NIPPON SHINYAKU CO., LTD.

Nippon Shinyaku Co., Ltd.

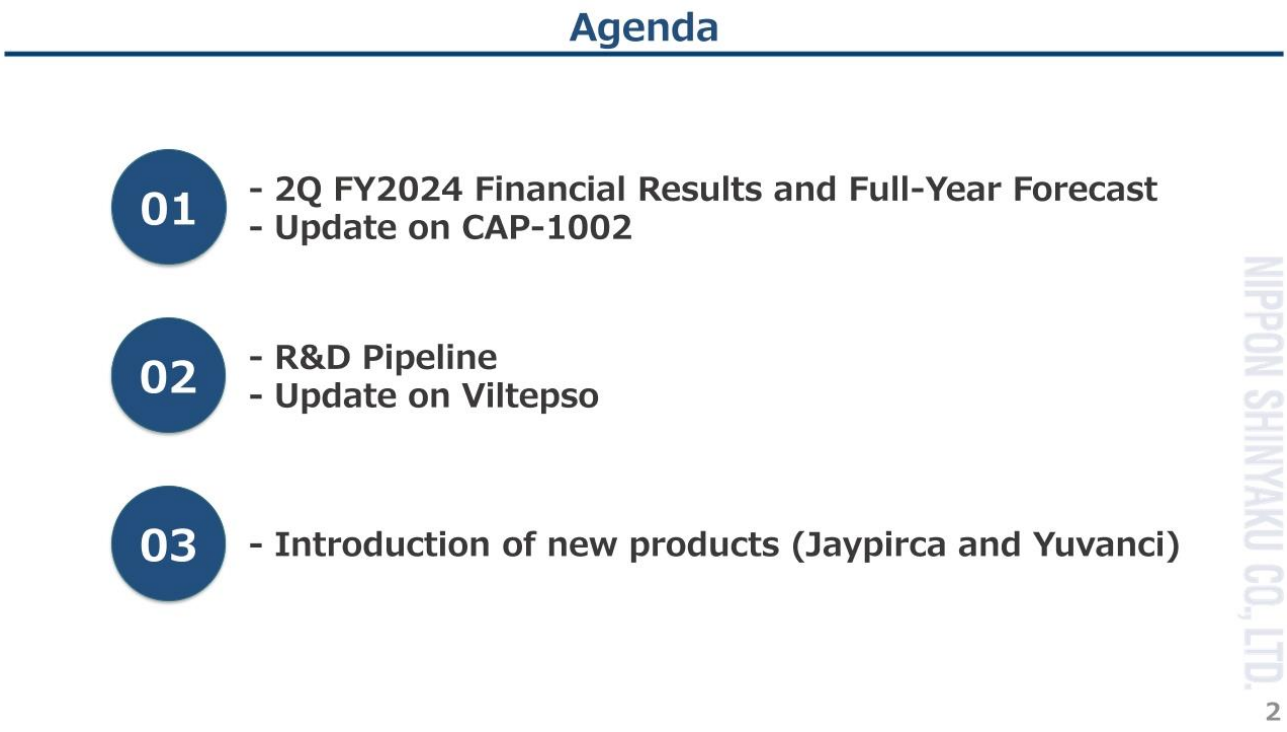
Financial Results Briefing for the 2nd Quarter Ended September 30, 2024

November 15, 2024

Presentation

Nakai: I am Toru Nakai, President of Nippon Shinyaku.

We appreciate you taking the time out of your busy schedule to participate in our financial results briefing for Q2 of FY2024. Thank you very much.



Today, I will be presenting our financial results for Q2 of FY2024 and our outlook for FY2024, as well as an update on CAP-1002.

Mr. Takagaki, in charge of R&D, will explain the progress of R&D items and an update on Viltepso, and finally, Mr. Sano, in charge of sales and marketing, will introduce our new products.

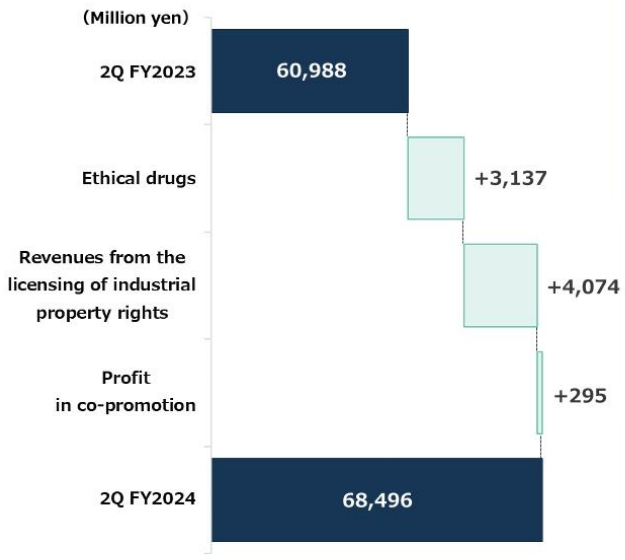
I will now explain our performance for Q2 of FY2024 and our outlook for FY2024.

2Q (Interim Period) FY2024 Summary

(Million yen)	2Q FY2023 Results	2Q FY2023 Ratio	2Q FY2024 Results	2Q FY2024 Ratio	YoY Change Amt	YoY Change %
Revenue	**73,314**	**100.0%**	**79,332**	**100.0%**	**+6,017**	**+8.2%**
(Pharmaceuticals)	(60,988)	(83.2%)	(68,496)	(86.3%)	(+7,507)	(+12.3%)
(Functional Food)	(12,325)	(16.8%)	(10,836)	(13.7%)	(-1,489)	(-12.1%)
Cost of sales	**25,320**	**34.5%**	**24,935**	**31.4%**	**-384**	**-1.5%**
SG&A expenses	**16,952**	**23.1%**	**18,031**	**22.7%**	**+1,079**	**+6.4%**
R&D expenses	**12,517**	**17.1%**	**16,732**	**21.1%**	**+4,215**	**+33.7%**
Other income	**2,596**	**3.5%**	**455**	**0.6%**	**-2,140**	**-82.5%**
(Foreign exchange gain)	(2,261)	(3.1%)	-	-	(-2,261)	(-100.0%)
Other expenses	**242**	**0.3%**	**2,219**	**2.9%**	**+1,976**	**+815.0%**
(Foreign exchange loss)	-	-	(1,935)	(2.4%)	(+1,935)	-
Operating profit	**20,878**	**28.5%**	**17,867**	**22.5%**	**-3,010**	**-14.4%**
Finance income	**326**	**0.4%**	**396**	**0.5%**	**+70**	**+21.6%**
Finance costs	**57**	**0.1%**	**65**	**0.1%**	**+7**	**+13.7%**
Profit before tax	**21,146**	**28.8%**	**18,198**	**22.9%**	**-2,947**	**-13.9%**
Income tax expense, etc	**4,970**	**6.8%**	**1,825**	**2.3%**	**-3,144**	**-63.3%**
Profit attributable to owners of parent	**16,176**	**22.1%**	**16,373**	**20.6%**	**+196**	**+1.2%**

As an overview of the business results for Q2 of FY2024, consolidated sales revenue was JPY79,332 million, operating profit was JPY17,867 million, profit before tax was JPY18,198 million, and profit attributable to owners of parent was JPY16,373 million.

Segmental Review - Pharmaceuticals -



Ethical drugs 41,140 million yen
(+3,137 million yen, +8.3%, YoY)
- ✓ Negative impacts of the NHI drug price revisions and generic drugs
- ✓ Sales growth of Uptravi and Viltepso, etc.
- ✓ New products including Vyxeos, which was launched in Japan in May

Revenues from the industrial property rights 22,655 million yen
(+4,074 million yen, +21.9%, YoY)
- ✓ Royalty revenue growth due to overseas sales of Uptravi

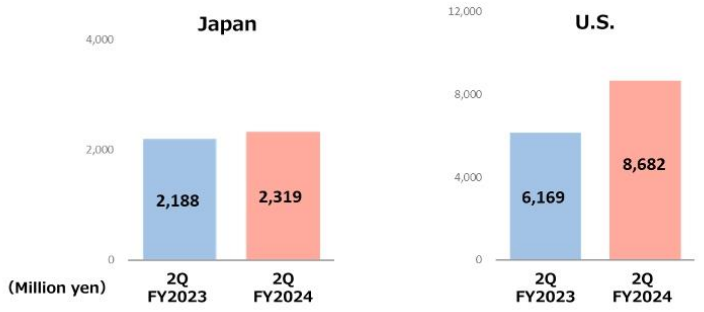
Profit in co-promotion 4,700 million yen
(+295 million yen, +6.7%, YoY)
- ✓ Sales growth of Opsumit and Erleada

In the pharmaceuticals business, consolidated net sales increased by 12.3% YoY to JPY68,496 million. This growth was driven by sales of Uptravi, royalty revenue from its overseas sales, sales of Viltepso, and the May launch of Vyxeos, despite the impact of NHI drug price revisions and generics.

Sales Trends of Viltepso® (viltolarsen)

(Million yen)		2Q FY2023 Results	2Q FY2024 Results	YoY Change Amt	YoY Change %	
Viltepso	Japan	2,188	2,319	+131	+6.0%	✓The number of patients currently being administered is more than two-thirds of the peak number of 128 patients in the data from Chuikyo (Central Social Insurance Medical Council) . ✓Currently working to increase sales by identifying and intervening early with patients who are eligible for the 53-skip treatment at a younger age.
	U.S.	6,169	8,682	+2,512	+40.7%	✓The number of patients receiving and wishing to receive Viltepso is increasing ✓In October 2024, the data from the Phase II (Study 211) was published in the journal Scientific Reports. The improvements in respiratory function and maintenance of motor function in both ambulatory and non-ambulatory patients were observed.
	total	8,358	11,002	+2,643	+31.6%	

Exchange rate	2Q FY2023 Actual rate	2Q FY2024 Actual rate
1US$	¥141.1	¥152.8

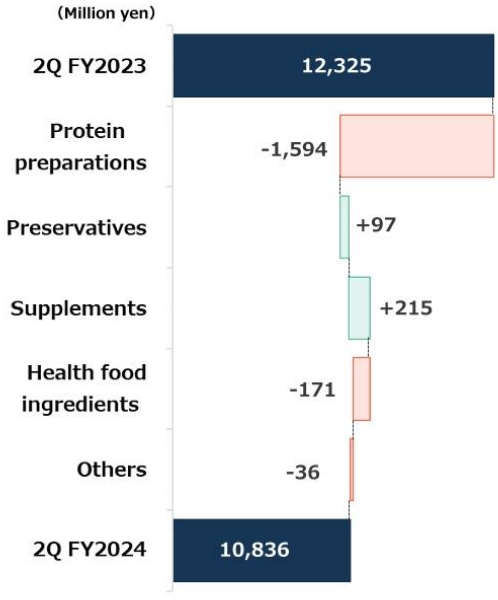


Here we show the sales of Viltepso in Japan and the US.

As for sales results for Q2 of FY2024, sales in both Japan and the US increased YoY, totaling JPY2,319 million in Japan and JPY8,682 million in the US.

In the US, sales in US dollar also increased YoY.

