R&D Day

June 8, 2026

ONO PHARMA

Forward-Looking Statements

Forecasts and other forward-looking statements included in this document are based on information currently available and certain assumptions that the Company deems reasonable.
Actual performance and other results may differ significantly due to various factors. Such factors include, but are not limited to:

Forward-looking statements:	This presentation contains forward-looking statements regarding the Company's future plans, strategies, and performance.
Current assumptions:	These statements are based on current expectations, assumptions, and information available to management at this time.
Risks and uncertainties:	Forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially.
No guarantee of outcomes:	Forecasts, targets, and projections are not guarantees of future performance or achievement of stated goals.
Official guidance:	Official financial guidance should be referred to in accordance with relevant regulatory requirements and disclosures.
Product/market risks:	Risks include, but are not limited to, product development challenges, regulatory approvals, market acceptance, and competition.
Economic/industry risks:	Additional risks may arise from changes in economic conditions, currency fluctuations, and healthcare policy reforms.
No obligation to update:	The Company undertakes no obligation to update or revise any forward-looking statements as a result of new information or future events.
Prevailing language:	In the event of any inconsistency between language versions, the original Japanese language version shall prevail.

Information about pharmaceutical products (including products currently in development) included in this document is not intended to constitute an advertisement of medical advice.

Today's Agenda

Opening

The data of POC Study

- ONO-4578 (ASCO2026)
- ONO-2808 (7th World Parkinson Congress)

Drug discovery activities in the Central Nervous System (CNS) field

Toichi Takino

Representative Director,
President and COO

Tatsuya Okamoto

Corporate Officer /
Executive Vice President,
Clinical Development

Seishi Katsumata

Corporate Officer /
Executive Vice President,
Discovery & Research

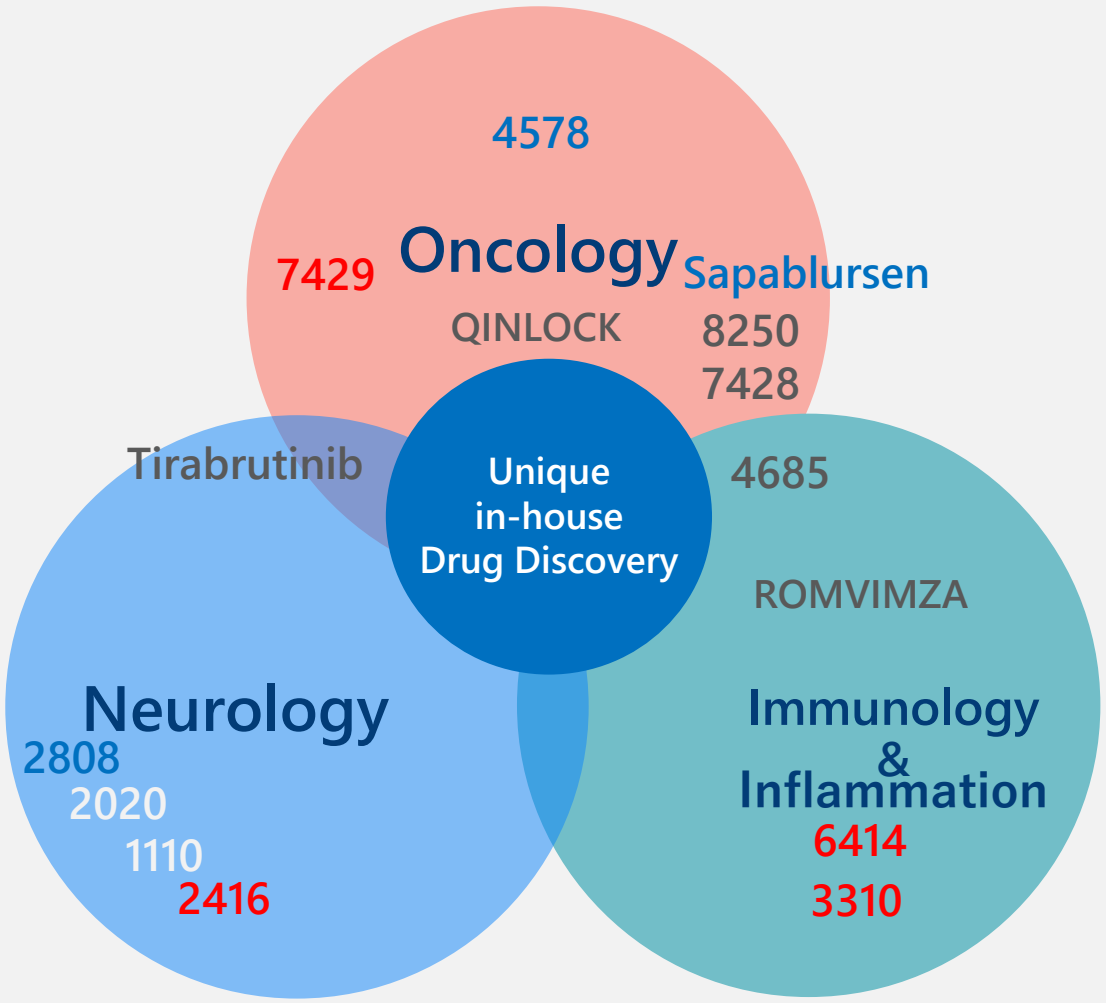
Commitment to Three Priority Areas

As of May 8, 2026

- Initiation of three global Phase 3 and data readouts from seven POC studies in FY2026
- In the priority areas of oncology, immunology & inflammation, and neurology, four new pipelines have initiated phase 1 study.

Open Innovation

License



Enter global Phase 3
POC data readouts
Initiate Phase 1

Upcoming Product Launches

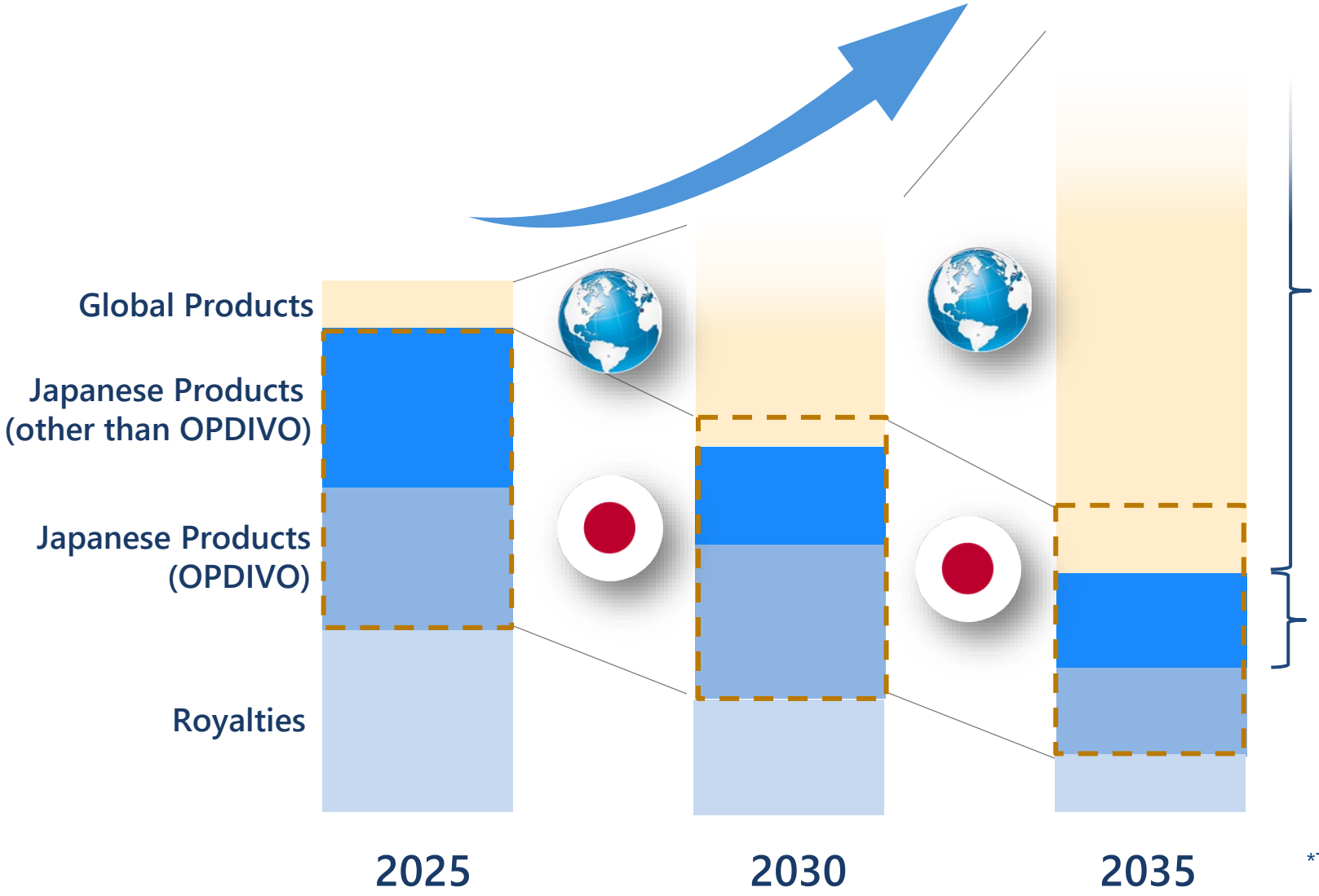
As of June 8, 2026

	FY2024	FY2025	FY2026	FY2027	FY2028+
US/EU	QINLOCK® GIST 4L	ROMVIMZA® Tenosynovial Giant Cell Tumor	Tirabrutinib ONO-4059 Primary CNS Lymphoma	QINLOCK® GIST 2L KIT Exon 11+17/18	Global Expansion Including Japan: Sapablursen ONO-0530 Polycythemia Vera; ONO-4685 T-cell Lymphoma/ Autoimmune Diseases; ONO-4578 Gastric Cancer 1L (in combination with OPDIVO); ROMVIMZA® Chronic Graft-versus-host Disease; ONO-2808 Multiple System Atrophy
Japan	OPDIVO MSI-H Colorectal Cancer 1L; OPDIVO Hepatocellular Carcinoma 1L; BRAFTOVI Capsules (FOLFOX) Colorectal Cancer 1L	Cenobamate ONO-2017 Partial-onset Seizures; QINLOCK® GIST 4L	OPDIVO Adjuvant Therapy for Hepatocellular Carcinoma	VELEXBRU Pemphigus 2L; QINLOCK® GIST 2L; povetacicept ONO-8531 IgA Nephropathy/ Chronic Kidney Disease; Cenobamate ONO-2017 Partial-onset Seizures (pediatric)/ Generalized Tonic-clonic Seizures	OPDIVO Subcutaneous Formulation; ROMVIMZA® Tenosynovial Giant Cell Tumor; Gel-One® ONO-5532 Osteoarthritis

Continued Launch of Specialty Products

In-house products　Deciphera　In-licensed products

Prospect for the Future



※Diagram does not represent actual sales of each product

Growth Drivers

Pipeline	Peak Sales (JPY bn)
Global	
QINLOCK (GIST)	50 – 70
ROMVIMZA (TGCT)	50 – 70
Tirabrutinib (PCNSL)	20 – 30
Sapablursen (PV)	50 – 100
ONO-4578 (GC)	100 -
ONO-2808 (MSA)	100 -
Japan*	
Povetacicept	50 -
Cenobamate	
Gel-One®	

*Total estimated peak sales, including products other than the three listed.

As of May 8, 2026

GIST: Gastrointestinal Stromal Tumor, TGCT: Tenosynovial Giant Cell Tumor, PCNSL: Primary Central Nervous System Lymphoma, PV: Polycythemia Vera, GC: Gastric Cancer, MSA: Multiple System Atrophy

Key Event Schedule for FY2026

	FY2026	
Approval		ONO-4059 (VELEXBRU) PCNSL
	ONO-2017, Cenobamate Partial-onset Seizures	QINLOCK GIST 4L
Phase3		ONO-4578 Gastric Cancer 1L
	ONO-0530, Sapablursen Polycythemia Vera	ONO-2808 Multiple System Atrophy
		QINLOCK GIST 2L
Phase2	ONO-1110 Postherpetic Neuralgia	ONO-2020 Alzheimer's Disease
	ONO-1110 Fibromyalgia	ONO-2020 Agitation Associated with Alzheimer's Disease
	ONO-1110 Hunner-type Interstitial Cystitis	ONO-2017 Generalized Tonic-clonic Seizures
	ONO-1110 Major Depressive Disorder	ONO-2017 Partial-onset Seizures (pediatric)
	ONO-1110 Social Anxiety Disorder	

Expected Approval　Study Initiation　Data Readout

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Today's Contents

- ✓ONO-4578 Latest Information
- ✓ONO-2808 Latest information

ONO-4578-08 Study

EP4 Receptor Antagonist

1L Treatment for HER2-negative Gastric Cancer

2026 ASCO® ANNUAL MEETING

ONO-4578 combined with nivolumab (NIVO) and chemotherapy (chemo) as First-line (1L) treatment for patients with HER2-negative unresectable advanced or recurrent (adv/rec) gastric/gastroesophageal junction cancer (G/GEJ): A randomized, double-blind, phase 2 trial (ONO-4578-08)

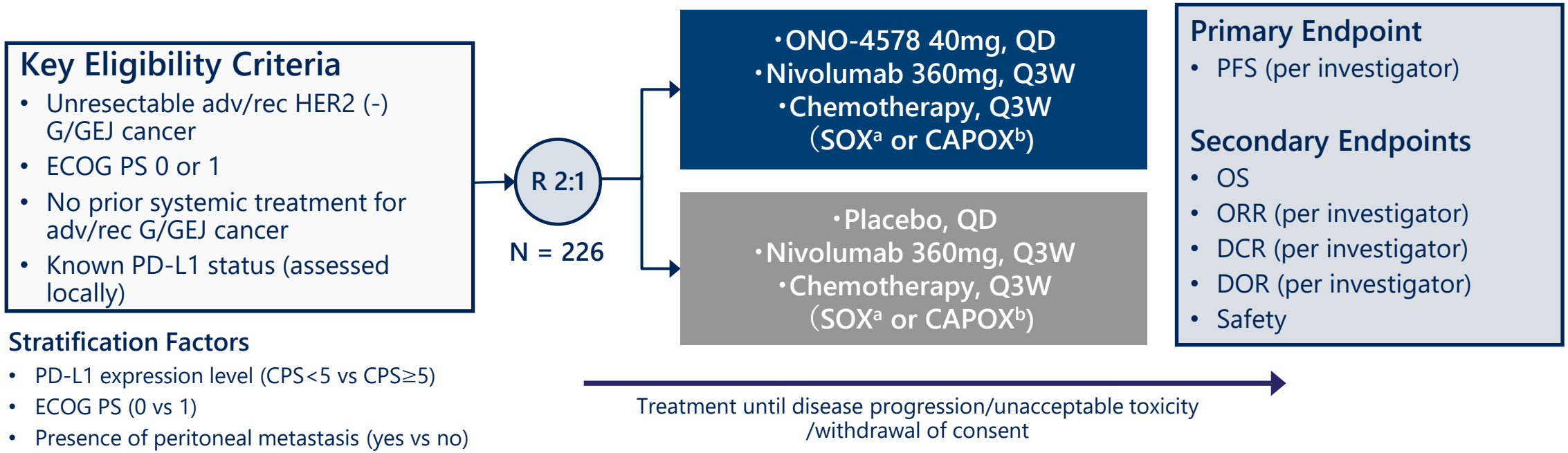
Sung Hee Lim[1*], Izuma Nakayama[2], Min-Hee Ryu[3], Jong Gwang Kim[4], Takeshi Omori[5], Sang Cheul Oh[6], Jin Young Kim[7], Sun Young Rha[8], Keun-Wook Lee[9], Nozomu Machida[10], Sun Jin Sym[11], Yukiya Narita[12], Young-Iee Park[13], Hiroki Hara[14], Hisashi Hosaka[15], Beodeul Kang[16], In-Ho Kim[17], Li-Yuan Bai[18], Kohei Shitara[2], ONO-4578-08 Study Group

[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [4]Kyungpook National University, Daegu, Republic of Korea; [5]Osaka International Cancer Institute, Osaka, Japan; [6]Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea; [7]Keimyung University Dongsan Hospital, Daegu, Republic of Korea; [8]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [9]Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; [10]Kanagawa Cancer Center, Yokohama, Japan; [11]Gachon University Gil Medical Center, Incheon, Republic of Korea; [12]Aichi Cancer Center Hospital, Nagoya, Japan; [13]Research Institute and Hospital, National Cancer Center, Goyang, Republic of Korea; [14]Saitama Cancer Center, Saitama, Japan; [15]Gunma Prefectural Cancer Center, Gunma, Japan; [16]CHA Bundang Medical Center, CHA University, Seongnam, Republic of Korea; [17]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; [18]China Medical University Hospital, Taichung, Taiwan

*Presenting

ONO-4578-08 Trial Design

ONO-4578-08: Asian (Japan/Korea/Taiwan), randomized, double-blinded, Phase 2 trial (NCT06256328)



- **Planned sample size: 210 patients, providing ≥70% power (two-sided α=0.10) to detect a HR of 0.65 (median PFS; 12.3 vs 8.0 months) with 117 events**
- **Patients were randomized from December 2023 to September 2024**
- **All analyses are based on a clinical data cutoff of 14th April 2025, with the median PFS follow-up of 8.5 months**

[a]**SOX therapy:** Oxaliplatin 130 mg/m^2 IV once daily (day1), and S-1 40 mg/m^2/dose orally twice daily (day1-14) , Q6W; [b]**CapeOX therapy:** Oxaliplatin 130 mg/m^2 IV once daily (day1), and Capecitabine 1000 mg/m^2/dose orally twice daily (day1-14), Q3W.

