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Nxera Pharma

Corporate Presentation

June 2025 | Nxera Pharma Co., Ltd. (TSE: 4565)

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Overview

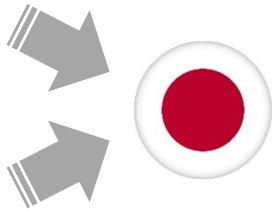
01

Nxera is a commercial stage, emerging biopharma from Japan

Founding

sosei

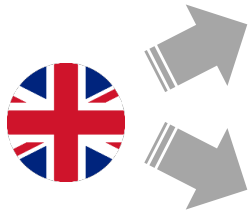
Founded with the purpose to bring the best biotech innovations to Japan…



2015

sosei HEPTARES

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



2024

Nxera

…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.

We are Nxera Pharma

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

OVERVIEW

$200m	Annual Revenues
$240m	Cash on Hand to Invest
400+	Employees in 5 locations
4565 (Ticker)	Tokyo Stock Exchange PRIME listed
6%+	Japan Govt. top long-term holder

PRODUCTS AND PROGRAMS

Sales

3	In Japan
1	In Global **(with Partner)**

Clinical (Global)

13	**With Partners**
3	In-House

Discovery

20+	In House and **With Partners**

PRODUCT FOCUS & SCIENCE

Market Size Of Product Focus

$120bn+	Neurology
$150bn+	Metabolic
$300bn+	Immunology/ GI

100+	GPCR Structures Solved with NxWave™ Platform
1,500	Patents Granted

Let's talk about our products and clinical pipeline

Nxera's Commercialized Products

1 Neurological disorders – diseases of ageing

PIVLAZ®

エンドセリン受容体拮抗薬 ピヴラッツ®点滴静注液 150mg 薬価基準収載

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

2 Neurological disorders – quality of life diseases

QUVIVIQ™

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

– 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

NEUROCRINE® BIOSCIENCES – ***Muscarinic agonists***

4 Neurological disorders – QOL diseases - sleep

CENTESSA PHARMACEUTICALS – ***Orexin 2 agonists***

5 Substance use disorders – QOL diseases - alcohol

TEMPERO BIO™ – ***mGlu5 NAM***

6 Metabolic diseases – QOL diseases - obesity

Pfizer – ***GLP-1 agonist***

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

Commercialized Products in Japan

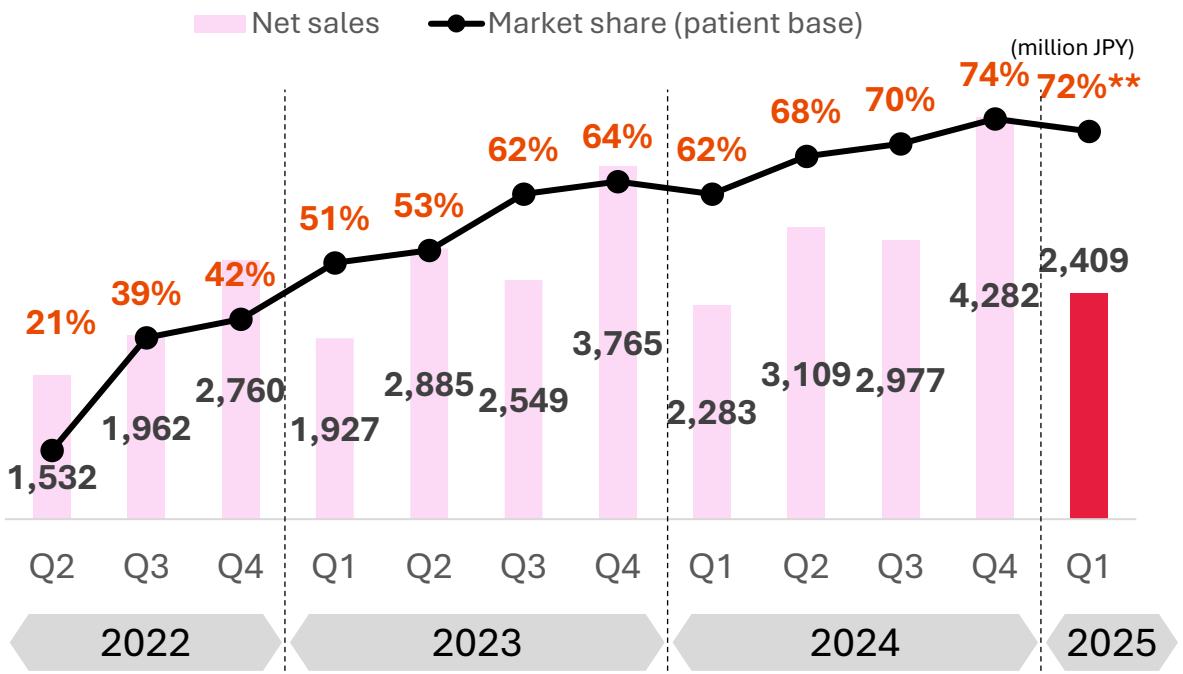
1 PIVLAZ® (clazosentan, an endothelin A antagonist)

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

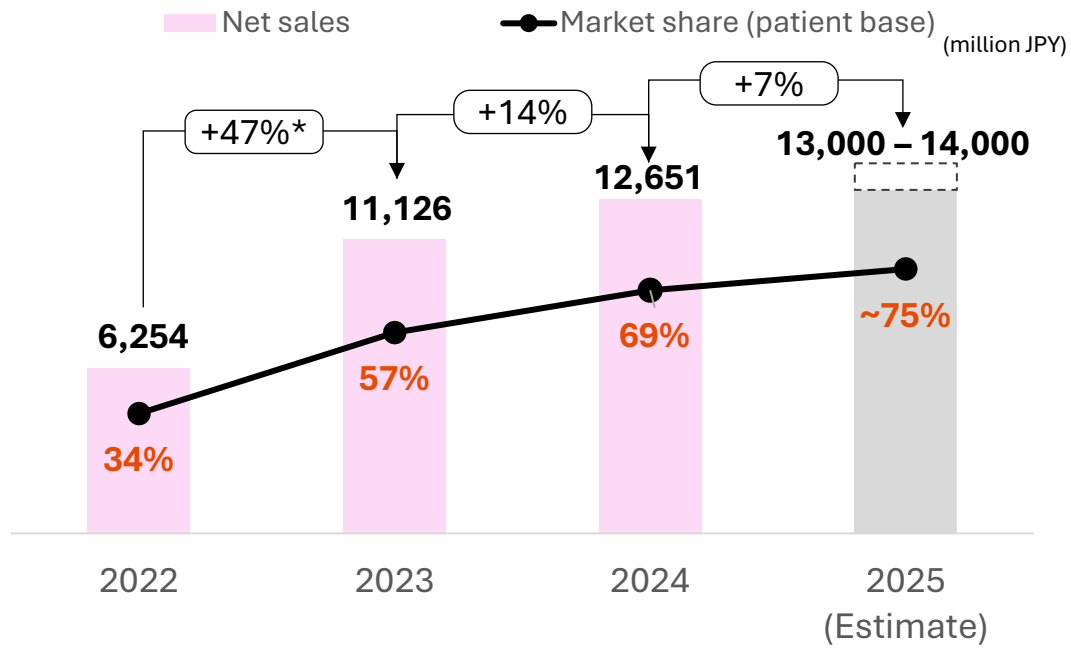
エンドセリン受容体拮抗薬 薬価基準収載
ピヴラッツ® 点滴静注液 150mg

Commercial

Quarterly PIVLAZ® Net Sales



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,

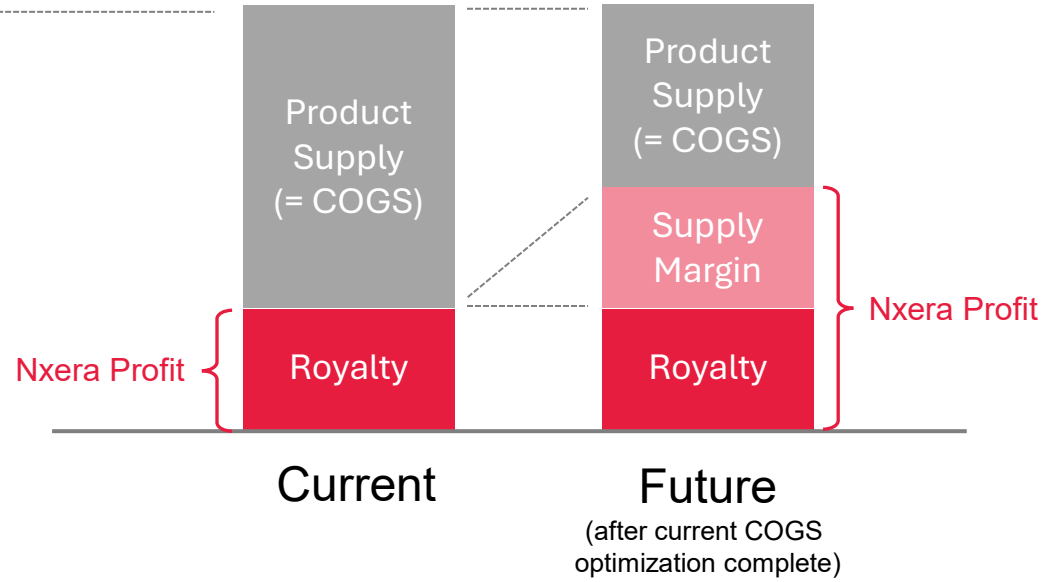
2 QUVIVIQ™ Business structure

Profit starts from royalties and supply margin will materialize within a few years