Segmental Review - Functional Food -



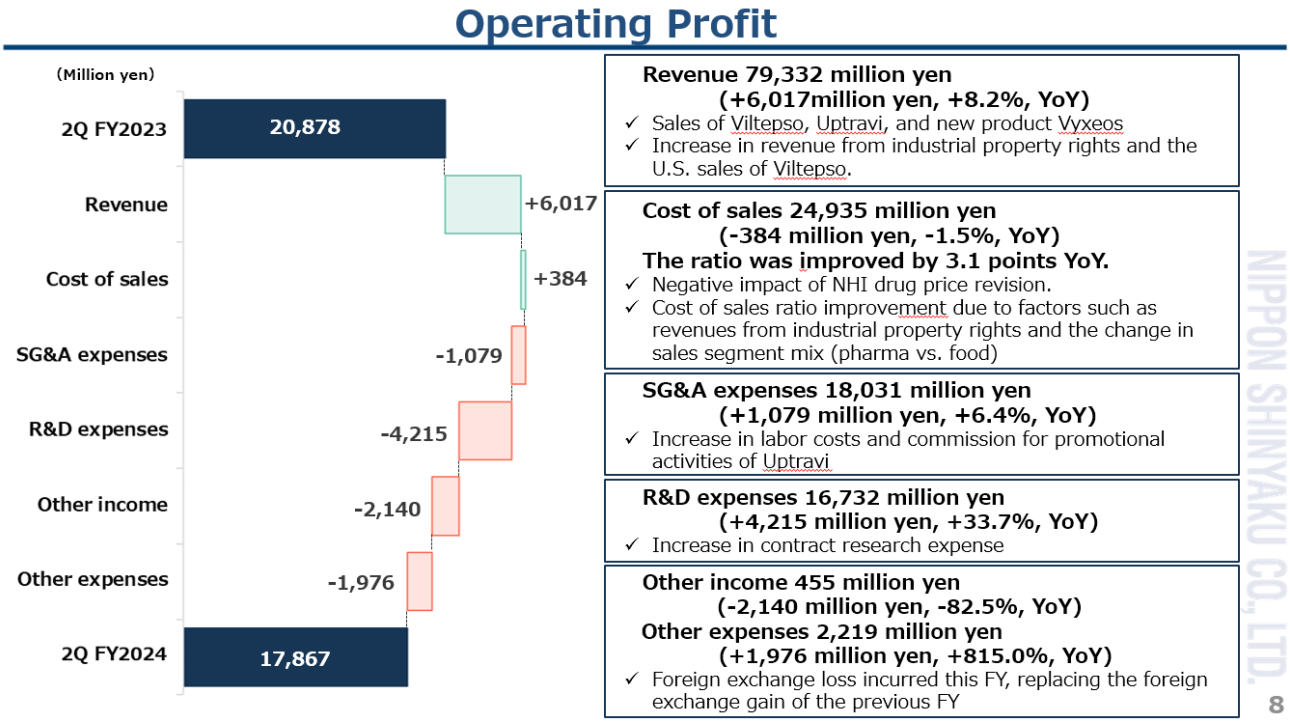
Protein preparations 6,893 million yen
(-1,594 million yen, -18.8%, YoY)
- ✓ Sales prices decline of protein preparations for the processed food industry
- ✓ Decrease in demand for milk protein due to customers switching to cheaper raw materials

Preservatives 1,620 million yen
(+97 million yen, +6.4%, YoY)
- ✓ Recovery in food service-related business due to active tourism and excursions

Supplements 1,202 million yen
(+215 million yen, +21.8%, YoY)
- ✓ Increase in demand from senior consumers in addition to the recovery in the number of sporting events held
- ✓ Growth in the anti-aging care category helped by sales measures

Health food ingredients 487 million yen
(-171 million yen, -26.1%, YoY)

In the functional food business, sales of supplements and other products increased, but sales of protein preparations and other products declined, resulting in consolidated net sales of JPY10,836 million, down 12.1% YoY.



Next, in terms of operating expenses, the cost of sales ratio improved by 3.1 percentage points YoY to 31.4%, due to factors such as industrial property rights and the segmental sales mix, despite the impact of the NHI drug price revision.

SG&A expenses increased 6.4% YoY to JPY18,031 million, mainly due to an increase in labor costs and an increase in sales promotion commission in line with increased sales of Uptravi.

R&D expenses totaled JPY16,732 million, up 33.7% YoY, mainly due to an increase in contract research expenses.

As a result, operating profit was JPY17,867 million, down 14.4% YoY.

Revised Business Forecast for FY2024 (consolidated)

(Million yen)	FY2023 2Q Results	Ratio	FY2024 2Q Results	Ratio	YoY Change Amt	%
Revenue	148,255	100.0%	157,000	100.0%	+8,745	+5.9%
(Pharmaceuticals)	(125,105)	(84.4%)	(135,500)	(86.3%)	(+10,395)	(+8.3%)
(Functional Food)	(23,150)	(15.6%)	(21,500)	(13.7%)	(-1,650)	(-7.1%)
Cost of sales	50,234	33.9%	50,500	32.2%	+266	+0.5%
SG&A expenses	34,959	23.6%	39,000	24.8%	+4,041	+11.6%
R&D expenses	31,676	21.4%	33,000	21.0%	+1,324	+4.2%
Other income	3,163	2.1%	900	0.6%	-2,263	-71.5%
Other expenses	1,252	0.8%	2,400	1.5%	+1,148	+91.6%
Operating profit	33,295	22.5%	33,000	21.0%	-295	-0.9%
Finance income	650	0.4%	700	0.4%	+50	+7.6%
Finance costs	329	0.2%	100	0.1%	-229	-69.7%
Profit before tax	33,616	22.7%	33,600	21.4%	-16	-0.0%
Income tax expense, etc	7,765	5.2%	3,600	2.3%	-4,165	-53.6%
Profit attributable to owners of parent	25,851	17.4%	30,000	19.1%	+4,149	+16.0%

The exchange rate assumed for the second half of FY2024 in the business forecast is 1 USD=140 yen. The sensitivity of the exchange rate is assumed to be an increase of approx. 200 million yen in revenue and approx. 300 million yen in operating profit for every 1 yen depreciation of the yen.

I would like to continue by explaining our outlook for FY2024.

Consolidated sales revenue is expected to be JPY157 billion.

As for operating expenses, the cost of sales ratio is expected to be 32.2%, an improvement of 1.7 percentage points YoY.

SG&A expenses are expected to be JPY39 billion and R&D expenses JPY33 billion.

As a result, we project operating profit of JPY33 billion, profit before tax of JPY33.6 billion, and profit attributable to owners of parent of JPY30 billion.

Business Forecast : Upward Full-Year Revision from August

(Million yen)	FY2024 Forecasts		Change	
	Previous*	Revised	Amt	%
Revenue	154,000	157,000	+3,000	+1.9%
(Pharmaceuticals)	(132,500)	(135,500)	(+3,000)	(+2.3%)
(Functional Food)	(21,500)	(21,500)	-	-
Cost of sales	51,000	50,500	-500	-1.0%
SG&A expenses	38,700	39,000	+300	+0.8%
R&D expenses	32,400	33,000	+600	+1.9%
Other income	500	900	+400	+80.0%
Other expenses	400	2,400	+2,000	+500.0%
Operating profit	32,000	33,000	+1,000	+3.1%
Finance income	600	700	+100	+16.7%
Finance costs	100	100	-	-
Profit before tax	32,500	33,600	+1,100	+3.4%
Income tax expense, etc	3,500	3,600	+100	+2.9%
Profit attributable to owners of parent	29,000	30,000	+1,000	+3.4%

* August 7th, 2024 (1Q FY2024 Financial Results)

Revenue 157,000 million yen (+3,000 million yen, +1.9% from previous forecast)
- ✓ Mainly due to the pharmaceutical business. Uptravi royalty income, Viltepso sales in the US, exchange rate fluctuations, etc.

R&D expenses 33,000 million yen (+600 million yen, +1.9% from previous forecast)
- ✓ Increase in research and development costs for in-licensed products

Other operating expenses 2,400 million yen (+2,000 million yen, +500.0% from previous forecast)
- ✓ Foreign exchange loss because of the 1USD=140JPY rate which is used for the second half of FY2024 in the business forecast.

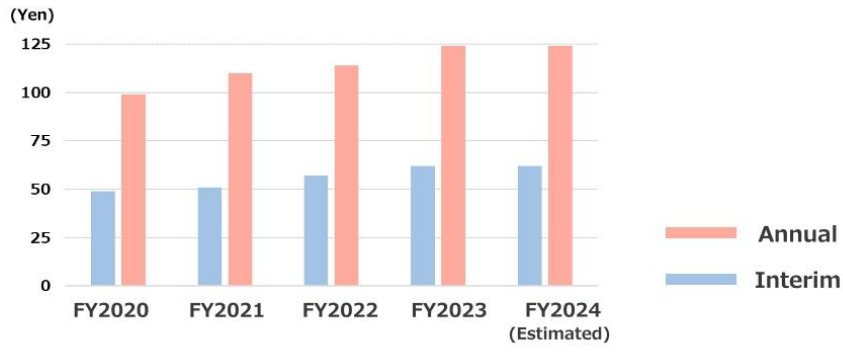
Here we show the difference between the previous and revised forecasts.

Sales revenue is expected to increase by JPY3 billion compared to the previous forecast due to strong royalty revenue from overseas sales of Uptravi and the impact of the weaker yen on sales in the US of Viltepso.

Operating profit is expected to increase by JPY1 billion. R&D expenses for in-licensed products are expected to increase by JPY0.6 billion from the previous forecast, and other expenses are expected to increase by JPY2 billion from the previous forecast due to foreign exchange losses resulting from the impact of foreign exchange rate fluctuations.

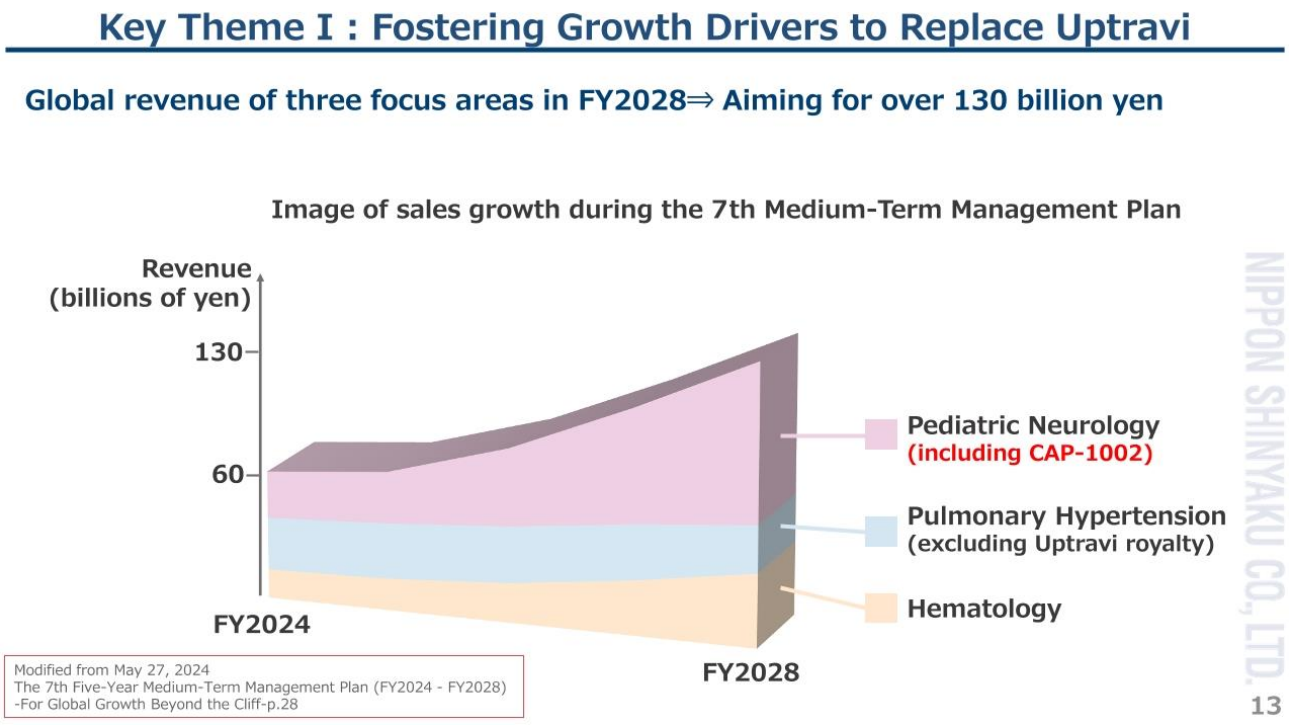
Dividends Forecast

		FY2023	FY2024
Dividends per share	Interim	¥62	¥62
	Annual	¥124	¥124
Basic earnings per share		¥383.82	¥445 (e)



The Company plans to pay an interim dividend of JPY62 per share and a year-end dividend of JPY62 per share, for an annual dividend of JPY124 per share for the current fiscal year.