Abbreviations: G/GEJ, gastric/gastroesophageal junction; PFS, progression free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; DOR, duration of response; Q3W, every 3 weeks; Q6W, every 6 weeks; SOX, S-1 (tegafur/gimeracil/oteracil)/oxaliplatin; CapeOX, capecitabine/oxaliplatin;

Demographics and Baseline Characteristics

	ONO-4578 group (n = 150)	Placebo group (n = 76)
Age, median (range), years	66.0 (27–84)	67.5 (36–86)
Male sex	113 (75.3)	64 (84.2)
Country		
Japan	54 (36.0)	37 (48.7)
Korea	87 (58.0)	35 (46.1)
Taiwan	9 (6.0)	4 (5.3)
ECOG PS		
0	78 (52.0)	41 (53.9)
1	72 (48.0)	35 (46.1)
Disease status		
Advanced	103 (68.7)	55 (72.4)
Recurrent	47 (31.3)	21 (27.6)
Primary Tumor location[*1]		
GEJ	17 (16.5)	7 (12.7)
Gastric	82 (79.6)	46 (83.6)
Unknown	4 (3.9)	2 (3.6)
Histologic type (Lauren's criteria)		
Intestinal type	72 (48.0)	31 (40.8)
Diffuse type	67 (44.7)	37 (48.7)
Others	11 (7.3)	8 (10.5)
Peritoneal metastasis		
Yes	82 (54.7)	42 (55.3)
No	68 (45.3)	34 (44.7)

	ONO-4578 group (n = 150)	Placebo group (n = 76)
Number of organs with metastases		
≤1	63 (42.0)	29 (38.2)
>1	87 (58.0)	47 (61.8)
PD-L1 expression level (CPS)		
<1	32 (21.3)	17 (22.4)
≥1 and <5	44 (29.3)	21 (27.6)
≥5	73 (48.7)	36 (47.4)
Indeterminate	1 (0.7)	2 (2.6)
Planned chemotherapy regimen		
SOX	89 (59.3)	45 (59.2)
CapeOX	61 (40.7)	31 (40.8)
Claudin 18.2		
Positive	50 (33.3)	28 (36.8)
Negative	96 (64.0)	47 (61.8)
Not Evaluated	4 (2.7)	1 (1.3)
MSI status[*2]		
MSS	32 (21.3)	19 (25.0)
MSI-low	2 (1.3)	0
MSI-high	4 (2.7)	0
Not determined	2 (1.3)	3 (3.9)

*2 The results of patients who locally underwent MSI test

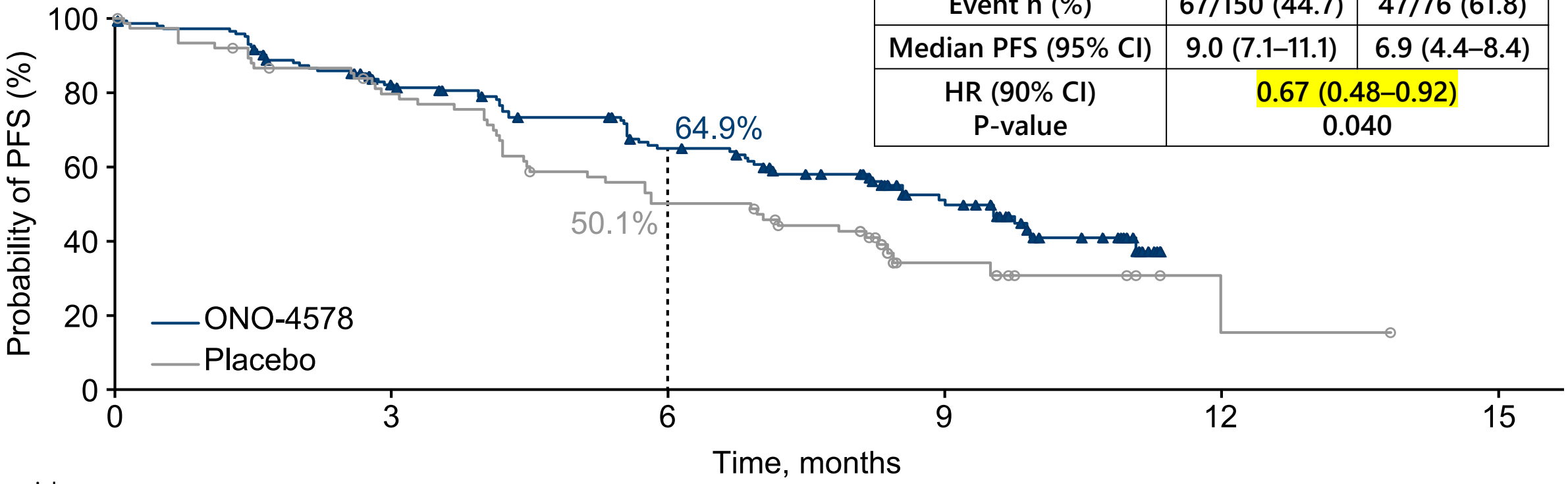
- Baseline characteristics were well balanced across the two groups

*1 Primary tumor location was categorized into three groups: gastroesophageal junction (GEJ; ICD-10 C16.0), gastric (C16.1–C16.4), and unknown ; percentages are based on the number of participants with advanced gastric cancer.

PFS per investigator : Primary Endpoint

median PFS follow-up of 8.5 months

	ONO-4578 group	Placebo group
Event n (%)	67/150 (44.7)	47/76 (61.8)
Median PFS (95% CI)	9.0 (7.1–11.1)	6.9 (4.4–8.4)
HR (90% CI) P-value	0.67 (0.48–0.92) 0.040	



No. at risk

ONO-4578	150	106	77	37	0	0
Placebo	76	57	35	10	1	0

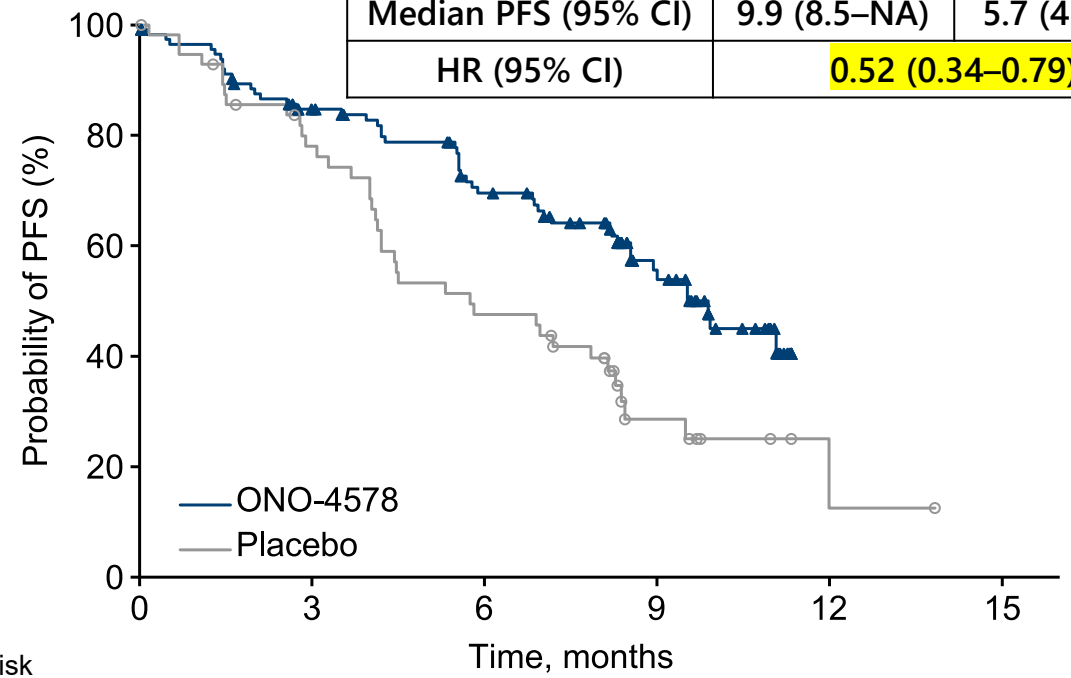
- **ONO-4578 group demonstrated a statistically significant improvement in PFS compared with placebo group**

PFS by PD-L1 CPS (≥1 vs <1)

median PFS follow-up of 8.5 months

CPS≥1

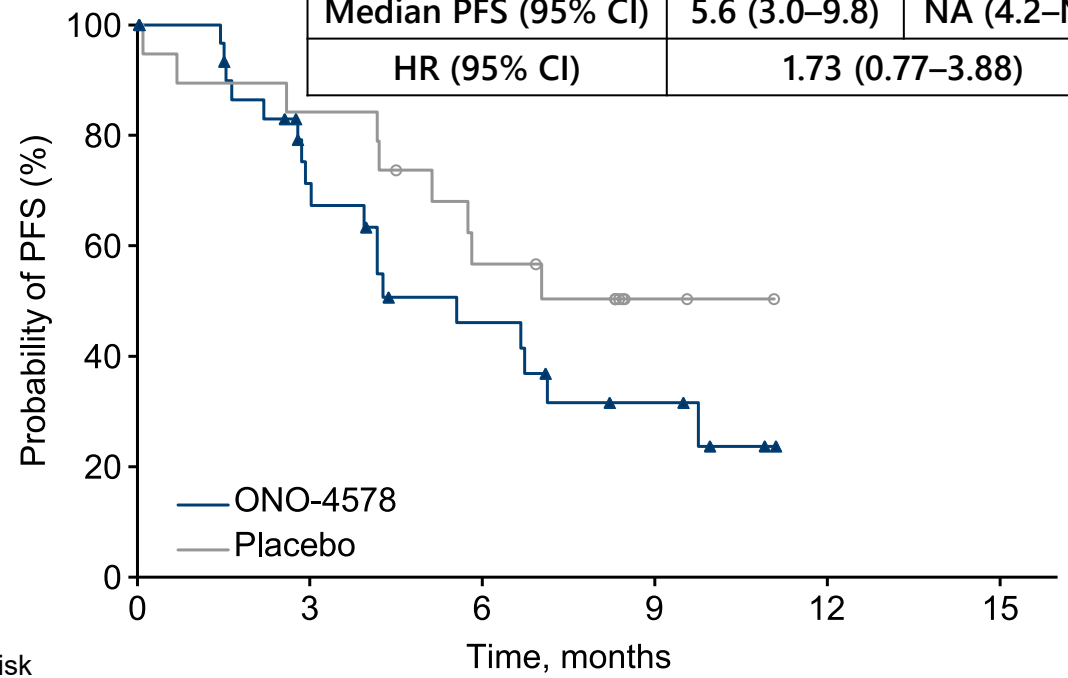
	ONO-4578 group	Placebo group
Event n (%)	49/117 (41.9)	38/57 (66.7)
Median PFS (95% CI)	9.9 (8.5–NA)	5.7 (4.1–8.3)
HR (95% CI)	0.52 (0.34–0.79)	



No. at risk						
ONO-4578	117	88	67	32	0	0
Placebo	57	41	25	8	1	0

CPS<1 or Indeterminate

	ONO-4578 group	Placebo group
Event n (%)	18/33 (54.5)	9/19 (47.4)
Median PFS (95% CI)	5.6 (3.0–9.8)	NA (4.2–NA)
HR (95% CI)	1.73 (0.77–3.88)	

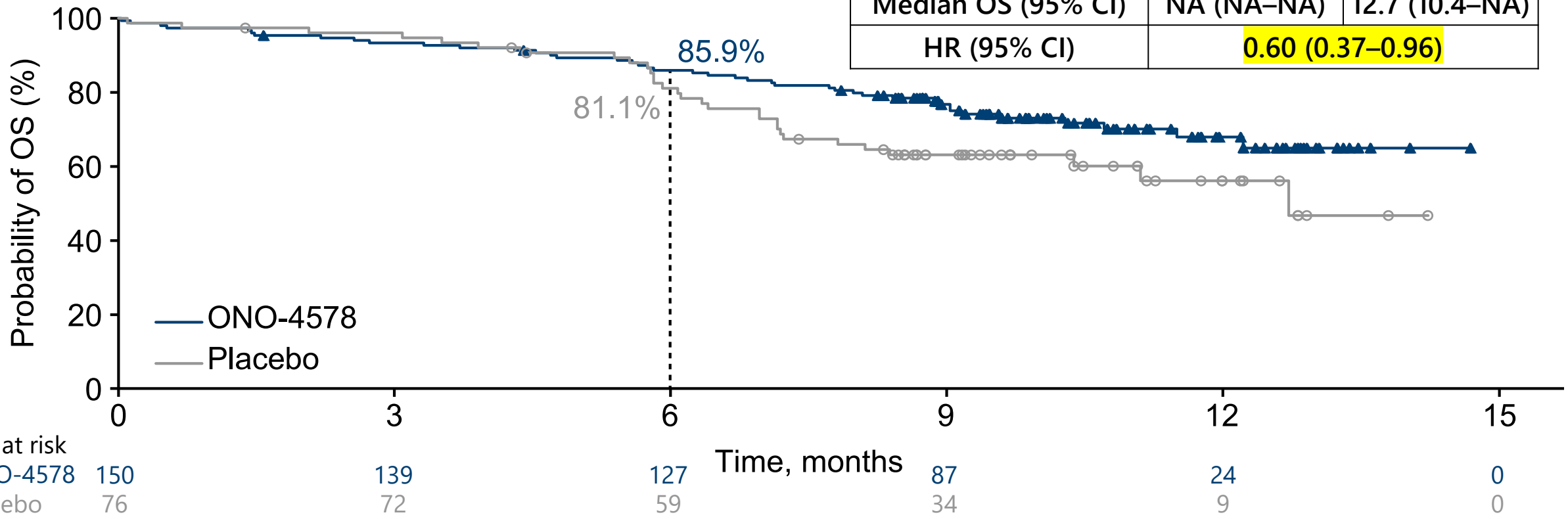


No. at risk						
ONO-4578	33	18	10	5	0	0
Placebo	19	16	10	2	0	0

- **PFS benefit of the ONO-4578 group appeared to be more pronounced in patients with CPS ≥1**

