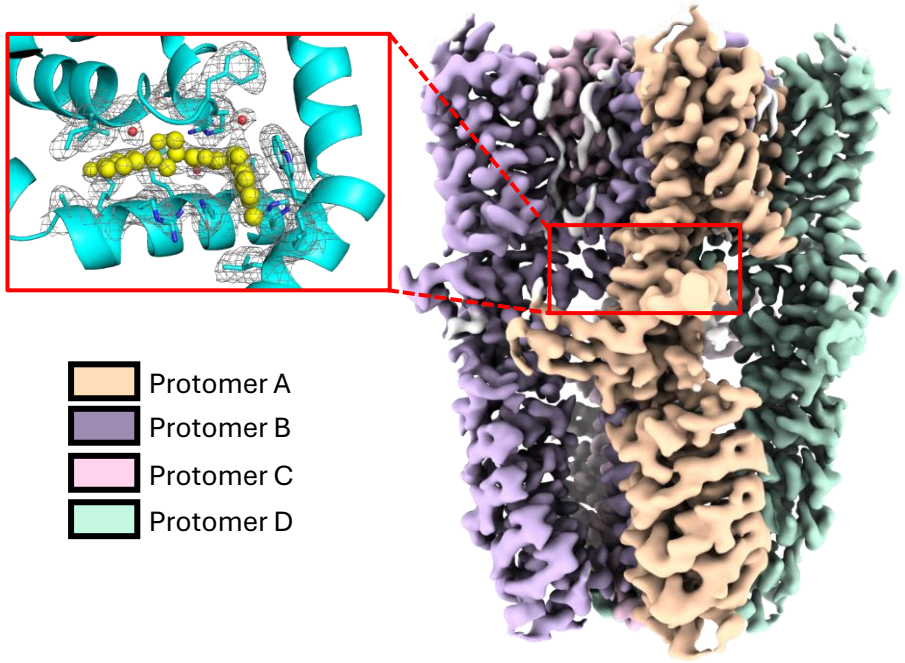
PrecisionLife's mechanism-based stratification example

Circles represent SNPs, **lines** indicate co-occurrence in >20% of patients. **Colours** represent different patient subgroups who share a specific mechanism driving their disease.

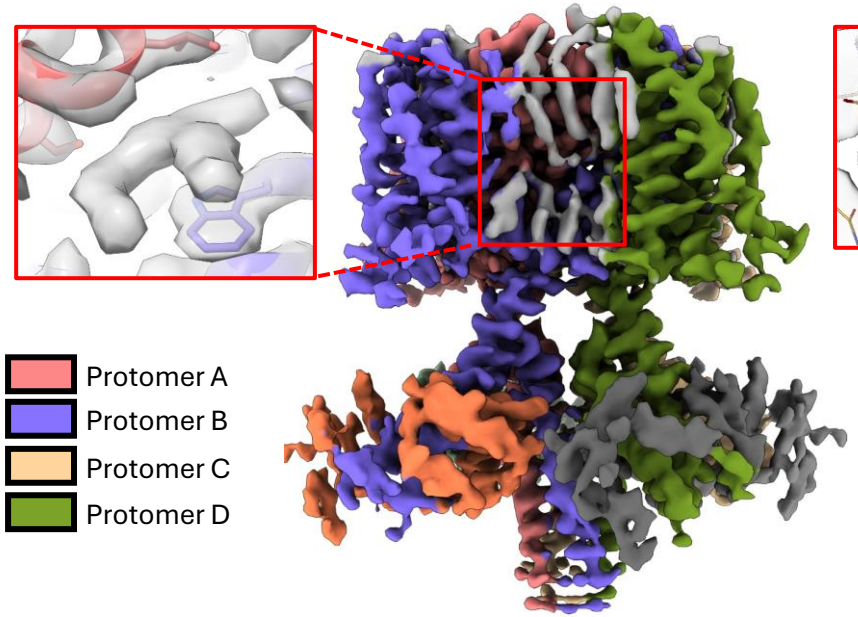
This helps select the best targets.