I will now explain the status of CAP-1002, which is a treatment for Duchenne muscular dystrophy cardiomyopathy.



In the 7th Five-Year Medium-Term Management Plan (FY2024-2028), one of the key themes is fostering growth drivers to replace Uptravi, and we are working to achieve global sales revenue of JPY130 billion or more by FY2028 in our three focus therapeutic areas of pediatric neurology, pulmonary hypertension, and hematology. In the pediatric neurology area, which accounts for the largest proportion of our three focus areas, we are pleased to provide you with an update on CAP-1002, which we expect to grow the most.

CAP-1002 (deramiocel) : U.S. development timeline updates

According to Capricor's announcement dated September 24, 2024, the timeline for the CAP-1002 BLA submission has been brought forward. NS Pharma, a U.S. subsidiary of Nippon Shinyaku, is currently preparing for the future commercialization of deramiocel.

	Before September 24, 2024	After September 24, 2024
Target date of BLA submission	2025	Rolling BLA submission initiated*
Target PDUFA (FDA approval) date	2026	Potentially 2H of 2025
Possible approval type	Full approval with the HOPE-3 (Cohort A) study data	Seeking full approval with existing cardiac data from the Phase 2 HOPE-2 and HOPE-2 Open Label Extension (OLE) trials compared to natural history data
Target indication of the drug	Duchenne muscular dystrophy (DMD)	Cardiomyopathy Associated with Duchenne Muscular Dystrophy
Key event	to report topline data from HOPE-3 (Cohort A) in the fourth quarter of 2024	to complete its rolling BLA submission by the end of 2024

* announced on October 9, 2024

Source: https://www.capricor.com/investors

Capricor has been conducting the HOPE-3 study for the indication of "Duchenne muscular dystrophy" and had informed us that it planned to disclose the top-line data of Cohort A by the end of this year, followed by an application. However, after discussions with the FDA, Capricor has decided to file a rolling BLA application for the indication of "Duchenne muscular dystrophy cardiomyopathy" with the results of the HOPE-2 trial, for which data are already available.

Complementing nucleic acid drugs by introducing a new DMD treatment option

Partnership with Capricor Therapeutics

Rights	Territory	Agreement signed in	Developed by	Development timeline	Distributed by
Exclusive Partnership for Commercialization and Distribution of CAP-1002 for the Treatment of Duchenne Muscular Dystrophy (DMD)	U.S.	January 2022	Capricor	See below	Nippon Shinyaku group
	Japan	February 2023		(TBD)	
	Europe	- LOI[1] and BTS[2] signed in Sep 2024 - Definitive Agreement now in discussion			(TBD)

1: Letter of Intent (LOI)
2: Binding Term Sheet (BTS)

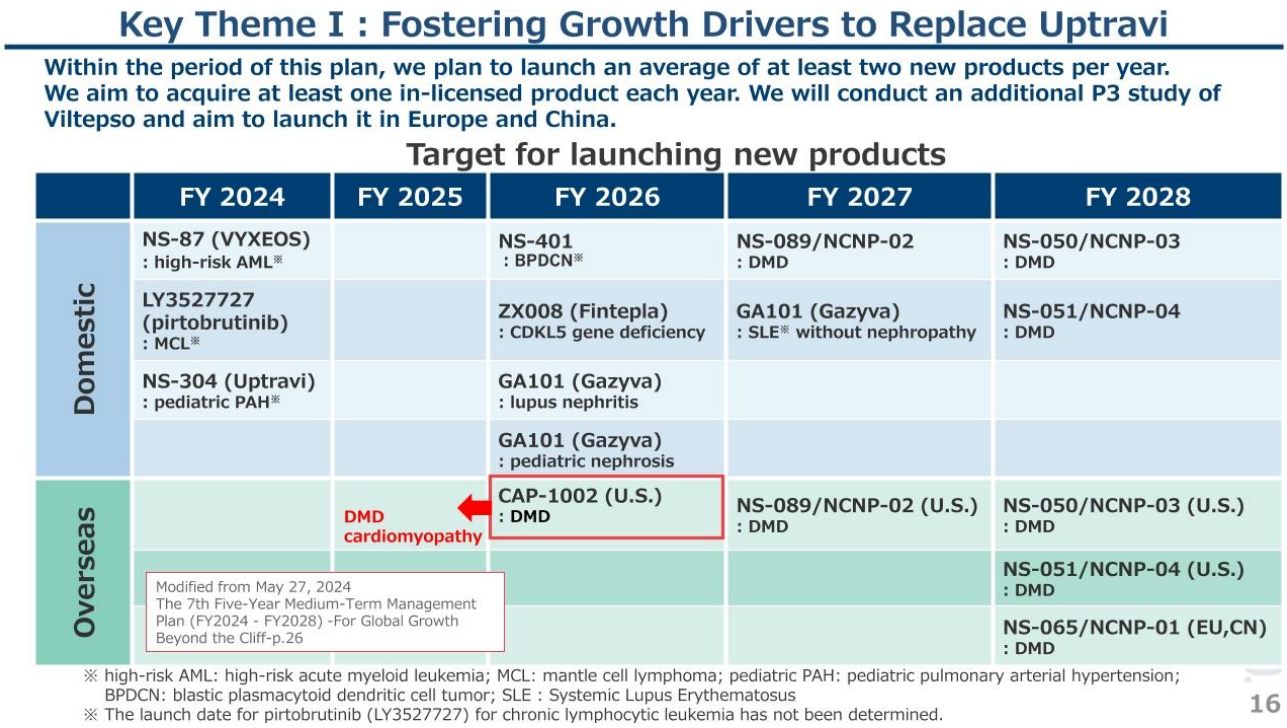
U.S. development timeline according to Capricor

Capricor is seeking full approval with a DMD-cardiomyopathy label

3: Biologics License Application (BLA)

Capricor began the rolling BLA submission in October for full approval for the indication of "Duchenne muscular dystrophy cardiomyopathy," which is expected to be completed by the end of this year. The PDUFA

date is expected in H2 of 2025 and the timing of the market launch may therefore be earlier than originally planned.



We had initially indicated that CAP-1002 would be launched in FY2026 in our new product launch targets for the 7th Medium-Term Management Plan period, but we expect the launch to be in FY2025 if the future schedule goes as planned.

We are also preparing for an earlier launch of the product.

This concludes our explanation of the results for Q2 of FY2024 and our full year forecast, as well as the CAP-1002 update.

Mr. Takagaki, in charge of R&D, will continue with an explanation of the progress of research and development.

Takagaki: I am Kazuchika Takagaki, in charge of R&D.

I will continue to explain the progress of R&D items that have been updated since Q1 of FY2024.

R&D Updates (1/2)

Recent status/event	Code No. (Generic name)	Product name	Indications and topics	Schedule
Launch	ZX008 (fenfluramine hydrochloride)	Fintepla	Lennox-Gastaut syndrome (additional indication)	March 2024
Launch	NS-87 (daunorubicin / cytarabine)	Vyxeos	high-risk acute myeloid leukemia	May 2024
Launch	LY3527727 (piltobrutinib)	Jaypirca	patients with relapsed or refractory mantle cell lymphoma who are resistant or intolerant to other BTK inhibitors	August 2024
Approval	ACT-064992D (macitentan / tadalafil)	Yuvanci	pulmonary arterial hypertension	September 2024
In application	NS-304 (selexipag)	Uptravi	pediatric pulmonary arterial hypertension	April 2024
Rolling submission	CAP-1002 (deramiocel)	–	Duchenne muscular dystrophy cardiomyopathy	October 2024 (U.S.)
Start of P2	NS-089/NCNP-02 (brogidirsen)	–	Duchenne muscular dystrophy	February 2024
Start of P2	NS-229	–	eosinophilic granulomatosis with polyangiitis	June 2024
Start of P1/ P2	NS-050/NCNP-03	–	Duchenne muscular dystrophy	October 2024
Temporarily suspended	NS-580	–	endometriosis chronic prostatitis / chronic pelvic pain syndrome	–

For updates since Q1 FY2024 financial results announcement on August 7, 2024, see highlighted text in red.

In August, we launched Jaypirca for the treatment for patients with relapsed or refractory mantle cell lymphoma who are resistant or intolerant to other BTK inhibitors, and the drug is already being used in clinical settings. In September, Janssen Pharmaceutical obtained approval for Yuvanci, a treatment for pulmonary arterial hypertension, and we are currently preparing for its launch.

As Mr.Nakai explained earlier, Capricor has initiated rolling BLA for CAP-1002 for the indication of Duchenne muscular dystrophy cardiomyopathy.

For NS-050/NCNP-03, FPI was completed in October and PI/II has been initiated.

R&D Updates (2/2)

Recent status/event	Code No. (Generic name)	Product name	Indications and topics	Schedule
In-license (Vicore Pharma)	C21	–	idiopathic pulmonary fibrosis	Contract signed in February 2024
Alliance agreement (Eli Lilly Japan)	LY3527727 (piltobrutinib)	Jaypirca	mantle cell lymphoma (MCL) chronic lymphocytic leukemia (CLL)	Contract signed in March 2024
Letter of Intent (Capricor Therapeutics)	CAP-1002 (deramiocel)	–	executed a Letter of Intent stipulating the exclusive right to negotiate over the next few months an exclusive distribution agreement for CAP-1002 in Europe	LOI signed in September 2024 (Europe)
In-license (Atsena Therapeutics)	ATSN-101	–	Leber congenital amaurosis caused by biallelic mutations in GUCY2D (LCA1)	Contract signed in November 2024
Preliminary analysis results	NS-065/NCNP-01 (viltolarsen)	Viltepso	global Phase 3 trial (RACER53 Study)	May 2024
Conference Presentations	NS-065/NCNP-01 (viltolarsen)	Viltepso	Phase 2 trial (Galactic53 trial): 2024 Muscular Dystrophy Association Clinical & Scientific Conference	March 2024
Orphan Drug Designation	NS-089/NCNP-02 (brogidirsen)	–	Duchenne muscular dystrophy	December 2023 (EU)
Orphan Drug Designation	NS-229	–	eosinophilic granulomatosis with polyangiitis	January 2024 (EU)
Rare Pediatric Disease Designation	NS-050/NCNP-03	–	Duchenne muscular dystrophy	August 2024 (U.S.)
Alliance (MiNA Therapeutics)	–	–	a joint research agreement with the aim of creating nucleic acid medicines that are expected to be applied to an intractable and rare disease in the CNS field	April 2024

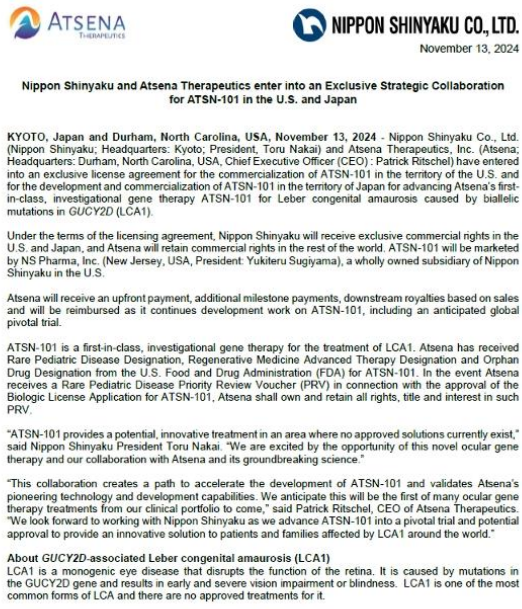
For updates since Q1 FY2024 financial results announcement on August 7, 2024, see highlighted text in red.