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
Commercial

Sales structure

Profit structure for Nxera



Nxera

Full year product sales guidance

Target 13.0 - 14.0 Bn JPY (PIVLAZ) as net sales, and 4.0 - 5.0 Bn JPY (QUVIVIQ) as royalty and supply

Commercial

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

Target sales in FY2025

13.0 – 14.0 Bn JPY

(NHI Sales:15.7 – 16.9Bn JPY)

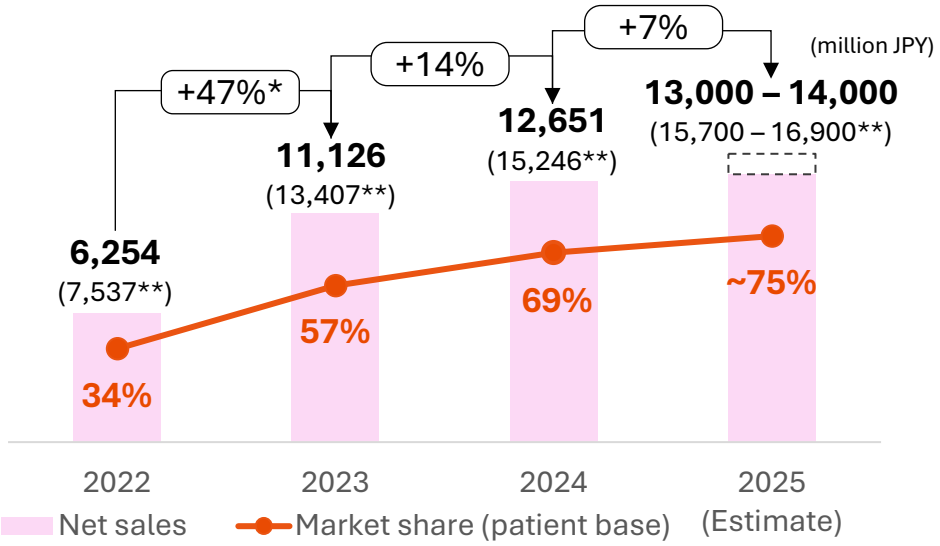
+7%

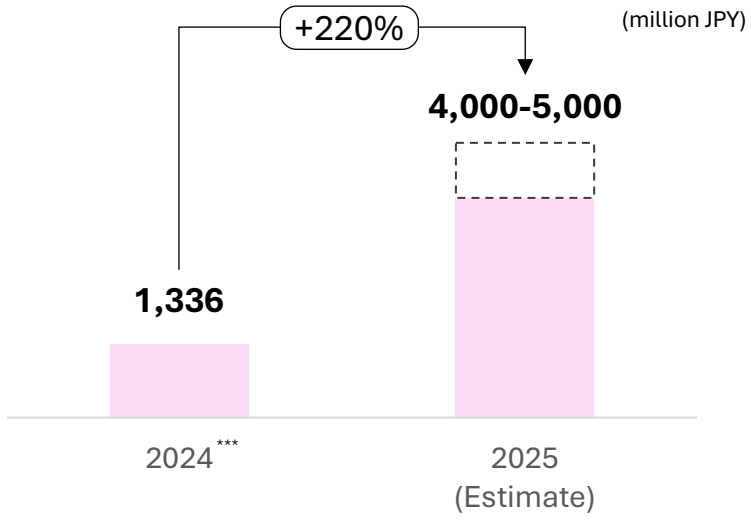
4.0 – 5.0 Bn JPY

(Shionogi:FY26/3E = 9.3 Bn JPY)

+220%

Sales trend





Source: MDV DPC hospital data

*: Comparison of 2-4Q of 2022 and 2023, ** NHI sales, *** 2024 sales includes upfront, milestone, royalty and product supply while 2025 sales includes royalty and product supply

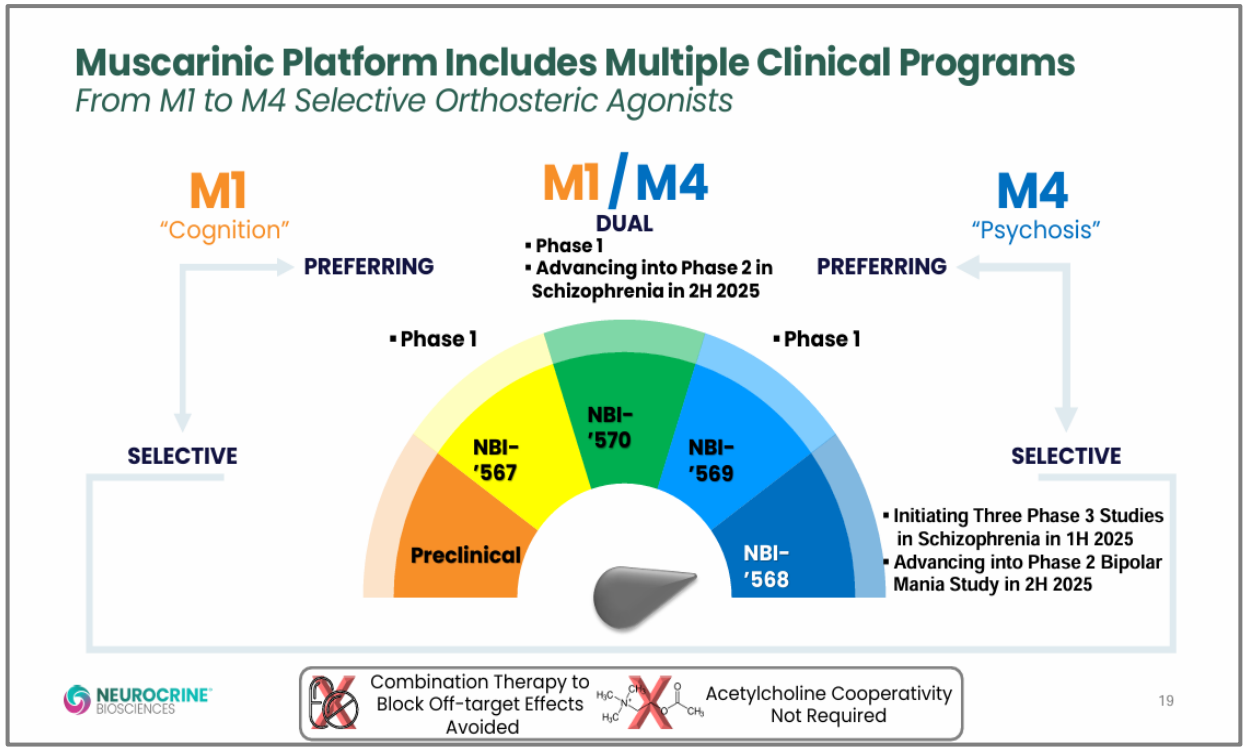
Partnered Products

03

3 Neurocrine is advancing the world's most comprehensive portfolio of muscarinic orthosteric agonists

– Phase 3 of NBI'568 initiated in May 2025

– discovered by Nxera using NxWave™



Program	Mechanism	Phase	Next Step Disease	Potential Areas
NBI'568	M4 agonist	3	Schizophrenia	Alzheimer's Disease Bipolar Disorder Lewy Body Dementia Parkinson's Disease Schizophrenia
NBI'567	M1 agonist	1	-	
NBI'569	M4 agonist	1	-	
NBI'570	M1/M4 agonist	1	Schizophrenia	

