

NXERO Pharma

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

43rd Annual J.P. Morgan Healthcare Conference
15 January 2025

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Chris Cargill

President & CEO

Nxera Pharma

(TSE:4565)

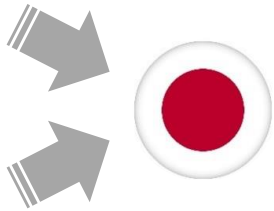


Nxera is a commercial stage, emerging biopharma from Japan

Founding



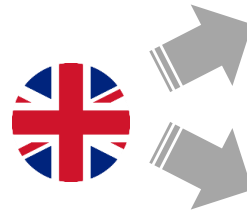
Founded with the purpose to bring the best biotech innovations to Japan...



2015



...and evolved with the NxWave™ GPCR structure-based drug discovery platform...



2024



...now accelerating the development and delivery of life-changing medicines.



5 Global Locations

Tokyo, Seoul, Cambridge, London, Basel



400+ Employees

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

By the numbers – a snapshot of our business

OVERVIEW

JPY29bn

Annual
Revenues

JPY36bn

Cash on Hand
to Invest

400+

Employees in
5 locations

PRODUCTS AND PROGRAMS

- 2** Commercially available products in Japan
- 13** Clinical-stage global programs (with partners)
- 3** Clinical-stage global programs (in-house)

THERAPEUTIC FOCUS

NEUROLOGY/
NEUROPSYCH

\$120bn+

MARKET SIZE

METABOLIC
DISEASES

\$150bn+

MARKET SIZE

IMMUNOLOGY/
GI

\$300bn+

MARKET SIZE

RESEARCH ACTIVITIES

- ✓ Focused on untapped potential of up to **400** GPCRs
- ✓ **1,500** patents granted
- ✓ **10+** programs active in discovery

4565 – our ticker on the Tokyo Stock Exchange PRIME segment

Not a traditional Japanese pharma. We think and innovate globally, and specialize locally

Global centers of excellence



CEO Research Finance Operations

Research & Early Clinical

- Proprietary StaR™ and NxWave™
- Cryo-EM Nobel Prize winning founder
- Structure-based drug design platform

Technical Operations

- Global CMC Operations
- Supply Chain
- Quality Management

~200 team members



~200 team members

Bilingual local leadership



Finance Development / Medical Commercial / Operations Compliance

Development & Commercial

- Bilingual management with global experience
- Significant development and regulatory
- Agile, technology-enabled teams
- Novel go-to-market approaches

Our team is committed to addressing some of the biggest healthcare challenges globally

Not a traditional Japanese pharma. Committed to speed and operational excellence

Core Values



Innovation



Focus



Speed



Operational excellence

Japan + APAC commercial business

Focusing on diseases that matter in the region

Focused on Age-related and QOL disorders

Highly experienced team

Nine PMDA approvals achieved to date

Japan's most effective & efficient salesforce

JPY 400m+ per sales representative

Global discovery business

NxWave™ discovery platform

GPCR focus (Muscarinics, Orexins, Incretins)

Innovating in areas that matter

Neurological disorders, Metabolic diseases, Immun./GI

World-leading development partners

Neurocrine, Pfizer, AbbVie, Lilly, Centessa + more

Focused strategy of wholly-owned R&D investment plus licensing initiatives to fuel long-term growth

Let's talk about our products and clinical pipeline

Nxera's Commercialized Products

1 Neurological disorders – diseases of ageing

PIVLAZ®



– prevention of cerebral vasospasm in patients with Aneurysmal Subarachnoid Hemorrhage (aSAH)

2 Neurological disorders – quality of life diseases

QUVIVIQ™



– treatment of adult patients with insomnia

JPY30–35bn product sales by 2030
(plus, multiple other programs in discovery/development)

Partnered Products (Discovered by Nxera/with NxWave™ tech)

3 Neurological disorders – psychiatric / cognition



– **Muscarinic agonists**

4 Neurological disorders – QOL diseases - sleep



– **Orexin 2 agonists**

5 Metabolic diseases – QOL diseases - T2D / obesity



– **GLP-1 agonist**

Up to JPY250bn royalty revenues at peak
(plus, multiple other programs in discovery/development)