Structure-Based Drug Discovery at other integral membrane protein target classes

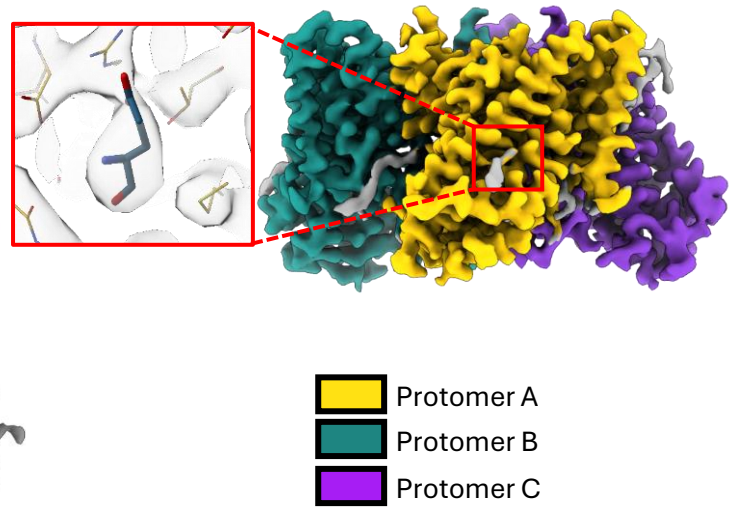
Ion channel 1



Ion channel 2



Transporter



- Use of in-house state-of-the-art membrane protein biochemistry to produce high quality protein reagents for functional and structural studies
- Multiple high resolution cryo-EM structures determined of liganded ion channels and transporter
- Establishment of network of trusted CRO to conduct electrophysiology experiments

NxWave™ SBDD platform delivering atomic resolution structures of liganded ion channels and transporters.

Designing Next Generation GPCR Antibody Therapeutics

Nxera Pharma and Antiverse Enter Collaboration To Design Novel GPCR-Targeted Antibody Therapeutics Using Generative AI

Why?

- Antibodies present an exciting opportunity for tackling GPCRs by offering high specificity and target occupancy with the potential of more convenient dosing regimens versus other modalities
- Nxera's NxStaR proteins have been utilised as antigens in the successful discovery of highly selective and potent antibodies

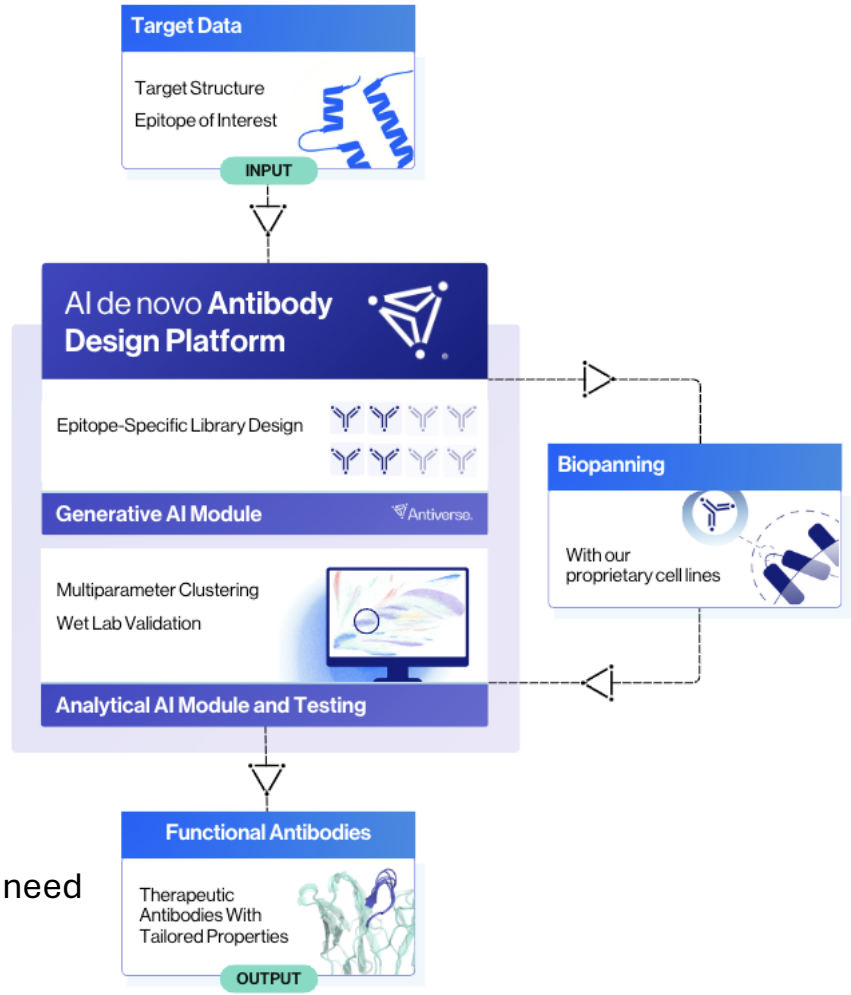
How?

