Outline of Consolidated Financial Results for the 2nd Quarter (Interim Period) Ended September 30, 2024

November 15, 2024
NIPPON SHINYAKU CO., LTD.

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Agenda

01
- 2Q FY2024 Financial Results and Full-Year Forecast
- Update on CAP-1002

02
- R&D Pipeline
- Update on Viltepso

03
- Introduction of new products (Jaypirca and Yuvanci)

2Q FY2024 RESULTS AND FULL-YEAR FORECASTS

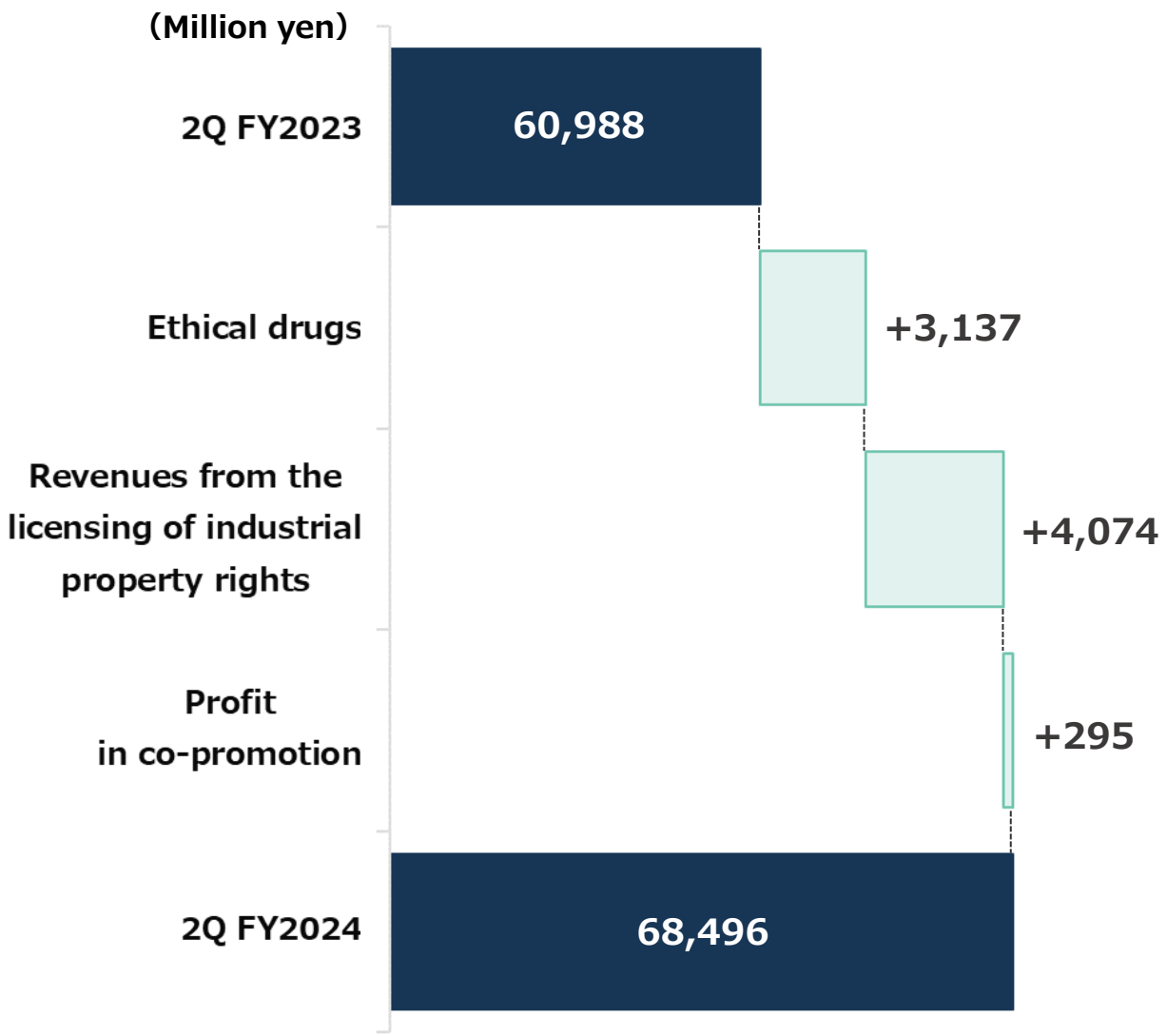
Toru Nakai

Representative Director, President

2Q (Interim Period) FY2024 Summary

(Million yen)	2Q FY2023		2Q FY2024		YoY Change	
	Results	Ratio	Results	Ratio	Amt	%
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%**

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

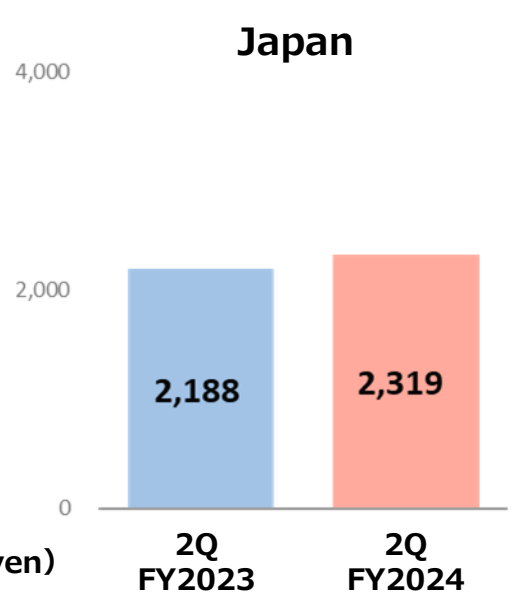
Profit in co-promotion 4,700 million yen
(+295 million yen, +6.7%, YoY)

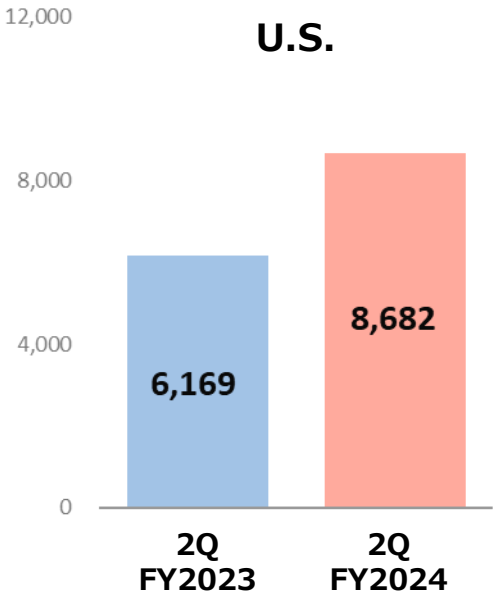
- ✓ Sales growth of Opsumit and Erleada

Sales Trends of Viltepso® (viltolarsen)

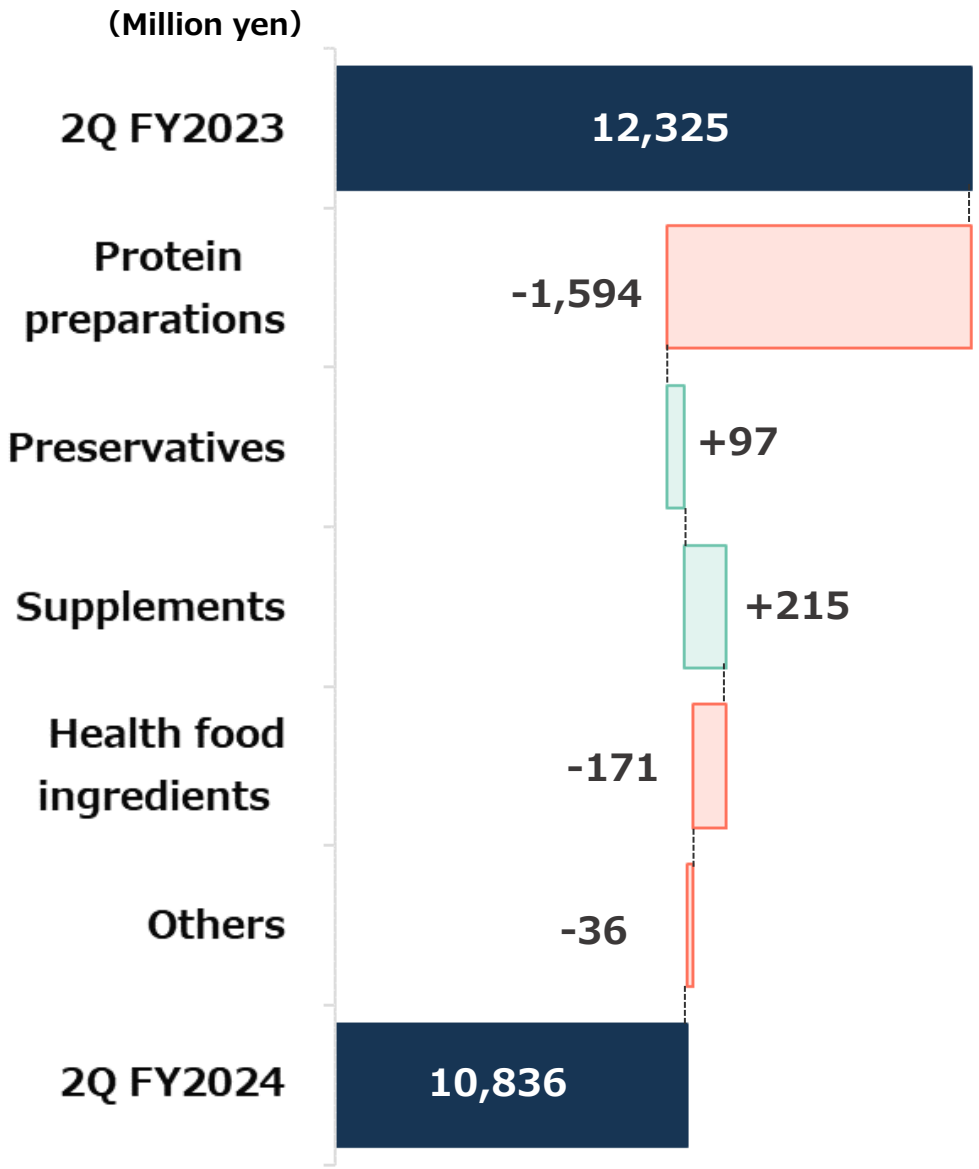
(Million yen)		2Q FY2023 Results	2Q FY2024 Results	YoY Change Amt	YoY Change %	
Viltepso	Japan	2,188	2,319	+131	+6.0%	✓The number of patients currently being administered is more than two-thirds of the peak number of 128 patients in the data from Chuikyo (Central Social Insurance Medical Council) . ✓Currently 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





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)