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

Source: Neurocrine investor presentation

3 Topline Results for Phase 2 Trial of M4 Agonist

20mg dose demonstrated statistically significant efficacy at Week 3, 4, 5 and 6 vs. placebo

NEUROCRINE BIOSCIENCES

Platform

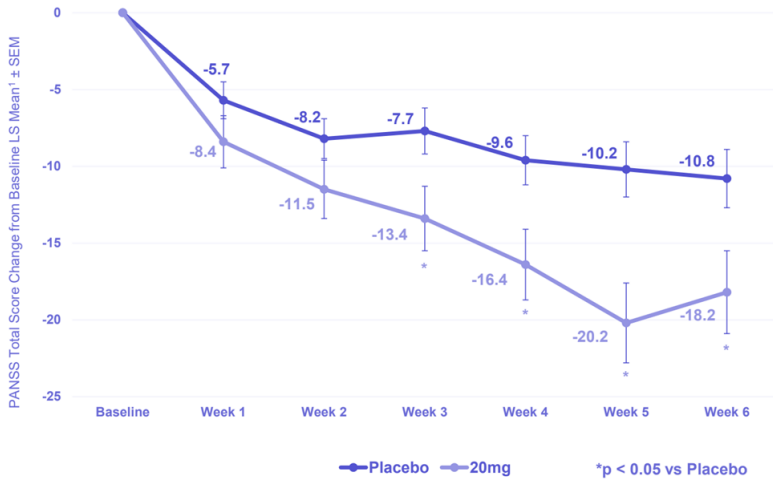
Once-Daily 20mg Dose Met Primary Endpoint

PANSS Total Score vs Placebo

Week 6	Placebo N=68	20mg QD N=35	40mg QD N=38	60mg QD N=34	30mg BID N=26
PANSS Total Score					
LS Mean Change from Baseline*	-10.8	-18.2	-12.6	-13.7	-15.8
LS Mean Difference vs. Placebo, p-value*		-7.5 p = 0.011	-1.9 p = 0.282	-2.9 p = 0.189	-5.0 p = 0.090
Effect Size**		0.61	0.27	0.39	0.23

*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.
**Effect size (Cohen's D) is based on observed data.

Once-Daily 20mg Dose Demonstrated Clinically Meaningful and Statistically Significant Efficacy at Week 3, 4, 5, and 6



20mg QD Efficacy Data
Week 4 – Week 6

Week	4	5	6**
PANSS Total Score			
LS Mean¹	-16.4	-20.2	-18.2
LS Mean Difference vs. Placebo¹	-6.8 p = 0.008	-10.0 p < 0.001	-7.5 p = 0.011
Effect Size²	0.53	0.72	0.61

** Primary Endpoint = Week 6

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.

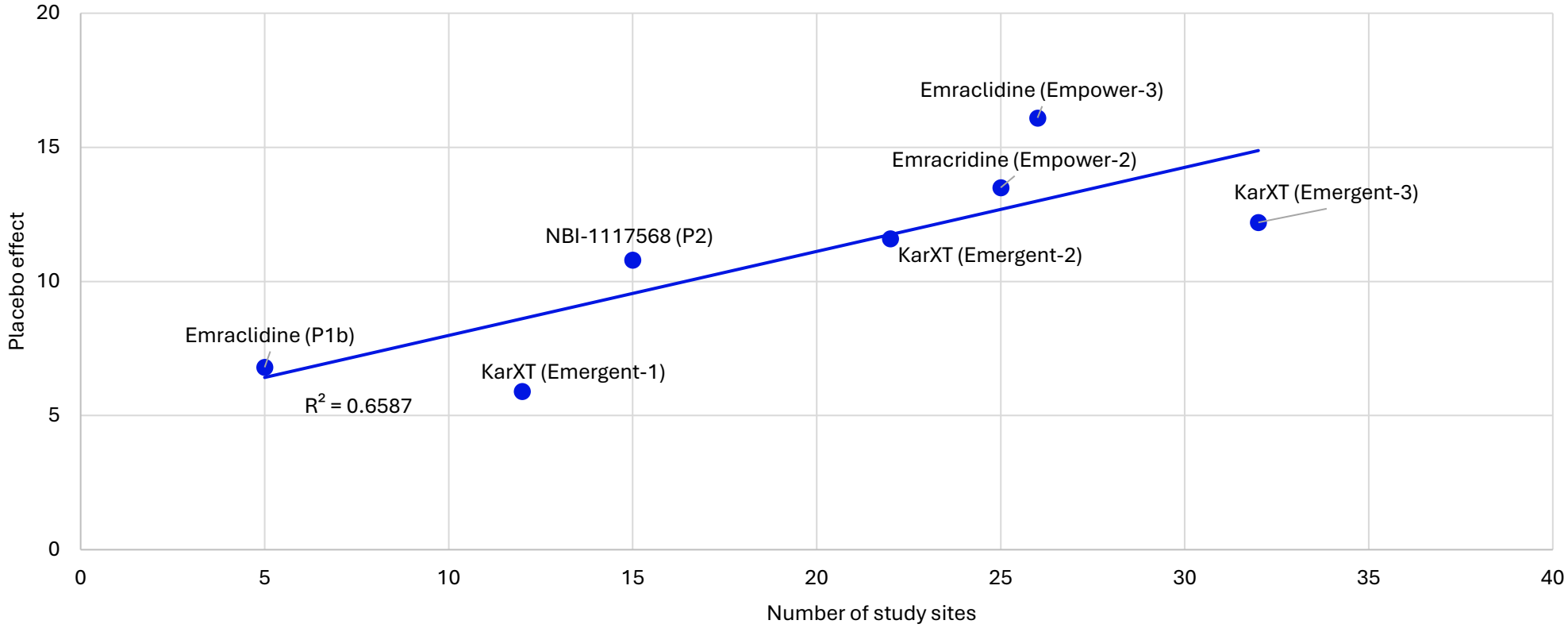
"The effects with the 20-milligram dose, you see statistical significance between Week 3, 4, 5, and six, meaning that you are seeing a reproducible response here."

Source: Neurocrine presentation – Topline Results for Phase 2 Trial of NBI-1117568 (NBI-'568) in Schizophrenia, August 28, 2024

NXera

3 Data comparison of placebo effects (Total PANSS)

Large number of study sites in a clinical trial of muscarinic program may be linked to a higher placebo response.



"Number of facilities is another important factor in managing the placebo effect"

Source: Neurocrine presentation – Topline Results for Phase 2 Trial of NBI-1117568 (NBI-'568) in Schizophrenia, August 28, 2024

3 Safety: Adverse Events Risk

The gastrointestinal and cardiovascular adverse events were higher than placebo in KarXT, but not on NBI-568

NEUROCRINE BIOSCIENCES

Platform

NBI-568

	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)

Cobenfy

Table 3.6. Pooled Treatment-Related Adverse Events in EMERGENT trials[20]

Adverse Event, %	KarXT (n= 340)	Placebo (n= 343)
★ Nausea	17.1%	3.2%
★ Constipation	15.0%	5.2%
★ Dyspepsia	12.1%	2.3%
★ Vomiting	10.9%	0.9%
★ Hypertension	5.9%	1.2%
Dry Mouth	5.0%	1.5%
Tachycardia	4.7%	2.0%

	Gastrointestinal (M2)	Cardiovascular (M3)	Others
NBI-568	★ Similar to placebo	Similar to placebo	Somnolence Dizziness
Cobenfy	★ x3-5 vs. placebo (Four items with 10% or more)	★ x4 vs. placebo (Occurred in 5.9%)	Dry mouth