The collaboration will combine:

- **Nxera's NxWave™ platform**, a powerful tool for GPCR target selection, validation and structure determination
- **Antiverse's AI *de novo* Antibody Design Platform**, which enables the rapid design of antibodies with tailored properties at scale – including epitope specificity, functionality, species cross-reactivity and enhanced affinity
- Developed over 7 years, Antiverse's platform integrates proprietary datasets and a multi-model, multi-step approach to efficiently generate and filter high-quality antibodies

What?

- A multi-target partnership and licensing agreement to target diseases of high unmet need by leveraging NxStaRs in combination with Antiverse's AI design approaches
- The first project will be aimed at designing antibodies with agonist function for a challenging GPCR target



FY2024 Q3 Financial Results

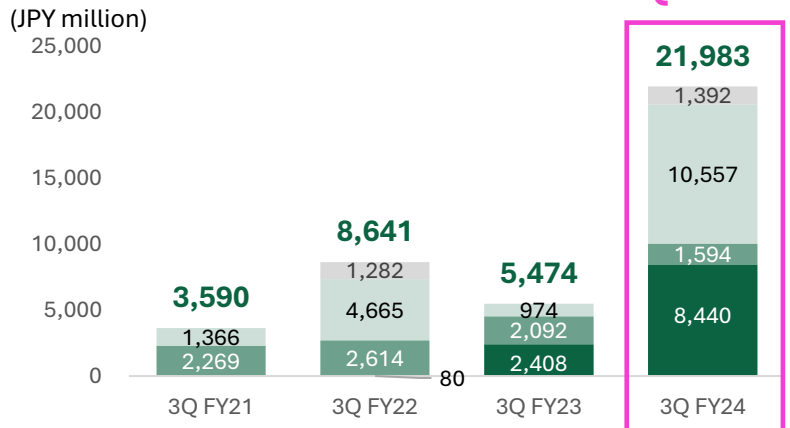
Hironoshin Nomura, Executive Officer, CFO

04

Key financial indicators

Full impact of NPJ/NPK product sales and cost base reflected in FY2024

Revenue

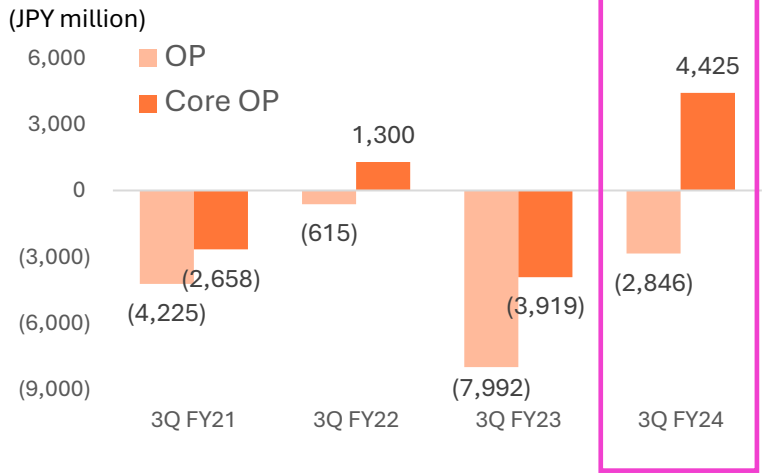


3Q result

Explanation for 1Q-3Q 2024

Upfront[1]	■ New option-to-license deal signed with Boehringer. (March)
Milestone[2]	■ $15m M4 development milestone from Neurocrine (April). ■ $4.6m milestone from Centessa (May). ■ $10m milestone from AbbVie (June). ■ $35m M4 Ph2 succusses milestone from Neurocrine (Sept).
Royalty / Other	■ Royalty from Respiratory Portfolio from Novartis decreased.
Product Sales	■ PIVLAZ® sales are increasing and fully impact for 2024.

Operating Profit / Loss



R&D	■ Increase investment in R&D activities for clinical trial. ■ Inclusion of NPJ/NPK related R&D costs.
Cost of Sales	■ Inclusion of PIVLAZ® product supply costs. ■ Additional non-cash CoS charge relating to PIVLAZ® inventory.
G&A	■ Inclusion of NPJ/NPK related G&A costs. ■ Integration costs (incl. company name change). ■ 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 3Q 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