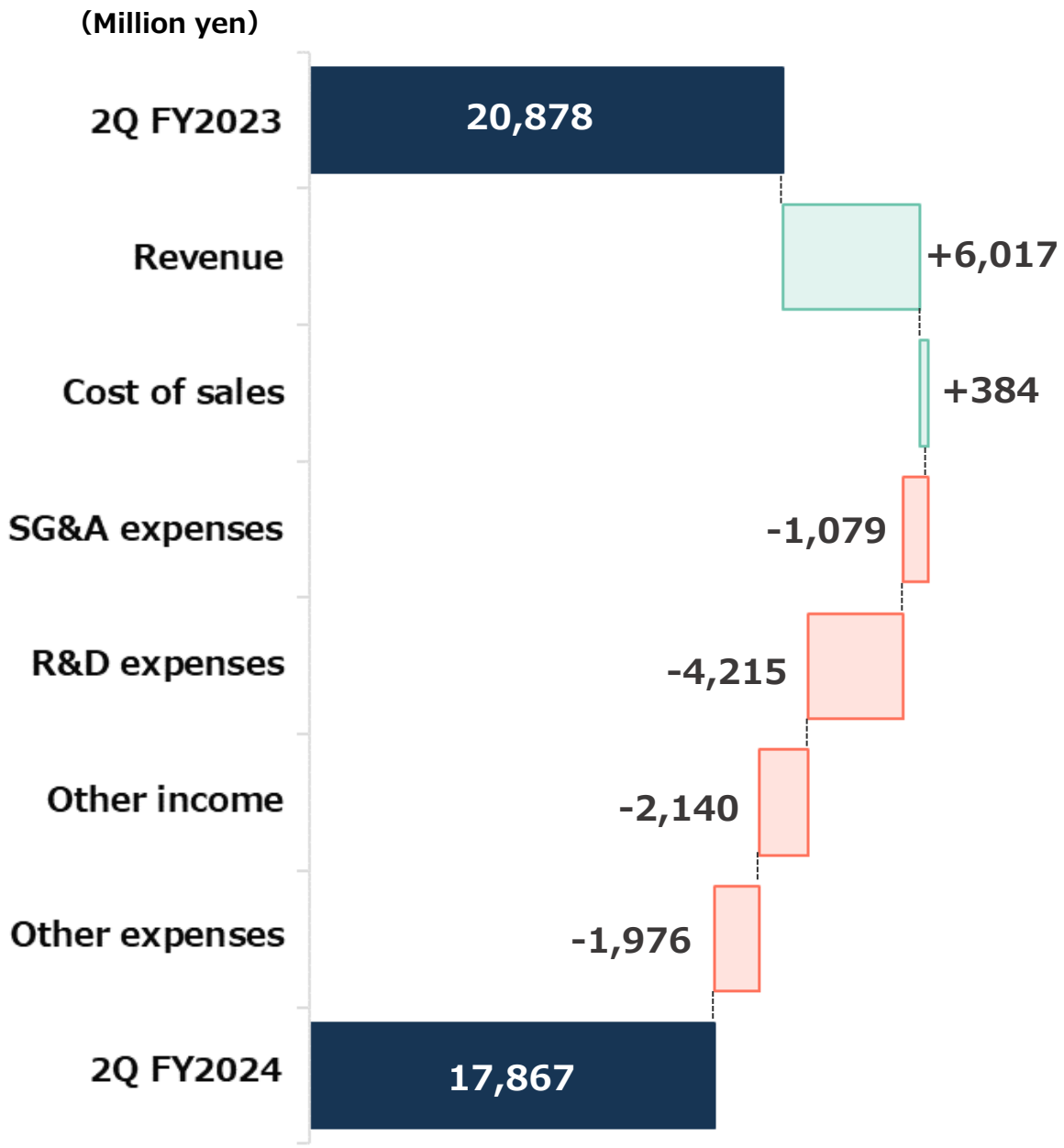
- ✓ Recovery in food service-related business due to active tourism and excursions

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)

Operating Profit



Revenue 79,332 million yen
(+6,017million yen, +8.2%, YoY)

- ✓ Sales of Viltepso, Uptravi, and new product Vyxeos
- ✓ Increase in revenue from industrial property rights and the U.S. sales of Viltepso.

Cost of sales 24,935 million yen
(-384 million yen, -1.5%, YoY)
The ratio was improved by 3.1 points YoY.

- ✓ Negative impact of NHI drug price revision.
- ✓ Cost of sales ratio improvement due to factors such as revenues from industrial property rights and the change in sales segment mix (pharma vs. food)

SG&A expenses 18,031 million yen
(+1,079 million yen, +6.4%, YoY)

- ✓ Increase in labor costs and commission for promotional activities of Uptravi

R&D expenses 16,732 million yen
(+4,215 million yen, +33.7%, YoY)

- ✓ Increase in contract research expense

Other income 455 million yen
(-2,140 million yen, -82.5%, YoY)
Other expenses 2,219 million yen
(+1,976 million yen, +815.0%, YoY)

- ✓ Foreign exchange loss incurred this FY, replacing the foreign exchange gain of the previous FY

Revised Business Forecast for FY2024 (consolidated)

(Million yen)	FY2023		FY2024		YoY Change	
	2Q Results	Ratio	2Q Results	Ratio	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.

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)

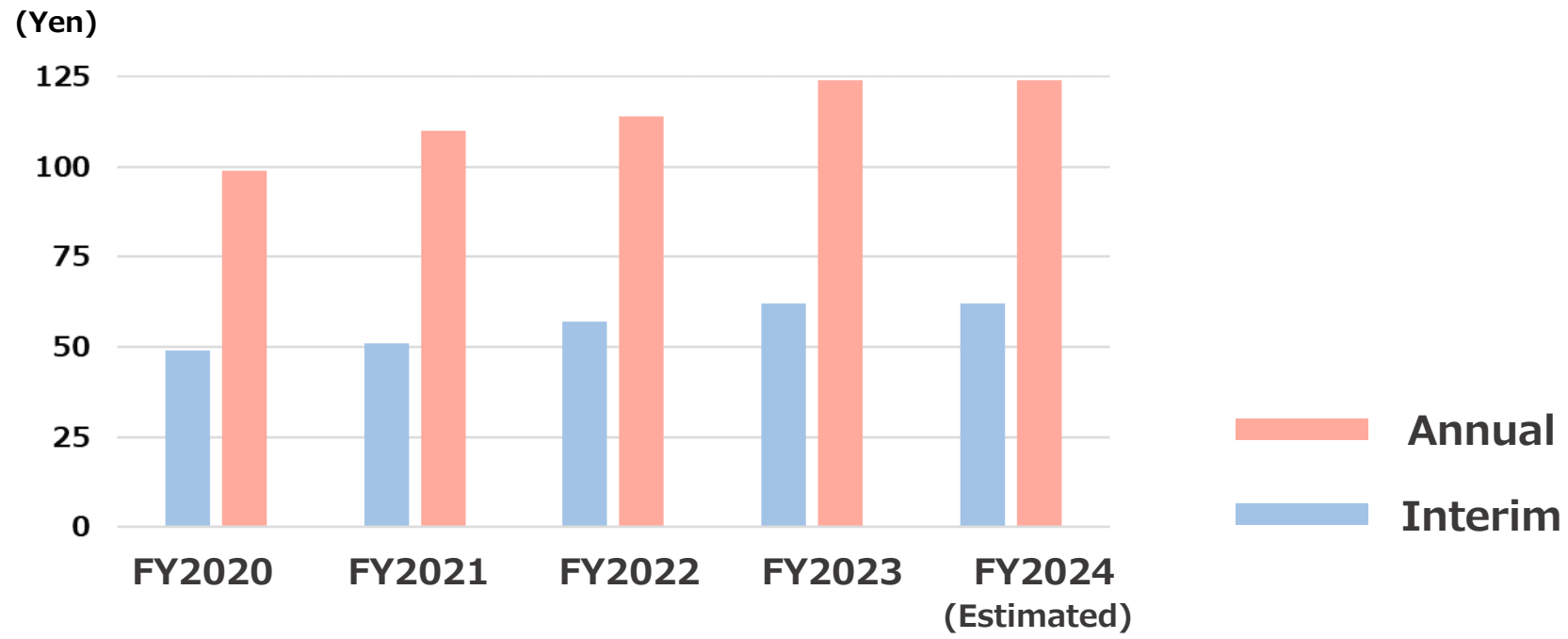
✓ Increase in research and development costs for in-licensed products

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.

Dividends Forecast

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



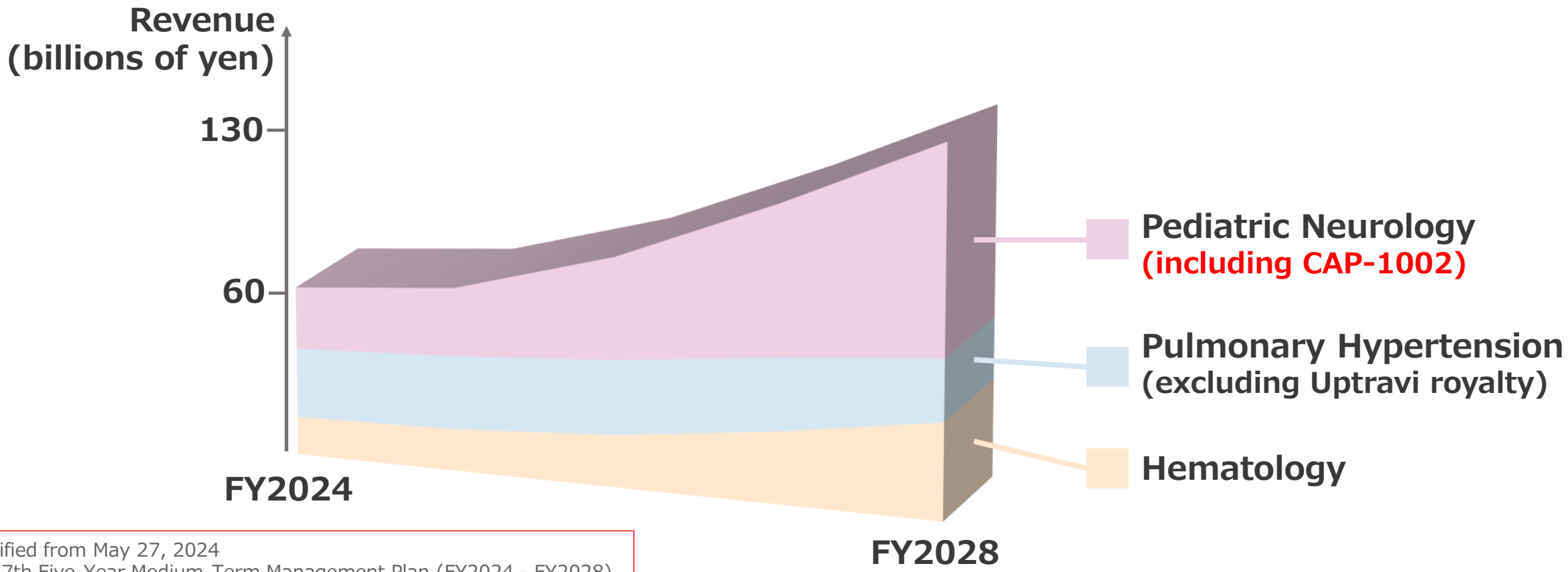
UPDATE ON CAP-1002 (DERAMIOCEL)

for the Treatment of Duchenne Muscular Dystrophy Cardiomyopathy

Key Theme I : Fostering Growth Drivers to Replace Uptravi

Global revenue of three focus areas in FY2028⇒ Aiming for over 130 billion yen

Image of sales growth during the 7th Medium-Term Management Plan



Modified from May 27, 2024
The 7th Five-Year Medium-Term Management Plan (FY2024 - FY2028)
-For Global Growth Beyond the Cliff-p.28

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

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

October 2024: Rolling BLA[3] submission initiated

By end of 2024: Rolling BLA submission planned to complete

By 2H of 2025: Potential PDUFA (FDA approval)

Capricor is seeking full approval with a DMD-cardiomyopathy label

3: Biologics License Application (BLA)

Key Theme I : Fostering Growth Drivers to Replace Uptravi

Within the period of this plan, we plan to launch an average of at least two new products per year. We aim to acquire at least one in-licensed product each year. We will conduct an additional P3 study of Viltepso and aim to launch it in Europe and China.