OS : Secondary Endpoint

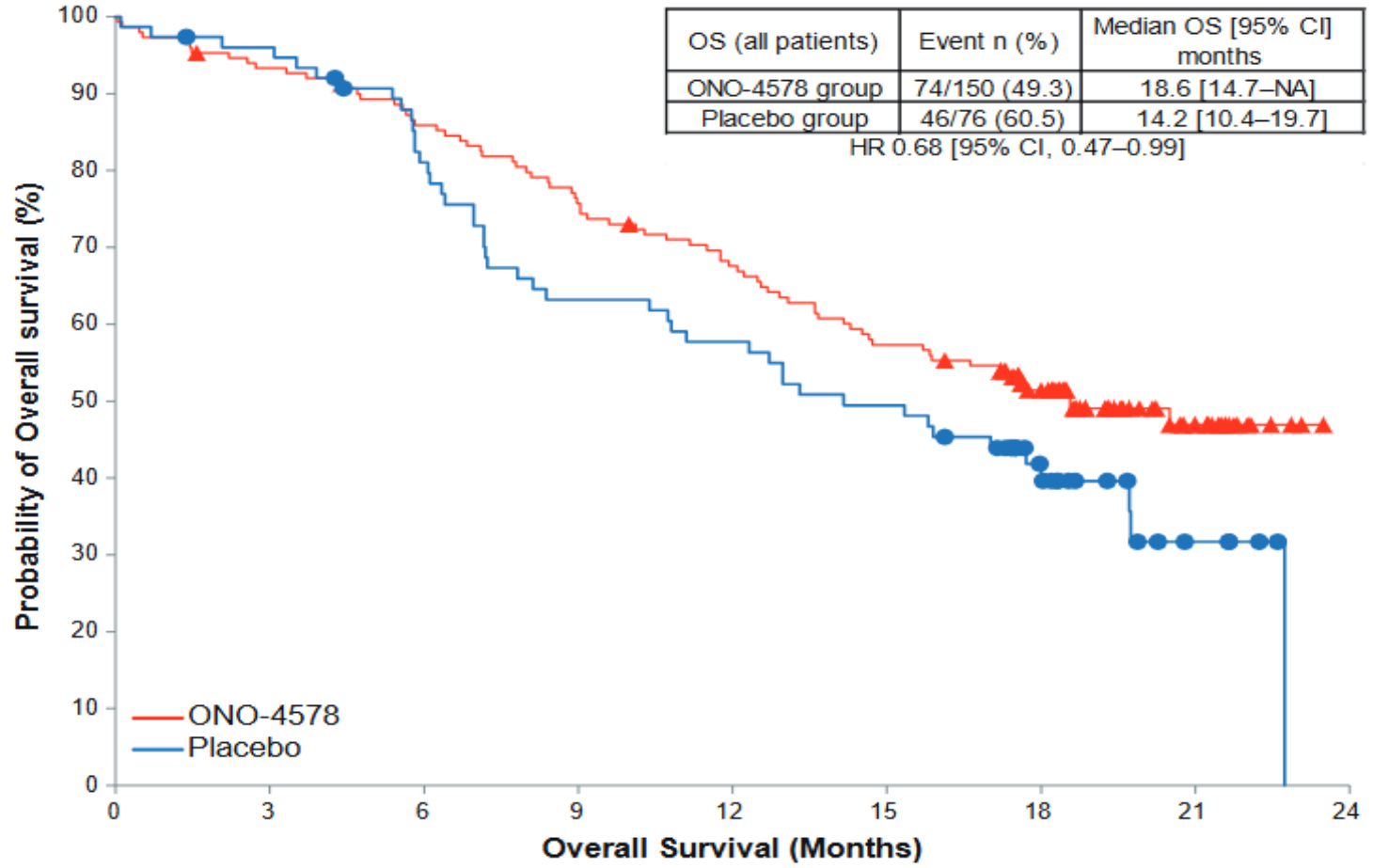
	ONO-4578 group	Placebo group
Event n (%)	42/150 (28.0)	30/76 (39.5)
Median OS (95% CI)	NA (NA–NA)	12.7 (10.4–NA)
HR (95% CI)	0.60 (0.37–0.96)	



- Although OS data are immature (minimum FU: 7.4 months) and should be interpreted with caution, OS favored the ONO-4578 group compared with the placebo group

Post-hoc extended OS

minimum OS follow-up of 16.1 months



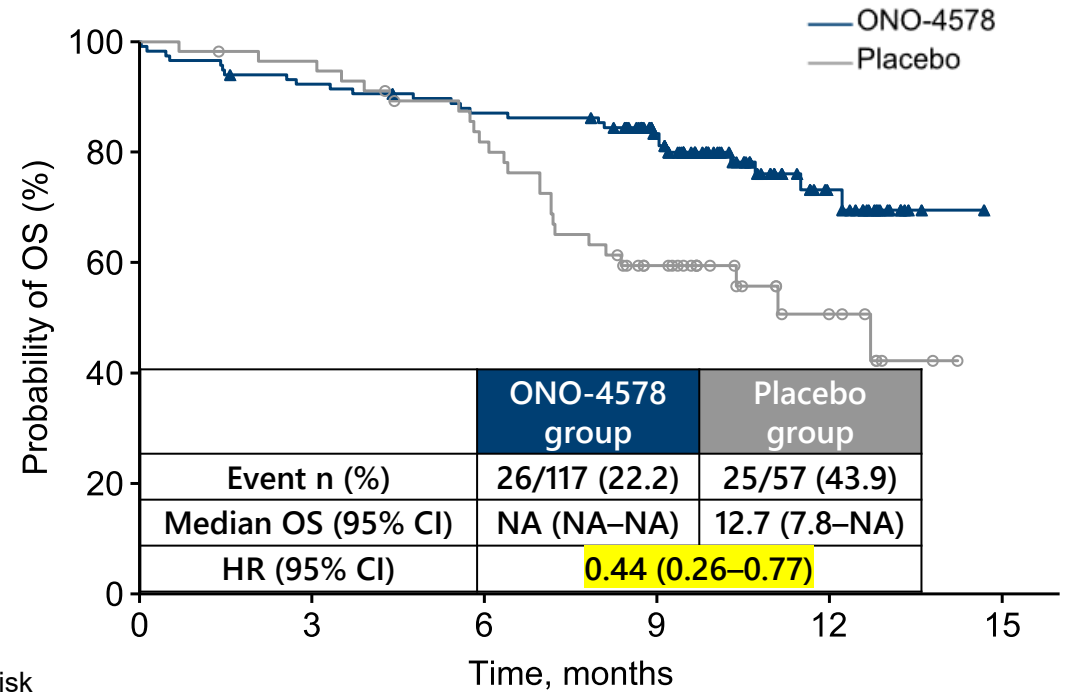
Number of Subjects at Risk

Months	0	3	6	9	12	15	18	21	24
ONO-4578	150	139	127	112	99	84	56	16	0
Placebo	76	72	59	46	42	36	19	5	0

Nakayama I, Ryu M-H, Lim S H, et al. Journal of Clinical Oncology10.1200/JCO-26-01072R1 Epub 2026 June 1.

Overall Survival by PD-L1 CPS (≥1 vs <1)

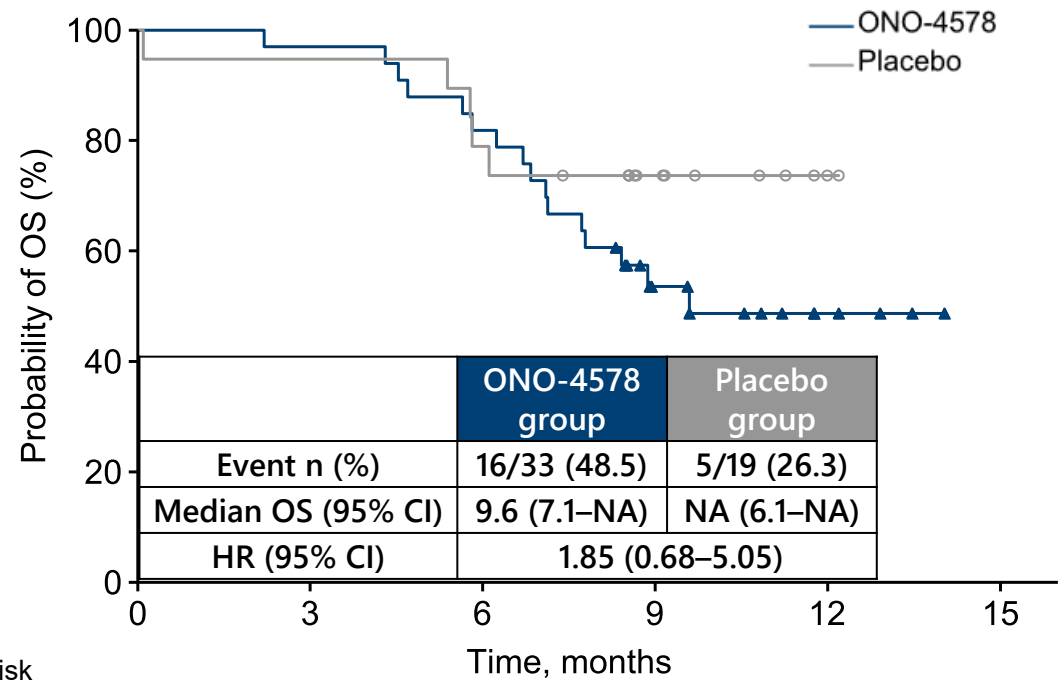
CPS≥1



	ONO-4578 group	Placebo group
Event n (%)	26/117 (22.2)	25/57 (43.9)
Median OS (95% CI)	NA (NA–NA)	12.7 (7.8–NA)
HR (95% CI)	0.44 (0.26–0.77)	

No. at risk						
ONO-4578	117	107	100	75	20	0
Placebo	57	54	44	26	8	0

CPS<1 or Indeterminate



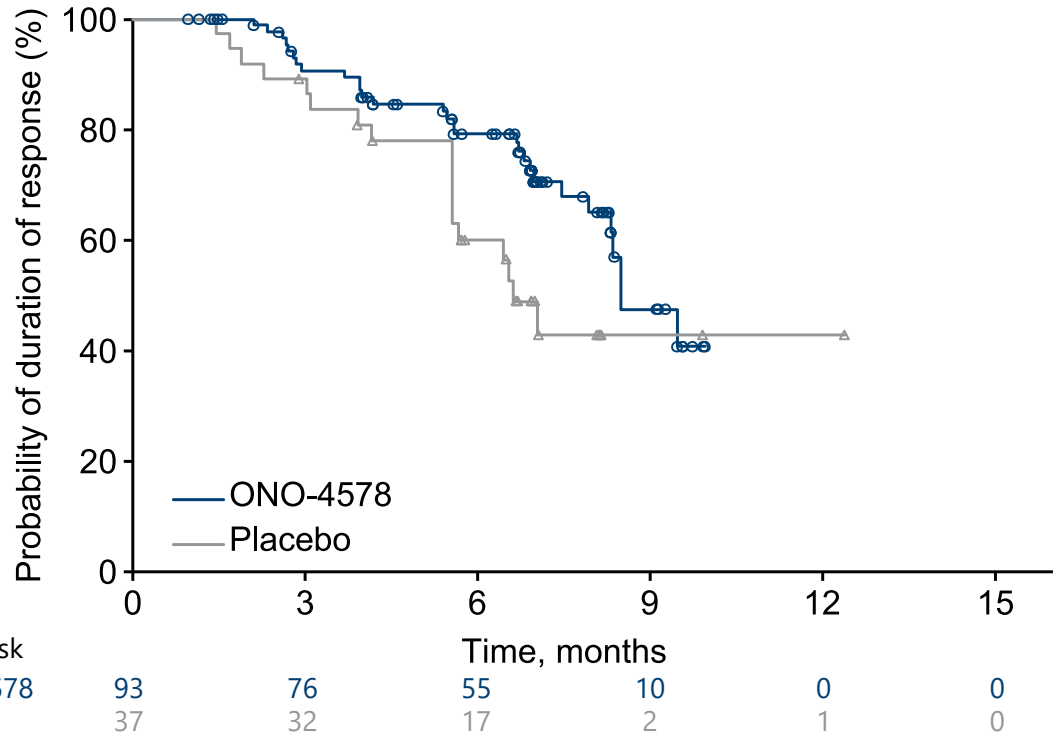
	ONO-4578 group	Placebo group
Event n (%)	16/33 (48.5)	5/19 (26.3)
Median OS (95% CI)	9.6 (7.1–NA)	NA (6.1–NA)
HR (95% CI)	1.85 (0.68–5.05)	

No. at risk						
ONO-4578	33	32	27	12	4	0
Placebo	19	18	15	8	1	0

- As with the PFS, the efficacy of the ONO-4578 group was more marked in patients with CPS ≥1

Summary of Anti-tumor Response

	ONO-4578 group (n = 150)	Placebo group (n = 76)
ORR (95% CI), %	62.0 (53.7–69.8)	48.7 (37.0–60.4)
Odds ratio (95% CI)	1.72 (0.98–3.00)	
BOR, n (%)		
CR	4 (2.7)	0
PR	89 (59.3)	37 (48.7)
SD	31 (20.7)	26 (34.2)
PD	12 (8.0)	9 (11.8)
NE	14 (9.3)	4 (5.3)
DOR, median (95% CI), months	8.5 (8.3–N.A.)	6.6 (5.6–N.A.)

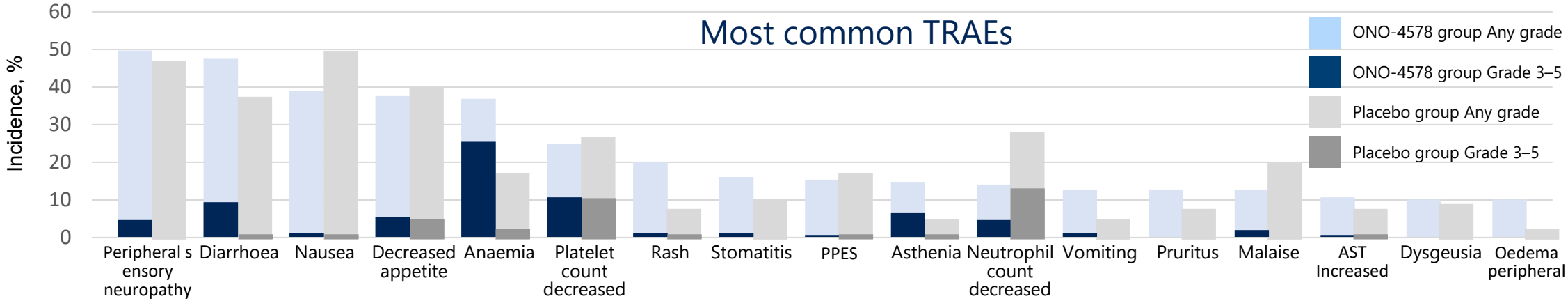


	CPS≥1		CPS<1	
	ONO-4578 group (n = 117)	Placebo group (n = 57)	ONO-4578 group (n = 33)	Placebo group (n = 19)
ORR (95% CI), %	70.9 (61.8–79.0)	50.9 (37.3–64.4)	30.3 (15.6–48.7)	42.1 (20.3–66.5)
Odds ratio (95% CI)	2.36 (1.22–4.54)		0.60 (0.18–1.94)	

- The ONO-4578 group showed higher ORR and longer DOR compared with the placebo group

Overall Safety Summary

All treated	ONO-4578 group (n = 149)		Placebo group (n = 75)	
	Any grade	Grade3–5	Any grade	Grade3–5
Any AEs	149 (100.0)	118 (79.2)	75 (100.0)	52 (69.3)
Serious AEs	80 (53.7)	72 (48.3)	32 (42.7)	26 (34.7)
AEs leading to death	12 (8.1)		3 (4.0)	
Any TRAEs	146 (98.0)	89 (59.7)	74 (98.7)	37 (49.3)
Serious TRAEs	51 (34.2)	46 (30.9)	19 (25.3)	16 (21.3)
TRAEs leading to discontinuation of ONO-4578/Placebo	12 (8.1)	7 (4.7)	1 (1.3)	1 (1.3)
TRAEs leading to discontinuation of nivolumab/chemotherapy	58 (38.9)	24 (16.1)	20 (26.7)	6 (8.0)
TRAEs leading to death	4 (2.7)		2 (2.7)	



- TRAEs leading to death were pneumonia klebsiella, febrile neutropenia and hepatitis in the ONO-4578 group, pneumonia interstitial and pneumonia in the placebo group
- The safety profile of ONO-4578 regimen appeared manageable with appropriate supportive care

Abbreviations: PPES, Palmar-plantar erythrodysaesthesia syndrome; AST, Aspartate aminotransferase

Discussion on the Results of ONO-4578-08 Study

[Prognostic Factors] Comparison with Checkmate-649 study (CM649)

- ✓ The proportion of patients aged ≥65, with diffuse type and peritoneal metastasis was approximately 10–30% higher than in CM649.
- ✓ The proportion of patients with PS 1 and ≥2 metastatic organs was approximately 10–20% lower than in CM649.