With regard to the partnership for CAP-1002 in Europe, in September we signed a Letter of Intent with Capricor allowing us to negotiate an exclusive distribution agreement with them.

NS-050/NCNP-03 received a Rare Pediatric Disease designation in the US in August.

Finally, we would like to introduce ATSN-101, which was released on November 13.

ATSN-101



ATSENA THERAPEUTICS

NIPPON SHINYAKU CO., LTD.

November 13, 2024

Nippon Shinyaku and Atsena Therapeutics enter into an Exclusive Strategic Collaboration for ATSN-101 in the U.S. and Japan

KYOTO, Japan and Durham, North Carolina, USA, November 13, 2024 - Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters: Kyoto; President, Toru Nakai) and Atsena Therapeutics, Inc. (Atsena; Headquarters: Durham, North Carolina, USA, Chief Executive Officer (CEO) : Patrick Ritschel) have entered into an exclusive license agreement for the commercialization of ATSN-101 in the territory of the U.S. and for the development and commercialization of ATSN-101 in the territory of Japan for advancing Atsena's first-in-class, investigational gene therapy ATSN-101 for Leber congenital amaurosis caused by biallelic mutations in *GUCY2D* (LCA1).

Under the terms of the licensing agreement, Nippon Shinyaku will receive exclusive commercial rights in the U.S. and Japan, and Atsena will retain commercial rights in the rest of the world. ATSN-101 will be marketed by NS Pharma, Inc. (New Jersey, USA, President: Yukiteru Sugiyama), a wholly owned subsidiary of Nippon Shinyaku in the U.S.

Atsena will receive an upfront payment, additional milestone payments, downstream royalties based on sales and will be reimbursed as it continues development work on ATSN-101, including an anticipated global pivotal trial.

ATSN-101 is a first-in-class, investigational gene therapy for the treatment of LCA1. Atsena has received Rare Pediatric Disease Designation, Regenerative Medicine Advanced Therapy Designation and Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for ATSN-101. In the event Atsena receives a Rare Pediatric Disease Priority Review Voucher (PRV) in connection with the approval of the Biologic License Application for ATSN-101, Atsena shall own and retain all rights, title and interest in such PRV.

"ATSN-101 provides a potential, innovative treatment in an area where no approved solutions currently exist," said Nippon Shinyaku President Toru Nakai. "We are excited by the opportunity of this novel ocular gene therapy and our collaboration with Atsena and its groundbreaking science."

"This collaboration creates a path to accelerate the development of ATSN-101 and validates Atsena's pioneering technology and development capabilities. We anticipate this will be the first of many ocular gene therapy treatments from our clinical portfolio to come," said Patrick Ritschel, CEO of Atsena Therapeutics. "We look forward to working with Nippon Shinyaku as we advance ATSN-101 into a pivotal trial and potential approval to provide an innovative solution to patients and families affected by LCA1 around the world."

About *GUCY2D*-associated Leber congenital amaurosis (LCA1)
LCA1 is a monogenic eye disease that disrupts the function of the retina. It is caused by mutations in the GUCY2D gene and results in early and severe vision impairment or blindness. LCA1 is one of the most common forms of LCA and there are no approved treatments for it.

- ✓ **Adeno-associated virus type 5 gene therapy agent administered subretinally**
- ✓ **Signed an exclusive license agreement with Atsena Therapeutics, Inc. of the U.S. for Japan and the U.S.**
- ✓ **Received "Rare Pediatric Disease Designation", "Regenerative Medicine Advanced Therapy Designation" and "Orphan Drug Designation"**
- ✓ **Currently in Phase I/II Study in the U.S. by Atsena Therapeutics, Inc.**

Source: company press release on November 13, 2024
https://www.nippon-shinyaku.co.jp/file/download.php?file_id=7885

We have entered into an exclusive license agreement with Atsena Therapeutics, Inc. for ATSN-101, a gene therapy for hereditary retinal dystrophy, which is a gene therapy for adeno-associated virus type 5 administeredsubretinally, in Japan and in the US.

Under this agreement, we have acquired exclusive rights to distribute the product in the US and Japan. In the US, the product will be distributed by our US subsidiary NS Pharma.

Currently, Atsena Therapeutics is conducting Phase I/II trials in the US.

Background Information of viltolarsen

<Clinical Trial>

- Japan Phase I/II trials in (2016-2017)
- U.S. Phase II (Study 201: 2016-2018) and its extension study (Study 202)

Results:
Expressions of dystrophin protein were found in skeletal muscles of enrolled DMD patients.
Significant differences were observed in multiple endpoints compared to the natural history population, suggesting improved motor function.

<Approval and Sales>

Japan: Conditional Early Approval in March 2020, followed by product launch in May of the same year

U.S.: Accelerated Approval and product launch in August 2020

***As conditions for approvals in both the U.S. and Japan, Nippon Shinyaku is required to conduct a global Phase III study (Study 301) as a verification study.**

I will now explain an update on Viltepso.

Viltepso has been shown to induce the expression of dystrophin protein in the skeletal muscles of DMD patients in Phase I/II trials in Japan and Phase II in the US, suggesting improved motor function compared to the natural history of the disease. With these results, we received conditional early approval in Japan in March 2020 and accelerated approval in the US in August 2020.

The product was launched in Japan in May 2020 and in the US in August 2020 and is already being used by many patients in clinical settings.

Global Phase III Study (RACER 53 Study/Study 301)

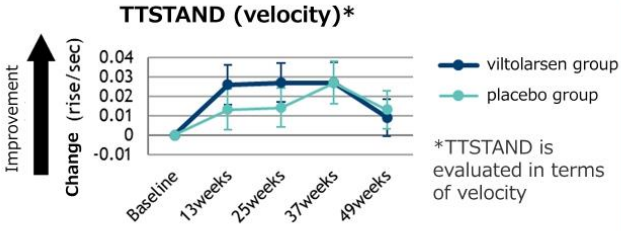
<Target Patients>

DMD patients between **4 and 7 years of age**, with a deletion of the dystrophin gene that can be treated by exon 53 skipping.

<Efficacy>

Primary endpoint: Time to Stand from the floor (TTSTAND)

*Change from baseline after 48 weeks of treatment



- **A trend of increased velocity was observed in the viltolarsen-treated group. On the other hand, the placebo group also showed an increase in velocity.**
- **No statistically significant differences were observed between the viltolarsen and placebo groups.**
- **There were similar trends in secondary endpoints (10-meter walk time, 4-step stair climbing time, 6-minute walk test, and NSAA).**

<Safety>

- The incidence of adverse events did not differ between the viltolarsen and placebo groups.
- All of the adverse events that occurred in the viltolarsen group were mild or moderate, and there were no cases that led to treatment was discontinued.

In May of this year, we announced the preliminary results of the RACER53/Study 301, which is global Phase III as a verificationstudy required as a condition for approval. The results showed no statistically significant difference in the primary endpoint of “time to stand from the floor” compared to the placebo group.

There were similar trends in the secondary endpoints of 10-meter walk time, 4-step stair climbing time, and 6-minute walk test. There was no difference in safety, including the incidence of adverse events, compared to the placebo group, and no cases resulted in treatment discontinuation.

FDA Meeting

- **A meeting with the FDA was scheduled in October 2024 to discuss conducting an additional Phase III study (Study 303) with keeping Viltepso (viltolarsen) on the market.**

- **The FDA requested the Clinical Study Report (CSR) including the full data set from Study 301, as a data review and further internal discussions were required in the FDA.**

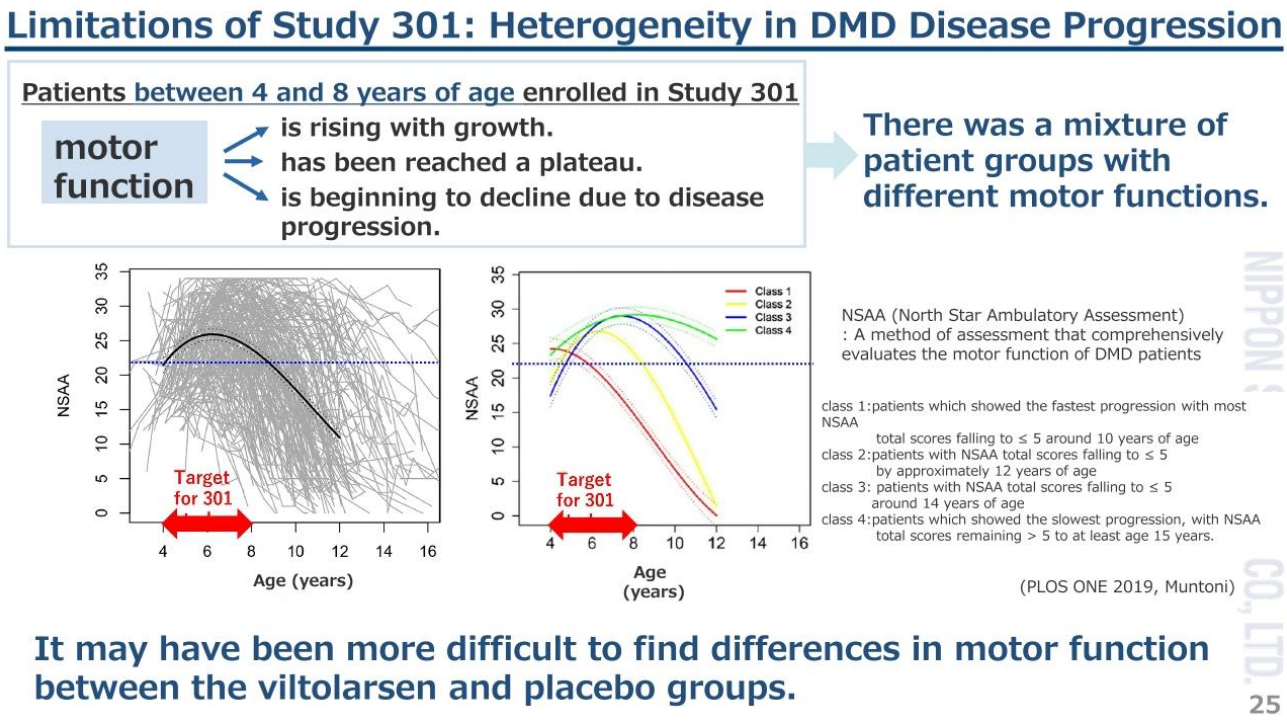
Next Step

- **Nippon Shinyaku will submit**
  - **Clinical Study Report, including the complete data set of Study 301**
  - **Protocol of Study 303**
- **After the FDA review is complete, we plan to hold a meeting with the FDA.**

Based on the results of Study 301, a meeting was scheduled in October with the FDA to discuss conducting Study 303, an additional Phase III study, with keeping Viltepso on the market.

However, the FDA has asked us to submit Clinical Study Report (CSR) of the trial, including the full data set of Study 301, as a data review and further internal discussions were required in the FDA.

We plan to hold a meeting with FDA after their review is complete.



I will now explain the limitations in Study 301.

The figure on the left displays the NSAA scores of 395 DMD patients over time, and the graph on the right divides them into classes according to age at which the NSAA score falls below 5.

In Study 301, the inclusion criteria specified patients aged four to seven years. However, within this age group, there was a variation in motor function, as some patients were experiencing improvement with growth, others had reached a plateau, and some had started to decline due to disease progression.

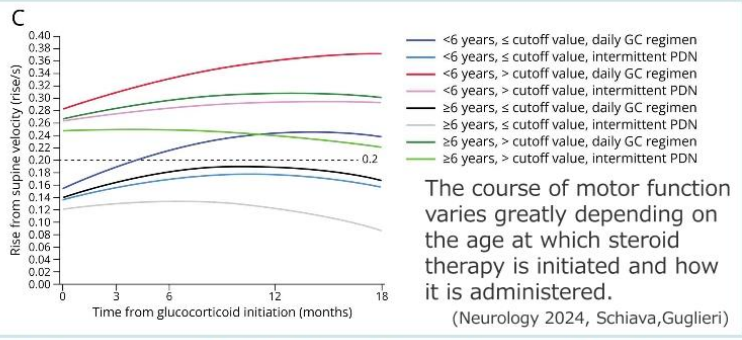
Although we cannot show the data, a subgroup analysis of Study 301 also showed a statistically significant improvement in NSAA scores in the viltolarsen group compared to the placebo group in the group of patients with advanced disease.