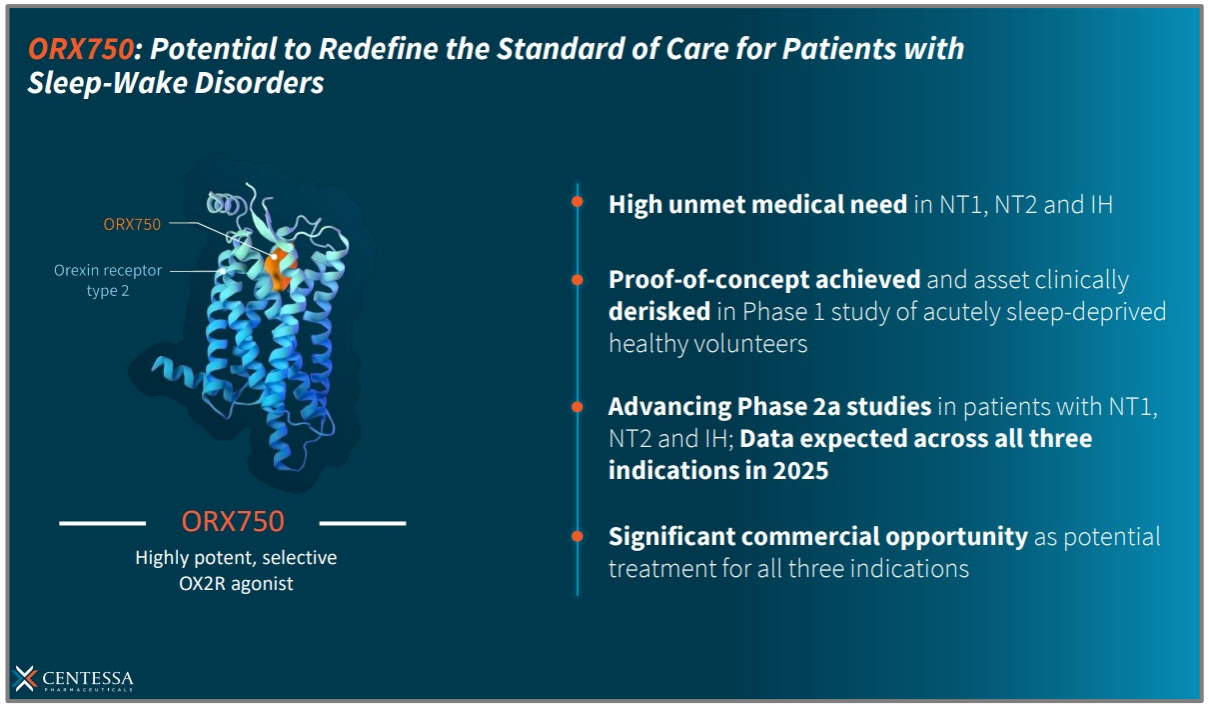
Source: Neurocrine presentation – Topline Results for Phase 2 Trial of NBI-1117568 (NBI-'568) in Schizophrenia, August 28, 2024, KarXT for Schizophrenia draft evidence report Nov. 28, 2023 (https://icer.org/wp-content/uploads/2023/07/ICER_Schizophrenia_Draft_Report_For-Publication_112823.pdf)

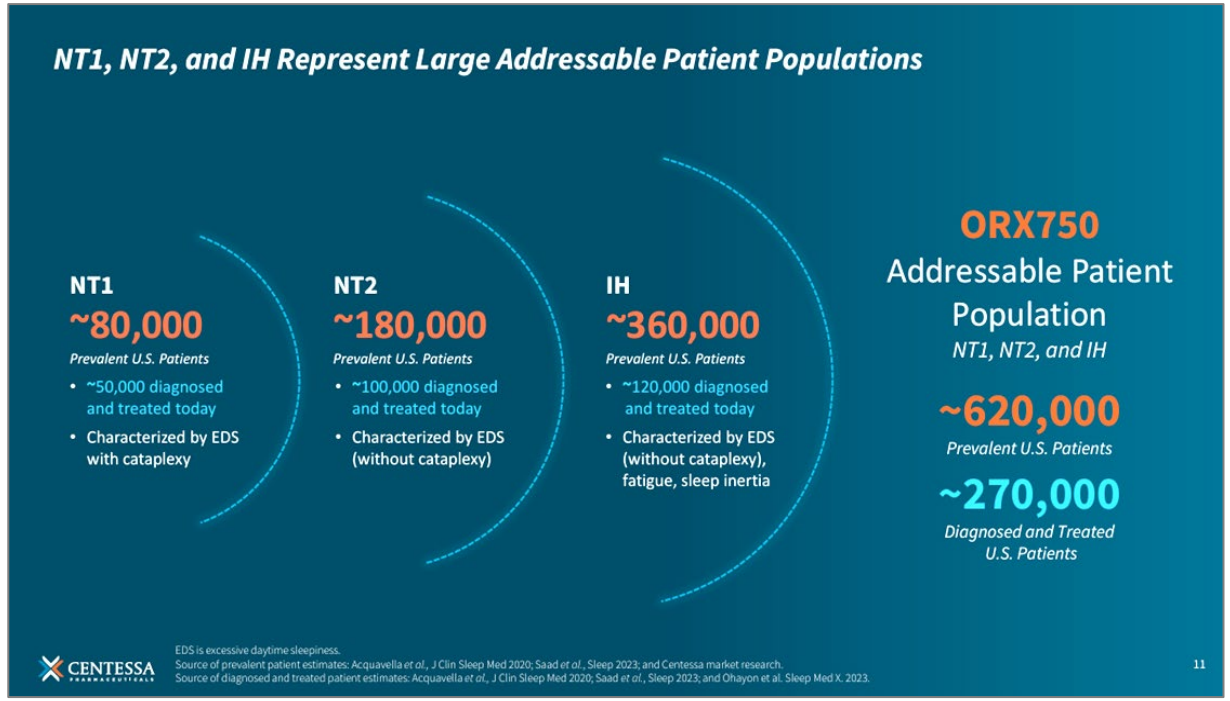
NXera

4 Centessa advancing Orexin 2 agonists

- ORX750 in Phase 2 as an improved treatment for Narcolepsy Type 1 and beyond
- ORX142, ORX489 as next generation for Neurological disorders
  – discovered using NxWave™

Platform





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

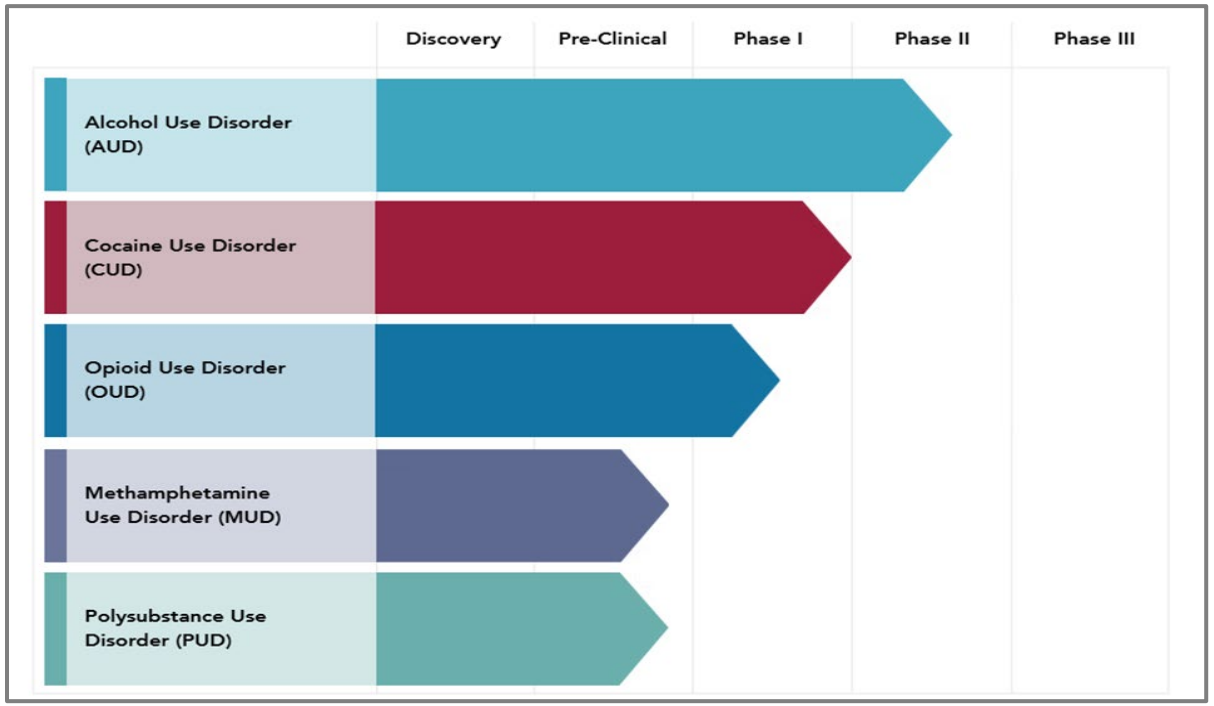
Source: Centessa, Pfizer investor presentations

5 TemperoBio advancing next-generation mGluR5 negative allosteric modulator - TMP301 in Phase 2 as an improved treatment for Alcohol Use Disorder and beyond – discovered using NxWave™