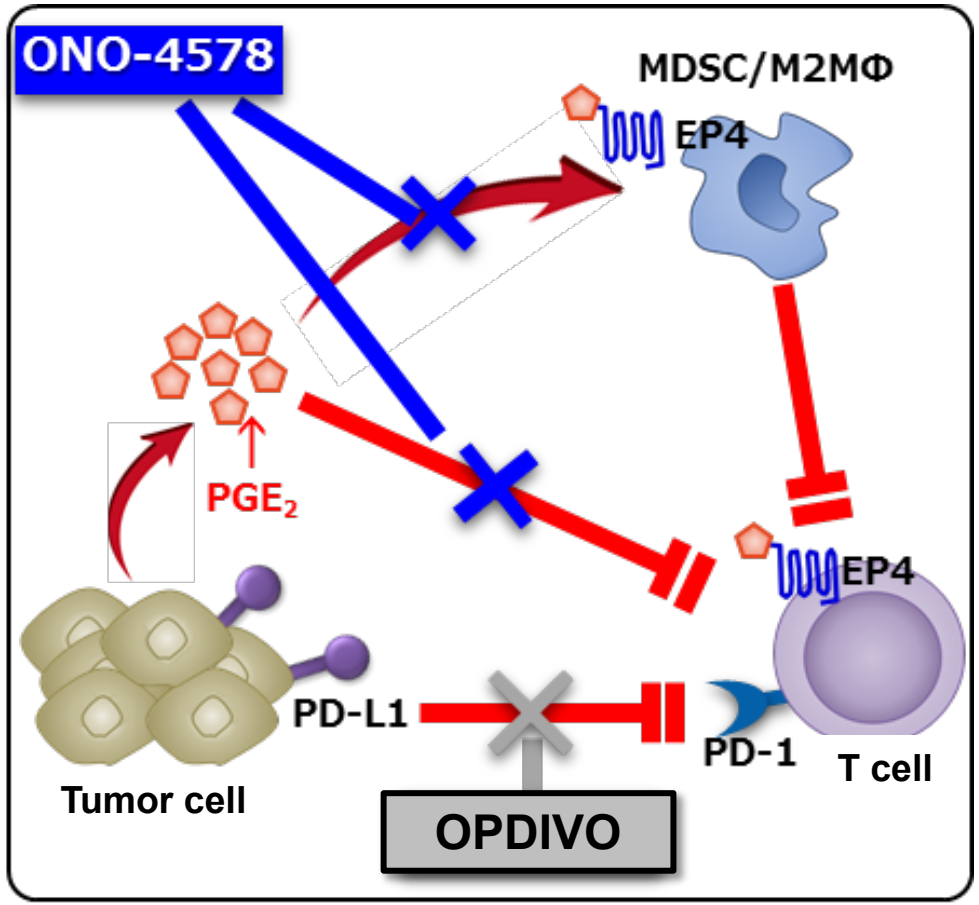
	ONO-4578-08 (Investigator-assessed CPS)		Checkmate-649 (Centrally-assessed CPS)	
	ONO-4578 group N=150	Placebo group N=76	Nivo + chemo N=789	chemo N=792
Age ≥65	80 (53.3%)	49 (64.5%)	316 (40%)	304 (38%)
ECOG PS 1				
0	78 (52.0%)	41 (53.9%)	326 (41%)	336 (42%)
1	72 (48.0%)	35 (46.1%)	462 (59%)	452 (57%)
Histologic type (Lauren's criteria)				
Intestinal type	72 (48.0%)	31 (40.8%)	272 (34%)	267 (34%)
Diffuse type	67 (44.7%)	37 (48.7%)	254 (32%)	273 (34%)
Others	11 (7.3%)	8 (10.5%)	263 (33%)	252 (32%)
Presence of peritoneal metastasis	82 (54.7%)	42 (55.3%)	188 (24%)	188 (24%)
Number of organs with metastases				
≤1	63 (42.0%)	29 (38.2%)	164 (21%)	183 (23%)
≥2	87 (58.0%)	47 (61.8%)	602 (76%)	583 (74%)

Mechanism of ONO-4578

- Prostaglandin E_2 (PGE_2) is derived from arachidonic acid via cyclooxygenase-2 (COX-2).
- COX-2 is overexpressed in solid tumor.[1] PGE_2PGE2 has been reported to induce myeloid-derived suppressor cells (MDSC) and M2 macrophages in the tumor microenvironment through one of its receptors, EP4, and suppress activation of cytotoxic T cells.[2]
- ONO-4578, a novel selective EP4 antagonist, is expected to have an antitumor effect by abolishing the tumor immunosuppressive mechanism that PGE2 constructs via EP4.

Concept: Addressing limitations of PD-1 antibody therapy alone

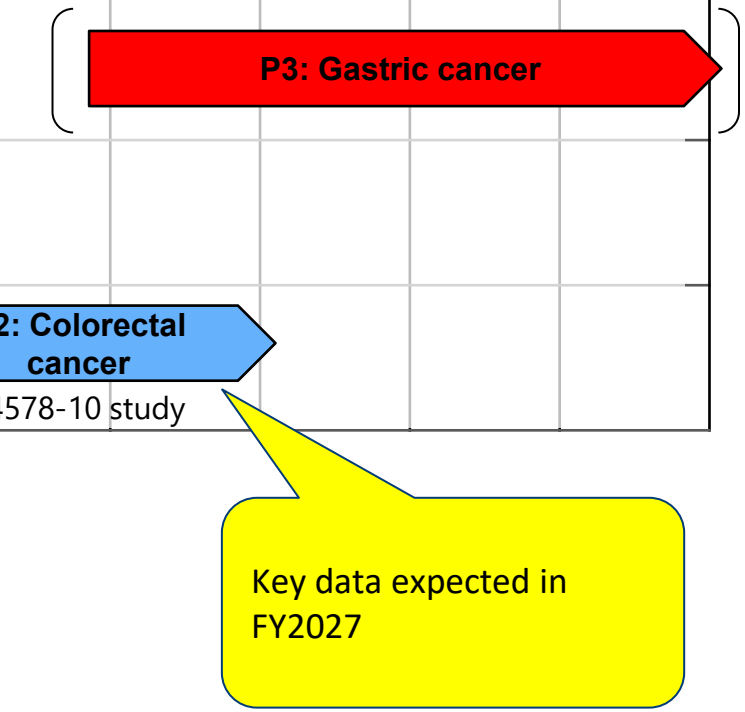
- **Increasing patients responding to PD-1 antibody therapy to improve response rates**
- **Reducing patients losing response to PD-1 antibody therapy to prolong progression-free survival (PFS)**



1. Bing L, et al. Cancer Cell Int; 2015:15:106
2. Yukinori T, et al. Front Immunol. 2020;11:324

ONO-4578 Development Status

Indication	Development phase	Status	Regions	Study ID
First-line gastric cancer*	PIII	In preparation		
First-line colorectal cancer*	P II	Key data obtained in FY2025	Japan, Korea, Taiwan	NCT06256328
First-line colorectal cancer*	P II	Key data expected in FY2027	Japan, US, EU, etc.	NCT06948448



*In combination with Opdivo and standard of care

2024 ESMO GASTROINTESTINAL CANCERS
Annual Congress
MUNICH GERMANY
26-29 JUNE 2024

Safety, Efficacy, And Biomarkers Of ONO-4578, An EP4 Antagonist, In Combination With Nivolumab And Chemotherapy In Treatment-naive And Proficient Mismatch Repair (pMMR)/Microsatellite Stable (MSS) Metastatic Colorectal Cancer (mCRC)

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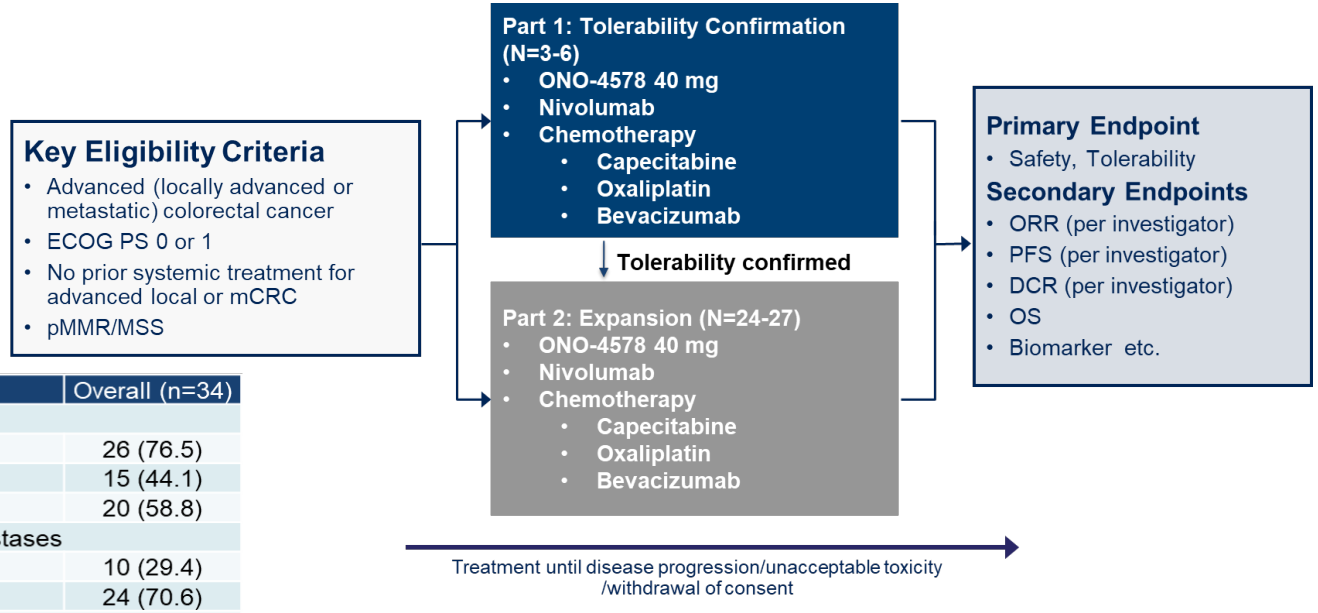
Study Design & Patient Characteristics

- The ONO-4578-02 study (NCT06547385) was an open-labelled, phase 1 study, conducted at 9 sites in Japan
- The minimum follow-up was 15.0 months at data cutoff (July 21, 2023)
- Patients with high frequency microsatellite instability (MSI-H) or mismatch repair mechanism deficiency (dMMR) were excluded per protocol



Characteristics	Overall (n=34)
Age (years)	
Median	66.0
Min-Max	40-80
Sex	
Female	17 (50.0)
Male	17 (50.0)
ECOG PS at baseline	
0	30 (88.2)
1	4 (11.8)
Initial or recurrent	
Initial	31 (91.2)
Recurrent	3 (8.8)
Organ location of initial disease	
Left	26 (76.5)
Rectum	16 (47.1)
Sigmoid colon	9 (26.5)
Rectosigmoid Junction	1 (2.9)
Right	8 (23.5)
Cecum	3 (8.8)
Ascending colon	2 (5.9)
Transverse colon	3 (8.8)
Disease stage	
IV	31 (91.2)
Missing	3 (8.8)

Characteristics	Overall (n=34)
Organ location of metastasis	
Liver	26 (76.5)
Lung	15 (44.1)
Lymph node	20 (58.8)
Number of organs showing metastases	
≤1	10 (29.4)
≥2	24 (70.6)
Prior treatment	
Colorectal cancer specific surgeries	8 (23.5)
Radiotherapies	0
Colorectal cancer specific medications	2 (5.9)
BRAF mutation status	
V600E	3 (8.8)
Wild type/No mutation	31 (91.2)
RAS mutation status[a]	
Mutated	21 (61.8)
Wild type	13 (38.2)
PD-L1 CPS	
<1	14 (41.2)
≥1	17 (50.0)
Indeterminate/Unknown	1 (2.9)
Missing	2 (5.9)
TMB (Muts/Mb)	
<10	29 (85.3)
≥10	0
Missing	5 (14.7)

Data presented as n (%) unless specified otherwise;
[a]*RAS* mutation present means *KRAS* or *NRAS* mutation present; CPS, combined positive score; ECOG PS, eastern cooperative oncology group performance status; Min, minimum; Max, maximum; Muts/Mb, mutations per megabase; PD-L1, programmed cell death-ligand 1; TMB, tumour mutation burden

Results: Efficacy (Overall Population)

	n (%)	[95% CI]
Objective response rate[a]	25 (73.5)	[55.6, 87.1]
Disease control rate[a]	31 (91.2)	[76.3, 98.1]
Best overall response[a]		
Complete Response	0	[0.0, 10.3]
Partial Response	25 (73.5)	[55.6, 87.1]
Stable Disease	6 (17.6)	[6.8, 34.5]
Progressive Disease	2 (5.9)	-
Not Evaluable	1 (2.9)	-
Progression free survival in months[b]		
Median [95% CI]	12.3	[7.0, 17.1]
Progression free survival rate[b]		
At 6 months (%) [95% CI]	84.7	[67.1, 93.4]
At 12 months (%) [95% CI]	50.3	[31.2, 66.7]

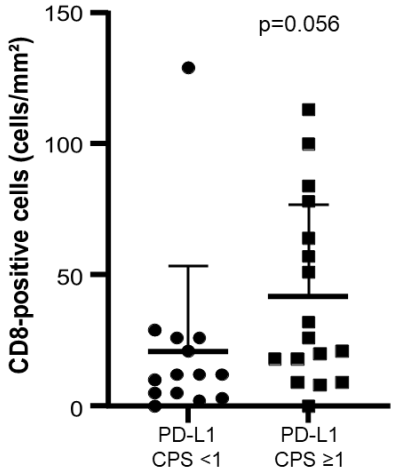
[a]by Clopper-Pearson method ; [b]by Kaplan-Meier method; CI, confidence interval

Results: Efficacy & BM Analysis (CPS-Positive/Negative)

	PD-L1 CPS ≥1 (n=17)	PD-L1 CPS <1 (n=14)
Objective response rate, n (%) [95% CI][a]	15 (88.2) [63.6, 98.5]	9 (64.3) [35.1, 87.2]
Progression free survival in months[b]		
Median [95% CI]	12.3 [6.9, NA]	7.4 [6.9, NA]
Progression free survival rate		
At 6 months (%) [95% CI]	88.2 [60.6, 96.9]	85.7 [53.9, 96.2]
At 12 months (%) [95% CI]	57.4 [30.6, 77.0]	46.8 [19.6, 70.2]

[a]by Clopper-Pearson method; [b]by Kaplan-Meier method; CI, confidence interval, CPS, combined positive score; NA, not available; PD-L1, programmed cell death-ligand 1

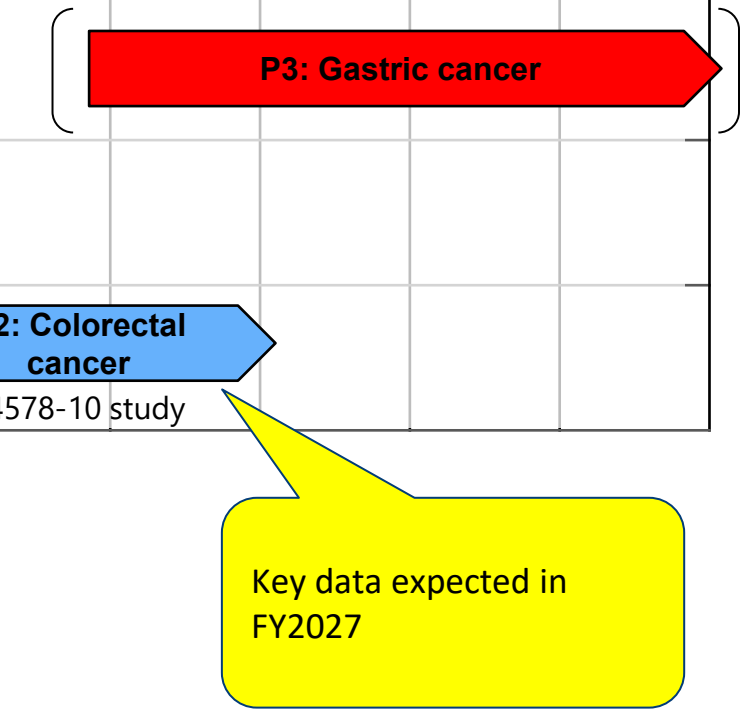
CD8⁺ Immunohistochemistry in PD-L1 CPS subgroups in Tumor Biopsies at Baseline



CPS, combined positive score; PD-L1, programmed cell death-ligand 1

ONO-4578 Development Status (Phase 2 and beyond)