We believe that this heterogeneity may have made it difficult to find differences in motor function between the viltolarsen and placebo groups.

Limitations in Study 301: Steroid Use

Heterogeneity of steroid use in Study 301

Variation in steroid dosage (0.11-1.11 mg/kg/day)
Mixture of daily dosing and intermittent dosing (10 days dosing, 10 days rest)
Pre-steroid period prior to starting viltolarsen administration※ variation in (3-12 months or more)
※Inclusion criteria: steroid preadministration for at least 3 months



The course of motor function varies greatly depending on the age at which steroid therapy is initiated and how it is administered.
(Neurology 2024, Schiava,Guglieri)

The inclusion criteria were "steroids administration for at least three months before participating in the study". However, depending on the dosing conditions, improvements in motor function of around one year have been confirmed due to steroid administration.

Heterogeneity in the steroid combination may have affected the comparison between the placebo and viltolarsen groups.

This is a graph showing the changes of motor function since the start of steroid treatment, with patients stratified around the age of six and grouped by the method of steroid administration. Compared to intermittent dosing, daily dosing tends to improve motor function by about 12 months. However, in Study 301, patients receiving intermittent dosing and daily dosing were not properly randomized.

In a subgroup analysis focused on patients who had received long-term steroid treatment for 12 months or more, or who had been treated with daily steroid dosing, statistically significant improvements were observed in quantitative muscle measurements and knee extension strength in the viltolarsen group, compared to the placebo group.

The inclusion criterion for steroid use was at least three months prior administration, but heterogeneity, such as variations in dosage and duration of administration prior to the start of viltolarsen administration, may have affected the comparison between the viltolarsen and placebo groups. We believe that the patient may have been affected by the effects of steroids, as some data have shown improvement in motor function over a period of about one year with steroid administration.

Here are the data confirming the efficacy of viltolarsen in the Phase II trial of Viltepso and its continuation trial, with a significant difference compared to natural history after 73 weeks.

Limitations in Study 301: Duration of Study

The one-year administration of viltolarsen may not have been long enough as a trial period.

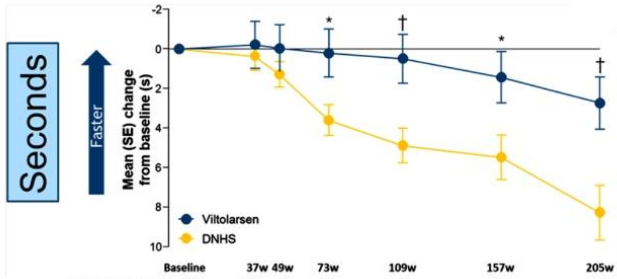
Improvements in motor function have been observed with long-term administration of viltolarsen.

(J Neuromuscul Dis 2023, Clemens)

"The participants learned that a typical 12-month clinical trial may be insufficient to discern the effectiveness of exon-skipping drugs. Although increases in dystrophin level may be evident within 12 months, the impact of increased dystrophin on clinical function is clearer over time and with the levels of dystrophin induced by first generation antisense compounds, a minimum of 18–24 months is necessary to appreciate divergence from untreated patients."

At the 269th ENMC (The European Neuromuscular Centre) international workshop (Neuromuscular Disorders 2023, Naarding)

Long-term efficacy of viltolarsen in the P2 study and its extension study



	Baseline	37w	49w	73w	109w	157w	205w
viltolarsen, e.g.	16	16	15	14	14	11	13
DNHS, e.g.	65	31	57	24	24	14	10

*p <0.05; †p <0.01; ‡p ≤0.001.
DNHS, Duchenne Natural History Study (DMD natural history control group)

(J Neuromuscul Dis 2023, Clemens)

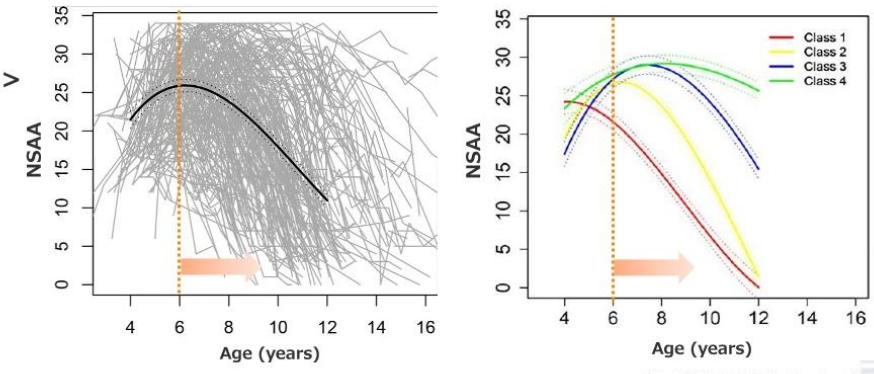
The primary endpoint of Study 301 was the time to stand from the floor after 48 weeks of treatment, but it has been pointed out that at least 18 to 24 months is needed to clearly demonstrate improvement in clinical function, since the improvement in motor function is delayed until after dystrophin level is increased. Therefore, it is possible that the duration of administration was not long enough.

The study design to be proposed as the additional Phase III study (Study 303)

<Age of the subject patient >
6 years old and up

<Primary endpoint>
NSAA

<Duration of treatment>
96 weeks



(PLOS ONE 2019, Muntoni)

<Inclusion criteria and conditions>

- ✓ Define the range of baseline NSAA scores
  - ↳ Reduce heterogeneity of motor function changes due to patient disease progression
- ✓ Strictly specified doses/regimens for steroids throughout the pre-dose period and study period

*This slide is based our current assumption. The final study design will be determined after consultation with the FDA in the future.

Based on these results, we plan to propose a study design to the FDA for an additional Phase III study, Study 303, with inclusion criteria such as patient age of at least six years, dosing period of 96 weeks, and strict stipulations on steroid administration.

Please note that this information about the design here has not yet been agreed with the FDA. We will disclose the official Study 303 design and other information as soon as it is finalized.

This concludes my explanation of the progress of research and development and the update on Viltepso.

Sano: My name is Shouzou Sano, and I am in charge of sales and marketing.

I will continue with an explanation of the features of Jaypirca, which was launched in August, and Yuvanci which received manufacturing and marketing approval in September.

About Jaypirca® tablets

First, let me explain the features of Jaypirca tablets, which was launched on August 21, 2024 after signing an alliance agreement with Eli Lilly Japan K.K. in March 2024.

Product Overview

Brand name	Jaypirca Tablet 50mg			Jaypirca Tablet 100mg		
Generic name	Pirtobrutinib					
NHI drug price	10,201.00 yen			19,465.80 yen		
Properties and dosage form	Blue triangular film-coated tablets			Blue circular film-coated tablets		
Externals	surface	back	side	surface	back	side
						
Indications or effects	Relapsed or refractory mantle cell lymphoma (MCL) that is resistant or intolerant to other BTK inhibitors					
Dosage and Administration	The usual adult dosage of pirtobrutinib is 200 mg orally once daily. The dose may be reduced according to the patient's condition.					
Manufacturing and marketing approval date	June 24, 2024					
Date of NHI drug price listing	August 15, 2024					
Release Date	August 21, 2024					
Manufacturer	Eli Lilly Japan K.K.					
Seller	Nippon Shinyaku Co.,Ltd.					

Jaypirca tablets, generic name Pirtobrutinib, are available in two dosage forms: 50 mg and 100 mg.

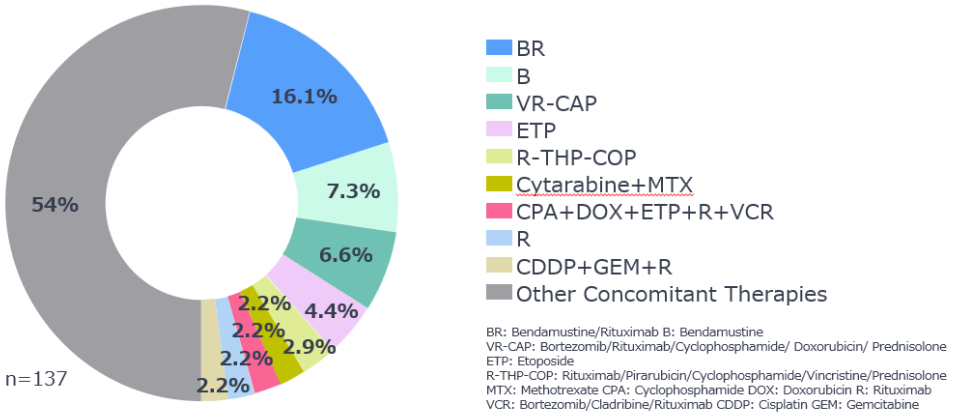
The indication is relapsed or refractory mantle cell lymphoma that is resistant or intolerant to other BTK inhibitors.

Based on the alliance agreement, Eli Lilly Japan will be in charge of product supply and we Nippon Shinyaku will be in charge of distribution, sales, and information provision activities.

Drug therapy for relapsed/refractory mantle cell lymphoma

In Japanese real-world data for relapsed/refractory mantle cell lymphoma, various agents were tried as next-line therapy after discontinuation of treatment with covalent BTK inhibitors.

<Next therapy after discontinuation of covalent BTK inhibitors: breakdown and percentage of each therapy >



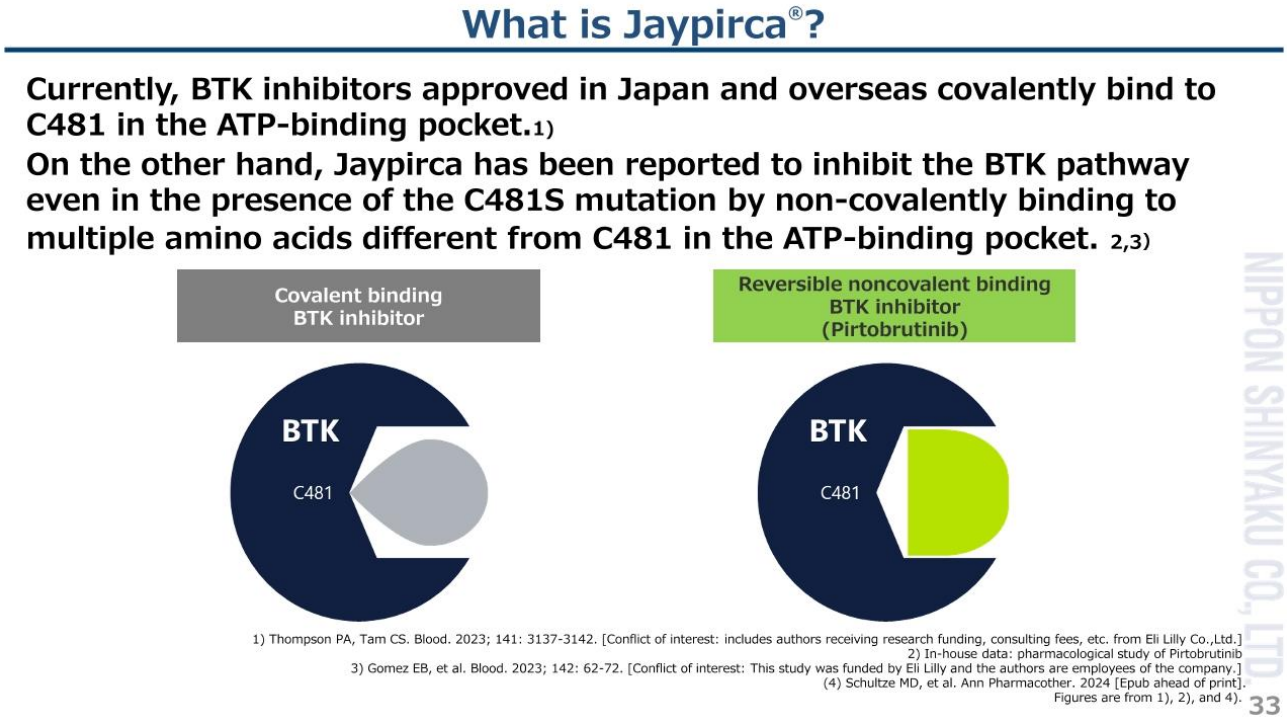
BR: Bendamustine/Rituximab B: Bendamustine
VR-CAP: Bortezomib/Rituximab/Cyclophosphamide/ Doxorubicin/ Prednisolone
ETP: Etoposide
R-THP-COP: Rituximab/Pirarubicin/Cyclophosphamide/Vincristine/Prednisolone
MTX: Methotrexate CPA: Cyclophosphamide DOX: Doxorubicin R: Rituximab
VCR: Bortezomib/Cladribine/Rituximab CDDP: Cisplatin GEM: Gemcitabine

The combination therapy with bortezomib approved in Japan is rituximab + cyclophosphamide + doxorubicin + prednisolone (VcR-CAP therapy). The generic version of bortezomib is not approved in Japan for MCL. Methotrexate is not approved in Japan for MCL.