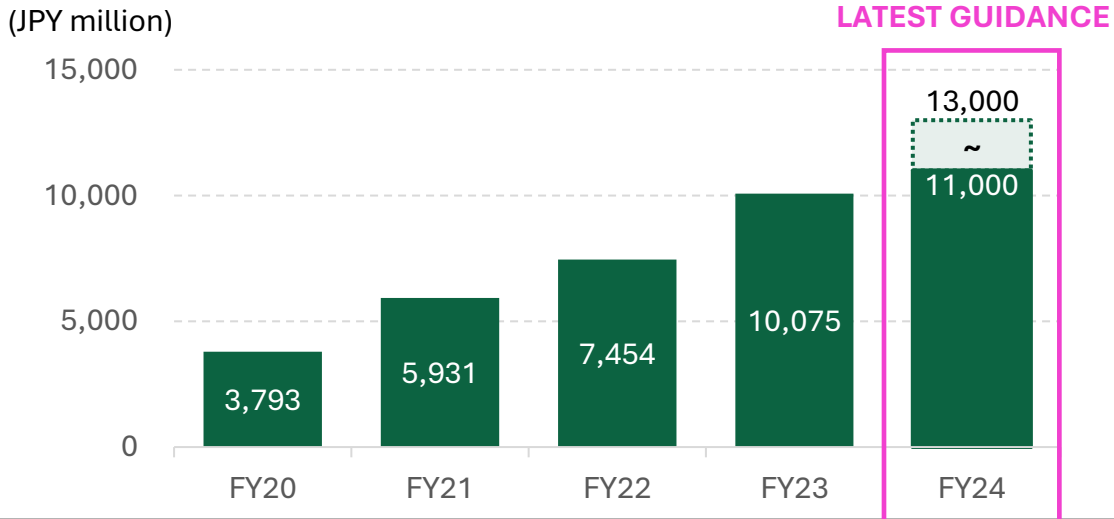
(JPY million)	NPC / NPU*1	+	NPJ / NPK*2	=	Consolidated P&L (Core)	+	Non-cash costs	+	Non-recurring Costs	=	Consolidated P&L (IFRS)
Revenue	13,613		8,370		21,983						21,983
Cost of Sales + SG&A	(4,823)		(6,100)		(10,923)		A (2,401) PIVLAZ® inventory adjustment		B (1,022) Amortization - Product IP / C (836) Integration / D (2,024) Other		(17,206)
R&D	(6,553)		(976)		(7,529)		D (988)				(8,517)
Other income	933		(39)		894		Total : 7,271				894
OP/Core OP	**3,170**		**1,255**		**Core OP 4,425**						**OP (2,846)**

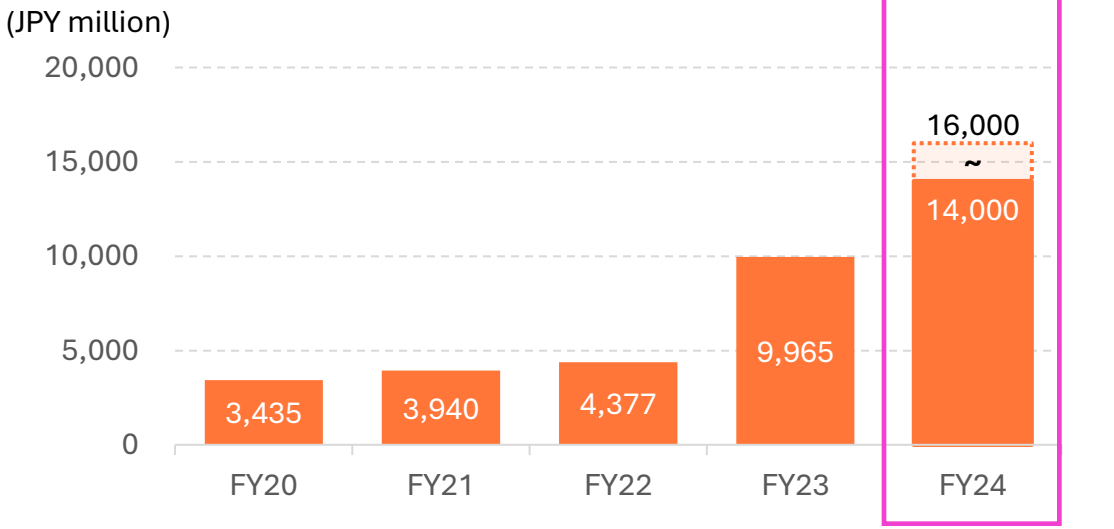
Integration related costs	A Additional CoS charge for PIVLAZ® stock which completed by 3Q 2024. This will no longer be recurring from 4Q 2024. B Amortization of intangible assets (currently relates to PIVLAZ®). Annual charge to increase to c. JPY 1,800m per year from 2025. C Integration costs including IT system integration and Corporate rebranding. Will significantly decrease in 2025.
Other	D Amortization of other intangible assets (e.g. IP), depreciation (e.g. laboratory equipment), share-based payments and other restructuring costs.