TEMPERO BIO™

Platform

Economic Condition:
Royalties: Mid to high single digits, Transaction: 2020



- Tempero Bio Secures $70 Million Series B Financing to Advance TMP-301 into Phase 2 Trials for Substance Use Disorders(March 24,2025)
- Phase 2 for alcohol use disorder and Phase 1 for cocaine use disorder will finish in 2H 2025.
- Tempero Bio plans to initiate Phase 2 trial for cocaine use disorder within the next year

Two clinical results on patient subjects may be reported later in the year or later

Source: Centessa, Pfizer investor presentations

NXera

6 Pfizer advancing PFE'522, once-daily, small molecule GLP-1 agonist in Phase 1 for Chronic weight management – discovered by Pfizer using NxWave™

Platform

Economic Condition:
Milestones received: $34m, Total potential milestones: $1.89bn, Royalties: Mid to high single digits, Transaction: 2015

Internal Medicine (1 of 2)

Discovery Projects | Phase 1: 6 | Phase 2: 4 | Phase 3: 2 | Registration: 1 | Total: 13

Compound Name	Mechanism of Action	Indication	Phase of Development	Submission Type
PAXLOVID™	SARS-CoV-2 3CL protease inhibitor (oral COVID-19 treatment)	COVID-19 Infection (Pediatric)	Registration	Product Enhancement
ibuzatrelvir (PF-07817883)	SARS-CoV-2 3CL protease inhibitor (oral COVID-19 treatment)	COVID-19 Infection (FAST TRACK – U.S.)	Phase 3	New Molecular Entity
►NURTEC® (rimegepant)	calcitonin gene-related peptide (CGRP) receptor antagonist	Menstrually-Related Migraine	Phase 3	Product Enhancement
ervogastat (PF-06865571)	Diacylglycerol O-Acyltransferase 2 (DGAT2) inhibitor	Metabolic Dysfunction-Associated Steatohepatitis (MASH)	Phase 2	New Molecular Entity
ervogastat (PF-06865571) + clesacostat (PF-05221304)	Diacylglycerol O-Acyltransferase 2 (DGAT2) inhibitor; Acetyl CoA-Carboxylase (ACC) inhibitor	Metabolic Dysfunction-Associated Steatohepatitis (MASH) (FAST TRACK – U.S.)	Phase 2	New Molecular Entity
ponsegromab (PF-06946860)	Growth Differentiation Factor 15 (GDF15) monoclonal antibody	Cachexia in Cancer (Biologic)	Phase 2	New Molecular Entity
PF-07976016	GIPR antagonist	Chronic Weight Management	Phase 2	New Molecular Entity

►Indicates that the project is either new or has progressed in phase since the previous portfolio update of Pfizer.com
Regulatory Designations – See Definitions in Backup

Pfizer

Internal Medicine (2 of 2)

Compound Name	Mechanism of Action	Indication	Phase of Development	Submission Type
PF-07258669	Melanocortin-4 receptor (MC4R) antagonist	Malnutrition	Phase 1	New Molecular Entity
PF-07328948	Branched chain ketoacid dehydrogenase kinase (BDK) inhibitor	Heart Failure	Phase 1	New Molecular Entity
PF-07293893	AMPKγ3 activator	Heart Failure	Phase 1	New Molecular Entity
PF-07853578	PNPLA3 modulator	Metabolic Dysfunction-Associated Steatohepatitis (MASH)	Phase 1	New Molecular Entity
PF-06954522	Glucagon-like peptide 1 receptor (GLP-1R) agonist	Chronic Weight Management	Phase 1	New Molecular Entity
PF-07941944	undisclosed	Respiratory Syncytial Virus Infection	Phase 1	New Molecular Entity

►Indicates that the project is either new or has progressed in phase since the previous portfolio update of Pfizer.com
Regulatory Designations – See Definitions in Backup

Pfizer

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

Source: Centessa, Pfizer investor presentations

NXera

Emerging wholly-owned pipeline

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

Platform

	OPTION TO LICENSE WITH Boehringer Ingelheim / DISCOVERED BY Nxera	DISCOVERED BY Nxera	DISCOVERED BY Nxera
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

Source : World Health Organization

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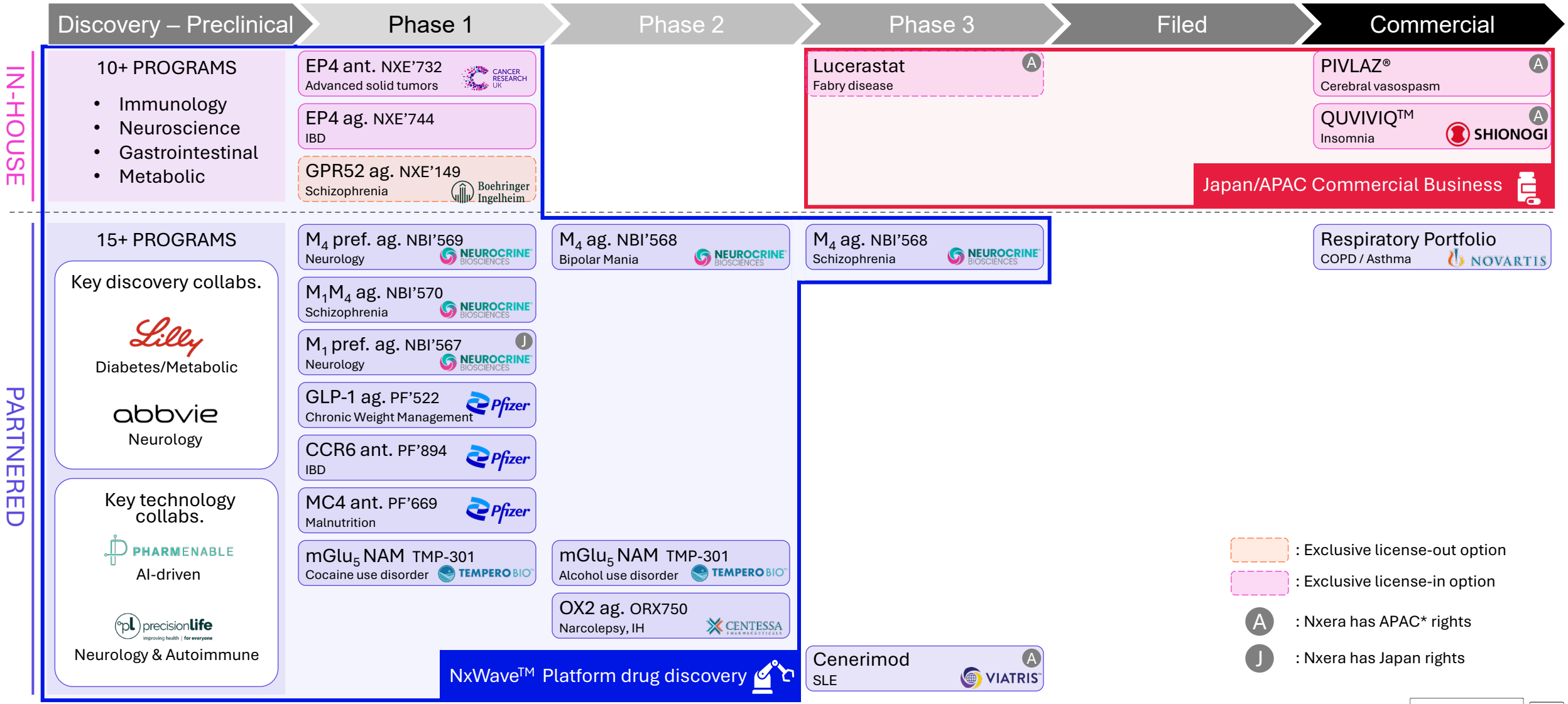
The Big Picture