Indication	Development phase	Status	Regions	Study ID
First-line gastric cancer*	PIII	In preparation		
First-line colorectal cancer*	P II	Key data obtained in FY2025	Japan, Korea, Taiwan	NCT06256328
First-line colorectal cancer*	P II	Key data expected in FY2027	Japan, US, EU, etc.	NCT06948448



*In combination with Opdivo and standard of care

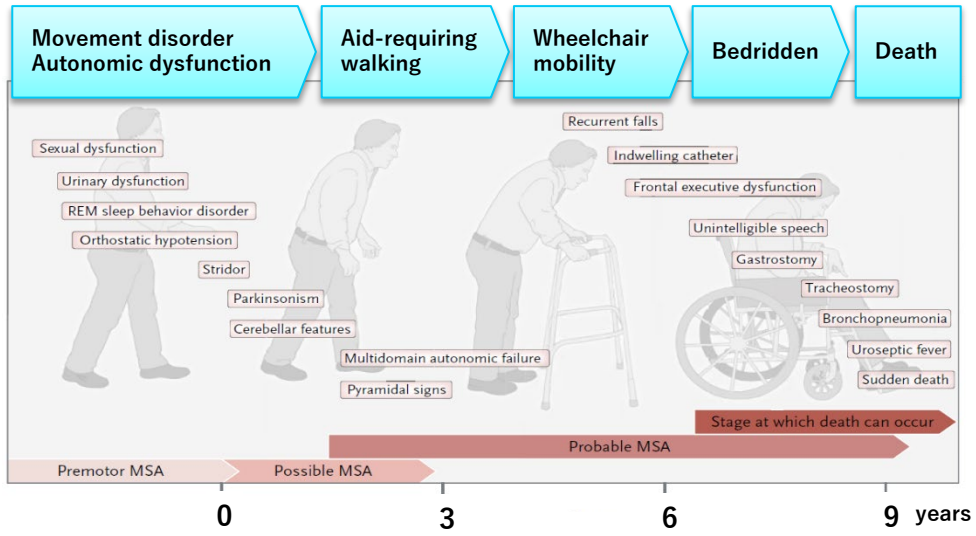
ONO-2808-03 study
S1P5 Receptor Agonist
Multiple System Atrophy (MSA)

ONO-2808 and MSA

Compound information

Compound	ONO-2808
Originator	ONO Pharma
Mechanism	S1P5 Receptor agonist
Formulation	Oral
Target indication	MSA (Multiple System Atrophy)
Development status	Phase II (US, Japan)

Multiple System Atrophy

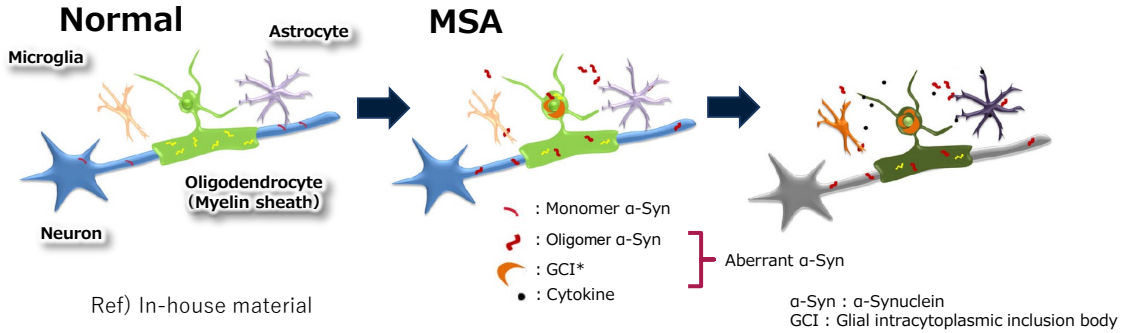


Gregor K. Wenning, N Engl J Med 2015; 372(3)

<Features>

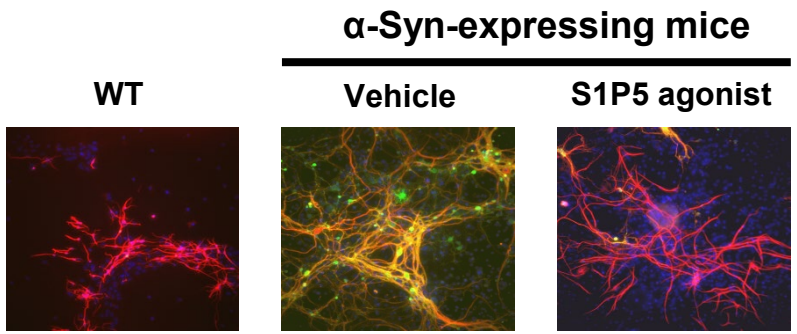
- Progressive neurodegenerative disease with cerebellar atrophy
- Average onset age: 55–60 years
- Severe and rapidly progressive
- Currently symptomatic treatment with limited efficacy
- Estimated patients (2031)
  US: 16,000, EU5* : 16,000, Japan : 12000

*EU5 : France, Germany, Italy, Spain, UK



Ref) In-house material

Primary whole-brain cultures from oligodendrocyte-specific human α-Syn-expressing mice



Blue : Nucleus
Green : α-Syn
Red : Neuron

S1P5 agonist suppressed α-Syn accumulation in neuronal axons

Poster: LBP37.09

Safety, Tolerability, and Preliminary Efficacy of ONO-2808, a Sphingosine-1-Phosphate Receptor 5 Agonist, in Multiple System Atrophy

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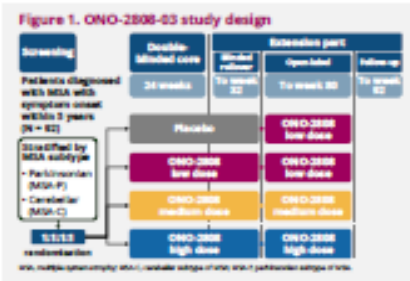
Introduction

- Multiple system atrophy (MSA) is a rare neurodegenerative disorder characterized by glial α-synuclein cytoplasmic inclusions[1]
- The sphingosine-1-phosphate receptor 5 (S1PR5) promotes mature oligodendrocyte survival and contributes to the regulation of myelination, which are key pathologic processes in MSA[2]
- Patients with MSA experience rapid progressive degeneration across motor, non-motor, and autonomic pathways leading to substantial reductions in quality of life and eventual death[1,3]
- MSA can be classified into 2 subtypes based on the predominant phenotype: MSA-P for parkinsonian features associated with striatonigral degeneration or MSA-C for cerebellar features associated with olivopontocerebellar atrophy[1,4]
- There are no approved treatments for MSA, and existing therapies are limited to symptomatic relief rather than addressing underlying pathogenic mechanisms, highlighting an urgent, unmet need for novel therapeutic strategies
- ONO-2808 is an investigational, first-in-class, oral, S1PR5 agonist that preclinically promoted remyelination and reduced α-synuclein accumulation
- Here, we report the safety and exploratory efficacy of ONO-2808 in patients with MSA from the phase 2 trial (NCT05923866)

Methods

- ONO-2808-03 is an ongoing, double-blind, placebo-controlled phase 2 trial in patients with MSA diagnosed per Movement Disorder Society Criteria with symptom onset within 5 years (**Figure 1**)
- The trial is composed of 2 parts, including the double-blinded core part (to week 24; the last patient reached week 24 on September 15, 2025) and extension part, comprising blinded rollover (to week 32), open-label treatment (to week 80), and follow-up (to week 92)
  - Patients who continued in the optional blinded rollover and open-label extension provided additional informed consent, which potentially influenced patient-reported outcomes
- The primary endpoints at week 24 included the incidence of treatment-emergent adverse events (TEAEs) and transaminase elevations assessed by an independent data monitoring committee
- Exploratory efficacy endpoints included here are mean change from baseline (CFB) in a modified Unified Multiple System Atrophy Rating Scale (mUMSARS) score and percent CFB in brain regions of interest as assessed via volumetric magnetic resonance imaging (vMRI)
  - The mUMSARS was an adjusted sum of 9 items (6 items from UMSARS part 1 and 3 items from UMSARS part 2) with scores ranging from 0 to 27 (lower scores indicate less impairment)

Figure 1. ONO-2808-03 study design



Results

- A total of 92 patients with MSA were enrolled across investigational sites in the US and Japan; there were no major imbalances in baseline characteristics between treatment arms (**Table 1**)
- Overall, 76% (70/92) of patients completed treatment in the double-blinded core part, and 57% (53/92) remained on treatment at data cutoff (February 24, 2026)

Table 1. Baseline demographics and clinical characteristics

Characteristic	Placebo (n = 23)	ONO-2808 low (n = 23)	ONO-2808 medium (n = 23)	ONO-2808 high (n = 23)	ONO-2808 total (n = 69)
Age, years					
Mean (SD)	59.6 (6.7)	63.2 (7.8)	63.6 (4.5)	60.4 (7.7)	62.4 (6.9)
Median (range)	58 (51–74)	63 (48–80)	65 (56–74)	60 (49–73)	62 (48–80)
Sex, n (%)					
Male	15 (65)	9 (39)	14 (61)	13 (57)	36 (52)
Female	8 (35)	14 (61)	9 (39)	10 (43)	33 (48)
Race, n (%)					
White	15 (65)	18 (78)	18 (57)	15 (65)	46 (67)
Asian	7 (30)	3 (13)	9 (39)	6 (26)	18 (26)
Other[a]	1 (4)	2 (9)	1 (4)	2 (9)	5 (7)
Years since diagnosis, n (%)					
0 to <1	8 (35)	6 (26)	10 (43)	8 (35)	24 (35)
1 to <2	10 (43)	10 (43)	6 (26)	9 (39)	25 (36)
2 to <3	3 (13)	4 (17)	3 (13)	2 (9)	9 (13)
3 to <4	2 (9)	2 (9)	3 (13)	3 (13)	8 (12)
4 to <5	0	1 (4)	1 (4)	1 (4)	3 (4)
MSA subtype, n (%)					
MSA-P	13 (57)	11 (48)	12 (52)	12 (52)	35 (51)
MSA-C	10 (43)	12 (52)	11 (48)	11 (48)	34 (49)

[a]Includes Native/American and American Indian/Alaska Native, multiple races, and unknown. MSA, multiple system atrophy; MSA-C, cerebellar subtype of MSA; MSA-P, parkinsonian subtype of MSA; SD, standard deviation.

Safety

- During the double-blinded core part, most patients experienced ≥1 any-grade TEAE (93% [64/69] across all ONO-2808 doses and 91% [21/23] in the placebo group)
- Treatment-related TEAEs led to treatment interruption in 4% (3/69) of patients across all ONO-2808 doses and 4% (1/23) in the placebo group, and discontinuation in 1.4% (1/69) and 4% (1/23), respectively
- The most frequent TEAEs with ONO-2808 were urinary tract infection, headache, constipation, fall, and nasopharyngitis (**Table 2**)
- Transaminase elevations occurred in 1.2% (1/69) of patients across ONO-2808 dose levels; all were reversible, and none met Hy's law criteria (**Table 3**)
- As of February 24, 2026, there were no new safety signals in the open-label extension period

Table 2. TEAEs in ≥10% of patients in any treatment group during the double-blinded core part

Preferred term, n (%)	Placebo (n = 23)	ONO-2808 low (n = 23)	ONO-2808 medium (n = 23)	ONO-2808 high (n = 23)	ONO-2808 total (n = 69)
Urinary tract infection	8 (35)	9 (39)	2 (9)	4 (17)	15 (22)
Headache	0	3 (13)	2 (9)	6 (26)	11 (16)
Constipation	0	1 (4)	0	4 (17)	5 (7)
Fall	3 (13)	3 (13)	2 (9)	0	5 (7)
Nasopharyngitis	1 (4)	0	2 (9)	3 (13)	5 (7)
Contusion	4 (17)	2 (9)	1 (4)	1 (4)	4 (6)
Fatigue	3 (13)	1 (4)	1 (4)	2 (9)	4 (6)
Arthralgia	4 (17)	1 (4)	1 (4)	1 (4)	3 (4)
Dizziness	1 (4)	0	0	3 (13)	3 (4)
Diarrhea	3 (13)	1 (4)	1 (4)	0	2 (3)
Skin abrasion	3 (13)	0	0	0	0

Data from the double-blinded core part, which included results with ≥4 weeks of follow-up.

Table 3. Transaminase elevations adjudicated by the IDMC at week 24

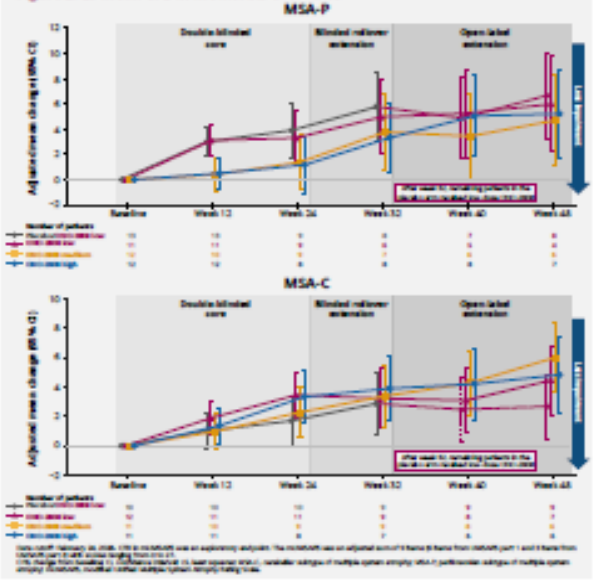
Category, n (%)	Placebo (n = 23)	ONO-2808 low (n = 23)	ONO-2808 medium (n = 23)	ONO-2808 high (n = 23)	ONO-2808 total (n = 69)
Any transaminase elevation confirmed by IDMC	0	1 (4)	3 (13)	4 (17)	8 (12)
Any treatment-related transaminase elevation by highest severity					
Mild	0	0	1 (4)	2 (9)	3 (4)
Moderate	0	0	1 (4)	2 (9)	3 (4)
Severe	0	1 (4)	1 (4)	0	2 (3)
Any treatment-related transaminase elevation leading to withdrawal of treatment	0	1 (4)	3 (13)	3 (13)	7 (10)
Any serious transaminase elevations	0	1 (4)	0	0	1 (1)
Treatment-related	0	1 (4)	0	0	1 (1)

Data from the double-blinded core part, which included results with ≥4 weeks of follow-up.
IDMC, independent data monitoring committee.