*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)

Full year cost guidance

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





R&D expenses (IFRS)

Old	New
¥12,000 ~ ¥14,000m	¥11,000 ~ ¥13,000m

- ¥1,000m

Major points on FY24

- Investment in discovery and translational medicine capabilities.
- 1 clinical trial initiated for in-house program (EP4 ag.)
- Advancing in-house programs further through the clinic will deliver higher out-licensing revenues

SG&A expenses (IFRS)

Old	New
¥18,000 ~ ¥20,000m	¥14,000 ~ ¥16,000m

- ¥4,000m

Major points on FY24

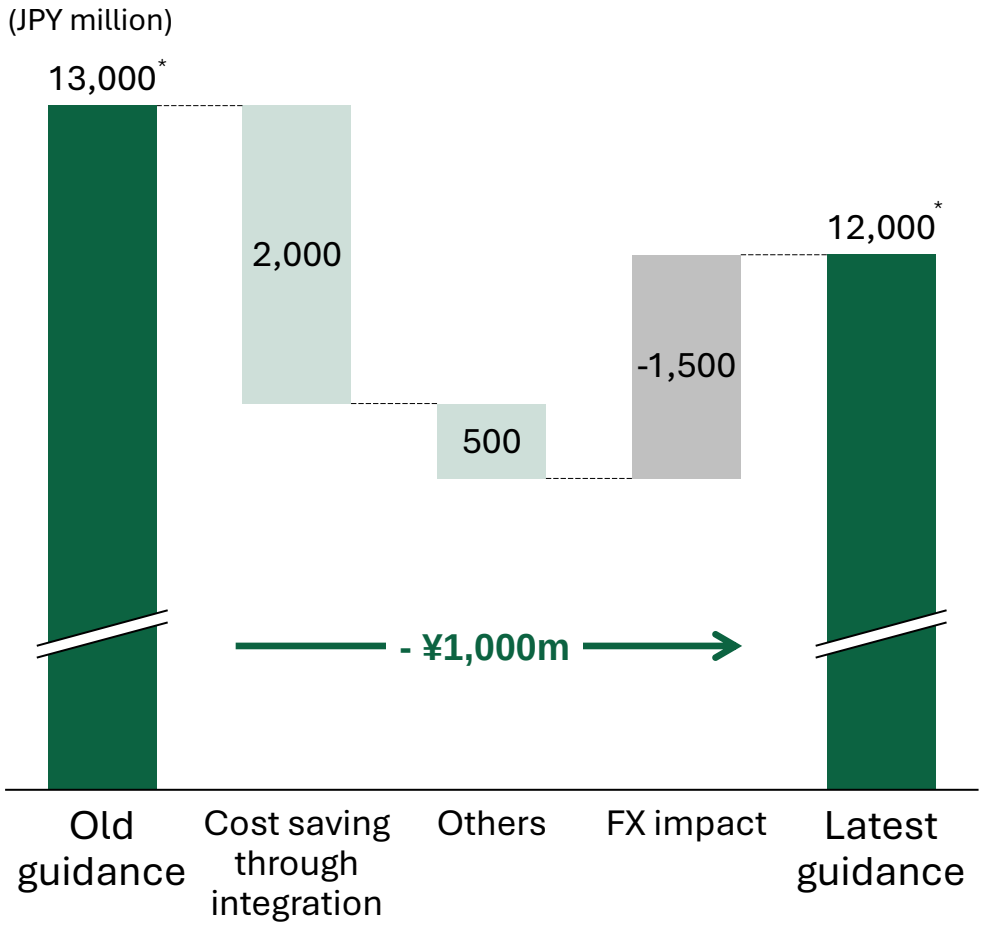
- Includes NPJ[1]/NPK[2] SG&A costs for a full year.
- Increase in support for PIVLAZ® to drive growth.
- Increase in amortization charge for PIVLAZ® and QUVIVIQ™(c. ¥1,600m)
- PMI relating costs for NPJ/NPK (c. ¥1,000m)