Commercialized Products in Japan

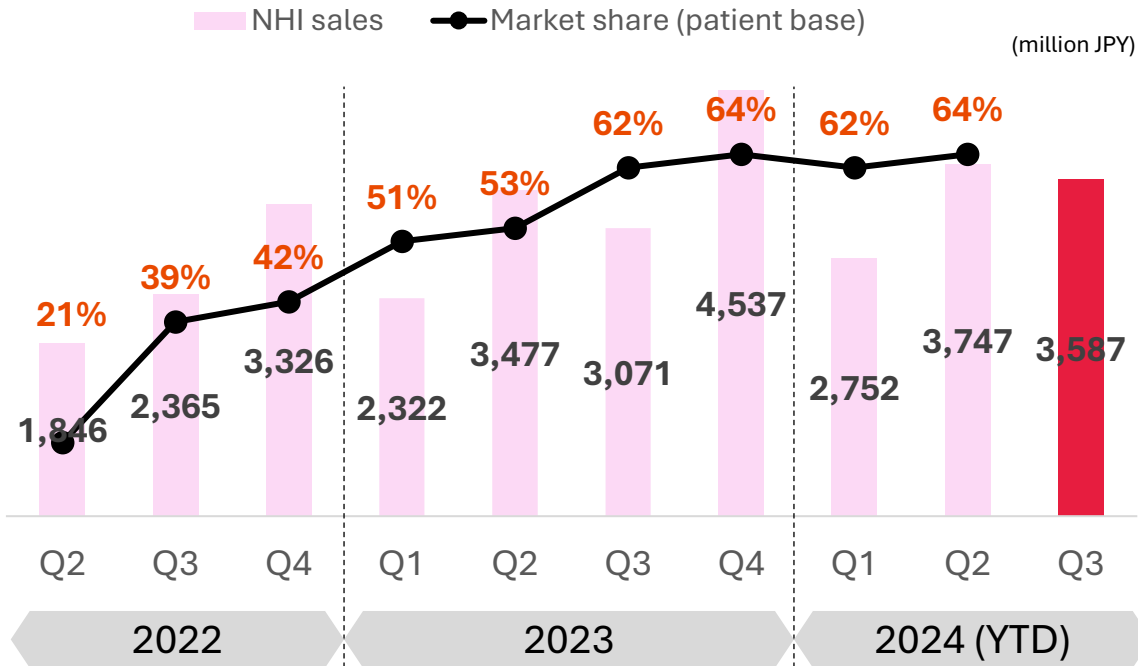


1 PIVLAZ[®] (clazosentan, an endothelin A antagonist)

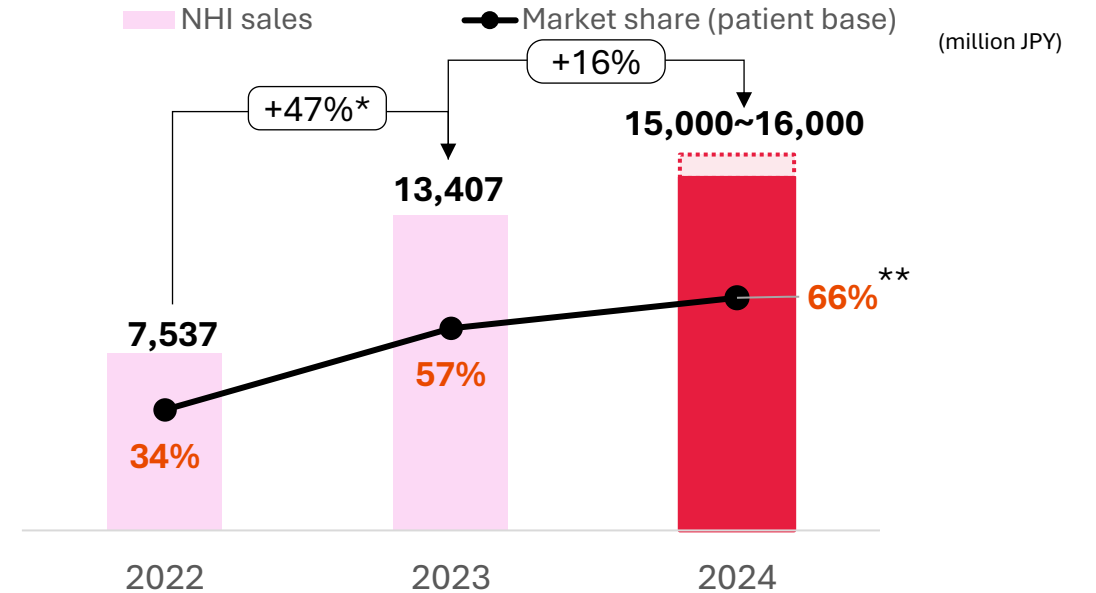
Our first commercially available product for the prevention of cerebral vasospasm in patients with Aneurysmal Subarachnoid Haemorrhage (aSAH)



Quarterly PIVLAZ[®] Sales (NHI-based)



Annual PIVLAZ[®] sales and its growth



PIVLAZ[®] has rapidly built awareness and is becoming the standard of care with neurosurgeons

Source: MDV DPC hospital data

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


2 QUVIVIQ™ (daridorexant, dual orexin antagonist)


PMDA approved September 2024, launched with partner Shionogi December 2024




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 hr** $T_{1/2}$: **about 6-9 hr**

Significant improvement in next-day sleepiness and daytime functioning confirmed in global phase 3 trials ²