Efficacy

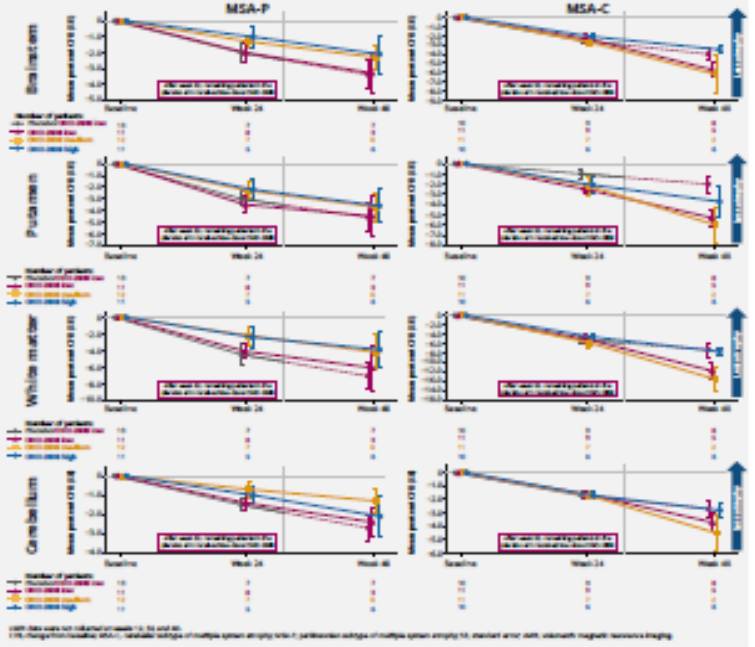
- The mean CFB (95% confidence interval [CI]) mUMSARS at week 24 showed attenuation of scores in patients with MSA-P in the ONO-2808 medium- (1.39 [−0.85 to 3.64]) and high-dose (1.16 [−1.1 to 3.41]) groups compared with placebo (3.90 [1.76 to 6.04]; **Figure 2**)
  - Attenuation of mUMSARS scores in patients with MSA-P were sustained up to week 48 in the ONO-2808 groups compared with patients randomized to placebo

Figure 2. LS Mean CFB in mUMSARS over time



- A dose-dependent response was observed in slowing of brain atrophy as assessed by vMRI in the brainstem, putamen, white matter, and cerebellum in patients with MSA-P treated with ONO-2808 vs those randomized to placebo placebo (**Figure 3**)

Figure 3. Mean percent CFB in vMRI measurements over time



CONCLUSIONS

- ONO-2808 had an acceptable safety profile in patients with MSA, and no new safety signals were observed with continued follow-up as of February 2026
  - All transaminase elevations across ONO-2808 doses were reversible, and none met Hy's law criteria
- In exploratory efficacy analyses up to week 48, ONO-2808 demonstrated a potential signal of efficacy as assessed by mUMSARS in patients with MSA-P
- ONO-2808 demonstrated slowing of brain atrophy over time vs placebo by vMRI in patients with MSA-P. The manageable safety profile and preliminary signs of efficacy support the continued investigation of ONO-2808 as a potential treatment to slow disease progression in patients with MSA

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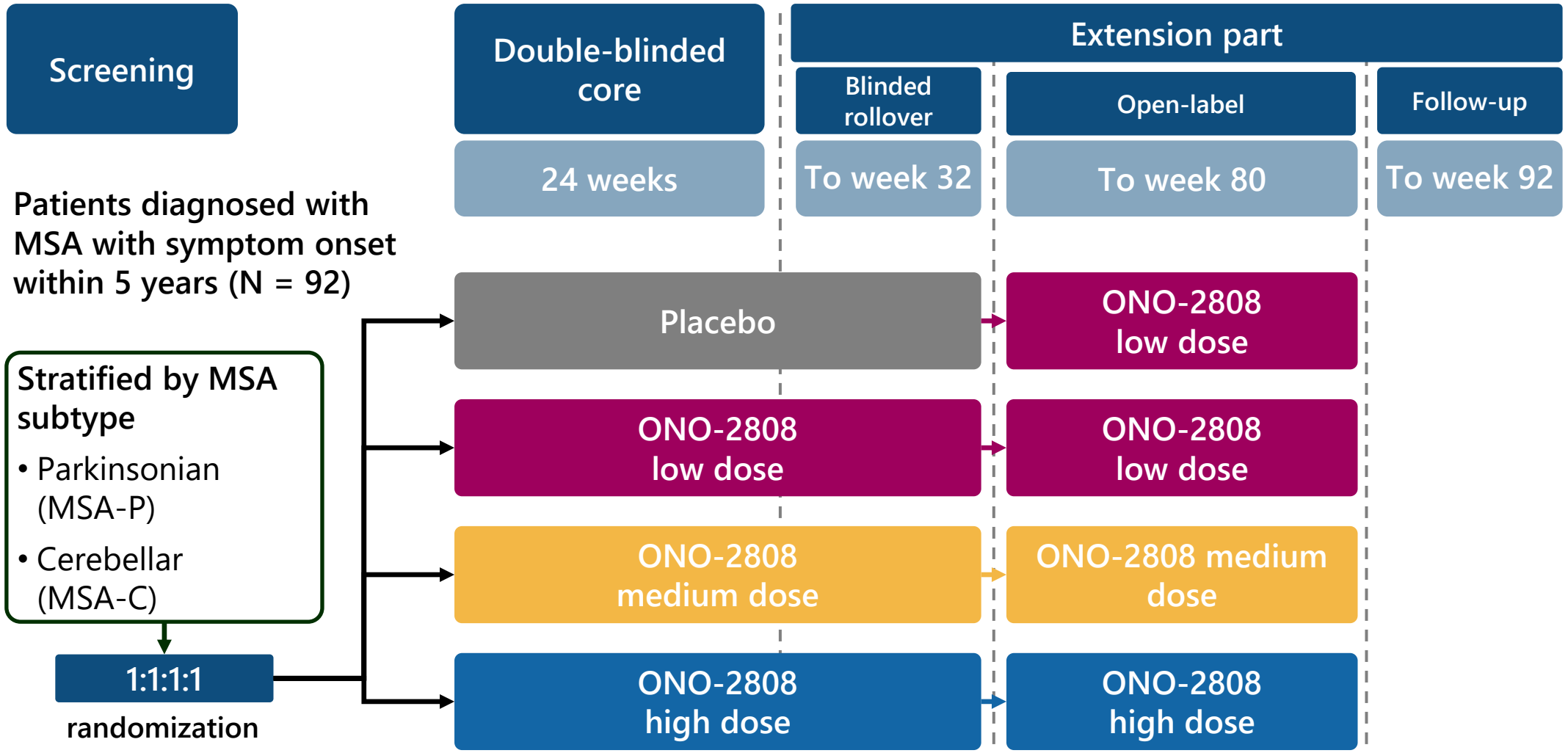
REFERENCES

ONO-2808-03 study design (NCT05923866)



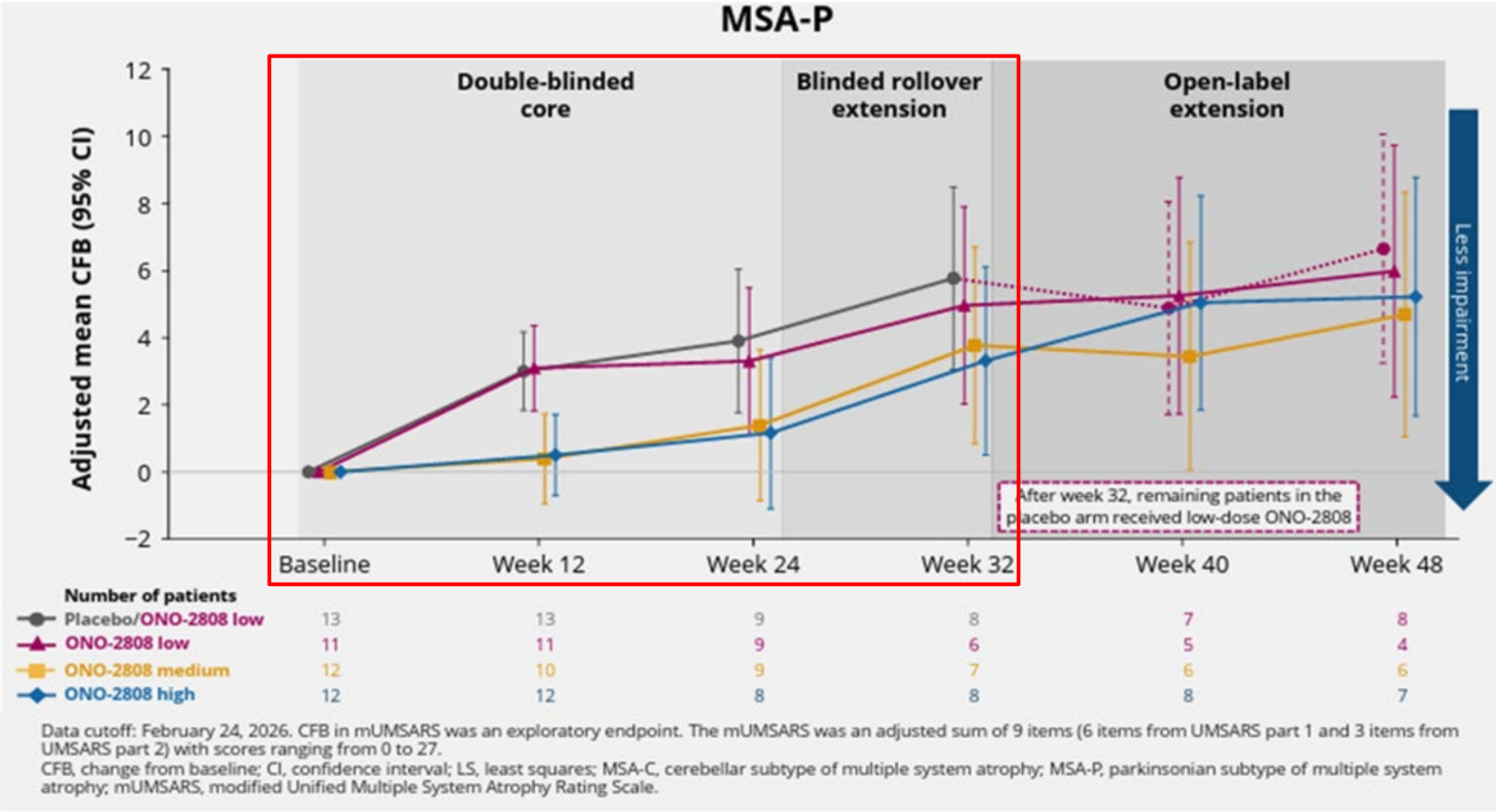
MSA, multiple system atrophy; MSA-C, cerebellar subtype of MSA; MSA-P, parkinsonian subtype of MSA.

Baseline demographics and clinical characteristics

Characteristic	Placebo n = 23	ONO-2808 low n = 23	ONO-2808 medium n = 23	ONO-2808 high n = 23	ONO-2808 total n = 69
Age, years					
Mean (SD)	59.6 (6.7)	63.2 (7.8)	63.6 (4.5)	60.4 (7.7)	62.4 (6.9)
Median (range)	58 (51–76)	63 (46–80)	65 (54–74)	60 (49–73)	62 (46–80)
Sex, n (%)					
Male	15 (65)	9 (39)	14 (61)	13 (57)	36 (52)
Female	8 (35)	14 (61)	9 (39)	10 (43)	33 (48)
Race, n (%)					
White	15 (65)	18 (78)	13 (57)	15 (65)	46 (67)
Asian	7 (30)	3 (13)	9 (39)	6 (26)	18 (26)
Other[a]	1 (4)	2 (9)	1 (4)	2 (9)	5 (7)
Years since diagnosis, n (%)					
0 to <1	8 (35)	6 (26)	10 (43)	8 (35)	24 (35)
1 to <2	10 (43)	10 (43)	6 (26)	9 (39)	25 (36)
2 to <3	3 (13)	4 (17)	3 (13)	2 (9)	9 (13)
3 to <4	2 (9)	2 (9)	3 (13)	3 (13)	8 (12)
4 to <5	0	1 (4)	1 (4)	1 (4)	3 (4)
MSA subtype, n (%)					
MSA-P	13 (57)	11 (48)	12 (52)	12 (52)	35 (51)
MSA-C	10 (43)	12 (52)	11 (48)	11 (48)	34 (49)

[a] Includes Black/African American and American Indian/Alaska Native.
MSA, multiple system atrophy; MSA-C, cerebellar subtype of MSA; MSA-P, parkinsonian subtype of MSA; SD, standard deviation.

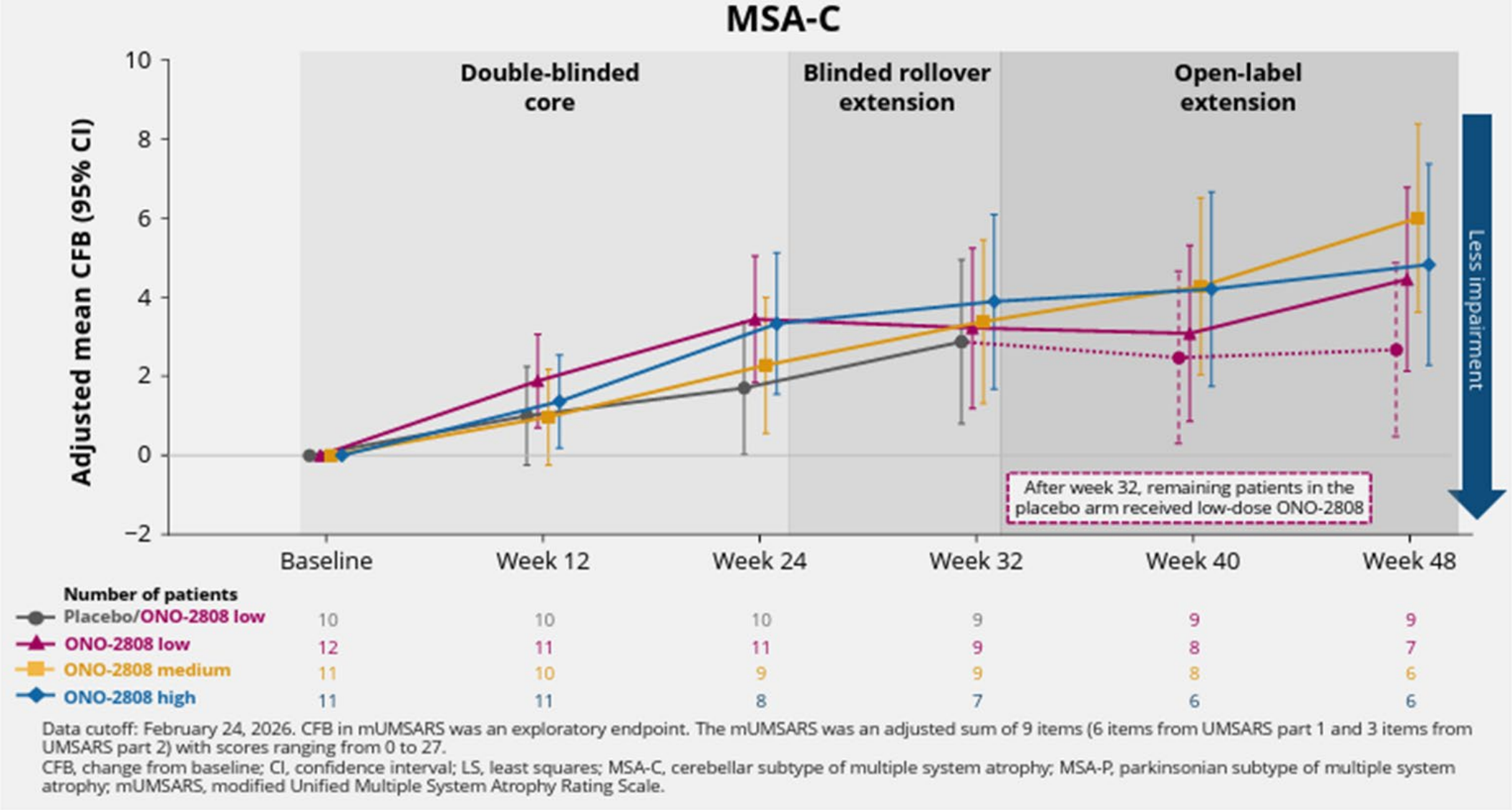
Efficacy-mUMSARS / MSA-P group



Data cutoff: February 24, 2026. CFB in mUMSARS was an exploratory endpoint. The mUMSARS was an adjusted sum of 9 items (6 items from UMSARS part 1 and 3 items from UMSARS part 2) with scores ranging from 0 to 27.
CFB, change from baseline; CI, confidence interval; LS, least squares; MSA-C, cerebellar subtype of multiple system atrophy; MSA-P, parkinsonian subtype of multiple system atrophy; mUMSARS, modified Unified Multiple System Atrophy Rating Scale.