Target for launching new products

	FY 2024	FY 2025	FY 2026	FY 2027	FY 2028
Domestic	NS-87 (VYXEOS) : high-risk AML※		NS-401 : BPDCN※	NS-089/NCNP-02 : DMD	NS-050/NCNP-03 : DMD
	LY3527727 (pirtobrutinib) : MCL※		ZX008 (Fintepla) : CDKL5 gene deficiency	GA101 (Gazyva) : SLE※ without nephropathy	NS-051/NCNP-04 : DMD
	NS-304 (Uptravi) : pediatric PAH※		GA101 (Gazyva) : lupus nephritis		
			GA101 (Gazyva) : pediatric nephrosis		
Overseas		DMD cardiomyopathy	CAP-1002 (U.S.) : DMD	NS-089/NCNP-02 (U.S.) : DMD	NS-050/NCNP-03 (U.S.) : DMD
					NS-051/NCNP-04 (U.S.) : DMD
					NS-065/NCNP-01 (EU,CN) : DMD

Modified from May 27, 2024
The 7th Five-Year Medium-Term Management Plan (FY2024 - FY2028) -For Global Growth Beyond the Cliff-p.26

※ high-risk AML: high-risk acute myeloid leukemia; MCL: mantle cell lymphoma; pediatric PAH: pediatric pulmonary arterial hypertension; BPDCN: blastic plasmacytoid dendritic cell tumor; SLE : Systemic Lupus Erythematosus
※ The launch date for pirtobrutinib (LY3527727) for chronic lymphocytic leukemia has not been determined.

R&D PIPELINE

Kazuchika Takagaki
Director, Research & Development

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.

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.

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

UPDATE ON VILTEPSO

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.**

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

<Target Patients>

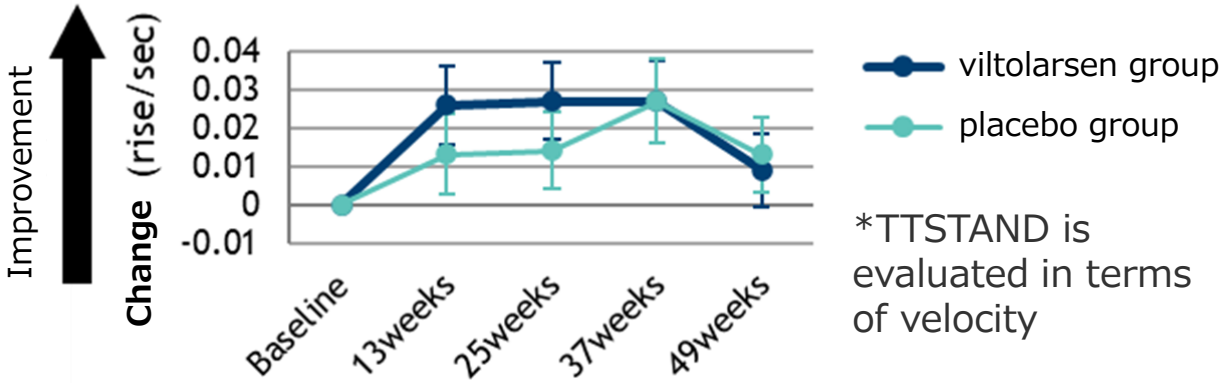
DMD patients between **4 and 7 years of age**, with a deletion of the dystrophin gene that can be treated by exon 53 skipping.

<Efficacy>

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

*Change from baseline after 48 weeks of treatment

TTSTAND (velocity)*



*TTSTAND is evaluated in terms of velocity

- **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.

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.

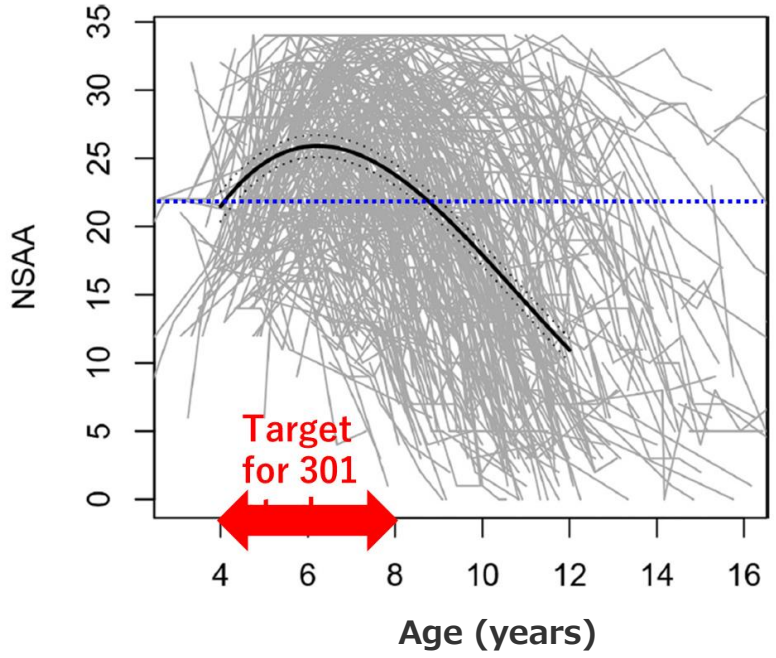
Limitations of Study 301: Heterogeneity in DMD Disease Progression

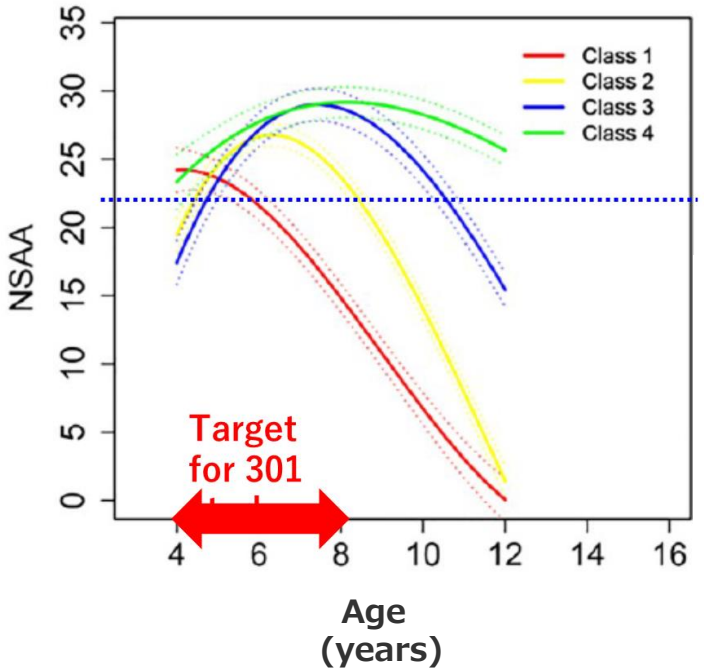
Patients between 4 and 8 years of age enrolled in Study 301

motor function

- is rising with growth.
- has been reached a plateau.
- is beginning to decline due to disease progression.

There was a mixture of patient groups with different motor functions.





NSAA (North Star Ambulatory Assessment)
: A method of assessment that comprehensively evaluates the motor function of DMD patients

class 1:patients which showed the fastest progression with most NSAA total scores falling to ≤ 5 around 10 years of age
class 2:patients with NSAA total scores falling to ≤ 5 by approximately 12 years of age
class 3: patients with NSAA total scores falling to ≤ 5 around 14 years of age
class 4:patients which showed the slowest progression, with NSAA total scores remaining > 5 to at least age 15 years.

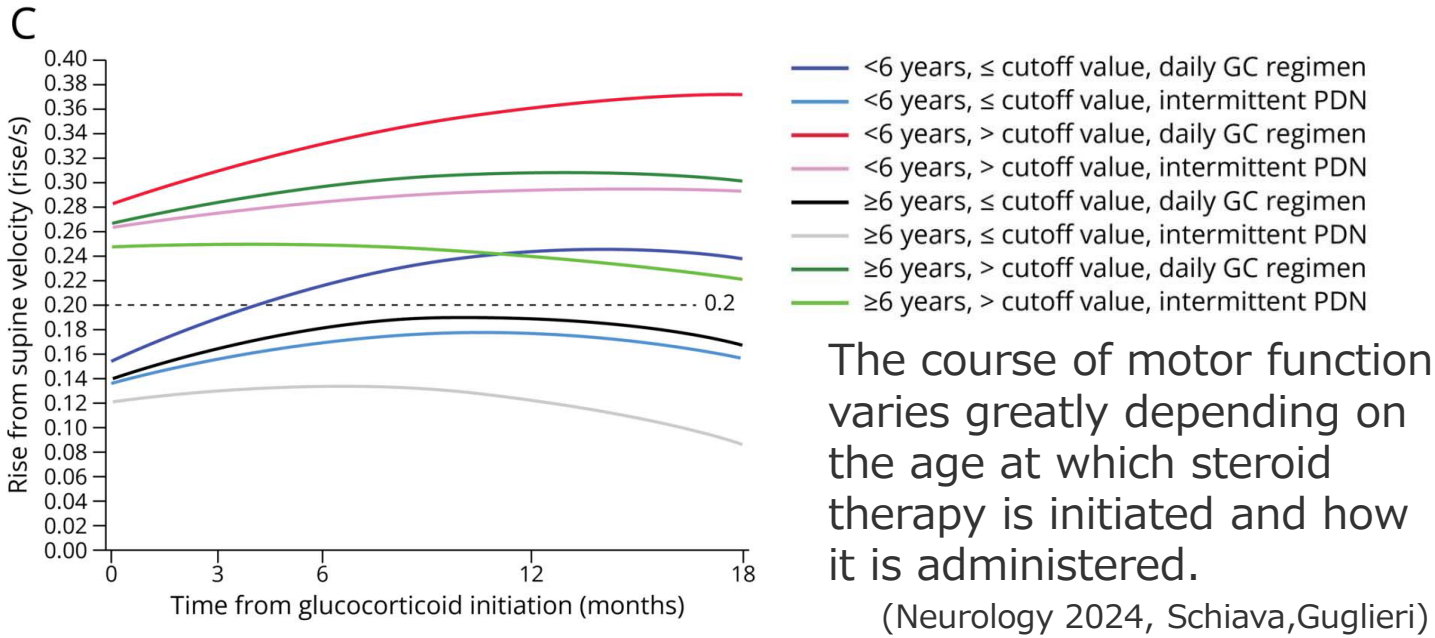
(PLOS ONE 2019, Muntoni)

It may have been more 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.