1. Nxera Pharma Japan 2. Nxera Pharma Korea

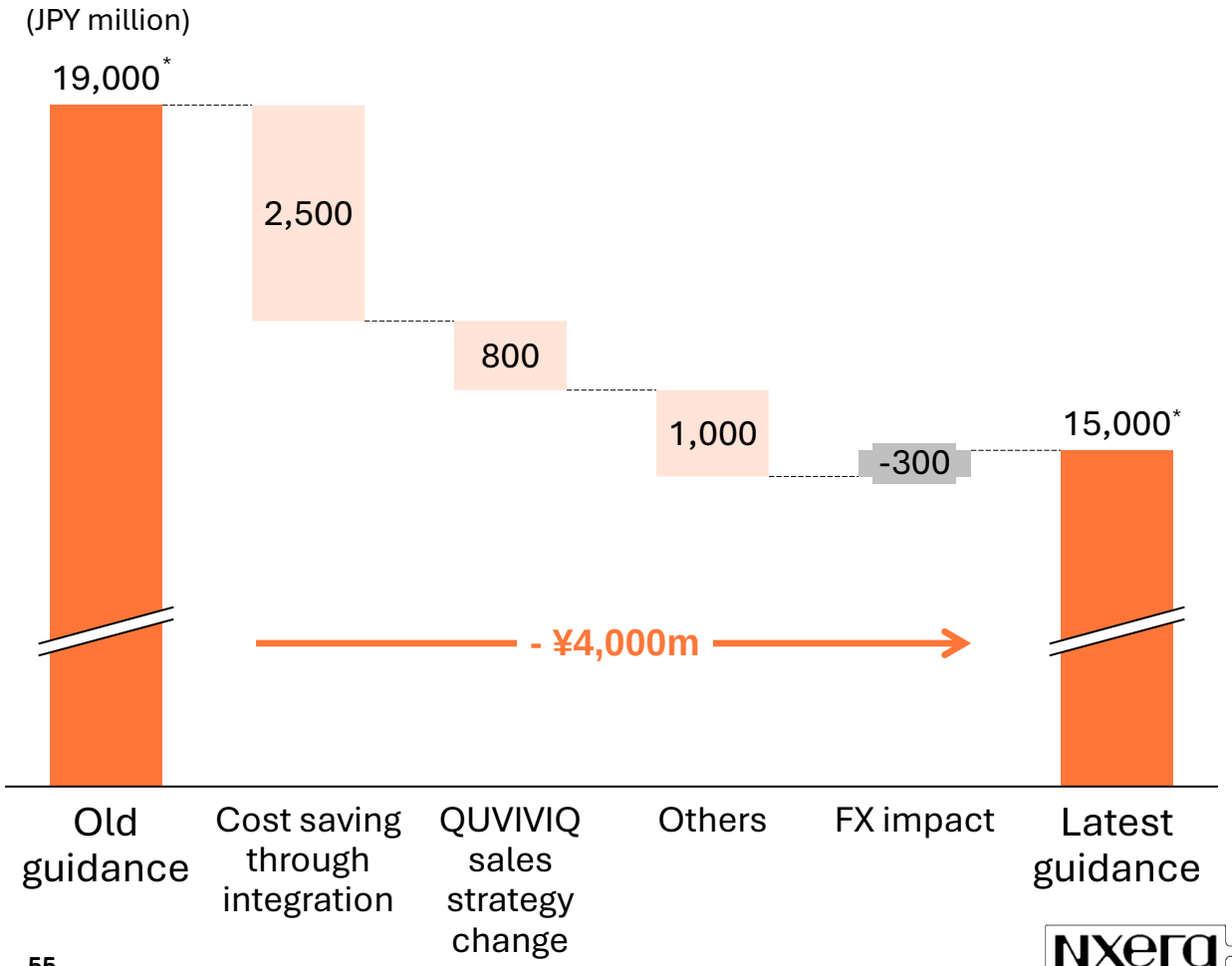
Cost expenses guidance gap vs. beginning of FY24

We expect downward trend in SG&A expenses to continue through optimization in 2025