Rai S, et al. Adv Ther. 2022; 39: 4792-4807.
[Conflict of interest: This study was supported by Eli Lilly and Company, and five of the authors are employees of Eli Lilly and Company or Eli Lilly Japan.]

Here we present Japanese real-world data for relapsed/refractory mantle cell lymphoma.

The most common treatment of choice as second-line therapy in relapsed/refractory mantle cell lymphoma was a covalent BTK inhibitor, but a variety of other treatments were also tried after discontinuation of treatment with covalent BTK inhibitors, as shown in the figure.



Currently, BTK inhibitors approved in Japan and abroad covalently bind to C481 of BTK.

On the other hand, Jaypirca binds noncovalently to several amino acids that differ from C481.

Therefore, it has been reported to inhibit the BTK pathway even when the C481S mutation, a known mechanism of resistance to existing BTK inhibitors, occurs, and it is expected to be effective when resistance occurs with covalent BTK inhibitors. We believe this could be a new treatment option after discontinuation of treatment with covalent BTK inhibitors.

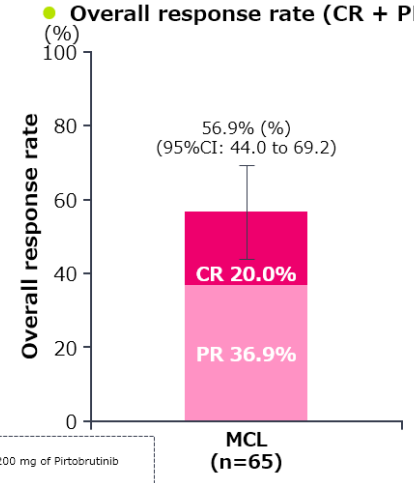
Global Phase I/II study (including dose finding study: BRUIN-18001)

[overseas data]

Overall response rate [primary endpoint], Best overall response [secondary endpoint]

The overall response rate was 56.9% (95%CI: 44.0-69.2), the lower limit of the 95%CI was above the pre-defined threshold of 20%.

● Overall response rate (CR + PR)



Includes dose-finding studies*
*6. The usual adult dosage for oral use is 200 mg of Pirtobrutinib once daily.
The dose may be reduced according to the patient's condition.

● Breakdown of Best Overall Response

	MCL (n=65)
Complete response (CR)	13 (20.0)
Partial response (PR)	24 (36.9)
Stable disease(SD)	9 (13.8)
Disease progression (PD)	10 (15.4)
Not evaluable (NE)	9 (13.8)

n (%)

This phase I/II study was not a confirmatory clinical trial, but the results of the efficacy and safety obtained in this study were used as the basis for approval in Japan.

In-house data: Phase I/II study of Pirtobrutinib (LOXO-BTK-18001 study) (evaluation data at the time of approval)

We will now present the efficacy results of the international Phase I/II BRUIN-18001 study, which is the data on the basis of which the product was approved in Japan.

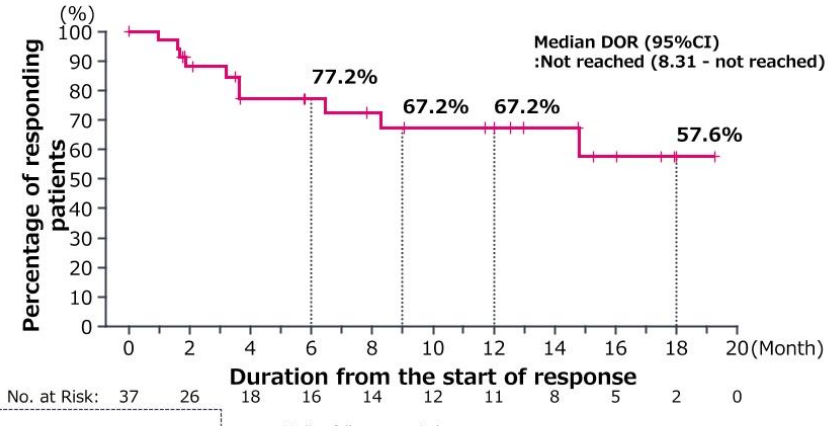
These are the results for the patient group with the approved indication of 'relapsed/refractory mantle cell lymphoma with resistance or intolerance to other BTK inhibitors.' The primary endpoint, response rate, was 56.9%, with 37 responders, including 13 complete responses or CRs, and 24 partial responses or PRs.

Global Phase I/II study (including dose finding study: BRUIN-18001)

Duration of response [secondary endpoint]

The median duration of response (DOR) was not reached (95%CI: 8.31 to not reached). The proportion of patients with a sustained response at 18 months was 57.6%.

● Kaplan-Meier curves for DOR, response cases (n=37)



Includes dose-finding studies*
*6. The usual adult dosage for oral use is 200 mg of Pirtobrutinib once daily.
The dose may be reduced according to the patient's condition.

Median follow-up period
9.10 months (interquartile range: 3.52-15.31)

In the BRUIN-18001 study, adverse events were observed in 681 of the 725 patients (93.9%) in the safety analysis set. The most common (15% or more) were fatigue in 191 patients (26.3%), diarrhea in 160 patients (22.1%), and contusion in 138 patients (19.0%). In addition, adverse events were observed in 146 out of 164 patients (89.0%) with MCL. The main ones (15% or more) were fatigue in 49 cases (29.9%), diarrhea in 35 cases (21.3%), and dyspnea in 27 cases (16.5%).

In-house data: Phase I/II study of Pirtobrutinib (LOXO-BTK-18001 study) (evaluation data at the time of approval)

The median duration of response, a secondary endpoint, was not reached, with 57.6% of patients having a sustained response at 18 months.

We believe that the results of this clinical trial will make Jaypirca a new treatment option for mantle cell lymphoma who are resistant or intolerant to covalent BTK inhibitors and address the unmet medical needs of patients.

Jaypirca is also currently in five Phase III studies for mantle cell lymphoma and chronic lymphocytic leukemia.

These studies are international clinical trials including Japan, and domestic development is underway.

We believe that expanding the indications will help even more patients in the future.

This concludes the description of the features of Jaypirca tablets.

Background of the development of YUVANCI® combination tablets

In recent years, various pulmonary vasodilators have been developed and evidence has accumulated regarding combination therapy of drugs with different mechanisms of action. Therefore, the Japanese pulmonary hypertension treatment guidelines[1)] recommended initial combination therapy with two or three drugs for some low-risk patients (NYHA/WHO functional class I to II degree), intermediate-risk patients (NYHA/WHO functional class II to III degree), and high-risk patients (NYHA/WHO functional class IV). Additional combination therapy may be considered if clinical response to initial therapy is insufficient.

The ESC/ERS Guideline for diagnosis and treatment of pulmonary hypertension[2)] also recommends "initial combination therapy with macitentan and tadalafil for IPAH, HPAH, and DPAH without cardiopulmonary comorbidities" as Class I.※

The introduction of a combination drug containing macitentan and tadalafil has the potential to improve convenience by reducing the number of tablets to be taken and simplifying the prescription, so the development of Yuvanci® combination tablets had been promoted.

※In initial combination therapy, the combination should be started cautiously after confirming the tolerability of each drug.[3)]

1) Japanese Society of Cardiology. Guidelines for the Treatment of Pulmonary Hypertension (Revised 2017), https://www.j-circ.or.jp/cms/wp-content/uploads/2017/10/JCS2017_Fukuda_h.pdf (viewed September 2024).
2) Humbert M, et al. Eur Respir J. 2023; 61: 2200879., 3) Burks M, et al. Am J Cardiovasc Drugs. 2018; 18: 249-257.

Reference **Initial therapy in ESC/ERS pulmonary hypertension diagnosis and treatment guidelines**
Recommendations for initial oral combination therapy (IPAH/HPAH/DPAH without cardiopulmonary comorbidities)

recommendation	class[a]	level[b]
Initial combination therapy with ambrisentan and tadalafil is recommended	I	B
Initial combination therapy with macitentan and tadalafil is recommended	I	B
Initial combination therapy with other ERAs and PDE5 inhibitors should be considered	IIa	B
Initial combination therapy with macitentan, tadalafil and selexipag is not recommended	III	B

a: Recommended class b: Level of evidence

Humbert M, et al. Eur Respir J. 2023; 61: 2200879

I would like to continue by explaining the features of Yuvanci combination tablets.

In recent years, various pulmonary vasodilators have been developed for the treatment of pulmonary hypertension, and evidence supporting combination therapy with drugs that have different mechanisms of action has been accumulating. As a result, the Japanese guidelines for the treatment of pulmonary hypertension now recommend initial combination therapy with two or three drugs for patients with various levels of risk.

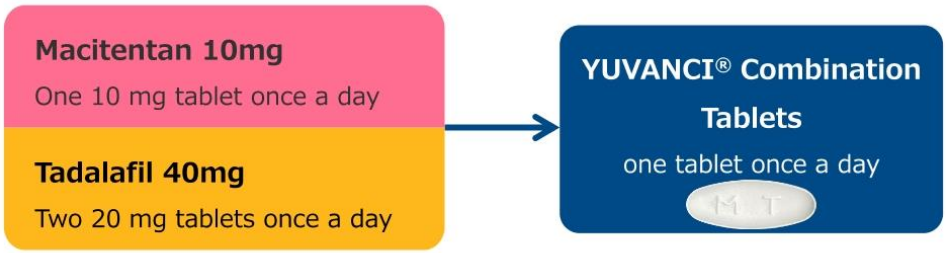
The ESC/ERS Guidelines for Diagnosis and Treatment of Pulmonary Hypertension also recommend initial combination treatment with macitentan and tadalafil for IPAH, HPAH, and DPAH without cardiopulmonary disease as Class I.

The introduction of a combination drug containing macitentan and tadalafil as ingredients was promoted by the possibility of improving convenience by reducing the number of dosing tablets and simplifying prescriptions.

What is YUVANCI® Combination Tablets?

YUVANCI® Combination Tablets is the first oral combination drug approved in Japan for the treatment of pulmonary arterial hypertension that contains the endothelin receptor antagonist (ERA) macitentan and the selective phosphodiesterase 5 (PDE5) inhibitor tadalafil.