Limitations in Study 301: Duration of Study

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

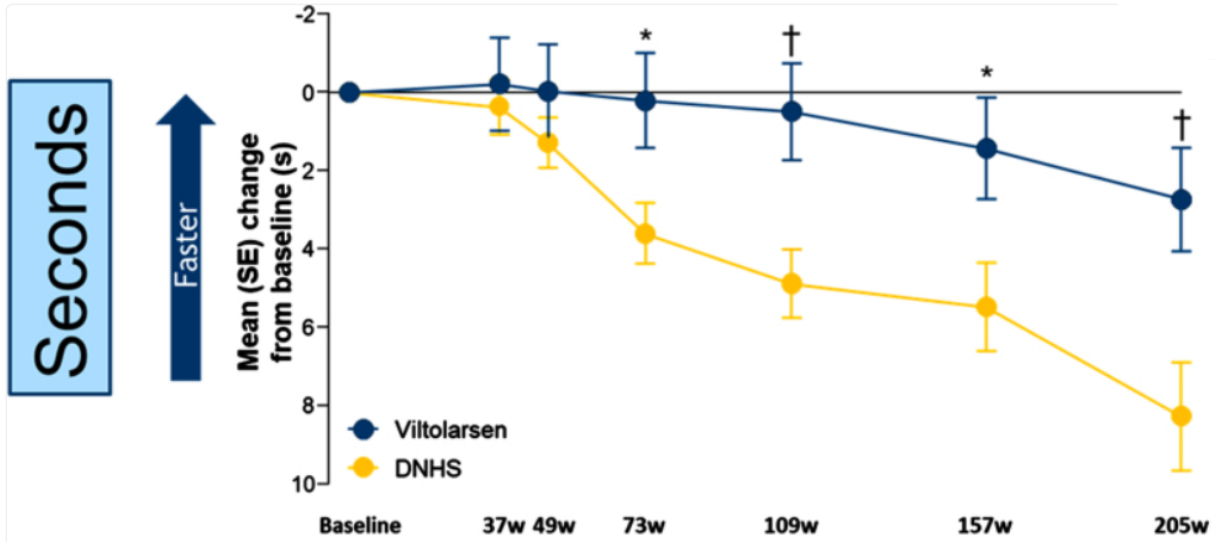
Improvements in motor function have been observed with long-term administration of viltolarsen.

(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)

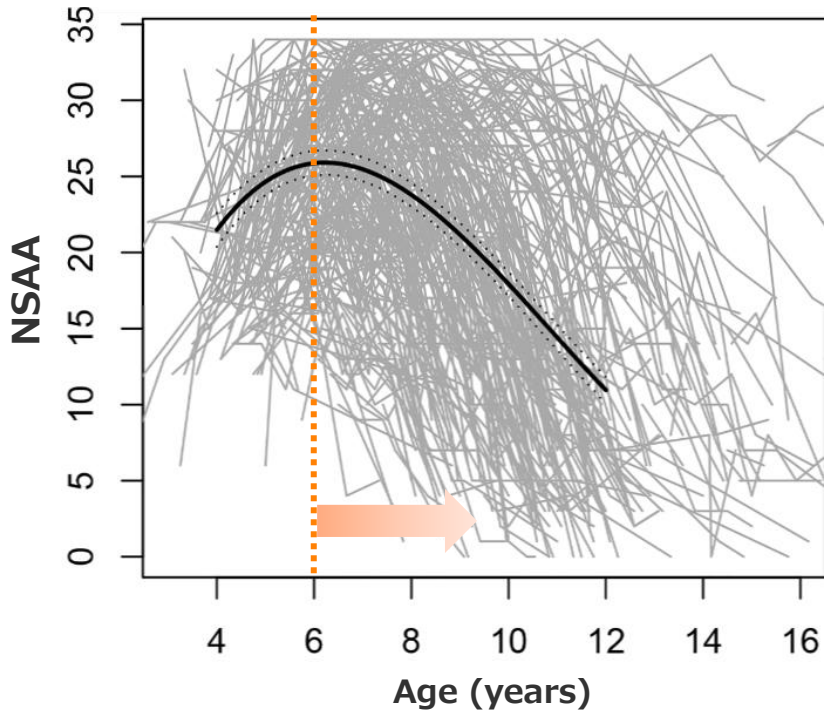
(J Neuromuscul Dis 2023, Clemens)

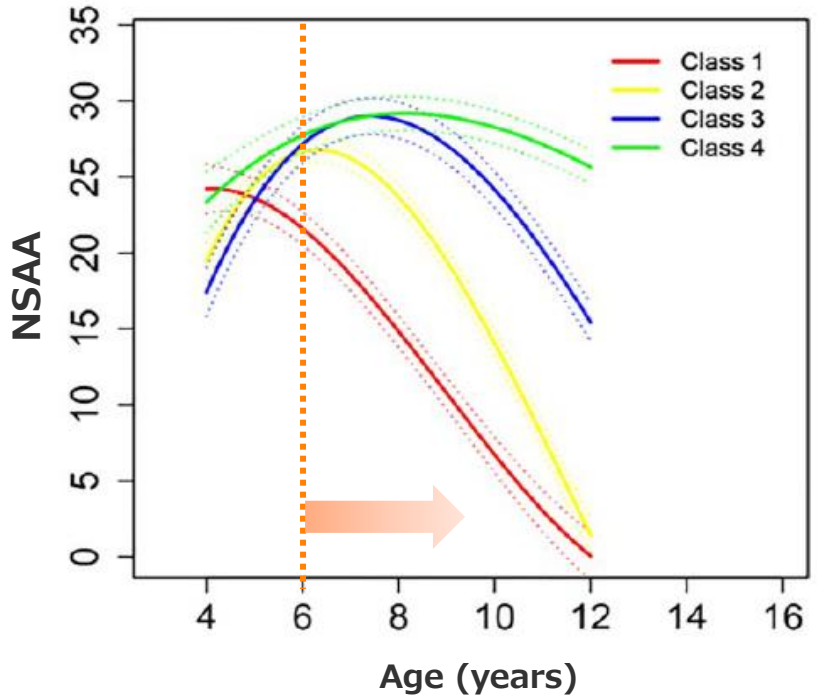
The study design to be proposed as the additional Phase III study (Study 303)

<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.

INTRODUCING NEW PRODUCTS

Shouzou Sano

Managing Director, Sales and Marketing

About Jaypirca® tablets

抗悪性腫瘍剤 可逆的非共有結合型BTK注）阻害剤

注）BTK：Bruton's Tyrosine Kinase（ブルトン型チロシンキナーゼ）

薬価基準収載

ジャイパーカ®錠 50mg 100mg

Jaypirca® Tablets 50,100mg

ピルトブルチニブ錠

劇薬 処方箋医薬品*

*注意－医師等の処方箋により使用すること

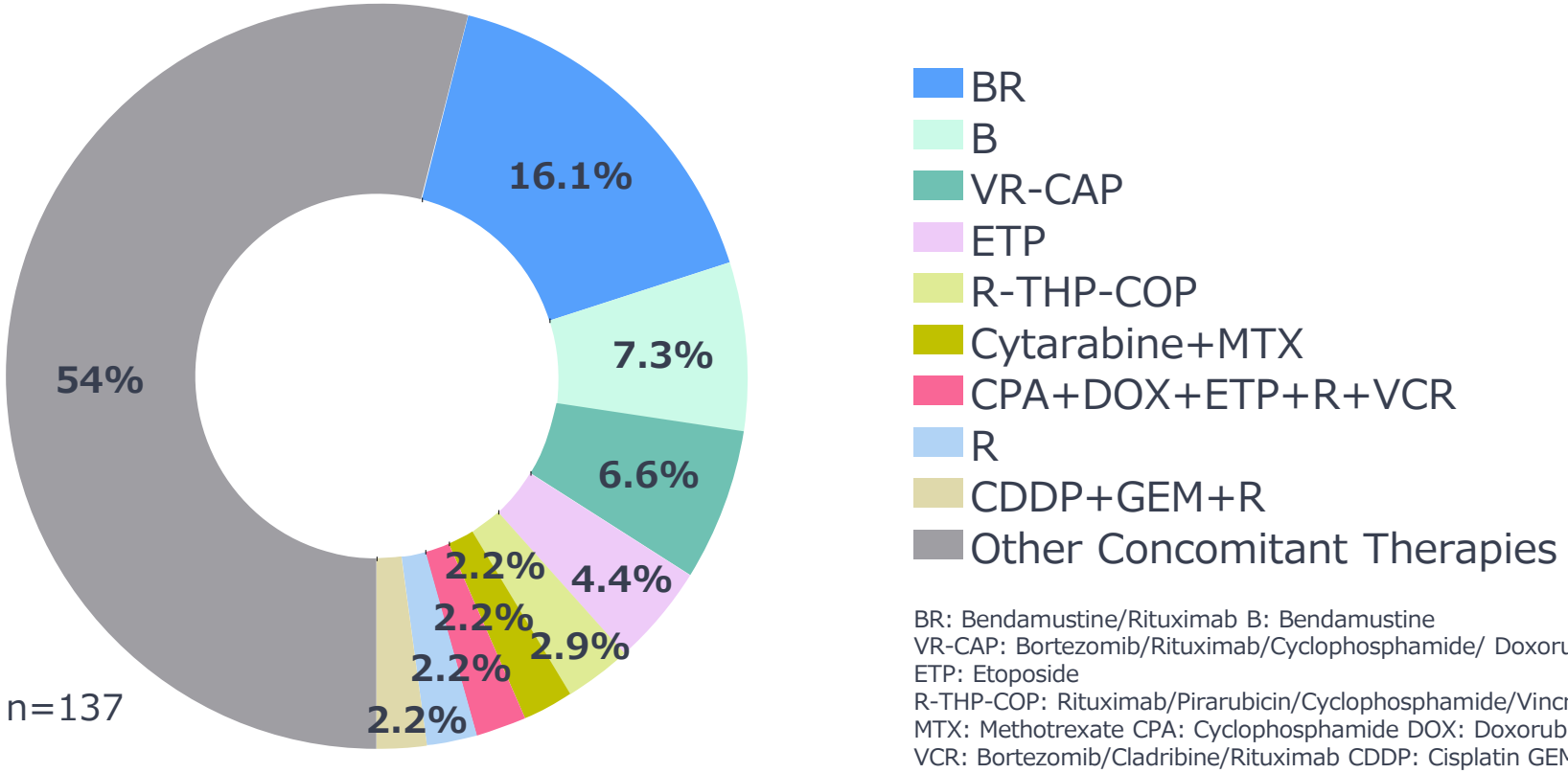
Product Overview

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.					

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.]

What is Jaypirca®?