R&D expenses (IFRS) guidance



SG&A expenses (IFRS) guidance



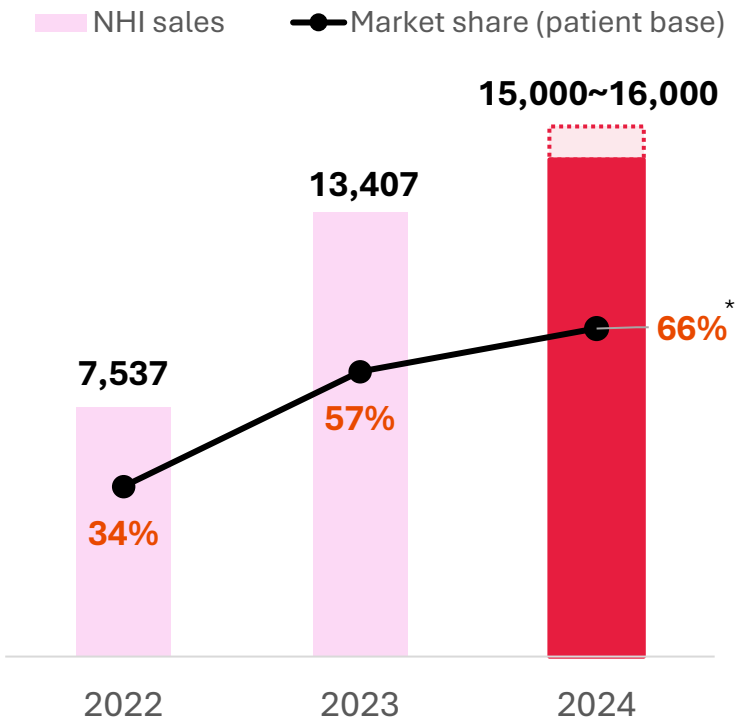
* The median of range is given as an example
Assumed exchange rate: 140 JPY/USD | 172 JPY/GBP (old guidance), 152 JPY/USD | 193 JPY/GBP (latest guidance)

PIVLAZ® sales guidance update

Updated sales guidance due to SAH occurrence decrease and cancellation of inventory adjustment plan

Sales guidance of PIVLAZ®

Updated sales guidance though PIVLAZ's market share is continuously growing



* Estimation from previous trend

Background of sales guidance update

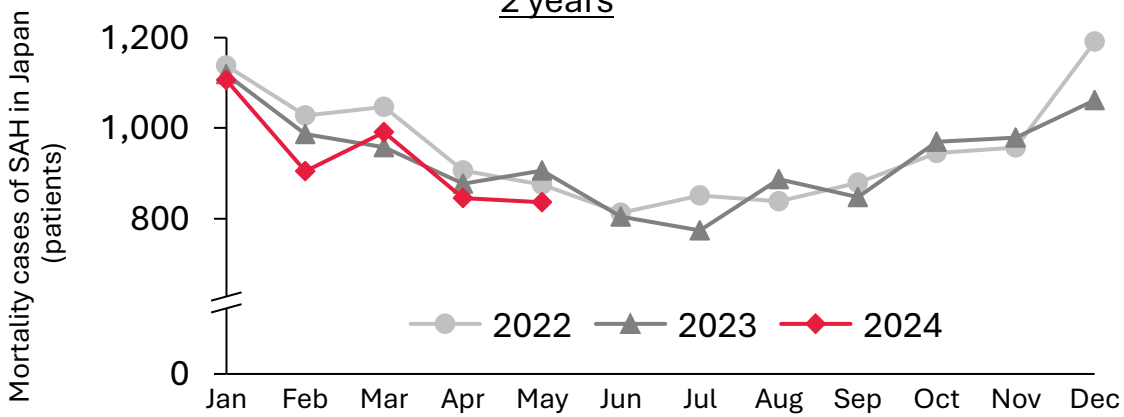
SAH occurrence decrease in 2024

c. JPY800m ↓

Optimization of year-end inventory

c. JPY200m ↓

Mortality cases of SAH in 2024 (Jan-May) was 4-6% lower than past 2 years



2023

In anticipation of increasing demand over the year-end and New Year period, the inventory for distributor was adjusted (excess of **c. JPY 200 million** than monthly forecast)

2024

Inventory adjustment was cancelled based on the track records in 2022-2023

Thank you

Appendix

05

Exclusive Opt-in Rights And ROFN/ROFR[1]

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]	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"

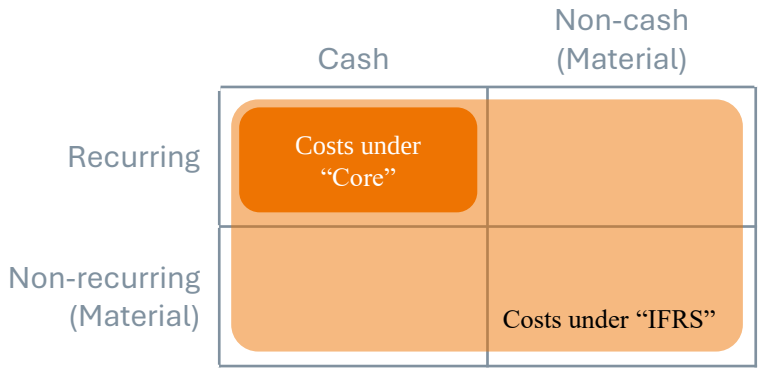
- Core Operating Profit/ Loss is a key financial indicator that highlights the underlying recurring cash generating capability of our business.
- Core Operating Profit/Loss is defined as IFRS Operating Profit + material Non-cash costs + material non-recurring costs
- Material Non-cash Costs include depreciation, 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.)