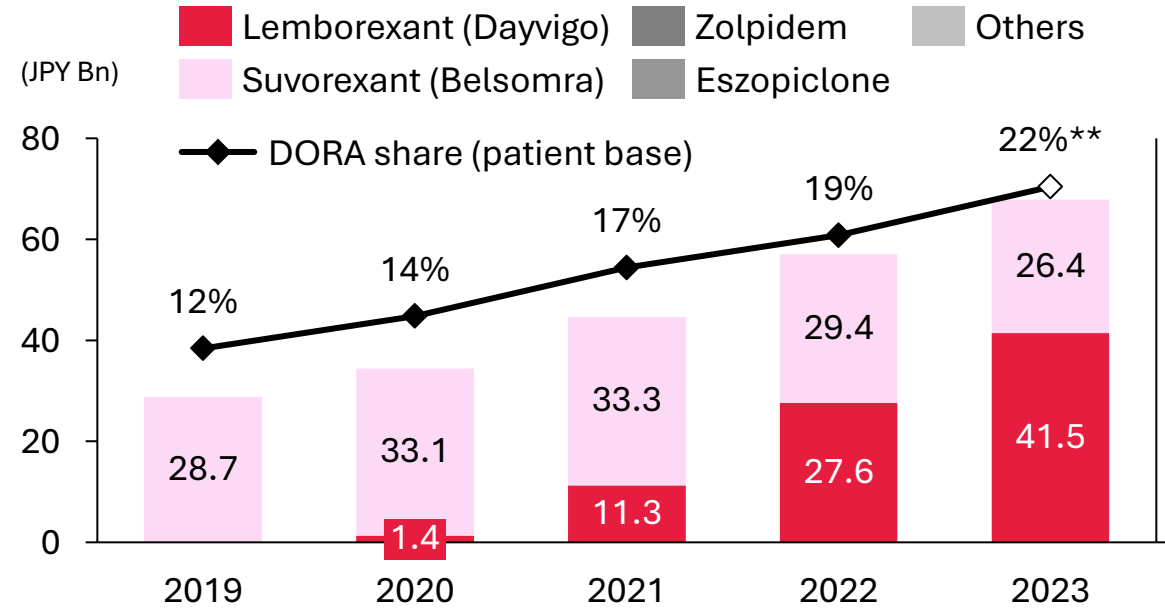
QUVIVIQ™ has the potential to be the best-in-class DORA treatment

2 QUVIVIQ™ (daridorexant, dual orexin antagonist “DORA”)

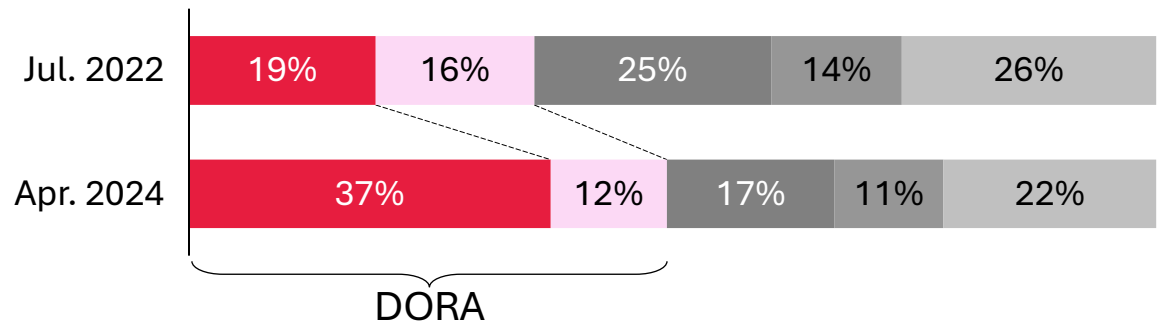
DORA is rapidly establishing its position in the treatment paradigm for insomnia



Sales and market share (NHI-base)



Prescription share (Most frequently prescribed sleeping pills)



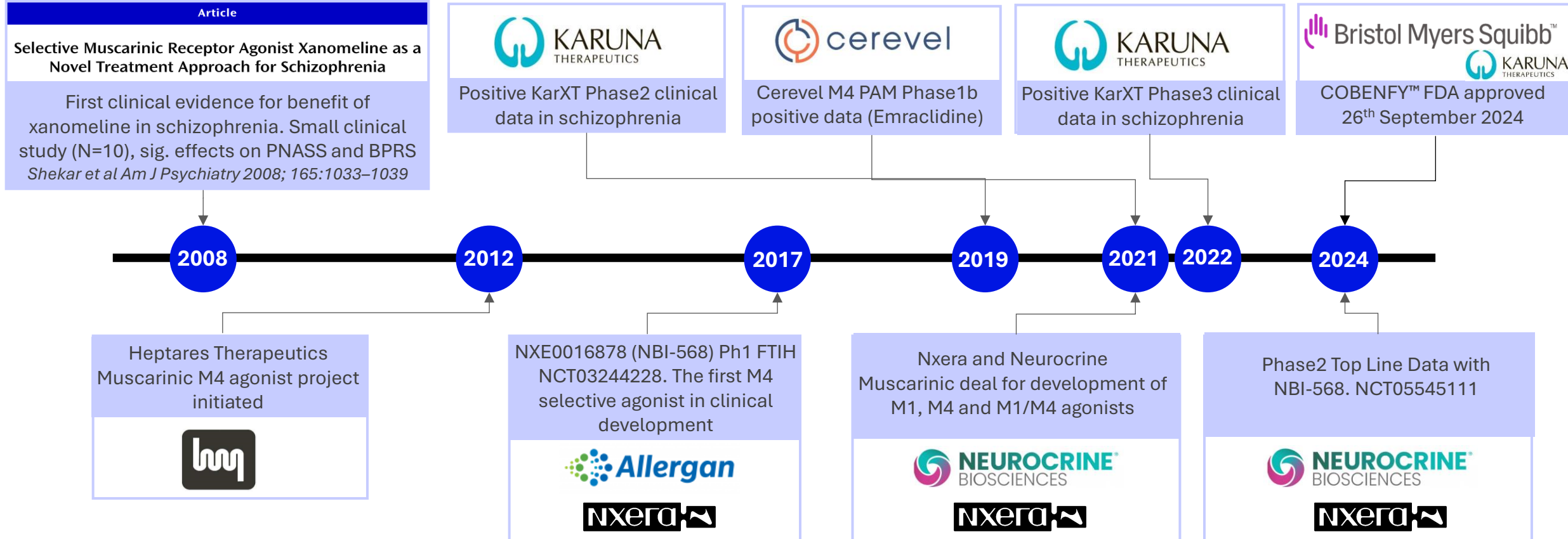
- ✓ DORAs are rapidly penetrating the insomnia treatment market in Japan, where traditional anti-anxiety and z-class drugs are not preferred by physicians
- ✓ Japan is one of the largest DORA markets globally – estimated at up to US\$1bn
- ✓ Together with partner Shionogi, we aim to provide the best-in-class product