Currently, BTK inhibitors approved in Japan and overseas covalently bind to C481 in the ATP-binding pocket.1)

On the other hand, Jaypirca has been reported to inhibit the BTK pathway even in the presence of the C481S mutation by non-covalently binding to multiple amino acids different from C481 in the ATP-binding pocket. 2,3)

Covalent binding BTK inhibitor

Reversible noncovalent binding BTK inhibitor (Pirtobrutinib)

1) Thompson PA, Tam CS. Blood. 2023; 141: 3137-3142. [Conflict of interest: includes authors receiving research funding, consulting fees, etc. from Eli Lilly Co.,Ltd.]
2) In-house data: pharmacological study of Pirtobrutinib
3) Gomez EB, et al. Blood. 2023; 142: 62-72. [Conflict of interest: This study was funded by Eli Lilly and the authors are employees of the company.]
(4) Schultze MD, et al. Ann Pharmacother. 2024 [Epub ahead of print].
Figures are from 1), 2), and 4).

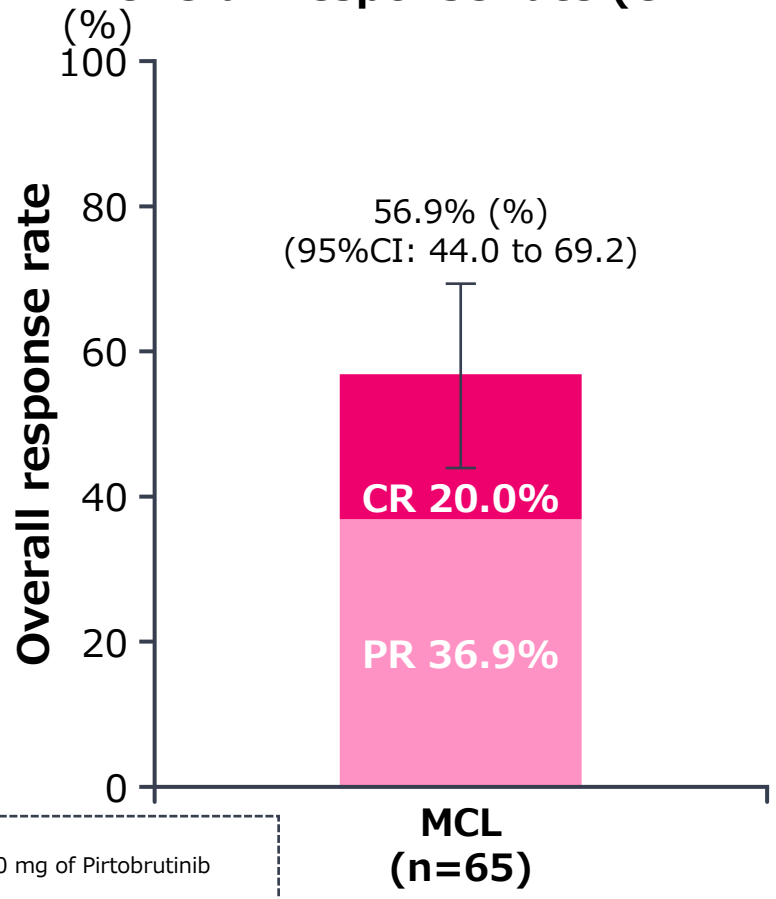
Global Phase I/II study (including dose finding study: BRUIN-18001)

[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)**



● **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 (%)

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.

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.

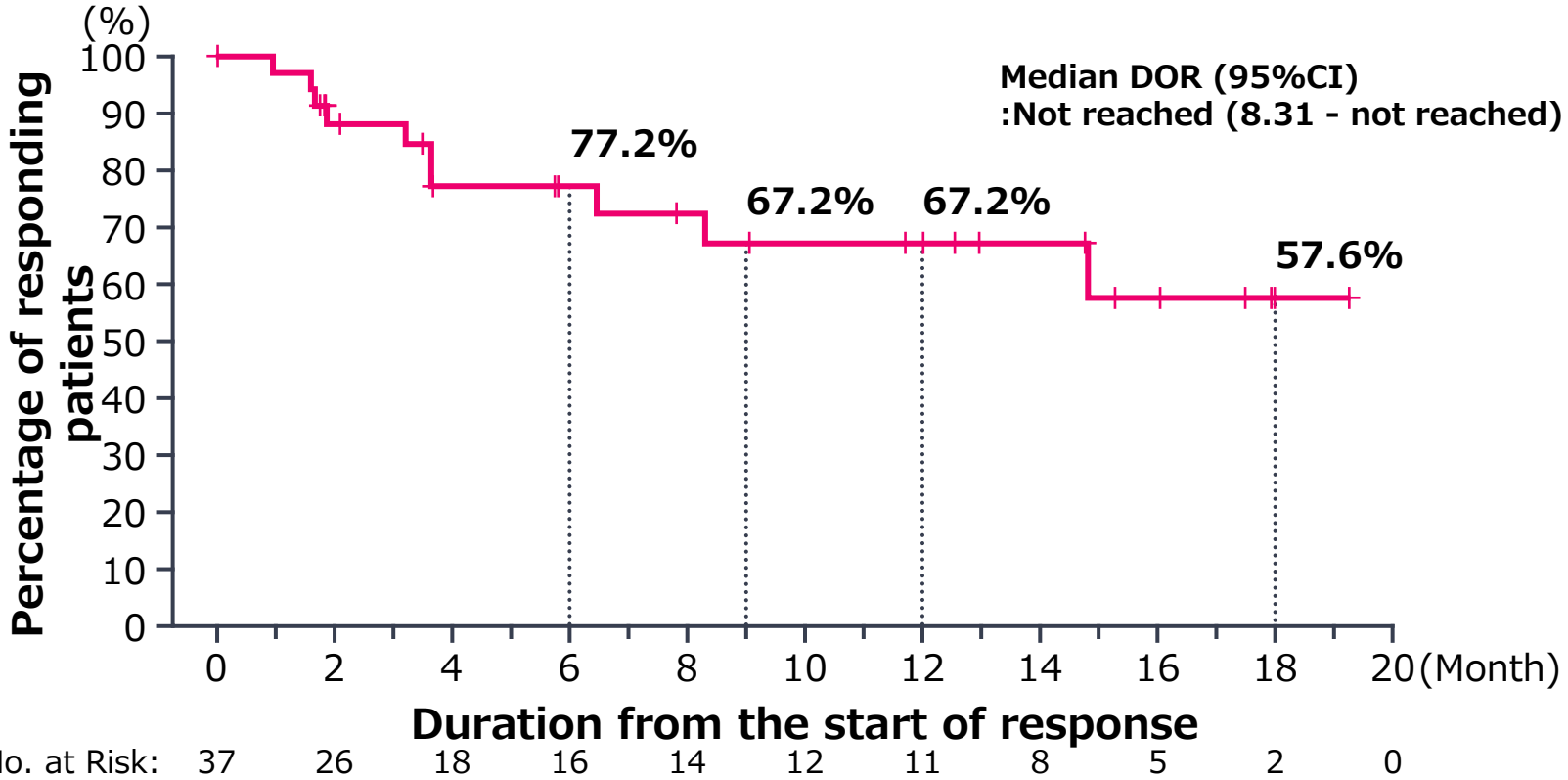
In-house data: Phase I/II study of Pirtobrutinib (LOXO-BTK-18001 study) (evaluation data at the time of approval)

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)**



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%).

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

About YUVANCI® Combination 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

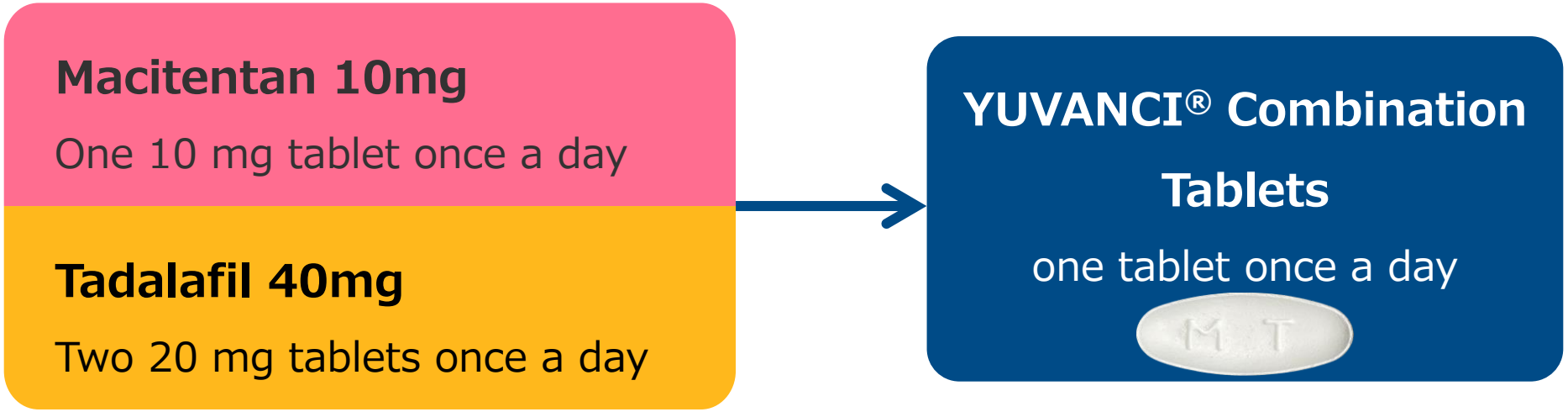
a: Recommended class b: Level of evidence

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

What is YUVANCI® Combination Tablets?

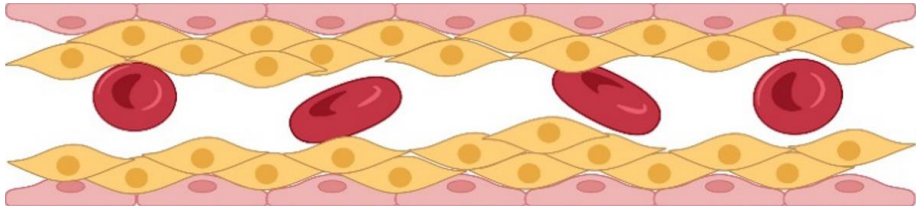
YUVANCI® Combination Tablets is the first oral combination drug approved in Japan for the treatment of pulmonary arterial hypertension that contains the endothelin receptor antagonist (ERA) macitentan and the selective phosphodiesterase 5 (PDE5) inhibitor tadalafil.