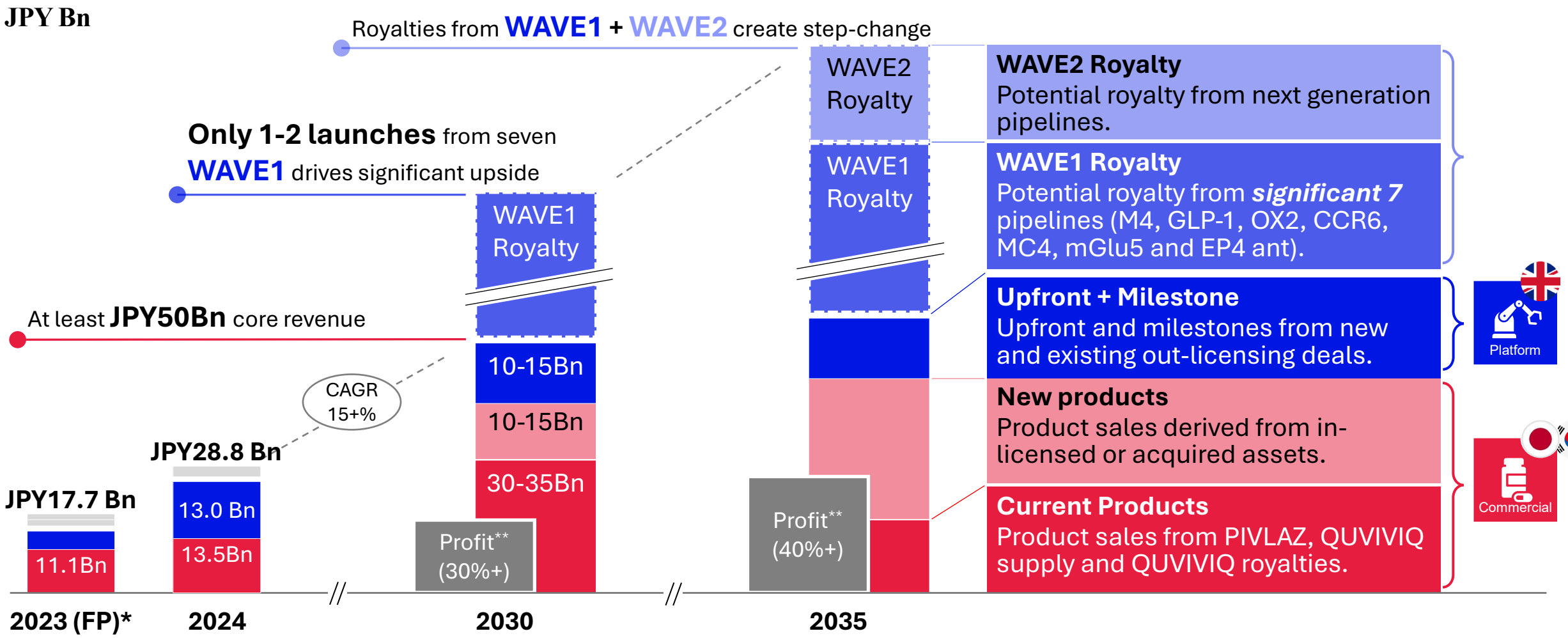
Major pipeline Overview (By business categories)



Note: Pref. ag. : Preferring agonist

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

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



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*

✓ : Progress in 2025

PROGRAM	PARTNER	TIMING	EVENT
✓ Cenerimod	idorsia VIATRIS	Feb. 2025	Assignment of JAPAC rights
✓ TMP-301 (mGlu5 NAM)	TEMPERO BIO	Mar. 2025	Phase 2 study start in alcohol use disorder
✓ NBI'568 (M4 agonist)	NEUROCRINE BIOSCIENCES	Apr. 2025	Phase 3 study start in Schizophrenia
Lucerastat	idorsia	H1 2025	Exclusive opt-in decision
NXE'732 (EP4 antagonist)	Nxera CANCER RESEARCH UK	H1 2025	Phase 2a study start in Advancing Solid Tumours
NBI'568 (M4 agonist)	NEUROCRINE BIOSCIENCES	H2 2025	Phase 2 study start in Bipolar Mania
NBI'570 (M1/M4 agonist)	NEUROCRINE BIOSCIENCES	H2 2025	Phase 2 study start in Schizophrenia
NXE'744 (EP4 agonist)	Nxera	H2 2025	Phase 2 study start in IBD
NXE'149 (GPR52 ag)	Nxera Boehringer Ingelheim	H2 2025	Phase 1b completion
NXE'732 (EP4 antagonist)	Nxera CANCER RESEARCH UK	H2 2025	Phase 1b topline data
ORX750 (OX2 agonist)	CENTESSA PHARMACEUTICALS	H2 2025	Phase 2 data readout (NT1/NT2/IH)
TMP-301 (mGlu5 NAM)	TEMPERO BIO	End 2025	Phase 2 result in alcohol use disorder
Multiple discovery collaboration progress	abbvie Lilly	2025	Progression through discovery stage
NBI'567 (M1 ago) / NBI'569 (M4 ago) / NBI'570 (M1/M4 ago)	NEUROCRINE BIOSCIENCES	2025	Phase 1 data readout
✓ QUVIVIQ™	Holling Bio-Pharma Corp.	Feb. 2025	Out licensing in Taiwan
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

* Partnered product progress is as already signaled or disclosed by partner

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
TECTONIC Therapeutic	2019	NASDAQ (2024)	$440M	SME, Biologics	3+	1
septerna	2019	NASDAQ (2024)	$440M	SME	3+	1
STRUCTURE THERAPEUTICS	2019	NASDAQ (2023)	$1,440M	SME	4	2
Nxera	**2007***	**TSE PRIME**	**$510M**	**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 20-May-2025
*Relates to the founding of Heptares Therapeutics Ltd (now known as Nxera Pharma UK Limited).
** Team members of Nxera Pharma UK Limited.

Questions?

Locations

Midtown East,
9-7-2 Akasaka
Minato-ku
Tokyo 107-0052

Japan

F17, 410 Teheran-Ro
GangHam-Gu
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South Korea

Steinmetz Building
Granta Park,
Cambridge
CB21 6DG

United Kingdom

Spaces Grosspeter Tower,
Grosspeteranlage 29,
4052 Basel

Switzerland

Thank you

Company Name: Nxera Pharma Co., Ltd. (JSS.F)
Event: Jefferies Global Healthcare Conference
Date: June 4, 2025

<<Analyst, Jefferies LLC>>

Jefferies analyst covering Japan biotech companies. In this session, we have Matt Barnes, Head of R&D of Nxera; and Hironoshin Nomura, CFO of Nxera.

So we're going to start with presentation. So Matt, I'll hand it over to you.

<<Matt Barnes, Chief Scientific Officer and President of Nxera Pharma UK>>

Yes, thank you so much and thank you to the organizers for giving us this slot.

So I'm going to – my name is Matt Barnes, so I am the CSO of Nxera Pharma. So, we're just going to give you a few slides, introduction to the company, for the Q&A.

So Nxera is a commercial stage, emerging biopharma company from Japan. It was founded as Sosei with the purpose of bringing best biotech innovations to Japan. And then a key acquisition for the company was in 2015 where Sosei acquired Heptares, a UK-based biotech company with a really interesting NxWave GPCR structure based drug design platform. And then following the acquisition of the Idorsia's business unit in Japan, we rebranded as Nxera Pharma in 2024. We're currently across five global locations and we have around 400 employees.

So, as a background overview, so we have about $200 million annual revenues. We have, as I said, about 400 employees across five locations. We're listed on the stock exchange in Japan. We have a number of products on the market. And we also have a very healthy clinical stage pipeline, so 13 clinical candidates with partners and three in-house. And behind that we have more than 20 discovery programs with again in-house and within partnerships.

We focus on a number of different therapeutic areas, so neurology, metabolic disease and immunology, GI. And we've generated – as part of our platform, we've generated more than 100 GPCR structures with that NxWave platform that I mentioned.

So, if we talk about the products and the clinical pipeline, so these are just the highlights really. So, I mentioned that we do have marketed products or commercialized products. The first one is called PIVLAZ and that's for the prevention of cerebral vasospasm in patients with ASAH.

Secondly, and recently launched in December last year was QUVIVIQ, which is for treatment of patients with insomnia and that's a co-marketing deal with our partner Shionogi.

In terms of our partner products, we have a number of muscarinic agonist programs in clinical development with our partner Neurocrine. The latest is within, has just initiated a Phase 3 study, NBI-'568, and I will talk a little bit more about that one. But there are a number of other muscarinic agonists behind that as well.

Also, we have a partnership with Centessa. So this is on orexin 2 agonist, which is in Phase 2. I will mention briefly this later as well. And also, we have a collaboration with Tempero Bio around an mGlu5 NAM compound for substance use disorder as well.

And of course, finally there with Pfizer, we have a collaboration on a number of molecules, actually three in clinical development, one of which is a GLP-1 small molecule agonist.

So, in terms of the commercialized products in Japan, Hiro?