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

Partnered Products



3 Following recent approval of BMS' COBENFY™, muscarinic agonism became the first new mode of action to treat schizophrenia patients in decades

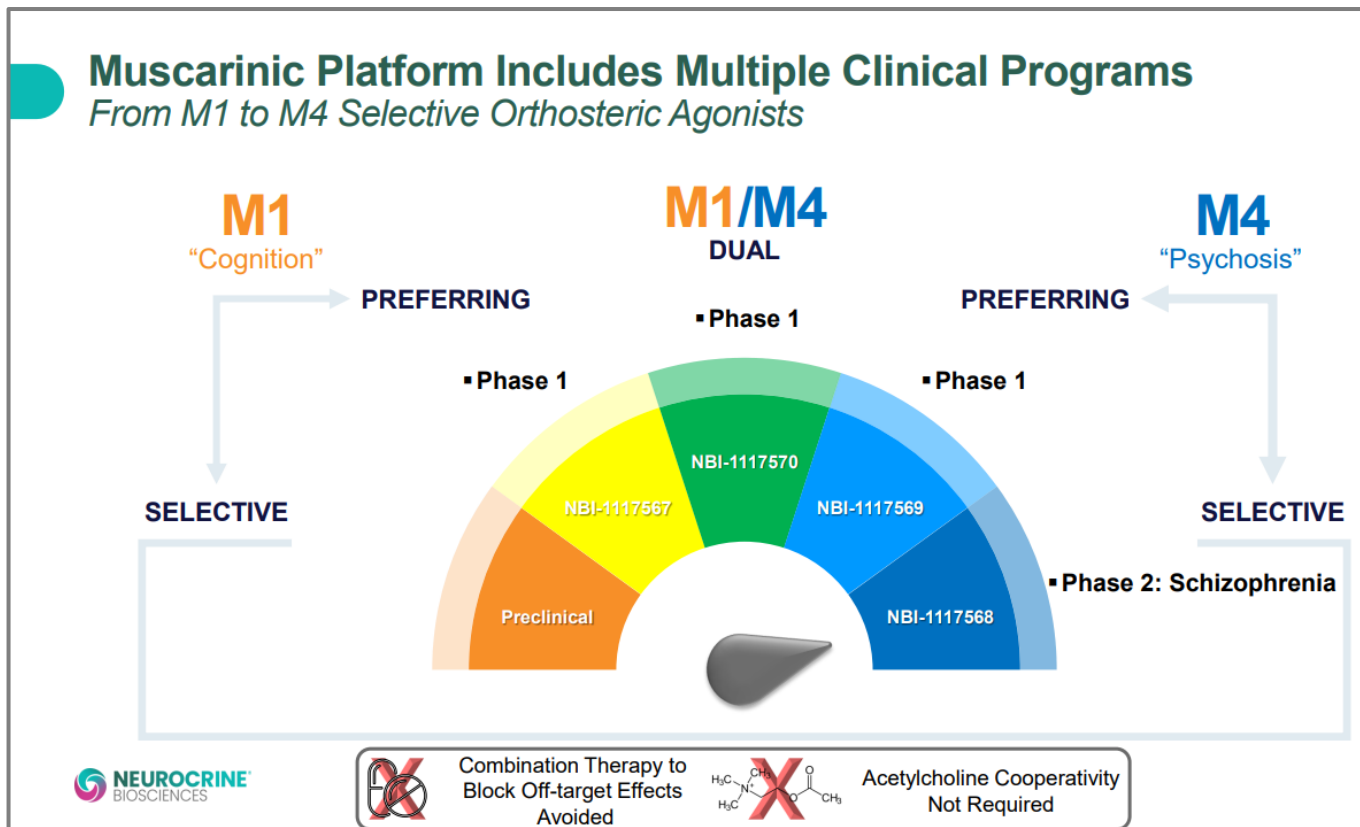


Nxera's research team began working on muscarinic agonists over 10 years ago. Opportunity remains wide open for best-in-class approaches across a myriad of potential indications

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



3 Neurocrine is advancing the world's most comprehensive portfolio of muscarinic orthosteric agonists – discovered by Nxera using NxWave™



Highlights

- NxWave™ platform enabled full suite of Structurally-enabled small molecule programs across key receptors
- Comprehensive approach to maximising the potential of muscarinic agonism
- Lead program, NBI'568, M4 selective orthosteric agonist, completed Phase 2 in 2024 with additional studies planned

From M1 through to M4, multiple pathways to potentially treat cognitive or psychosis related conditions