A combination tablets containing 10 mg of macitentan and 40 mg of tadalafil, taken once daily



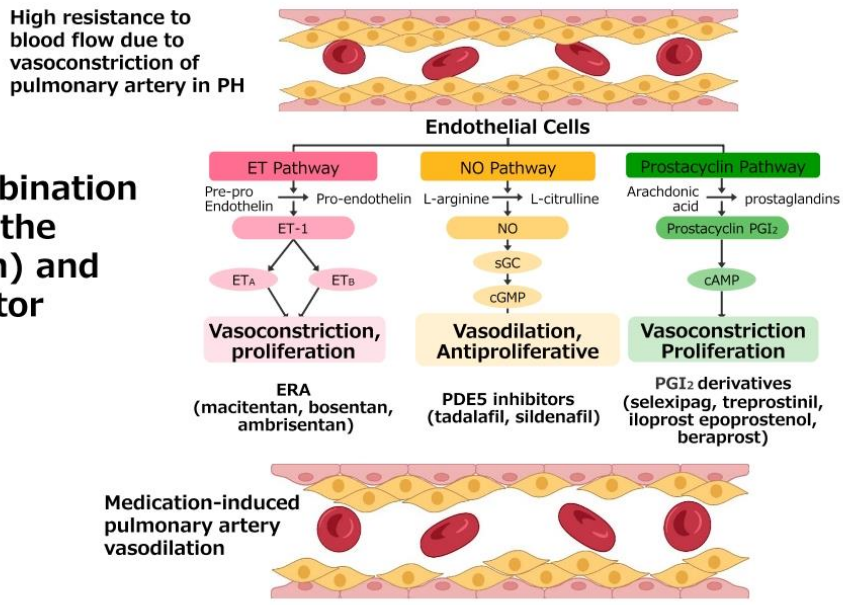
Yuvanci combination tablets is the first oral combination drug approved in Japan for the treatment of pulmonary arterial hypertension, containing the endothelin receptor antagonist, macitentan, and the selective phosphodiesterase 5 inhibitor, tadalafil.

It is a combination tablet containing 10 mg of macitentan and 40 mg of tadalafil, to be taken once daily.

For patients being treated for PAH, this is expected to improve convenience by reducing the number of medication tablets and simplifying prescriptions.

Treatment pathway of PAH and YUVANCI® Combination Tablets

YUVANCI® Combination Tablets contain the ERA(macitentan) and the PDE5 inhibitor (tadalafil).



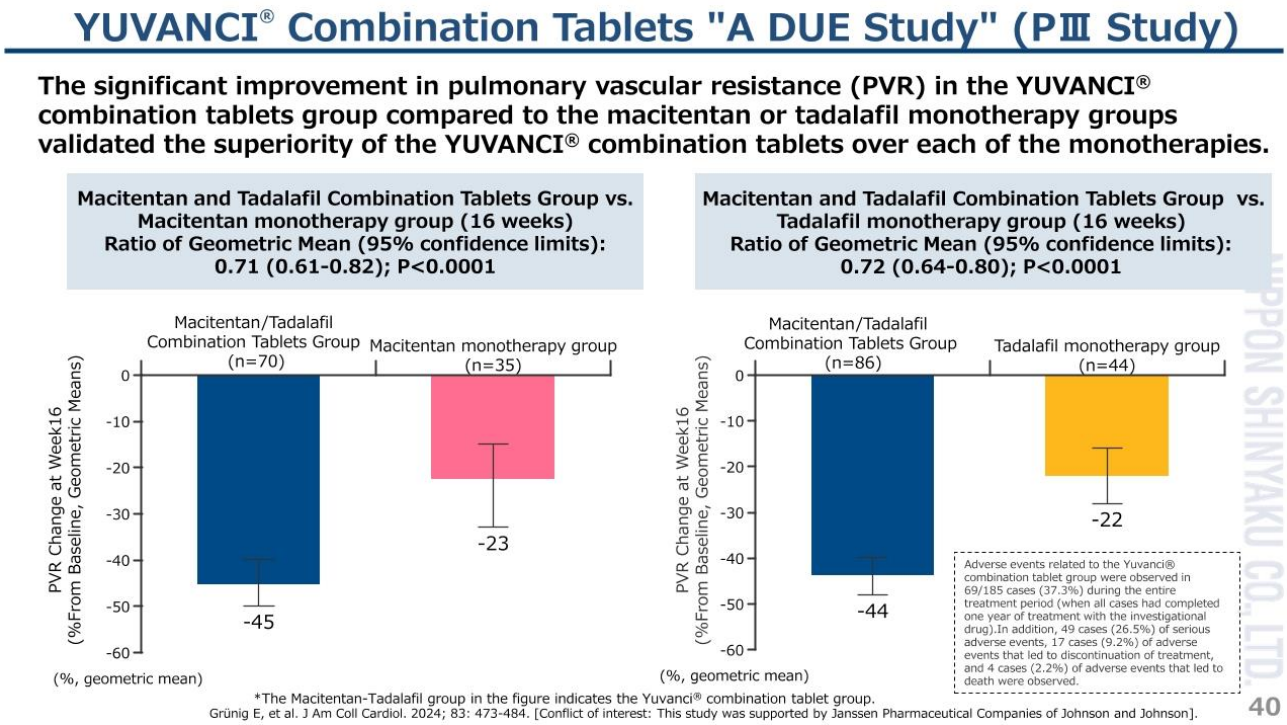
cAMP: cyclic adenosine monophosphate
cGMP: cyclic guanosine monophosphate
ET: endothelin
ERA: endothelin receptor antagonist
NO: nitric oxide
PDE5: phosphodiesterase 5
PGI_2: prostacyclin
sGC: soluble guanylate cyclase

Modified from Dhoble S, et al. Int J Pharm. 2022; 621: 121792

PAH is a poor prognosis disease in which the blood pressure in the pulmonary artery, which carries blood from the heart to the lungs, rises abnormally for some reason, and is designated as an Intractable Disease by the Ministry of Health, Labor and Welfare.

Three types of pulmonary vasodilators, rostacyclins, endothelin receptor antagonists, and phosphodiesterase 5 inhibitors, are the main drugs used in this therapy, and combinations of two or three of these drugs are also used.

Yuvanci combination tablets is a combination drug containing macitentan, an endothelin receptor antagonist, and tadalafil, a phosphodiesterase 5 inhibitor.



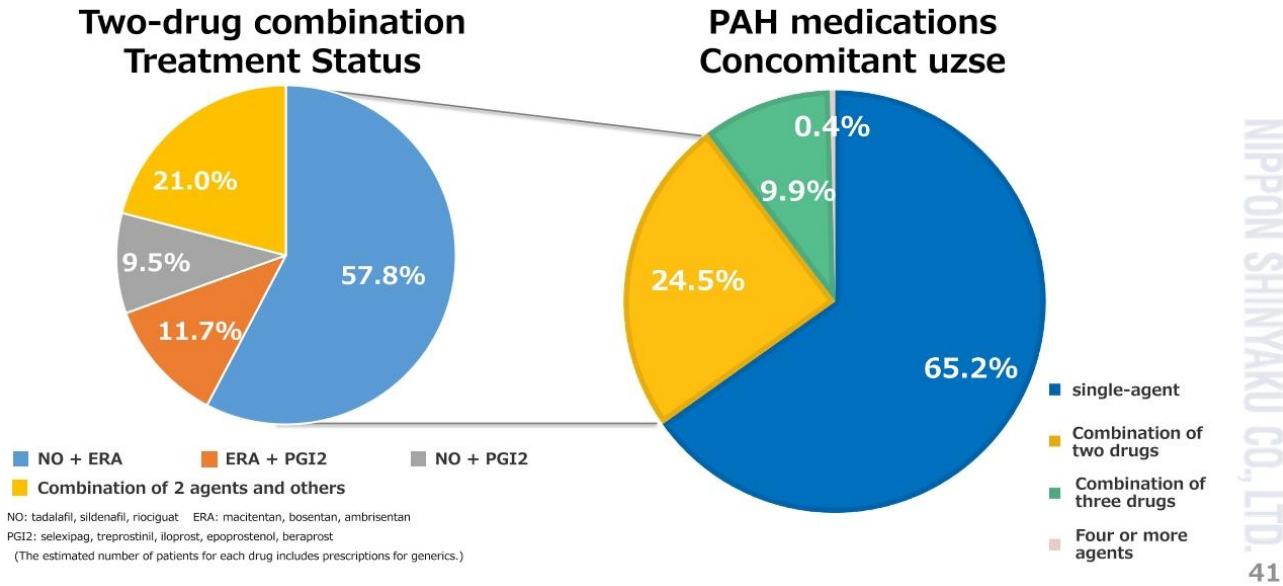
Here are the results of the A DUE study, a global Phase III study.

The subjects were 186 patients with PAH.

The macitentan and tadalafil group showed significant improvement in pulmonary vascular resistance in both the macitentan and tadalafil monotherapy groups, confirming the superiority of the Yuvanci combination tablets over each monotherapy group.

We believe that we can contribute to the treatment of PAH by appropriately delivering this drug to patients and healthcare professionals who need it.

Pulmonary Hypertension Market in Japan (Estimated Patient Percentage)



This page shows the estimated percentage of patients in the pulmonary hypertension market in Japan.

More than half of PAH patients are treated with a single drug, but about 35% are treated with two or more drugs in combination.

About 25%, or a quarter of all patients, are taking two drugs together, including nearly 60% who are taking an ERA in combination with a NO-based drug, which is the combination of Yuvanci combination tablets.

We believe that the use of Yuvanci combination tablets in these patients will help reduce the number of tablets they take and improve adherence.

This concludes the introductions of our new products.

Q&A for 2Q FY2024 Financial Results (Summary)

November 15, 2024

No.	Questions	Answer
1	Regarding the business forecast, the exchange rate is assumed to be 140 yen to the dollar in the 2H, but what is the exchange rate in 2Q results and FY2024 full year?	The exchange rate for 2Q results is 152.8 yen, and the assumed rate for 2H is 140 yen.
2	If the exchange rate remains at the current rate of 150 yen to the dollar, there would be a foreign exchange gain between the current rate and the company's forecast rate of 140 yen for the second half, resulting in an increase in operating income of approximately 3 billion yen. Is my assumption correct?	We have the same view. We shared the sensitivity of the exchange rate in today's presentation material. It is assumed to be an increase of approximately 300 million yen in operating profit for every 1 yen depreciation of the yen. In addition, assets are revalued at the end of every fiscal year, so there will be some fluctuation depending on their values at that point.
3	The "Revenue in the Rest of World" listed in the Semiannual Securities Report (2H Yuka-shoken-houkokusho) is about 2.3 billion yen for this fiscal year, an increase compared to 1.2 billion yen for the same period last year. Compared to the April-June period of this year, did it slow down in the July-September period?	It is not slowing down compared to April-June, but is growing.
4	I understand that CAP-1002 is expected for the FDA approval in DMD-cardiomyopathy in the second half of next year, and that the results of the HOPE-3 study summarizing cohorts A and B will probably be announced at the same time. If the results of HOPE-3 differ from expectations, what scenarios are possible? Could you tell us your thoughts on whether the product can continue to be marketed with additional studies like Viltepso, or whether the approval will be withdrawn?	The DMD-cardiomyopathy indication for CAP-1002 is different from the case of Viltepso. It is the full approval process based on data from HOPE-2, which has already come out, and its open label extension (HOPE-2 OLE) trial. We believe that the approval for cardiomyopathy would remain even if the data of HOPE-3 was not favorable because approval based on the results of HOPE-3, which will include skeletal muscle data, would be an indication expansion.