<<Hironoshin Nomura, Chief Financial Officer>>

Yeah, thank you, Matt. Thank you everyone for your time. So I'm the CFO of the company, Hironoshin Nomura. I'd like to make a brief update about Japan part of commercial business.

So as you see on the screen, we have only two products in Japan. One is the PIVLAZ, this is the emergency used to prevent the vasospasm basically. And this was run four years ago, sorry, three years ago and now is the year four. And basically this product is the only product on this indication. So we are very, how can I say, satisfied and we are very happy about this penetration. It's going very well. So after three years launch this year, we are targeting around US$90 million to US$100 million as our top line and we are also happy this product as I said, there's no competition, so it's basically very high profitability product.

But the market is already penetrated by 75%. Of course, we are expecting to gain another 10% to 20% for next three years or something. But this is very good cash cow product for us now. So this is our first product.

So second product is insomnia drug. This is QUVIVIQ and different from fast-track. Of course, fast-track, we are selling this by ourselves by using the SIMD marketing salespeople. But QUVIVIQ is an insomnia drug and this is very, I can say, primary care area, and there's so many hospitals, clinic are taking – and there's a doctor who is taking this drug to prescribe this drug. So, basically, we licensed this QUVIVIQ out to Shionogi Pharma. This is one of the major pharmaceutical company in Japan.

So the profit structure is different from PIVLAZ. We are getting the royalty and now we only enjoying royalty. But in near future from 2027 basically, we will also enjoy the sales supply product margin.
So from 2027 and after, we will enjoy a supply margin compared with sharing top line sales. This is the second product.

So, combining these products, this is this year's target. So PIVLAZ is a ER4 product. So we are expecting 7% of share, of course, internally we have more aggressive target. And the QUVIVIQ, we are – this was just launched six months ago. So this year is mostly a past year for this product. So we are expecting ¥4 billion to ¥5 billion sales. It is around US$30 million.

And just one thing I add is Shionogi is of course, it is a public listed company. So they disclosed their fiscal year target, this is ¥9.3 billion for their fiscal year. This is actually

around 1.5 times to 2 times our expectation. So we are very happy with that number. Of course, it depends how – it depends on Shionogi how it is going, but we really appreciate their strong commitment on this product.

So now I direct back to Matt about the R&D part.

<<Matt Barnes, Chief Scientific Officer and President of Nxera Pharma UK>>

Yeah. Thank you, Hiro. So as well as those commercial products, as I mentioned previously, we have a host of clinical stage assets in partnership with a number of companies. One of the most notable is this collaboration with Neurocrine. And we just wanted to highlight the most advanced asset, which is NBI-'568. So this recently was initiated in a Phase 3 trial in schizophrenia. It's an M4 selective agonist discovered by Nxera using its NxWave platform. So, we're really, really excited about that program to see where that lands.

And then behind that, there's also three other further assets in clinical – early clinical development. So there's an M1 agonist, NBI-'567, a second M4 agonist, NBI-'569, and a dual M1/M4 agonist, NBI-'570 for schizophrenia. So there's lots of potential, I think, in this suite of muscarinic assets – dependent on the particular molecule profile that we have here.

So just some highlights from the output from the Phase 2 trial for NBI-'568. So, the once a day 20 mg dose met its primary endpoint there with a mean difference placebo-adjusted PANSS score of -7.5. And you can see on the right there the kinetic or the temporal profile of the study week by week. And you can see that there is a really strong, significant, placebo-adjusted reduction in the PANSS score for the 20 mg dose.

So moving on, one of the things you have to be extremely careful about when you're doing these clinical studies in patients in the neuropsychiatric area is the placebo response. And I think we've been extremely impressed with the way that Neurocrine have managed this process. And some of the competitors in this space such as KarXT, which is now called Cobenfy, which now aligns with BMS and Emraclidine, I think, this graph quite nicely shows that really the number of study sites that are utilized in some of these studies does really seem to correlate with the extent of the placebo effect. So, I think Neurocrine are very, very conscious and mindful about this as they move into the Phase 3 study. And so they'll be trying to mirror what they did in the Phase 2 in terms of the clinical trial design and the number of sites that they use.

And I also mentioned Cobenfy before. And so this is an approved treatment now. So the mechanism is to some degree validated, it caused a lot of excitement in the schizophrenia space because this was really the first approval for many decades with an alternative mechanism to atypical antipsychotics. And so that, I think, was great.

So mechanistically, these two assets are quite similar. What we would say, though, is with Cobenfy, so that's a non-selective muscarinic agonist. So it has to be co-dosed with a muscarinic antagonist, which is peripherally restricted. And actually, if you look at the adverse event profile that was observed in the emerging trials, you still are seeing some of those adverse events break through when you look at that compared to placebo. But what you'll see with NBI-568, which is a purely selective M4 muscarinic agonist, is that the side effect profile is really, really similar to placebo.

So I think we believe that this molecule has a really great safety profile and really encouraging efficacy profile as well. So, we're really excited as that moves into Phase 3.

I also mentioned about Centessa, so orexin-2 agonists are quite an emerging area. I think I'm capturing a lot of attention for the narcolepsy space. Very largely unmet medical need in this particular area, particularly around these three types, NT1, NT2, and IH. So proof-of-concept has been achieved. There are a few companies in this space. So Takeda, Centessa and Alkermes.

Centessa is the company that we have the collaboration with. The Centessa molecule, ORX750, was actually discovered using our NxWave platform a few years ago and we've been really pleased to see the progress that Centessa have made of moving that rapidly into clinical development and really actually catching up somewhat, I think, with the other companies and becoming – positioning themselves in a very competitive space. So it's in Phase 2 right now and so we're hoping to see some data start to read out from these Phase 2 studies towards the end of the year. I mean there really is a significant opportunity in this space and it's really capturing a lot of attention as we move forward. So, I think watch this space with this particular molecule.

And also, I just wanted to highlight another asset we have in partnership. So this is with Tempero Bio. Again, an asset, this is an mGlu5 negative allosteric modulator that again was discovered using our NxWave platform. And so Tempero Bio are moving this forward in substance use disorder. And they initially have started a Phase 2 trial in alcohol use disorder. But of course, there are other substance use disorders that could be captured with this particular asset as it moves forward, so including cocaine, opioid, et cetera. So earlier this year, Tempero secured $70 million Series B financing round to advance these clinical studies, and we're really hoping that to see some of that initial Phase 2 data from the alcohol use disorder study by the end of the year and really hoping to see some progress on initiating the cocaine use disorder trial as well.

And then briefly just to mention Pfizer as well. So, the GLP-1 small agonist space is a very competitive area with Lilly recently reporting some positive Phase 2 data in diabetes trial. Later we'll see some data, I think, later in the year with ultra GLP-1 in obesity as well. But this is really just to remind people that although Pfizer has discontinued some molecules, small molecules in this space, there is still a molecule 522, which is still in Pfizer's – portfolio, which is listed as chronic weight management. So, we're really optimistic, I think, to see what Pfizer does with this molecule going forward.

And I can't not talk about our own in-house programs, of course, as well. Not everything we do is in partnership, about 50% is and 50% is internal. And actually, in the last two or three years, we've progressed three of our own in-house programs into the clinic. And so they are NXE'149, which is currently in Phase 1b with a target indication of schizophrenia. That actually has an option to license with Boehringer Ingelheim. That's a novel, selective GPR52 agonist, which is first-in-class. We are the only company that has a clinical stage asset against this target. Really excited about that particular program.

Then we have NXE'732, which is an EP4 receptor antagonist in combination with a checkpoint inhibitor for advanced solid tumors. So we're working very closely with colleagues in Cancer Research UK, which is a nonprofit charity in the UK who are

actually sponsoring the study and are very well connected into the clinical trial network in the cancer space. We're hoping to advance this into Phase 2 later this year also.

And then finally, NXE'744, which is currently in Phase 1 for IBD. This is an EP4 agonist. So this is actually a GI targeted molecule, and it's actually based on some very early clinical validation data from Ono Pharmaceuticals from a small IBD study, which was done about 15 years ago. So there is a degree there of validation around this target, but the Ono molecule was systemically available and of course saw some hemodynamic effects. And so what we've done is we've built this molecule using our platform to really design to target the GI and avoid those hemodynamic effects. And so we're really excited about that program as it moves forward hopefully towards Phase 2 by the end of this year as well.

And I think really I'll maybe just stop there and leave on this pipeline for people's orientation as we move into the Q&A. Thank you.