3 NBI-568 is positioned for a Phase 3 start in schizophrenia in H1 2025



First compound discovered using Nxera's NxWave™ technology to progress into Phase 3



Clinically Effective

Efficacy at 20mg dose comparable to all competitors



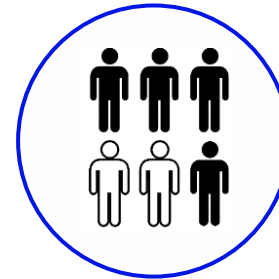
Good Tolerability

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 clinical trial was successful and confirmed a safe, well tolerated and efficacious dose to progress into Phase 3 studies H1 2025. **Additional Phase 2 studies are planned in H2 2025** (i) **NBI-568** in Bipolar Mania and (ii) **NBI-570**, a dual M1/M4 agonist in Schizophrenia.

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

4 Centessa advancing Orexin 2 agonists - ORX750 in Phase 2 as an improved treatment for Narcolepsy Type 1 and beyond – discovered using NxWave™



ORX750: Potential to Redefine the Standard of Care for Patients with Sleep-Wake Disorders

ORX750
Orexin receptor type 2

- **High unmet medical need** in NT1, NT2 and IH
- **Proof-of-concept achieved** and asset clinically **derisked** in Phase 1 study of acutely sleep-deprived healthy volunteers
- **Advancing Phase 2a studies** in patients with NT1, NT2 and IH; **Data expected across all three indications in 2025**
- **Significant commercial opportunity** as potential treatment for all three indications

ORX750
Highly potent, selective OX2R agonist

Significant commercial opportunity for best-in-class lead program ORX750 across NT1, NT2, and IH

5 Pfizer advancing PFE'522, once-daily, small molecule GLP-1 agonist in Phase 1 for T2D and obesity – discovered by Pfizer using NxWave™



Select Pipeline Advancements in Internal Medicine*

Cachexia¹

- **Ponsegromab**
 - Weight increases at all doses in Phase 2 cancer cachexia study, with improvements in appetite, cachexia symptoms, physical activity, muscle mass at highest dose
 - Aim to start registration-enabling study in 2025

Obesity

- **Danuglipron**
 - Expected 1Q25 update will inform registration enabling studies
- **Oral small molecule GIPR** antagonist phase 2 expected to start in 2024
- **Once-daily GLP-1** in Phase 1

Strategic focus on portfolio prioritization and continued improvement of productivity metrics

*See Slide 29 for Glossary: Select Pipeline Assets
1. Wasting (muscle mass loss with or without fat loss) due to severe chronic illness.
GIPR=glucose-dependent insulinotropic polypeptide receptor; GLP-1=glucagon-like peptide 1

Third Quarter 2024 Earnings

15





Pfizer “all-in” on oral small molecules for metabolic disease. Huge need for convenient, cost effective, scalable products



Emerging wholly-owned pipeline



Fuelling the Wave 1 and Wave 2 launches with novel programs in neurology and immunology

	OPTION TO LICENSE WITH  Boehringer Ingelheim	DISCOVERED BY  NXE	DISCOVERED BY  NXE	DISCOVERED BY  NXE
Compound & Stage	NXE-149 (Ph 1b)	NXE-732 (Ph 1)	NXE-744 (Ph 1)	
Target Indication	Schizophrenia	Advanced solid tumors	IBD	
Global Patient Population	24 million	18 million	10 million	
Mechanism	Novel, selective GPR52 receptor agonism	Selective EP4 receptor antagonist in combo with PD-L1	Novel, selective EP4 receptor agonist	
Novelty	First-in-Class	Best-in-Class	First-in-Class	

Continuing to design convenient, cost effective, easy to manufacture, oral small molecule medicines with the potential to change the treatment paradigm for major diseases

Leveraging and expanding the world's most comprehensive platform for GPCRs – NxWave™