5	Regarding the definition of patients eligible for DMD-cardiomyopathy in CAP-1002, I remember that a subgroup analysis of patients with a LVEF (left ventricular ejection fraction) of 45% or greater demonstrated an improvement. I guess it depends on the label, but does that mean that patients with an LVEF of 45% or greater are eligible regardless of age or ambulation status?	It depends on the outcome of the labeling discussions, but I think your guess is correct.
6	Capricor mentioned* that 50-60% of all DMD patients in the U.S. has DMD-cardiomyopathy, which is about 8,000 people. Do you agree to this? CAP-1002 originally targeted non-ambulatory DMD patients who account for about half of all DMD patients, and will the number of eligible patients not change much? * Capricor Therapeutics Third Quarter 2024 Financial Results and Corporate Update Conference Call on November 13, 2024	We have also researched on the number of eligible patients for CAP-1002 and shared the results with Capricor, but both companies' understanding is almost the same. We believe that patients aged 10 and over, who are the target of the HOPE-3 study, are also the target of CAP-1002, and our company estimates a slightly higher percentage than Capricor's. However, the total number of patients estimated by both companies is almost the same. We are also researching the willingness of insurance companies to reimburse and doctors to prescribe in the U.S., but we cannot provide an estimate of the number of patients at this time.
7	According to Capricor's conference call (see note above), 100 patients who had participated in clinical trial would be switching directly to commercial products. If the product is successfully launched in the market, will sales of these 100 patients be generated right after the product launch?	Once the period of open label extension (OLE) after HOPE-2 is over, the 100 patients will then move to commercial products. Although it will take some time after approval, we expect a smoother start compared to Viltepso, which started with 14 patients.

8	If CAP-1002 receives indication of DMD-cardiomyopathy, do you think you will be able to achieve the revenue expansion envisioned in the 7th Five-Year Medium Term Management Plan? If so, will the results of the HOPE-3 trial be a further upside?	It will be an upside factor. The market which we originally contemplated for CAP-1002 can be covered only with an indication for DMD-cardiomyopathy. Most of the patients who are over the age of 10, which is one of the inclusion criteria in HOPE-3, have heart problems, and there is currently no drug on the market that acts on and protects the heart of DMD patients, so demand for the product could expand quickly once it is launched. We believe that the HOPE-3 data can be used for patients who are young and have not experienced a decline in cardiac function but have reduced motor function.
9	Although CAP-1002 is likely to penetrate in the market quickly after its launch, is there any possibility that the supply will be a bottleneck when it expands all at once?	We have confirmed with Capricor that the current manufacturing site is sufficient to meet the immediate demand and Capricor is currently in the process of expanding its manufacturing site. If demand far exceeds expectations, there may be a possibility of a bottleneck occurring on the supply side, but we are currently preparing for this while confirming the number of patients.
10	Both your company and Capricor are expecting that CAP-1002 will spread rapidly in the market. Do you think you can handle the expected increase in demand with the current manufacturing sites?	Yes, we do.
11	Capricor announced that they can make thousands of doses of CAP-1002 from a single heart, is this correct?	That's correct. One heart is enough to cover one whole clinical trial. There are several steps involved in making a drug, but one heart is enough to cover that much.

12	Did you purchase 20% of Capricor's shares? Is that stock purchase for European rights of CAP-1002? I think that CAP-1002 sales in Europe were not included in the 7th Five-Year Medium Term Management Plan. What are your plans for Europe over the next couple of years?	We have invested in Capricor, and now hold a 15% stake in the company. We purchased the shares this time to obtain exclusive negotiating rights for distribution in Europe. We had previously invested a small amount in Capricor, and the total now stands at around 15%. Capricor is planning to start discussions with European authorities early next year. In discussions with the FDA, it was decided to use the results of the HOPE-2 trial to move forward with approval for DMD-cardiomyopathy, but it is not known what will happen in Europe. If the European authorities have the same opinion as the FDA, the product launch timing will be accelerated, but there is also the possibility that data from the HOPE-3 trial or a new trial will be required. Therefore, the timing of the product launch in Europe is uncertain.
13	Will you invest in European market entry after all is known with CAP-1002?	We will consider how to proceed after checking the situation of the negotiations in Europe next year.
14	Is the number of patients expected to be treated with the gene therapy ATSN-101, for which a partnership has just been announced, likely to be higher than that for Luxturna*? Will the economic terms be similar to those of Capricor? Is there a possibility that the drug will be launched during the 7th Five-Year Medium Term Management Plan? *ATSN-101 is a gene therapy for the treatment of hereditary retinal dystrophy caused by biallelic RPE65 mutation-associated retinal dystrophy.	CAP-1002 has been developed by Capricor and will be distributed by our group under the distribution partnership. For ATSN-101, we will bear the development costs for the P3 trial. Therefore, it is a form of in-licensing of a product under development, and the profit structure differs from that of CAP-1002. The exact launch timing of ATSN-101 has not been disclosed, but we hope to be able to bring it to market within the timeframe of the 7th Five-Year Medium Term Management Plan. According to epidemiological research, the number of patients targeted by ATSN-101 is slightly higher than that of Luxturna. As it is a gene therapy that targets a different population to Luxturna, we are expecting a similar price.
15	Luxturna has sold over $600 million globally. Do you expect the same level of sales?	In our understanding, Luxturna had global sales of 210 million dollars in 2023, of which 50 million dollars were in the U.S.

16	I would like to ask about future events for Viltepso. When do you think you will be able to submit the Clinical Study Report (CSR) to the FDA, receive the review, and hold a meeting with them?	The Clinical Study Report and Study 303 protocol are scheduled to be submitted this year. We expect the FDA review to take around 2-3 months, so we would like to hold a meeting with the FDA by the end of FY2024 (March 2025).
17	Regarding the FDA's stance on Viltepso, is it positive for you that the meeting, which was previously scheduled for October, has been delayed because they want to see a little more data?	We did not have a meeting this time, but we did receive comments from the FDA. We expect that the FDA will review and comment on the Study 303 protocol in advance, and that it has not been said that Viltepso will be withdrawn from the market right now. We are positive about this.
18	Do you have any concern that Viltepso cannot continue to be on the market?	We do not believe there are any at this time.
19	If we apply the range of the NSAA* score to Study 303, can we narrow down the patients from the heterogeneous patient group? *North Star Ambulatory Assessment	It is difficult to define patients based on the range of the NSAA alone. However, if we select cases that have progressed to a certain extent in terms of the NSAA and age, we believe we can narrow down the patient group with declining motor function. In Study 301, there was a mix of different types patients, but in Study 303, we think we can reduce the patient variation.
20	Is it generally acceptable to narrow down patients by NSAA and age?	Based on the results of Study 301, we have so inferred, and KOLs have said that it is reasonable.
21	If the FDA approves the patient narrowing criteria for Viltepso's Study 303, will it affect clinical trials for other PMO products under development? We believe that the same patient population as Study 303 will be targeted in the confirmatory trial, but will it affect the ongoing P1/2 study?	The endpoint of the P1/2 trial for the other PMO products is the expression of dystrophin protein, so it will not be affected. For a confirmatory trial, we will utilize the design of Study 303 based on the experience of Study 301 to come up with a design that will result in a significant difference.

22	Study 303 is to set up a very strict protocol, and it may take time to recruit patients. The 7th Five-Year Medium Term Management Plan had a plan to launch Viltepso in Europe and China in FY2028, but is there any change in the schedule? At the 7th Five-Year Medium Term Management Plan briefing (May 28th, 2024), you mentioned hiring a chief medical officer in the U.S. for the upcoming negotiations with the FDA.	The protocol for Study 303 that we introduced today has stricter inclusion criteria than Study 301. If we agree with the FDA on our current study design, we cannot deny the possibility that the schedule will be pushed back slightly, since the schedule we presented during the 7th Five-Year Medium Term Management Plan briefing is an estimate for a study that is almost identical to Study 301. However, we would like to complete the trial as soon as possible, taking full advantage of our experience in conducting a global trial once. As for the chief medical officer in the U.S., we have not yet been able to hire one. Interviews are underway, and some finalists have been shortlisted; in addition to a qualification of MD (Medical Doctor), we are screening to see if a successful candidate can perform well within the company, so it will take some more time.
23	In slides today, you presented the results of two subgroup analyses of the Study 301, one of which was for patients with progressed symptoms. I would like to know again the results of the other subgroup analysis regarding steroids.	Among the patients who participated in the clinical trial, intermittent dosing and daily dosing were mixed in terms of steroid administration methods, but when these were narrowed down to patients who received daily dosing, significant results were observed in terms of knee flexor measurement.
24	Will you be presenting the data from Study 301 for Viltepso, which was disclosed as part of today's IR meeting material, to KOLs and patient advocacy groups?	We have already presented the data to KOLs. Patient advocacy groups will learn the data through today's disclosure.
25	What is the response from KOLs?	KOLs discussed the limitations of Study 301 and gave us advice on how to make a significant difference in the next study. The tendency of steroids was first reported in an academic paper in 2024, and KOLs pointed out that this may have also affected the study.

26	I think that the protocol for Study 301 of Viltepso was quite rough because the use of steroids was not adequately controlled. Steroids are a standard drug, but they were not controlled. Was this because you left everything to the CRO?	As a result, the trial ended up being rather rough. In Japan and the U.S., the steroids were administered daily, but in Europe they were administered intermittently. It was also discovered after the trial began that there was a tenfold difference in the dosage between countries. We would like to reflect on these issues and conduct the next trial.
27	Viltepso sales are strong in Q2. Is there any impact of gene therapy so far on Viltepso sales and NS-050 recruiting?	We do not think there is any impact. I actually spoke to physicians in the U.S., and they acknowledged the effectiveness of exon skipping drugs. I have not heard of any cases where Viltepso was not effective and the patient was switched to gene therapy. One reason why gene therapy has not expanded as much as expected may be the burden on medical institutions of having to continuously monitor patients. In the clinical trials for NS-050 and NS-089, patients are also informed of the trials before gene therapy if they meet the protocol. We do not think that the impact of gene therapy will prevent the recruitment of patients for the trials.
28	Sarepta Therapeutics has ended development of all the new nucleic acid drugs over a safety problem in kidney function. I would like to hear your opinion on whether this is due to the modality or is specific to the Sarepta case.	We were also developing a peptide-conjugated PMO (PPMO), but this was put on hold due to unexpected toxicity in non-clinical trials. Sarepta's Peptide-conjugated PMO (PPMO) has previously been reported to have the side effect of hypomagnesemia. While PMO itself is safe, we believe that an extra care should be taken when adding peptides, antibodies, etc. From a passive perspective, it is safest to not add anything, but for convenience, some approach should be considered after ensuring safety.

29	Is it overly optimistic to think that Sarepta's decision to discontinue development of PPMO will result in less focus on future marketing activities for exon skipping products, which in turn will positively impact Viltepso and your company's upcoming exon skipping products?	Regarding the competition for the exon 53 skipping drug, Viltepso is currently trying to catch up with golodirsen (Vyondys 53) in the U.S. market. We are not developing an exon 45 skipping agent, so there will be no competition with them in that category. However, we believe that the exon 51 skipping agent will give us a competitive advantage in the PMO market if their focus on PMO decreases. It is also important for us to speed up drug developments.
30	At the time of the drug price calculation for Vyxeos, the peak sales were estimated to be 2 billion yen (as disclosed by the Central Social Insurance Medical Council on May 15, 2024), but the company's forecast for this fiscal year is 4.6 billion yen. What was different from the assumptions made at the time of the drug price calculation? Is it 7+3 therapy and/or switching from other therapies? Based on this, how much of the upside of sales do you think remains?	Because AML progresses very quickly, it is necessary to use drugs as early as possible, and the adoption of Vyxeos prescriptions progressed more quickly than expected. While we had expected that Vyxeos would be prescribed mainly for new-onset acute myeloid leukemia (AML) in patients aged 60 to 75 years who were suitable for chemotherapy, in actual clinical practice, it is also being prescribed for relapsed/refractory AML patients who had already used various treatment drugs and were waiting for the launch of Vyxeos. Basically, Vyxeos is a drug that is expected to be most effective for patients who are 65 to 70 years old and who are suitable for chemotherapy. We hope that the drug will first be used in that age group and that its efficacy will be recognized. The peak sales figures in the data from the Central Social Insurance Medical Council were based on the assumption that the drug would be prescribed within the range of 60 to 75 years of age for new-onset AML, for which there is evidence. In reality, the product got off to a strong start because it was also prescribed for patients with relapsed/refractory AML and other conditions who were awaiting treatment. We think that the further growth of prescriptions for new-onset AML will lead to further growth, regardless of age group. The sales guidance will be provided after the situation has been confirmed for a while, as it has only been six months since it was launched.