Progression Suppression

Efficacy-mUMSARS / MSA-C group



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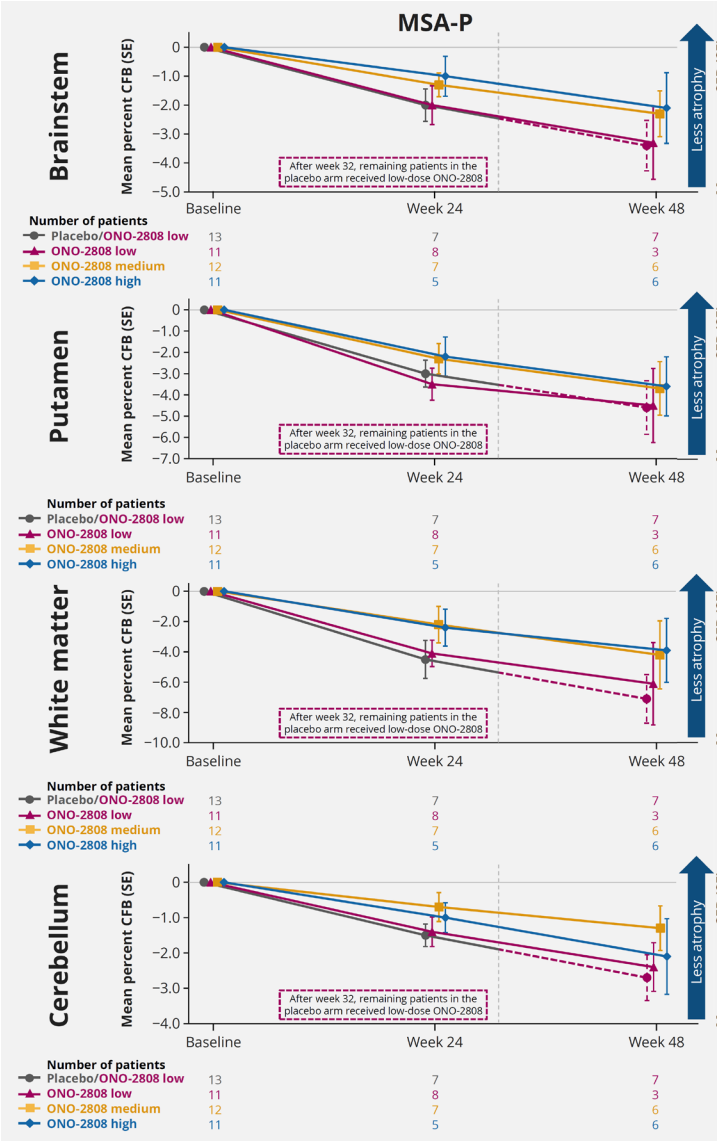
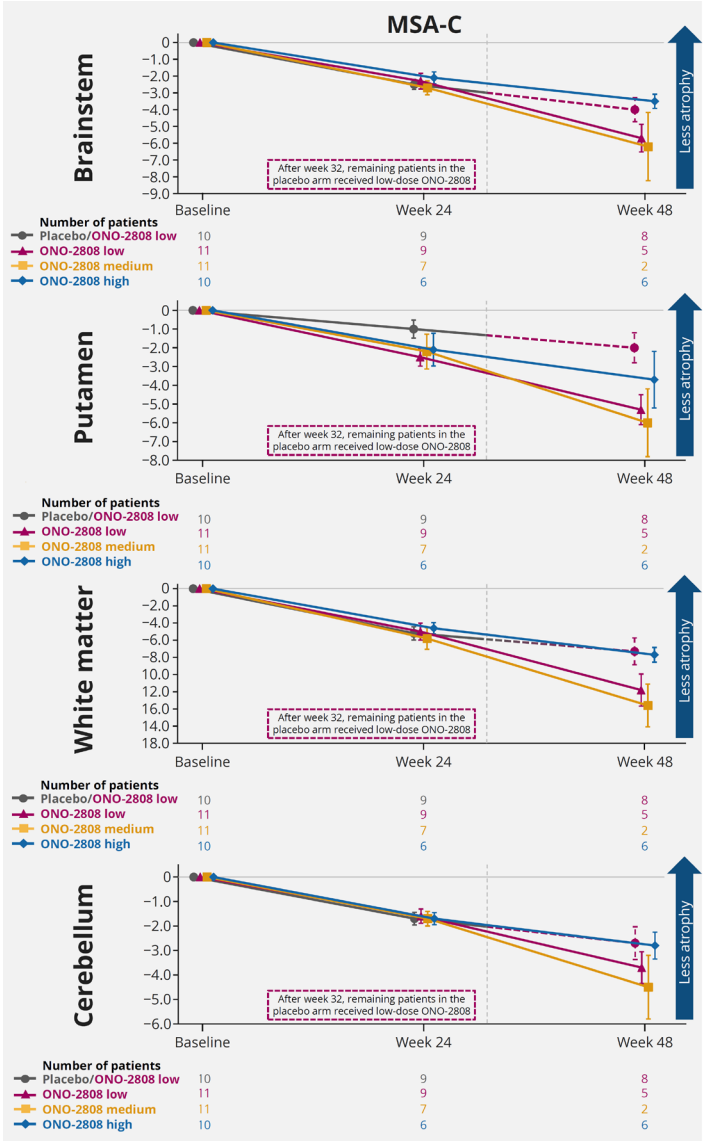
CFB, change from baseline; CI, confidence interval; LS, least squares; MSA-C, cerebellar subtype of multiple system atrophy; MSA-P, parkinsonian subtype of multiple system atrophy; mUMSARS, modified Unified Multiple System Atrophy Rating Scale.

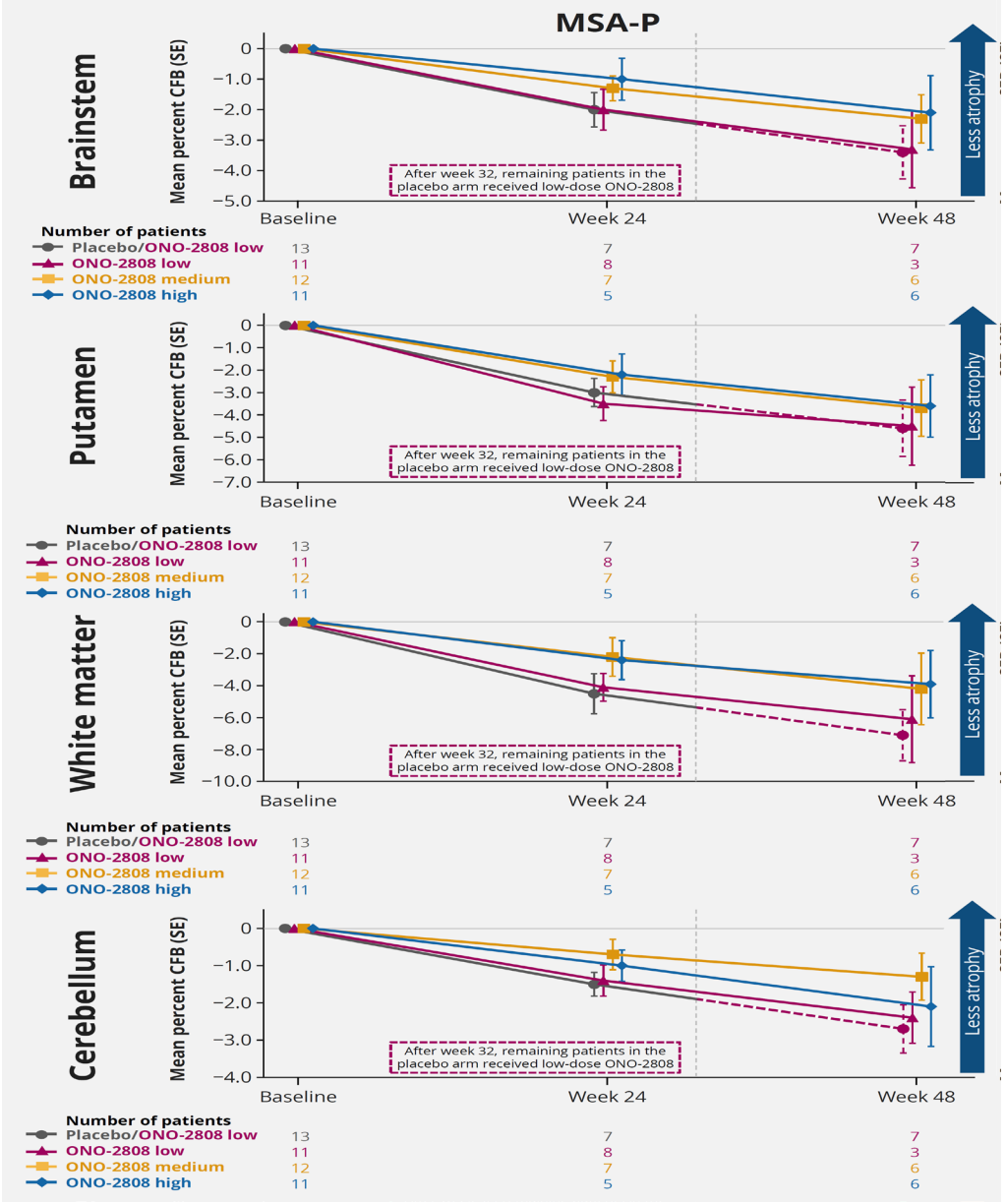
Progression
Suppression

Efficacy-vMRI measurements

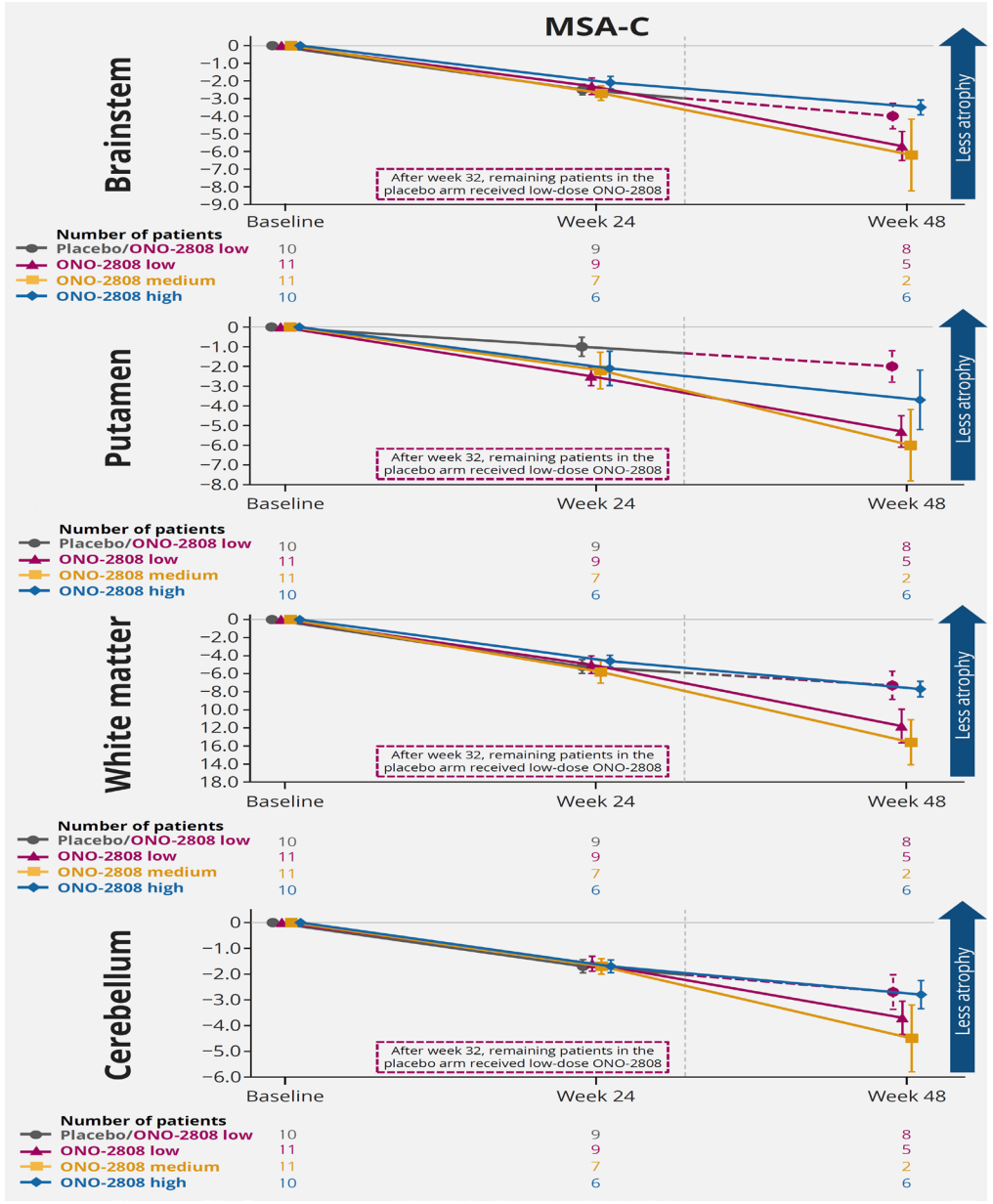




Efficacy-vMRI measurements / MSA-P group



Efficacy-vMRI measurements / MSA-C group



TEAEs in ≥10% of patients in any treatment group during the double-blinded core part

Preferred term, n (%)	Placebo n = 23	ONO-2808 low n = 23	ONO-2808 medium n = 23	ONO-2808 high n = 23	ONO-2808 total n = 69
Urinary tract infection	8 (35)	9 (39)	2 (9)	4 (17)	15 (22)
Headache	0	3 (13)	2 (9)	6 (26)	11 (16)
Constipation	0	1 (4)	0	4 (17)	5 (7)
Fall	3 (13)	3 (13)	2 (9)	0	5 (7)
Nasopharyngitis	1 (4)	0	2 (9)	3 (13)	5 (7)
Contusion	4 (17)	2 (9)	1 (4)	1 (4)	4 (6)
Fatigue	3 (13)	1 (4)	1 (4)	2 (9)	4 (6)
Arthralgia	4 (17)	1 (4)	1 (4)	1 (4)	3 (4)
Dizziness	1 (4)	0	0	3 (13)	3 (4)
Diarrhea	3 (13)	1 (4)	1 (4)	0	2 (3)
Skin abrasion	3 (13)	0	0	0	0

Data from the double-blinded core part , which included results with 24 weeks of follow-up. Adjudicated transaminase elevation events are described in Table 3.
TEAE, treatment-emergent adverse event.

Transaminase elevations adjudicated by the IDMC at week 24

Category, n (%)	Placebo n = 23	ONO-2808 low n = 23	ONO-2808 medium n = 23	ONO-2808 high n = 23	ONO-2808 total n = 69
Any transaminase elevation confirmed by IDMC	0	1 (4)	3 (13)	4 (17)	8 (12)
Any treatment-related transaminase elevation by highest severity					
Mild	0	0	1 (4)	2 (9)	3 (4)
Moderate	0	0	1 (4)	2 (9)	3 (4)
Severe	0	1 (4)	1 (4)	0	2 (3)
Any treatment-related transaminase elevation leading to withdrawal of treatment	0	1 (4)	3 (13)	3 (13)	7 (10)
Any serious transaminase elevations	0	1 (4)	0	0	1 (1)
Treatment-related	0	1 (4)	0	0	1 (1)

Data from the double-blinded core part, which included results with 24 weeks of follow-up.
IDMC, independent data monitoring committee.