NxWave™ Platform



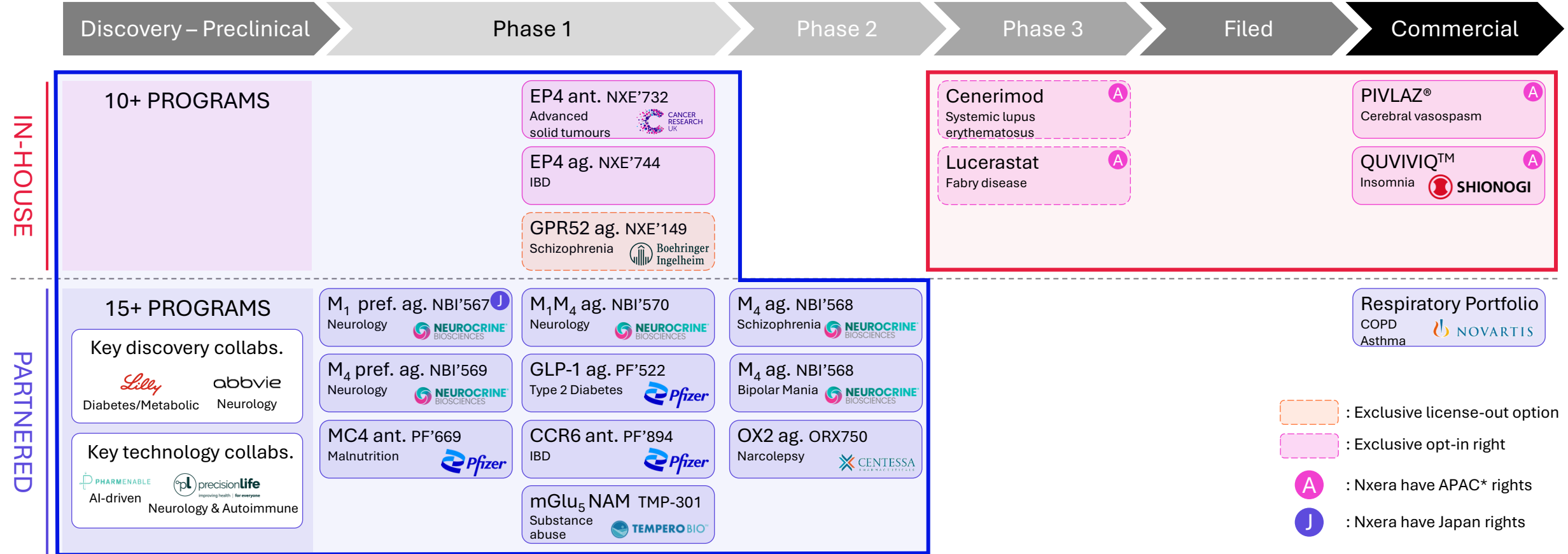
Our core strength is in small molecules.

Expanding the NxWave™ platform to other modalities to address needs where small molecules cannot.

The Big Picture



Broad and balanced pipeline with two recently launched products driving top line growth



Clinical pipeline rapidly shifting towards late-stage clinical development

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

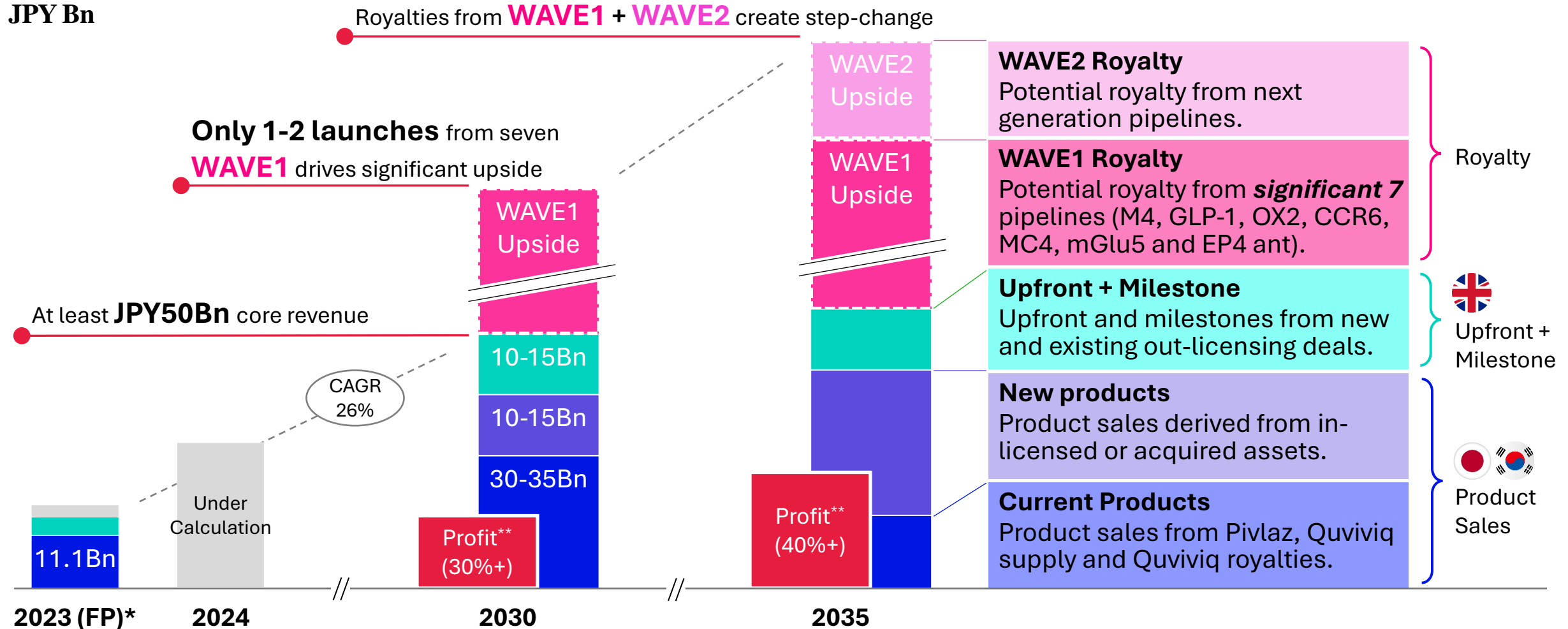
Our Wave 1 and Wave 2 programs are positioned across fast growing areas of healthcare