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

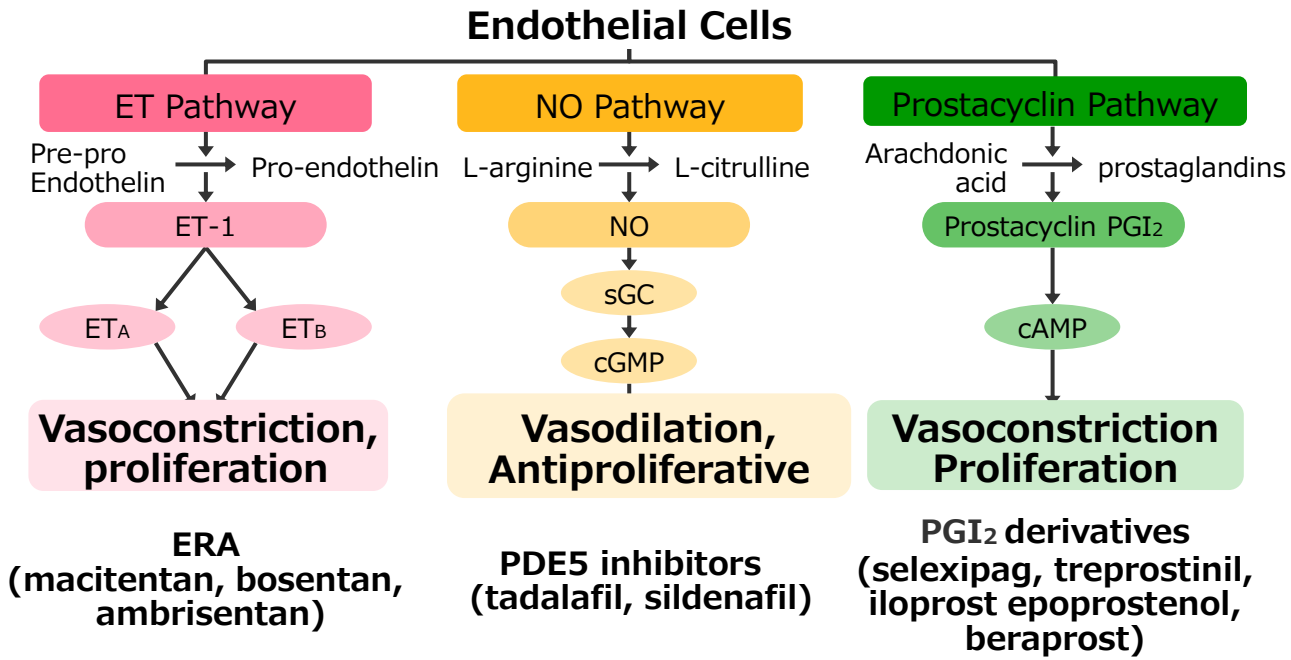


Treatment pathway of PAH and YUVANCI® Combination Tablets

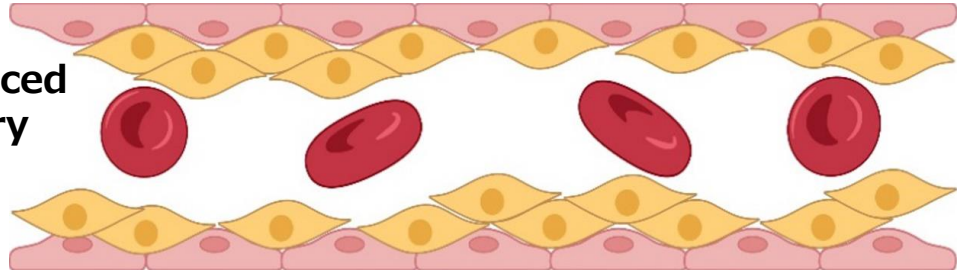
High resistance to blood flow due to vasoconstriction of pulmonary artery in PH



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



Medication-induced pulmonary artery vasodilation



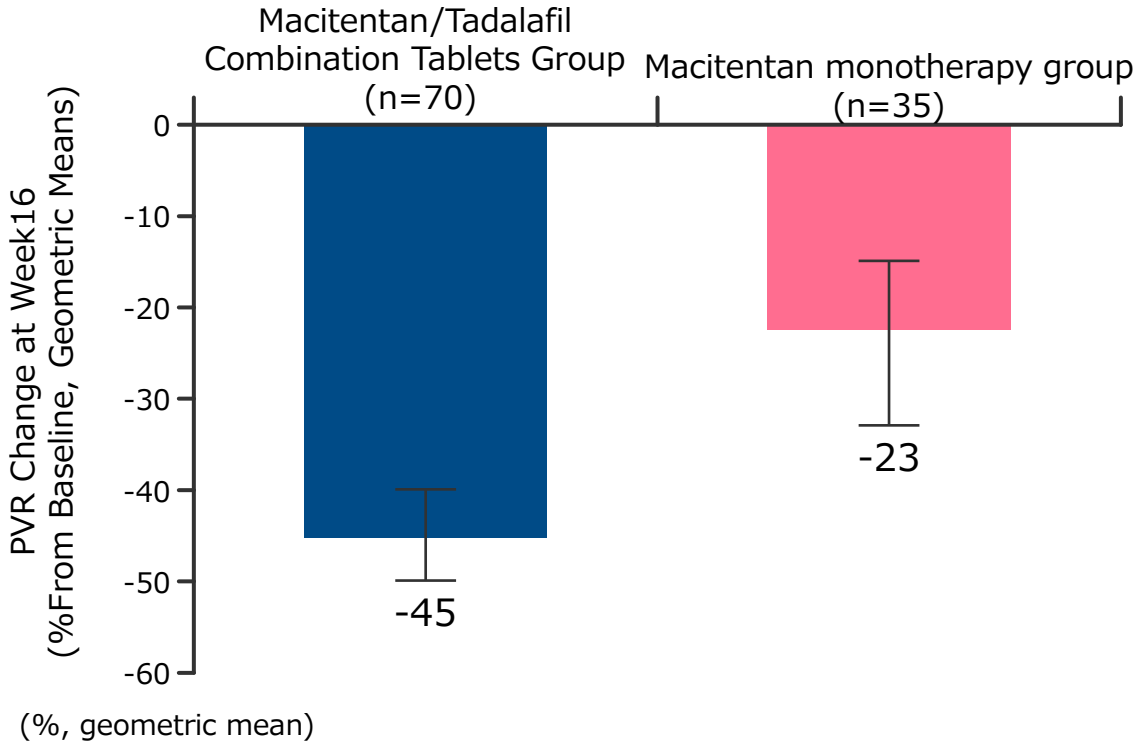
cAMP: cyclic adenosine monophosphate
cGMP: cyclic guanosine monophosphate
ET: endothelin
ERA: endothelin receptor antagonist
NO: nitric oxide
PDE5: phosphodiesterase 5
PGI_2: prostacyclin
sGC: soluble guanylate cyclase

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

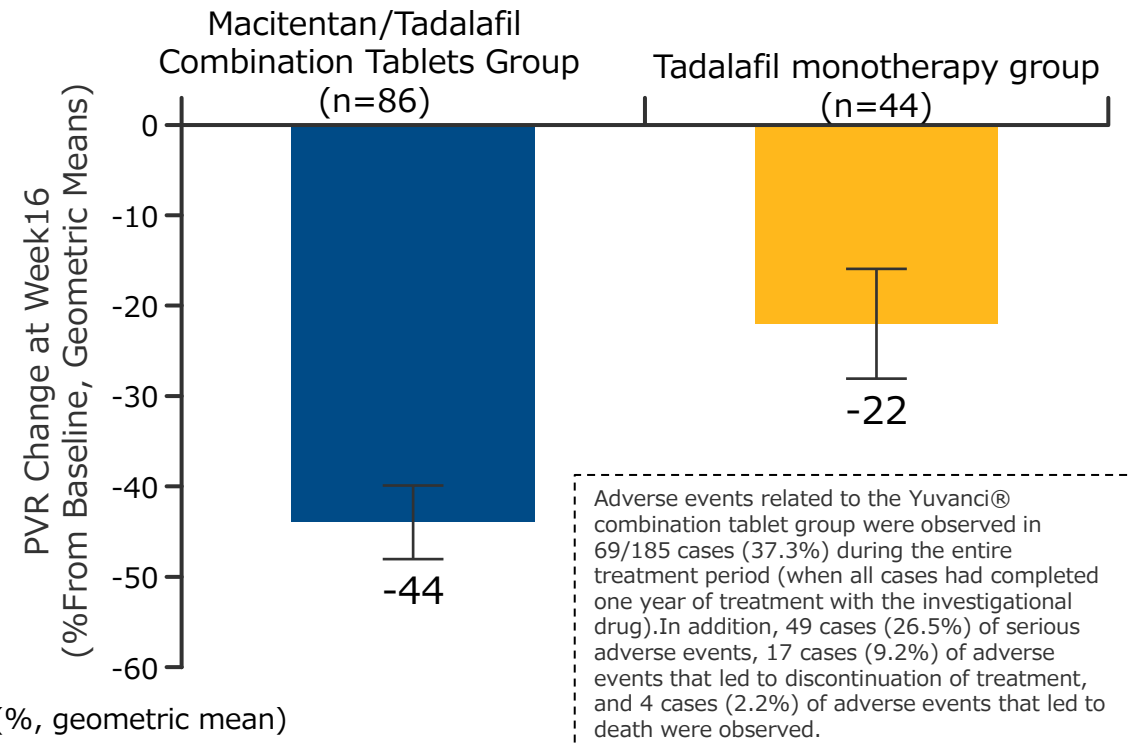
YUVANCI® Combination Tablets "A DUE Study" (PⅢ Study)

The significant improvement in pulmonary vascular resistance (PVR) in the YUVANCI® combination tablets group compared to the macitentan or tadalafil monotherapy groups validated the superiority of the YUVANCI® combination tablets over each of the monotherapies.

Macitentan and Tadalafil Combination Tablets Group vs. Macitentan monotherapy group (16 weeks)
Ratio of Geometric Mean (95% confidence limits): 0.71 (0.61-0.82); P<0.0001



Macitentan and Tadalafil Combination Tablets Group vs. Tadalafil monotherapy group (16 weeks)
Ratio of Geometric Mean (95% confidence limits): 0.72 (0.64-0.80); P<0.0001



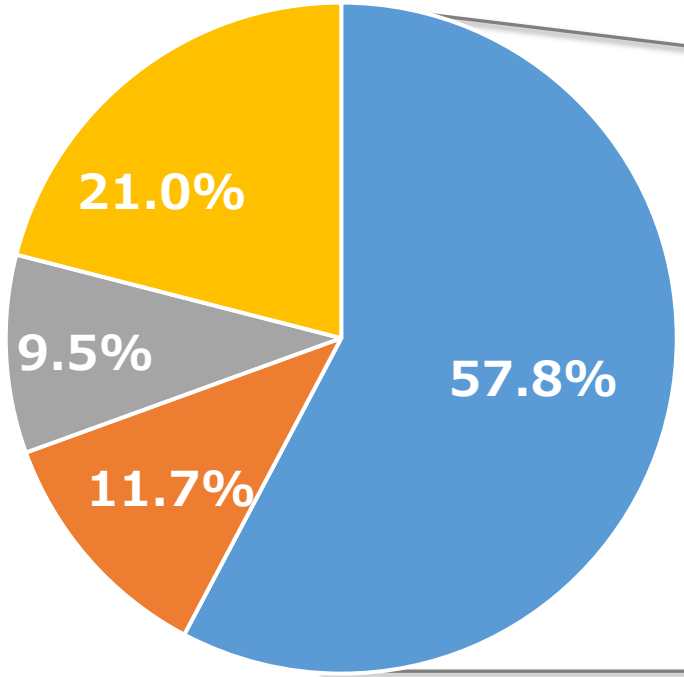
Adverse events related to the Yuvanci® combination tablet group were observed in 69/185 cases (37.3%) during the entire treatment period (when all cases had completed one year of treatment with the investigational drug).In addition, 49 cases (26.5%) of serious adverse events, 17 cases (9.2%) of adverse events that led to discontinuation of treatment, and 4 cases (2.2%) of adverse events that led to death were observed.