<<Analyst, Jefferies LLC>>

Thank you very much, Matt and Hironoshin. Now we move into Q&A Session. If you have any questions, please raise your hand. If not, let me ask about questions on orexin agonist fast. So yeah, how do you estimate the probability of success of ORX750 Phase 2 trial? And also what will be the positioning of following pipelines such as – sorry one, yeah, ORX142 and ORX489 in the narcolepsy or sleep disorder treatment?

<<Matt Barnes, Chief Scientific Officer and President of Nxera Pharma UK>>

Yeah, thank you. Yes, thanks for the question. So, I think this is a really exciting area actually. So, there's a lot of genetics support around the orexin axis from a sleep disorder point of view, right? Of course, a lot of people already be aware of the orexin antagonists for insomnia and actually Hiro earlier on mentioned one of our products that we have on the market, QUVIVIQ, which is an antagonist for insomnia. This is the kind of the reverse, right? So this is looking at agonists for preventing narcolepsy or excessive daytime sleepiness.

So, there are effectively three companies in this space. So, Takeda is the more advanced and has generated some early proof-of-concept data, which looks really encouraging. Not far behind is the Centessa molecule and the Alkermes molecule as well. This is going to be really interesting to see how these molecules stack up against each other when we start to get to patient studies. And I think one thing to point out with Centessa actually is they're really going after the broad sweep of these indications, right? So they're going after the NT1, NT2 and the IH. So, they're really trying to gain a lot of momentum in a very broad sense across these different indications.

What's going to be key, I think, about this is not only the molecule profiles in terms of the potency, but I think also the pharmacokinetic profile of these particular molecules is going to be important. You only really want to reduce excessive daytime sleepiness, you don't want to have that in the night time, of course, but it's going to be a really, really interesting area.

<<Analyst, Jefferies LLC>>

Got it. Thank you. Please go ahead.

Q&A

<Q>: [Question Inaudible]

<A – Matt Barnes>: Yeah, good. Yeah, great point. So actually we should have made that clear. So actually, the commercial products are Japan, APAC and some of these other clinical stage programs are actually in partnership often with U.S. companies. So generally, just the way to think about it is our business model is we have half our employees in the UK, they are doing everything up to Phase 2 and we have half of our employees in Japan that do late stage development and sales and marketing. So the business model is very much is in the UK we take things forward to Phase 2, we look to partner with say you know a pharma company, U.S. based company they'll move it forward from a global point of view but we'll retain the rights for Japan and APAC and funnel that into our business unit in Japan that's the business model.

<Q>: Okay thank you very much. Any other questions? Please go ahead.

<Q>: Do you mind just going through some of the milestones and royalty structures that you have of the major partner products?

<A – Matt Barnes>: Hiro, do you want to comment about that?

<A – Hironoshin Nomura>: Yeah. So you can see a lot of partners on this slide. So of course, it depends on partners in the final moment. But actually, for example, the Neurocrine contract, so we are getting – our contract is $1.5 billion as a development milestone and $1.1 billion as a commercial milestone. And the royalty start high single digit to mid-teen percent. So this is one of the basic, our contract style. So most of our royalties, for example, it's a range is mid-single digit to the mid-teen. So that is our basic.

<A – Matt Barnes>: So I think, actually, that's a good point just to add. So I think from a revenue point of view, so you'll have seen there, we're actually generating, we're starting to generate revenues from our commercial business in Japan. So I mentioned that figure around $200 million. So as we move forward to 2030, what we want to try to do is build that capability more through in licensing for Japan and APAC. And so we really wish to try to get five products on the market by 2030, which will start to generate significant revenues that will help us fund the rest of the business.

But right now, actually, this part of the business on the left-hand side, we're still generating revenues from upfront payments, from milestone payments, and hopefully in the future from royalty payments. So, we've actually got two independent royalty streams at the moment. It's just that the commercial side is much more reliable and consistent and the other side is less reliable. So, that's why we want to move towards that five products by 2030 on the market. Yeah.

<Q>: Okay, thank you very much. And this is another question. Are you thinking about different modality, like antibody other than small molecules?

<A – Matt Barnes>: Yeah. Yeah, that's a great question, thank you. So most of what you see on the slide here are small molecule based. So traditionally our platform, which is all

about using rational structure-based drug design for GPCRs, which are and still remain a really, really attractive drug and validated drug target class. So we've used that in earnest to generate small molecules. It's very much suited to small molecule drug discovery, of course.

But of course, we are flexible and we remain open to other modalities as well. We've done some peptide programs previously, we've done some antibody programs previously as well in collaboration with different companies using different antibody platforms. But late last year, I think, we announced a collaboration with a company called Antiverse, which actually is an AI-driven antibody platform. And why we're excited about that one is because they can utilize the structural biology information that we have on the GPCRs to help them design antibody libraries or nanobody libraries or VHH libraries.

And so in many ways, that is almost a structure-based drug design approach, but with antibodies. And I think that really, really appealed to us, that kind of more AI-driven approach. And so we've started that collaboration with them. It's going very well. And so we're excited to see what antibodies come out of that particular collaboration.

And one thing just to say as well is that because of the way our NxWave platform works, traditionally it's been very, very difficult to identify antibodies to GPCRs generally. But we think that we might be able to generate antibodies that have agonist function as well as antagonist function. And so we're really excited to see whether we can demonstrate that and maybe be a world's first at doing that.

<Q>: Sounds very interesting. Thank you very much. Could you talk a little bit more about your novel programs?

<A – Matt Barnes>: Yeah.

<Q>: So I believe there are some interesting pipelines such as GPR52 in schizophrenia or EP4 agonist for cancer. So which pipeline do you think?

<A – Matt Barnes>: Yeah, thanks, Steve [ph]. I mean, I love them all. And I think these are really in all interesting propositions. What you'll see there as well is that we're very mindful about the targets we select, right, when we start the process right at the front end. So what we're trying to do is we're trying to balance our risk profile. profile in terms of focusing on targets where there may be some clinical validation. So, maybe focusing on a more best-in-class approach and using our platform to help us to do to identify molecules that have a superior profile. And actually, the Neurocrine collaboration is a really great example of that, of course.

But we're also – we do work also on some novel targets, and GPR52 is a good example of that. So, what we're trying to do is to spread the risks, right? We're not all about novel targets and high risk, high reward. We're actually trying to manage and mitigate that sort of risk profile. And those three are a really good example of that sort of risk mitigation. GPR52 specifically, this is for schizophrenia. And I mentioned in my talk that we are the only company that has a Phase 1 asset in this space. We know other companies have had interest in this pre-clinically but we're the only people that have managed to progress to the clinic.

The reason that this is really exciting program apart from its novelty is that based on the mechanistic hypothesis we think that GPR52 agonists might have efficacy across positive, negative and cognitive domains and in particular negative and cognitive are very – there is very high unmet need there.

And it's just really around the unique mechanism of the way that GPR52 works. We've generated a really strong preclinical data package. The compound, as far as we can tell in the early clinical studies, is behaving extremely well. We've got a really nice pharmacokinetic profile consistent with a once-a-day profile. And we're now moving into a really interesting phase for the program which is a proof of mechanism clinical study. If that's successful we're hoping that that might then be enough for Boehringer Ingelheim to exercise their option to license and you'll start to see that story kind of emerging towards the end of this year moving into next year. But I think it's a really, really exciting area. Boehringer Ingelheim would then take the responsibility to move into Phase 2 in schizophrenia. And then we'd also have those downstream milestones and royalties that Hiro mentioned before.

<Q>: Thank you very much. We have one minute. So any last questions? Please go ahead.

<Q>: What gives you hope that Pfizer will move forward with GLP-1?

<A – Matt Barnes>: Thanks for the question. It's still such an attractive area, right? So GLP1s, so getting a small molecule position, I think, or for orforglipron, I think, Lilly have done an amazing job to get to Phase 3. I think Pfizer clearly have had their problems there with the molecules they move forward with. If anyone is going to make progress, it'll be Pfizer though. Right?

So, according to clinicaltrials.gov, so what's publicly known, so the Phase 1 MAD study in patients with diabetes with an option for obesity should have read out by now. And so, we're actually as eager as everybody else to find out what the data of that is, but we'll have to wait for Pfizer to release that data. Thank you.

<<Analyst, Jefferies LLC>>

Okay, thank you very much. We are running out of time. So this concludes this session. Thank you very much for joining.

<<Matt Barnes, Chief Scientific Officer and President of Nxera Pharma UK>>

Okay, thank you.

<<Hironoshin Nomura, Chief Financial Officer>>

Thank you.