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 form 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							
Enerzair® Breezhaler®	LAMA+LABA+ICS	SME	Asthma	NOVARTIS							
ORAVI®	Antifungal agent miconazole	SME	Oropharyngeal candidiasis	Hisamitsu							
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-07054894	CCR6 antagonist	SME	Inflammatory bowel disease	Pfizer							
PF-07258669	MC4 antagonist	SME	Malnutrition	Pfizer							
PF-06954522	GLP-1 agonist	SME	Type 2 Diabetes	Pfizer							
(Not disclosed)	CGRP antagonist	SME	Neurology diseases	Pfizer							
(Not disclosed)	Multi target	SME/LME	Multiple indications	Genentech A Member of the Roche Group							
(Not disclosed)	Multi target	SME	Neurology	abbvie							
(Not disclosed)	Multi target	SME	Diabetes/Metabolic	Lilly							

Note: SME = small molecule. LME = large molecule. Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG.

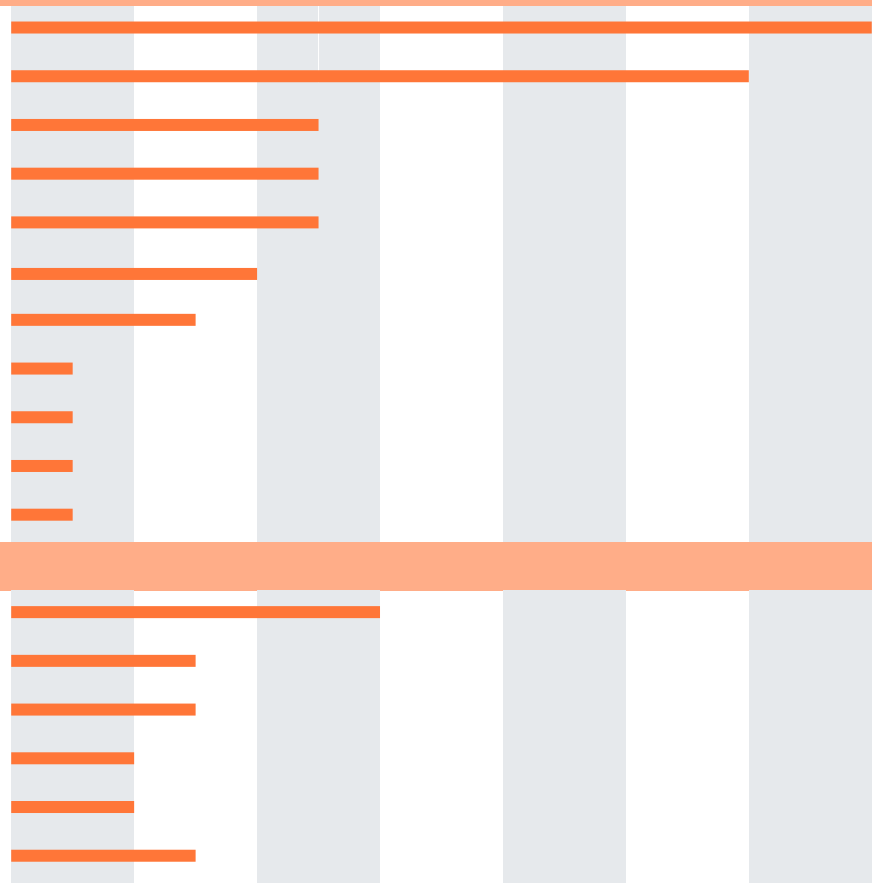
Partnered pipeline (2/2)

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	PeptiDream							
(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 Therapeutics							
ORX142	OX2 agonist (Oral)	SME	EDS in neurology	CENTESSA / Orexia Therapeutics							

Note: SME = small molecule. LME = large molecule

In-house pipeline

Compound	Target / Mechanism	Modality	Indication	Partner
In-house Programs				
PIVLAZ®	ETA antagonist	SME	Cerebral vasospasm	
QUVIVIQ™	Dual Orexin antagonist	SME	Insomnia	SHIONOGI
NXE0048149 [1]	GPR52 agonist	SME	Schizophrenia	Boehringer Ingelheim
NXE0039732	EP4 antagonist	SME	Immuno-oncology	
NXE0033744	EP4 agonist	SME	Inflammatory bowel disease	
NXE0027477	GPR35 agonist	SME	Inflammatory bowel disease	
(Not disclosed)	Muscarinic M1 agonist (JP)	SME	Neurology diseases	
(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: 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
NxStaR	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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