*The Macitentan-Tadalafil group in the figure indicates the Yuvanci® combination tablet group.

Grünig E, et al. J Am Coll Cardiol. 2024; 83: 473-484. [Conflict of interest: This study was supported by Janssen Pharmaceutical Companies of Johnson and Johnson].

Pulmonary Hypertension Market in Japan (Estimated Patient Percentage)

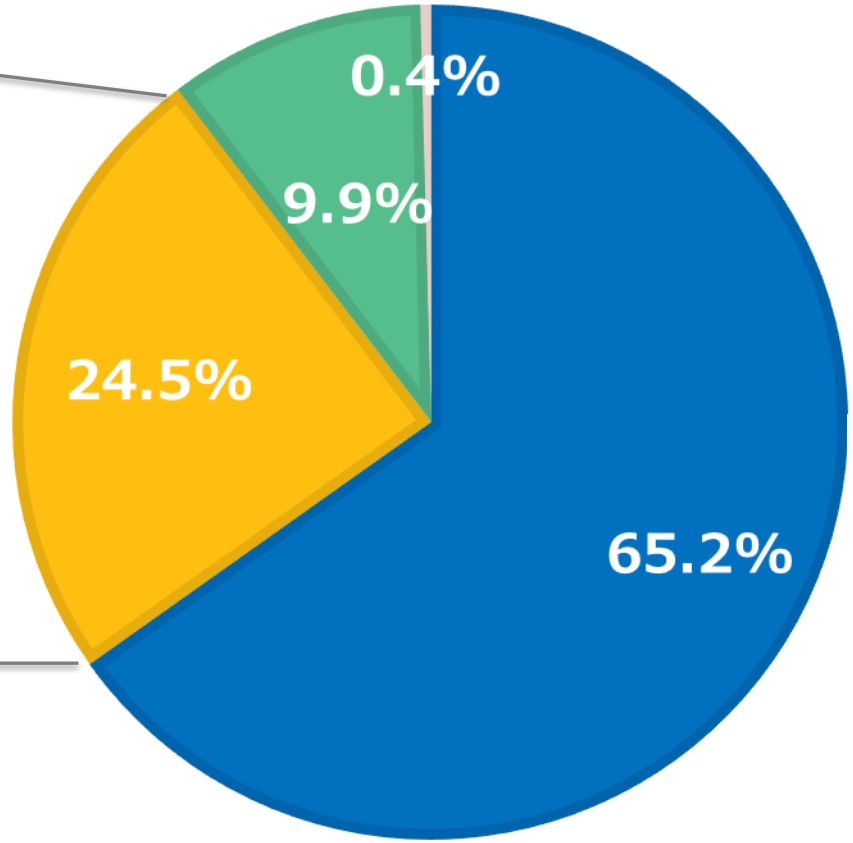
Two-drug combination Treatment Status



NO + ERA　ERA + PGI2　NO + PGI2
Combination of 2 agents and others

NO: tadalafil, sildenafil, riociguat　ERA: macitentan, bosentan, ambrisentan
PGI2: selexipag, treprostinil, iloprost, epoprostenol, beraprost
(The estimated number of patients for each drug includes prescriptions for generics.)

PAH medications Concomitant uzse



single-agent
Combination of two drugs
Combination of three drugs
Four or more agents

REFERENCE MATERIALS

Sales Forecast in Pharmaceutical Segment

(Million yen)

Brand name	Indications	2Q FY2023 Results	2Q FY2024 Results	YoY Change Amt	YoY Change %	FY2024 Forecast
Viltepso		8,358	11,002	+2,643	+31.6%	21,400
(Japan)	Duchenne muscular dystrophy	(2,188)	(2,319)	(+131)	(+6.0%)	(4,600)
(U.S.)		(6,169)	(8,682)	(+2,512)	(+40.7%)	(16,800)
Uptravi	pulmonary arterial hypertension/ chronic thromboembolic pulmonary hypertension	6,465	7,474	+1,008	+15.6%	15,000
Vidaza	myelodysplastic syndrome/ acute myeloid leukemia	5,526	2,757	-2,769	-50.1%	4,800
Gazyva	CD20-positive follicular lymphoma/ CD20-positive chronic lymphocytic leukemia	2,439	2,452	+13	+0.5%	4,800
Vyxeos	high-risk AML	-	2,236	+2,236	-	4,600
Tramal/Onetram	cancer pain, chronic pain	2,080	1,470	-609	-29.3%	2,700
Defitelio	sinusoidal obstruction syndrome	1,099	1,277	+178	+16.3%	2,400
Cialis	erectile dysfunction	1,250	1,219	-31	-2.5%	2,400
Zalutia	urinary disorder caused by benign prostatic hyperplasia	1,161	903	-258	-22.2%	1,600
Adcirca	pulmonary arterial hypertension	1,190	893	-297	-25.0%	1,600
Erizas	allergic rhinitis	584	511	-73	-12.5%	2,000
Profit in co-promotion		4,404	4,700	+295	+6.7%	9,400
Revenues from the licensing of industrial property rights		18,580	22,655	+4,074	+21.9%	44,100
Revenue		60,988	68,496	+7,507	+12.3%	135,500

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 for every 1 yen depreciation of the yen.

Sales Forecast in Functional Food Segment

(Million yen)	2Q FY2023		2Q FY2024		YoY Change		FY2024
	Results	Ratio	Results	Ratio	Amt	%	Forecast
Protein preparations	8,487	68.9%	6,893	63.6%	-1,594	-18.8%	13,000
Preservatives	1,522	12.3%	1,620	15.0%	+97	+6.4%	3,200
Supplements	987	8.0%	1,202	11.1%	+215	+21.8%	3,100
Health food ingredients	659	5.4%	487	4.5%	-171	-26.1%	1,100
Others	668	5.4%	632	5.8%	-36	-5.4%	1,100
Revenue	12,325	100.0%	10,836	100.0%	-1,489	-12.1%	21,500

Consolidated Balance Sheet

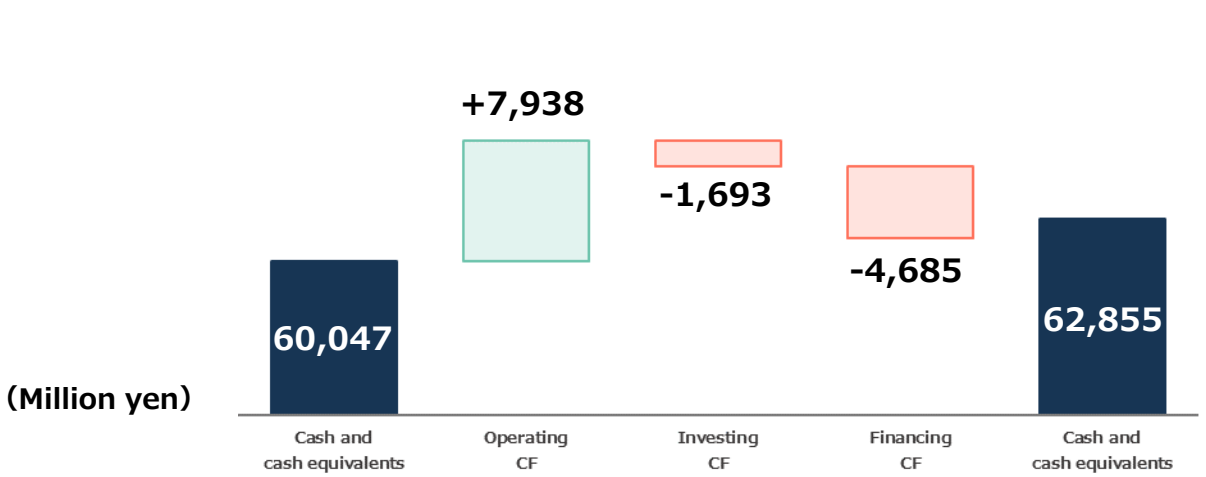
(Million yen)	End of 2Q FY2023	End of 2Q FY2024	Change Amt		End of 2Q FY2023	End of 2Q FY2024	Change Amt
Assets	263,404	268,542	+5,138	Liabilities	42,870	33,290	-9,579
Current assets	164,285	159,826	-4,458	Current liabilities	37,336	27,712	-9,624
Non-current assets	99,119	108,716	+9,596	Non-current liabilities	5,533	5,578	+45
				Equity	220,534	235,252	+14,718
Total aseets	263,404	268,542	+5,138	Total liabilities and equity	263,404	268,542	+5,138

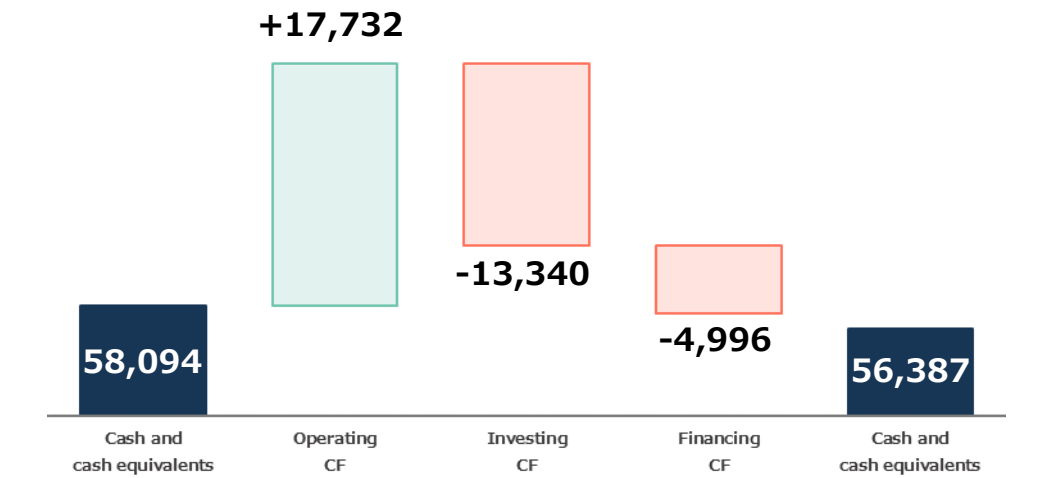
Assets	
Cash and cash equivalents	-1,706
Intangible assets	+3,959
Other financial assets (non-current)	+6,961

Liabilities and Shareholders' Equity	
Trade and other payables	-7,077
Income taxes payable	-2,038
Retained earnings	+12,197

Consolidated Statements of Cash Flows

(Million yen)	2Q FY2023 Results	2Q FY2024 Results	YoY Change Amt
Operating activities	7,938	17,732	+9,794
Investing activities	-1,693	-13,340	-11,646
Financing activities	-4,685	-4,996	-311
Cash and cash equivalents at end of period	62,855	56,387	-6,467





Pipeline（1/2）

Stage	Code No. (Generic name)	Origin	Application type	Indications	Schedule	Country
Launch P3	NS-065/NCNP-01 (viltolarsen)	In-house	NME	Duchenne muscular dystrophy	—	Japan/U.S.
Preparing for launch	ACT-064992D (macitentan/ tadalafil)	Co-promotion Janssen Pharmaceutical K.K.	NME	pulmonary arterial hypertension	Approval : September 2024	Japan
NDA filing	NS-304 (selexipag)	In-house	New dose New indication	pediatric pulmonary arterial hypertension	Study Completion : FY 2025 Application : April 2024	Japan
Rolling submission	CAP-1002 (deramiocel)	Partnership Capricor Therapeutics, Inc.	NME	Duchenne muscular dystrophy cardiomyopathy	Application completion : End of 2024	U.S.
P3	ZX008 (fenfluramine hydrochloride)	Distribution partnership UCB S.A.	New indication	CDKL5 deficiency disorder	Study Completion : FY2026	Japan
	GA101 (obinutuzumab)	In-license Chugai Pharmaceutical Co., Ltd.	New indication	lupus nephritis	Projected submission : 2026	Japan
				pediatric nephrotic syndrome	Projected submission : 2026	Japan
				extra renal lupus	Projected submission : 2027 and beyond	Japan
	CAP-1002 (deramiocel)	Partnership Capricor Therapeutics, Inc.	NME	Duchenne muscular dystrophy	—	U.S.
	LY3527727 (pirtobrutinib)	Alliance agreement Eli Lilly Japan K.K.	New indication	mantle cell lymphoma	—	Japan
				chronic lymphocytic leukemia	—	Japan

*Schedule is based on trial end dates, etc. from jRCT or ClinicalTrials.gov.