		WAVE1 (Potential Launch by 2030)	WAVE2 (Potential Launch by 2035)
Neurology	<p>MARKET SIZE (2030)</p> <p>\$120bn+</p>	<p>TEMPERO BIO™</p> <p>P1 mGlu5 NAM Substance Use Disorders</p> <p>CENTESSA PHARMACEUTICALS</p> <p>P2 Ox2 agonist Narcolepsy</p> <p>NEUROCRINE BIOSCIENCES</p> <p>P2 M4 agonist Schizophrenia</p> <p>P2 M4 agonist Bipolar Mania</p> <p>P1 M1/M4 agonist Schizophrenia</p>	<p>CENTESSA PHARMACEUTICALS</p> <p>PreC Ox2 agonists Neuropsych-related sleep disorders</p> <p>NEUROCRINE BIOSCIENCES</p> <p>P1 M4 pref. agonist</p> <p>P1 M1 pref. agonist Cognitive & psychosis-related disorders</p> <p>NXera</p> <p>P1 GPR52 agonist Schizophrenia</p> <p>abbvie</p> <p>Disc Multiple targets Neurology</p>
Metabolic	<p>MARKET SIZE (2030)</p> <p>\$150bn+</p>	<p>Pfizer</p> <p>P1 GLP-1 agonist T2D / Obesity</p> <p>P1 MC4 antagonist Malnutrition</p>	<p>Lilly</p> <p>Disc Multiple targets T2D/Obesity and Others</p>
Immunology / GI	<p>MARKET SIZE (2030)</p> <p>\$300bn+</p>	<p>Pfizer</p> <p>P1 CCR6 antagonist IBD</p> <p>NXera</p> <p>P1 EP4 antagonist + PD-L1 Immune-oncology for Advanced Solid Tumors</p> <p>CANCER RESEARCH UK</p>	<p>NXera</p> <p>P1 EP4 agonist IBD</p>
		JPY250bn (max total royalty potential at peak)	Multi billion USD milestones and royalties

Source: EvaluatePharma, News Research, Internal Analysis

Our 2030 vision is to build a high growth, highly profitable Japanese biopharma















JPY Bn



Note: * Revenue values are proforma the acquisition of Idorsia Pharmaceuticals Japan and Korea and reflect annual product sales of Pivlaz in 2023.





** WAVE1 and WAVE2 royalty is not included.

Looking ahead to potential catalysts in 2025*

PROGRAM	PARTNER	TIMING	EVENT
TMP-301 (mGlu5 NAM)		Q1 2025	Phase 2 study start in alcohol use disorder
Cenerimod (S1P1) / Lucerastat		Q1 2025	Exclusive opt-in decision
NXE'732 (EP4 antagonist)	 	Q1 2025	Phase 2 study start in Advancing Solid Tumors
NBI'568 (M4 agonist)		H1 2025	Phase 3 study start in Schizophrenia
NBI'568 (M4 agonist)		H2 2025	Phase 2 study start in Bipolar Mania
NBI'570 (M1/M4 agonist)		H2 2025	Phase 2 study start in Schizophrenia
NXE'744 (EP4 agonist)		H2 2025	Phase 2 study start in IBD
NXE'149 (GPR52 ag)	 	H2 2025	Phase 1b completion
ORX750 (OX2 agonist)		H2 2025	Phase 2a data across NT1, NT2, and IH
Multiple discovery collaboration progress	 	2025	Progression through discovery stage
NBI'567 (M1 ago) / NBI'569 (M4 ago) / NBI'570 (M1/M4 ago)		2025	Phase 1 data readout
New global out-licenses		Anytime	Out licensing and/or discovery collabs
New Japan / APAC in-licenses		Anytime	Acquire/in-license late-stage medicines
QUVIVIQ™		Anytime	APAC out-licensing deals

Rapidly executing on our 2030 vision to be Japan's high growth, emerging biopharma champion

Now is the time to invest in one of Japan's most transformative emerging biopharmas

	Year Founded	IPO / Listing	Value of Business	Modality	# Non-clinical Programs	# Clinical Programs
	2019	NASDAQ (2024)	\$600M	SME, Biologics	3+	1
	2019	NASDAQ (2024)	\$890M	SME	3+	1
	2019	NASDAQ (2023)	\$1,493M	SME	4	2
	2007*	TSE PRIME	\$560M	SME, Peptides, Biologics	25+	13

Comprehensive discovery capabilities, and a clinical pipeline positioned for mid and long term success

Source: Company Presentations, FactSet as at 10-Jan-2025

*Relates to the founding of Heptares Therapeutics Ltd (now known as Nxera Pharma UK Limited).

** Team members of Nxera Pharma UK Limited.

Questions?



Thank you

Japan is our home, and the best lynchpin market for broader APAC growth

Well understood healthcare challenges

- **Ageing population**
 - 1 in 3 Japanese citizens will be 65+ this year
 - Age-related / quality of life disease are prevalent and growing rapidly
- **Neurological disorders on the rise**
 - Growing awareness of mental health disorders
 - Patients seeking treatment for mental/neuropsych disorders have doubled over past 10 years
- **Drug lag and drug loss issues**
 - Hundreds of medicines approved globally are not approved in Japan