Pipeline（2/2）

Stage	Code No. (Generic name)	Origin	Application type	Indications	Schedule	Country
P2	NS-304 (selexipag)	In-house	New indication	arteriosclerosis obliterans	Study Completion : FY2024	Japan
	NS-580	In-house	NME	endometriosis	Temporarily suspended	Japan
				chronic prostatitis/ chronic pelvic pain syndrome	Temporarily suspended	Japan
	NS-089/NCNP-02 (brogidirsen)	In-house	NME	Duchenne muscular dystrophy	Study Completion : FY2025	Japan/U.S.
	NS-229	In-house	NME	eosinophilic granulomatosis with polyangiitis	Study Completion : FY2026	Japan/U.S.
P1/2	NS-401 (tagraxofusp)	In-license The Menarini Group	NME	blastic plasmacytoid dendritic cell neoplasm	Study Completion : FY2026	Japan
	NS-050/NCNP-03	In-house	NME	Duchenne muscular dystrophy	Study Completion : FY2027	Japan/U.S.
P1	NS-917 (radgocitabine)	In-license Delta-Fly Pharma, Inc.	NME	relapsed/refractory acute myeloid leukemia	Study Completion : FY2024	Japan
	NS-025	In-house	NME	urological diseases	Study Completion : FY2024	Japan
	NS-863	In-house	NME	cardiovascular diseases	Study Completion : FY2024	Japan

*Schedule is based on trial end dates, etc. from jRCT or ClinicalTrials.gov.

NS-065/NCNP-01 (viltolarsen)

- Treatment for Duchenne muscular dystrophy -

Development Phase	・Japan : Launch ・U.S. : Launch ・Global : P3 open-label extension study in progress
Origin	Co-development : National Center of Neurology and Psychiatry
Development	Nippon Shinyaku
Mechanism of action	Exon 53 Skipping
Indication	Duchenne muscular dystrophy
Dosage form	Injection
Feature	・Improvement in symptoms and prevention of the disease progression by recovery of dystrophin protein expression ・Morpholino based oligonucleotide with possible high safety profile and maximized activity

ZX008 (fenfluramine hydrochloride)

- Treatment for rare intractable epilepsy -

Development Phase	Japan : Launch (Dravet syndrome) Japan : Launch（Lennox-Gastaut syndrome) Japan : P3 (CDKL5 deficiency disorder)
Origin	[Mar. 2019] Distribution partnership in Japan : UCB S.A. (former Zogenix, Inc.)
Development	UCB S.A. (former Zogenix, Inc.)
Mechanism of action	5-HT (serotonin) releaser with agonist activity at several 5-HT receptors
Indication	Dravet syndrome Lennox-Gastaut syndrome CDKL5 deficiency disorder
Dosage form	Oral liquid agent
Feature	・Effective for Dravet syndrome, Lennox-Gastaut syndrome and CDKL5 deficiency disorder patients refractory to existing treatment options ・ZX008 can be used in combination with other drugs, as standard of care for intractable epilepsy based on combination therapy.

LY3527727(pirtobrutinib)

- Treatment for Mantle cell lymphoma, Chronic lymphocytic leukemia -

Development Phase	・Launch (for patients with relapsed or refractory mantle cell lymphoma who are resistant or intolerant to other BTK inhibitors) ・P3 (MCL and CLL)
Origin	[Mar. 2024] Alliance agreement in Japan : Eli Lilly Japan K.K.
Development	Eli Lilly Japan K.K.
Mechanism of action	A reversible non-covalent BTK inhibitor
Indication	mantle cell lymphoma (MCL) chronic lymphocytic leukemia (CLL)
Dosage form	Oral agent
Feature	・A highly selective, non-covalent (reversible) inhibitor of the enzyme Bruton's tyrosine kinase (BTK), with having a novel binding mechanism.

CAP-1002 (deramiocel)

- Treatment for Duchenne muscular dystrophy -

Development Phase	U.S. : P3 Rolling submission for Duchenne muscular dystrophy cardiomyopathy
Origin	[Jan. 2022] Partnership for commercialization in U.S. [Feb. 2023] Partnership for commercialization in Japan : Capricor Therapeutics, Inc.
Development	Capricor Therapeutics, Inc.
Mechanism of action	Exosomes released from cardiosphere-derived cells
Indication	Duchenne muscular dystrophy cardiomyopathy Duchenne muscular dystrophy
Dosage form	Injection
Feature	・Exosomes released from this drug are expected to reduce oxidative stress, inflammation, fibrosis, and increase cell energy and myocyte generation, resulting in improvement of motor and cardiac functions. ・ Its broad applicability makes it suitable for patients regardless of the type of genetic mutation.

GA101 (obinutuzumab)

- Treatment for lupus nephritis, pediatric nephrotic syndrome, extra renal lupus -

Development Phase	Japan : P3（LN） Global : P3（PNS） Japan : P3（ERL）
Origin	[Nov. 2012] Licensed-in from : Chugai Pharmaceutical Co., Ltd.
Development	Co-development : Chugai Pharmaceutical Co., Ltd.
Mechanism of action	Anti-CD20 monoclonal antibody
Indication	lupus nephritis (LN) pediatric nephrotic syndrome (PNS) extra renal lupus (ERL)
Dosage form	Injection
Feature	Anti-CD20 monoclonal antibody, increased antibody-dependent cellular cytotoxicity (ADCC) activity and direct cytotoxicity

NS-304 (selexipag)

- Treatment for pulmonary hypertension, arteriosclerosis obliterans -

Development Phase	Japan : P2b (ASO) Japan : P2, NDA filing (pediatric PAH)
Origin	Nippon Shinyaku
Development	Nippon Shinyaku
Mechanism of action	Selective IP receptor agonist
Indication	arteriosclerosis obliterans (ASO) pediatric pulmonary arterial hypertension (pediatric PAH)
Dosage form	Tablet
Feature	Long-acting oral drug

NS-580

- Treatment for endometriosis, Chronic prostatitis/Chronic pelvic pain syndrome -

Development Phase	Japan : P2b (endometriosis) Temporarily suspended Japan : P2a (CP/CPPS) Temporarily suspended
Origin	Nippon Shinyaku
Development	Nippon Shinyaku
Mechanism of action	Inhibition of membrane-associated prostaglandin E synthase-1
Indication	endometriosis chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)
Dosage form	Oral agent
Feature	・Treatment for endometriosis without hormonal effect and with possible analgesic potency ・Treatment for CP/CPPS with high safety and long-term pain control

NS-089/NCNP-02（brogidirsen）

- Treatment for Duchenne muscular dystrophy -

Development Phase	Global : P2
Origin	Co-development : National Center of Neurology and Psychiatry
Development	Nippon Shinyaku
Mechanism of action	Exon 44 Skipping
Indication	Duchenne muscular dystrophy
Dosage form	Injection
Feature	・Improvement in symptoms and prevention of the disease progression by recovery of dystrophin protein expression ・Morpholino based oligonucleotide with possible high safety profile and maximized activity

NS-229

- Treatment for Eosinophilic granulomatosis with polyangiitis -

Development Phase	Global : P2
Origin	Nippon Shinyaku
Development	Nippon Shinyaku
Mechanism of action	JAK1 inhibitor
Indication	eosinophilic granulomatosis with polyangiitis (EGPA)
Dosage form	Oral agent
Feature	・Potent and highly selective JAK1 inhibitor ・High efficacy and good safety profiles are expected in the treatment for EGPA

NS-401 (tagraxofusp)

- Treatment for blastic plasmacytoid dendritic cell neoplasm -

Development Phase	Japan : P1/2
Origin	[Mar. 2021] Licensed-in from: The Menarini Group
Development	Nippon Shinyaku
Mechanism of action	Induction apoptosis of cells by inhibiting protein synthesis by specifically targeting cancer cells expressing CD123
Indication	blastic plasmacytoid dendritic cell neoplasm (BPDCN)
Dosage form	Injection
Feature	・Composed of diphtheria toxin (DT) fusion protein and recombinant human IL-3 ・Novel targeted therapy directed to CD123 on tumor cells ・IL-3 binds to CD123-expressing tumor cells and delivers the cytotoxic diphtheria toxin to the cells, resulting in the blockage of protein synthesis in the cell and causing cell death in CD123-expressing cells

NS-050/NCNP-03

- Treatment for Duchenne muscular dystrophy -

Development Phase	Global : P1/2
Origin	Co-development : National Center of Neurology and Psychiatry
Development	Nippon Shinyaku
Mechanism of action	Exon 50 Skipping
Indication	Duchenne muscular dystrophy
Dosage form	Injection
Feature	・Improvement in symptoms and prevention of the disease progression by recovery of dystrophin protein expression ・Morpholino based oligonucleotide with possible high safety profile and maximized activity

NS-917 (radgocitabine)

- Treatment for relapsed or refractory acute myeloid leukemia -

Development Phase	Japan : P1
Origin	[Mar. 2017] Licensed-in from : Delta-Fly Pharma, Inc.
Development	Nippon Shinyaku
Mechanism of action	DNA strand-break by incorporating itself into DNA
Indication	relapsed or refractory (r/r) acute myeloid leukemia (AML)
Dosage form	Injection
Feature	・Significant anti-leukemic activity with unique mechanism of action from other nucleoside analogs at low dose continuous infusion ・Tolerable safety profile available to elderly patients with r/r AML

NS-025

- Treatment for urological diseases -

Development Phase	Japan : P1
Origin	Nippon Shinyaku
Development	Nippon Shinyaku
Mechanism of action	–
Indication	Urological diseases (to be determined)
Dosage form	Oral agent
Feature	–

NS-863

- Treatment for cardiovascular diseases -

Development Phase	Japan : P1
Origin	Nippon Shinyaku
Development	Nippon Shinyaku
Mechanism of action	–
Indication	Cardiovascular diseases (to be determined)
Dosage form	Oral agent
Feature	–

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