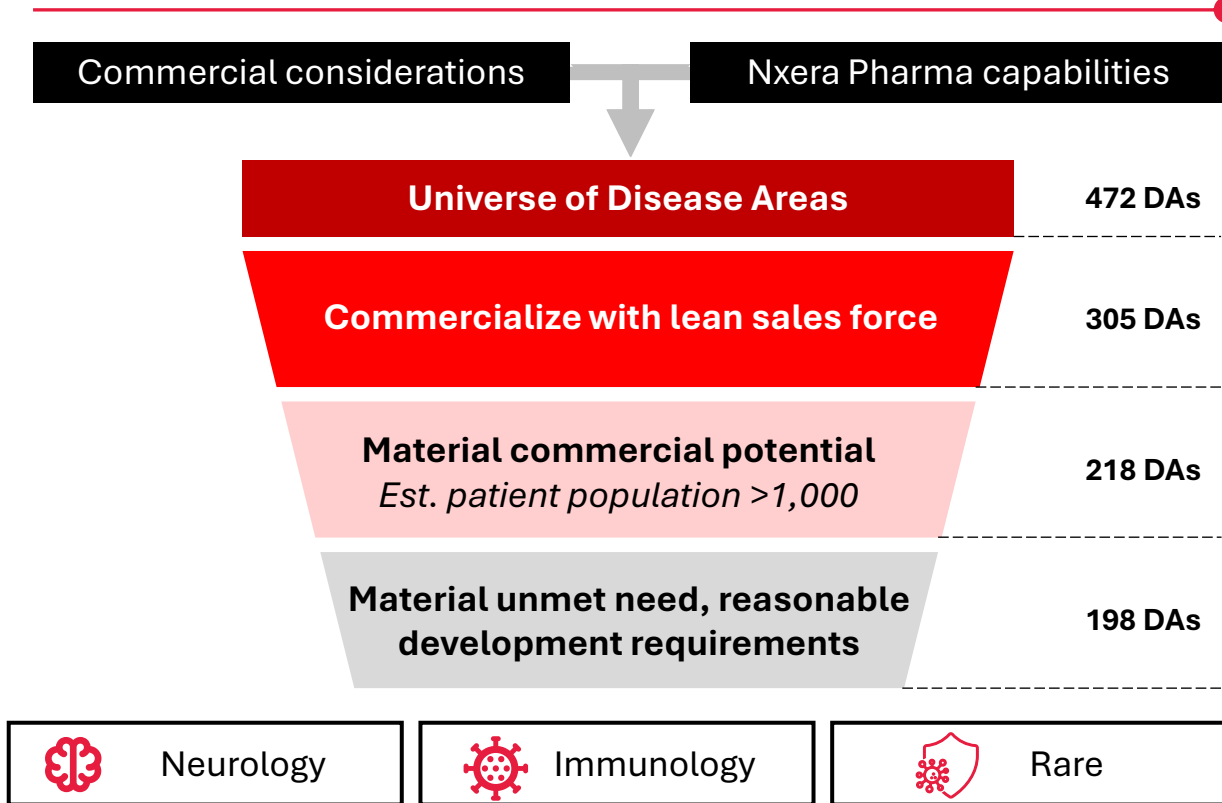
Excellent place to do business

- **Stable, growing market**
 - In an increasingly unstable world, Japan is an extremely stable place to do business
- **Second largest pharma globally (ex-China)**
 - \$85bn market size and growing
- **Supportive government and regulatory environment**
 - Universal healthcare system
 - Pricing incentives in place for innovation and paediatric development
 - Strengthened alignment with FDA, accelerated development pathways increasingly available

Focussed on addressing Neurology (age-related and QOL), Immunology and Rare Diseases in Japan

Nxera is the partner of choice to develop your medicines in Japan, Korea and APAC

Diseases that matter to us in Japan & APAC



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



7 opportunities currently at term sheet or contracting stage

Actively hunting for new product opportunities in 2025

Lead program, NBI'568 demonstrated positive phase 2 data in H2 2024

Once-daily 20 mg dose showed efficacy and good safety/tolerability profile for schizophrenia patients



<p>Clinically meaningful and statistically significant efficacy (Once-daily 20 mg dose)</p>	<ul style="list-style-type: none"> ➤ PANSS total score change -18.2 ➤ PANSS total score change vs. Placebo -7.5 (p = 0.011) ➤ Effect size 0.61 ➤ Marder Factor score change vs Placebo: <ul style="list-style-type: none"> • Positive -3.0 (p=0.004) • Negative -1.9 (p=0.028) 	<p>Met primary and additional endpoints and demonstrated efficacy on both positive and negative symptoms</p>
<p>Generally safe and well-tolerated across all doses tested</p>	<ul style="list-style-type: none"> ➤ Treatment discontinuation rate due to adverse events across all NBI'568 arms 5.0% (placebo: 4.3%) ➤ GI and CV adverse event frequency (Cobenfy (BMS/Karuna): 3-5x (GI), ~4x (CV) vs. placebo) Similar to placebo 	<p>NBI'568 showed safety and tolerability for all doses</p>
<p>Rapidly advancing to Phase 3 development</p>	<ul style="list-style-type: none"> ➤ Received successful milestone of Ph2 trial US\$ 35 m ➤ Ph3 clinical trial begin in H1 2025 ➤ Additional Ph2 trial in Bipolar Mania begin in H2 2025 ➤ Advancing follow-on compounds in muscarinic agonist portfolio 	<p>Expanding potential of muscarinic agonist portfolio</p>

Source: Presentation of Neurocrine Sciences (Aug.28 2024), KarXT for Schizophrenia draft evidence report (Nov. 28, 2023)