Discussion on the Results of ONO-2808-03 Study

Modified UMSARS for ONO-2808

Used in the ONO-2808 Phase 2 study (maximum score: 27)

-	**Part I: Historical Review** (Activities of Daily Living) Assesses average function over the past 2 weeks based on an interview with the patient and/or caregiver	**Part II: Motor Examination Scale** (Motor Function Assessment) Rated on the more affected side
1	Speech	Facial expression
2	Swallowing	Speech
3	Handwriting	Oculomotor dysfunction
4	Cutting food/handling utensils	Tremor at rest
5	Dressing	Action tremor
6	Hygiene	Increased tone
7	Walking	Rapid alternating movements
8	Falls	Finger taps
9	Orthostatic symptoms	Leg agility
10	Urinary function	Heel-knee-shin test
11	Sexual function	Arising from chair
12	Bowel function	Posture
13	---	Body sway
14	---	Gait
-	**Minimum 0, maximum 18**	**Minimum 0, maximum 9**

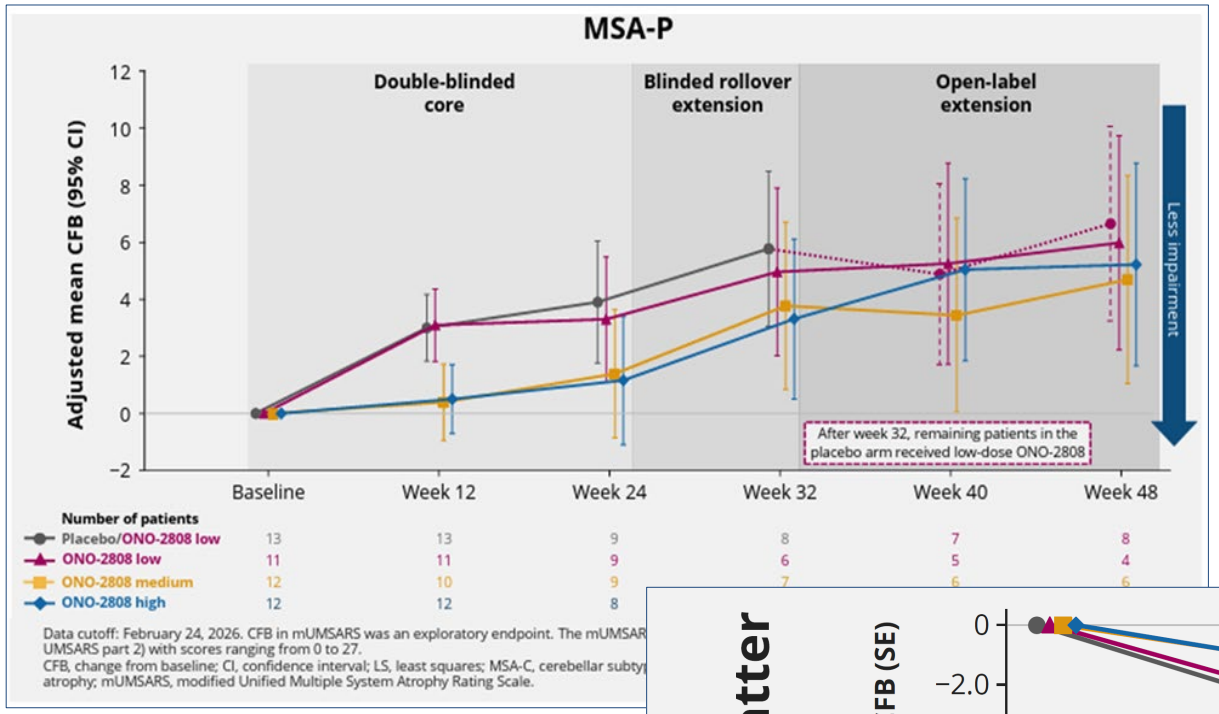
Modified UMSARS for Amlenetug (Lu AF82422)

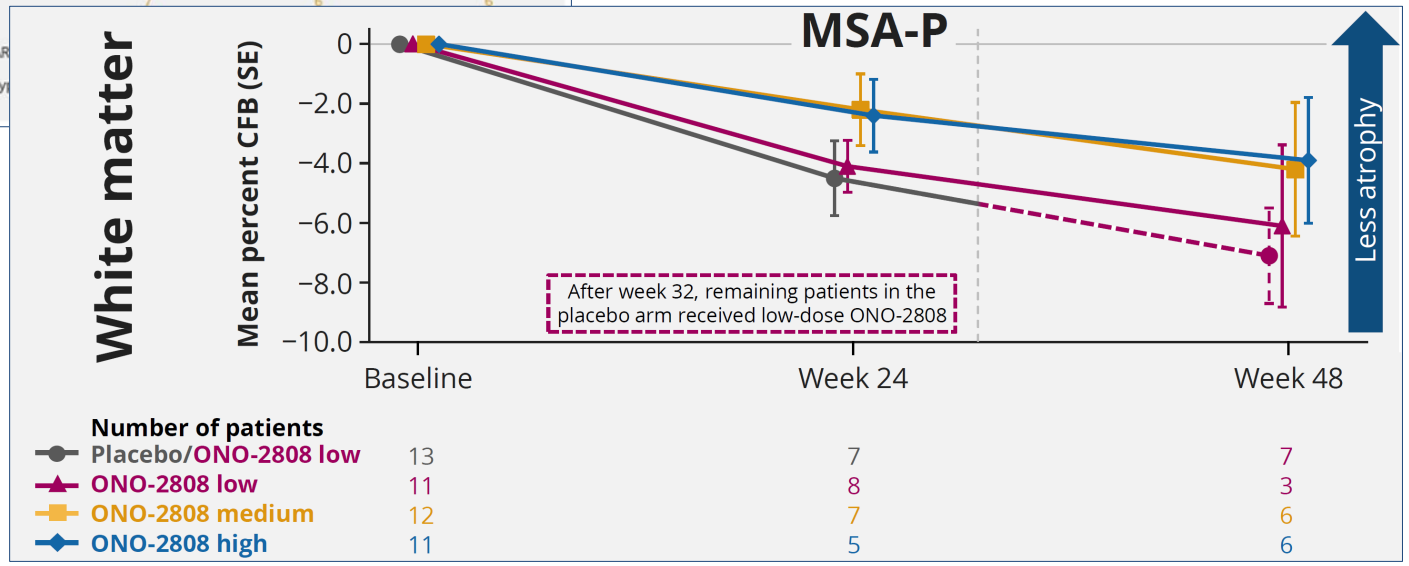
Used in Phase 2 study of Lundbeck's investigational drug (Amlenetug, Lu AF82422; maximum score, 48)

-	**Part I: Historical Review** (Activities of Daily Living) Assesses average function over the past 2 weeks based on an interview with the patient and/or caregiver	**Part II: Motor Examination Scale** (Motor Function Assessment) Rated on the more affected side
1	Speech	Facial expression
2	Swallowing	Speech
3	Handwriting	Oculomotor dysfunction
4	Cutting food/handling utensils	Tremor at rest
5	Dressing	Action tremor
6	Hygiene	Increased tone
7	Walking	Rapid alternating movements
8	Falls	Finger taps
9	Orthostatic symptoms	Leg agility
10	Urinary function	Heel-knee-shin test
11	Sexual function	Arising from chair
12	Bowel function	Posture
13	---	Body sway
14	---	Gait
-	**Minimum 12, maximum 48**	**0**

Adapted from Kjærsgaard L et al., Lancet Neurol. 2026 Jun;25(6):560–570.

ONO-2808 Summary





ONO-2808 Development Status

Indication(s)	Development phase	Status	Regions	Study ID	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
MSA (MSA-P)	P3	In preparation	Planned in Japan, the US, and EU (TBD)	TBD						**P3: MSA** (planned) ONO-2808-03-001 study				
MSA	P2	Key data obtained in FY2025	Japan and the US	NCT05923866			**P2: MSA** ONO-2808-03 study							

Today's Agenda

Opening

The data of POC Study

- ONO-4578 (ASCO2026)
- ONO-2808 (7th World Parkinson Congress)

Drug discovery activities in the Central Nervous System (CNS) field

Toichi Takino

Representative Director,
President and COO

Tatsuya Okamoto

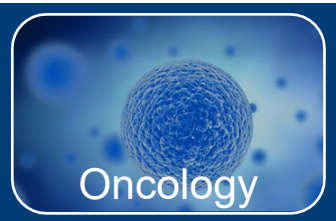
Corporate Officer /
Executive Vice President,
Clinical Development

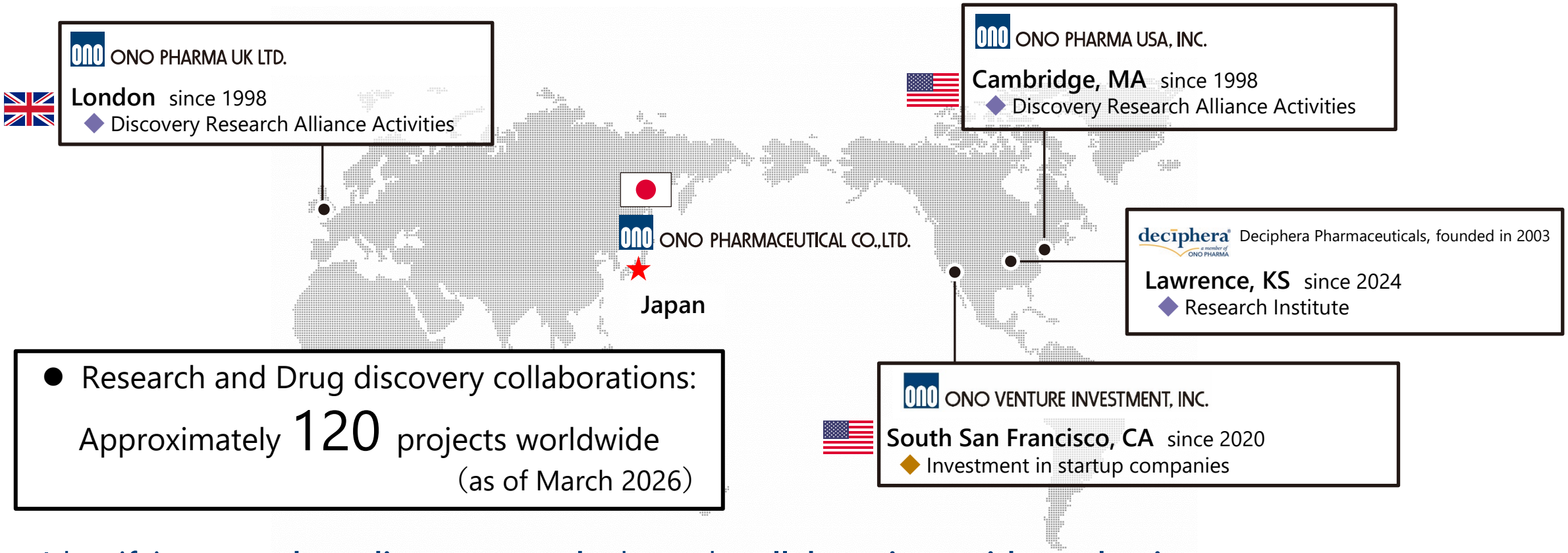
Seishi Katsumata

Corporate Officer /
Executive Vice President,
Discovery & Research

ONO's Drug Discovery

Focus Area





ONO PHARMA UK LTD.
London since 1998
◆ Discovery Research Alliance Activities

ONO PHARMA USA, INC.
Cambridge, MA since 1998
◆ Discovery Research Alliance Activities

ONO PHARMACEUTICAL CO.,LTD.
Japan

deciphera Deciphera Pharmaceuticals, founded in 2003
Lawrence, KS since 2024
◆ Research Institute

ONO VENTURE INVESTMENT, INC.
South San Francisco, CA since 2020
◆ Investment in startup companies

- Research and Drug discovery collaborations:
  Approximately **120** projects worldwide
  (as of March 2026)

- Identifying **new drug discovery seeds** through **collaborations with academia**
- Advancing drug discovery using **the optimal modality** through **collaborations with biotech companies**

Drug Discovery Strategy in Neurology

- ✓ Elucidate disease biology to address unmet medical needs
- ✓ Develop disease-modifying therapies, not only symptomatic treatments
- ✓ Target glial cells, not only neurons
- ✓ Leverage clinical insights to improve translatability to humans

Deliver new drugs through cutting-edge technology and open innovation

Pipeline Overview (Neurology)

AD : Alzheimer's Disease
ALS : Amyotrophic Lateral Sclerosis
ACI : Acute Cerebral Infarction
CH : Cerebral Hemorrhage
CIPN : Chemotherapy-Induced Peripheral Neuropathy
CINV : Chemotherapy-Induced Nausea and Vomiting
DPN : Diabetic Peripheral Neuropathy
IBS : Irritable Bowel Syndrome
PD : Parkinson's Disease
MS : Multiple Sclerosis
MSA : Multiple System Atrophy
SH : Subarachnoid Hemorrhage

Neurodegenerative Disorders

CATACLOT®
SH, CH

ONO-1603
AD

ONO-2506
AD, PD, ALS, ACI
(Out-licensed to Merck)

RIVASTACH®
AD
(In-licensed from Novartis)

ONO-4641
MS
(Out-licensed to Merck Serono)

ONO-2160
PD

ONGENTYS®
PD
(In-licensed from Bial)

Psychiatric & Neurological Disorders

ONO-2333MS
Depression

ONO-2745
Short-acting General Anesthesia
(In-licensed from Paion)

ONO-2909
Narcolepsy

Pain & Nerve Disorders

KINEDAK®
DPN

ONO-9902
Pain

OPALMON®
Spinal Stenosis

EMEND®
CINV
(In-licensed from Merck)

ONO-2921
Neuropathic Pain

ONO-2952
IBS

ONO-2910
CIPN, DPN

In Development

ONO-2020
AD, Agitation in AD
P2 Ongoing

ONO-2808
MSA
POC Established

ONO-2017
Epilepsy (Filed)
(In-licensed from SK bio)

ONO-1110
Depression,
Social Anxiety Disorder
P2 Ongoing

ONO-2416
Psychiatric Disorders
P1 Ongoing

ONO-1110
Postherpetic Neuralgia,
Fibromyalgia,
Hunner Type Interstitial Cystitis
P2 Ongoing

Glial Cell-targeted Drug Discovery

AD : Alzheimer's Disease
CIPN : Chemotherapy-Induced Peripheral Neuropathy
DPN : Diabetic Peripheral Neuropathy
IBS : Irritable Bowel Syndrome
MSA : Multiple System Atrophy

Pioneering Glial Drug Discovery

ONO-2506（Arocyte, injection）
Research and Development

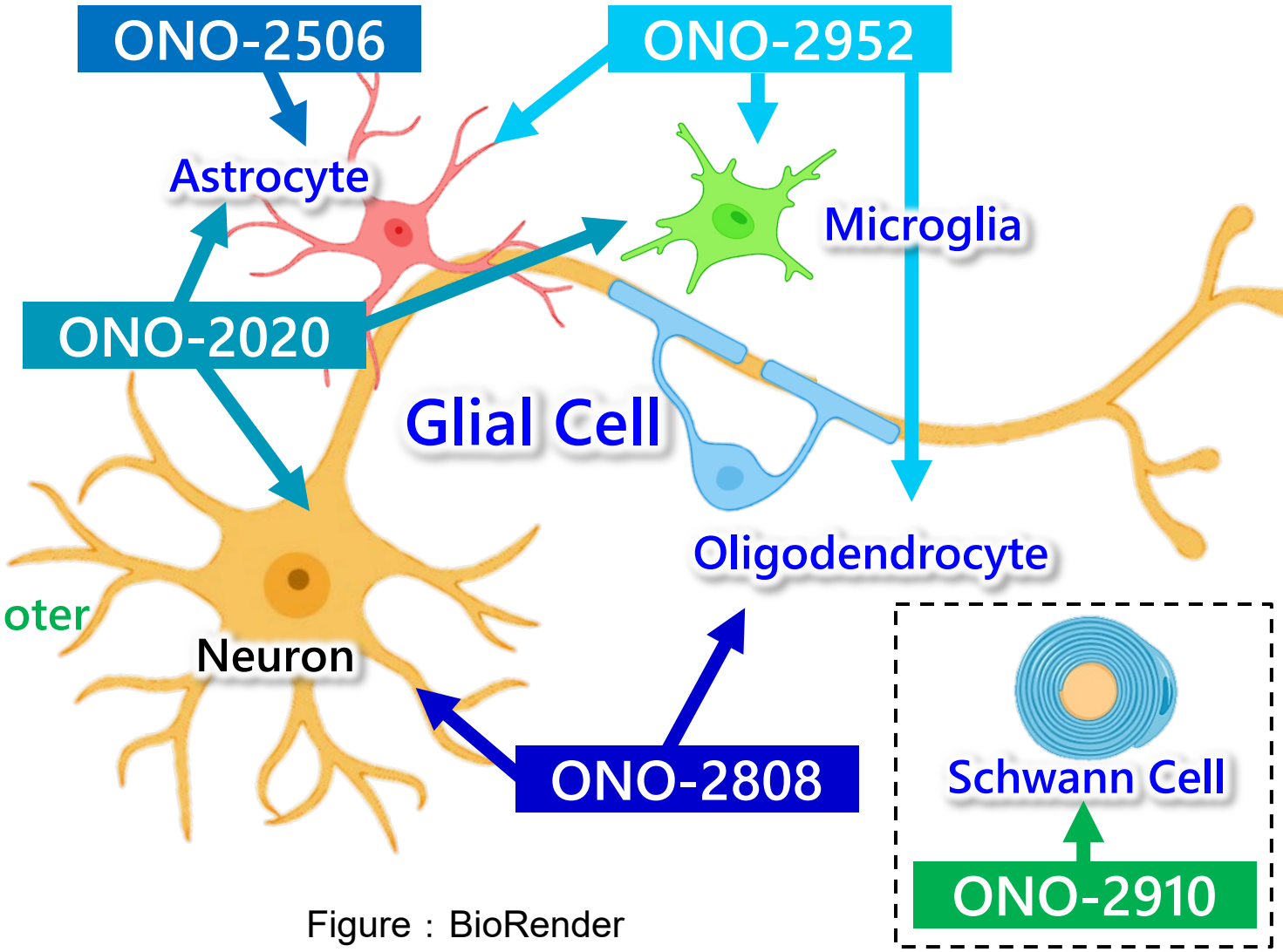
Advancing Drug Discovery Leveraging KOL Networks

ONO-2952：TSPO Antagonist
(stress disorders, IBS)

ONO-2910：
Schwann Cell Differentiation Promoter
(CIPN, DPN)

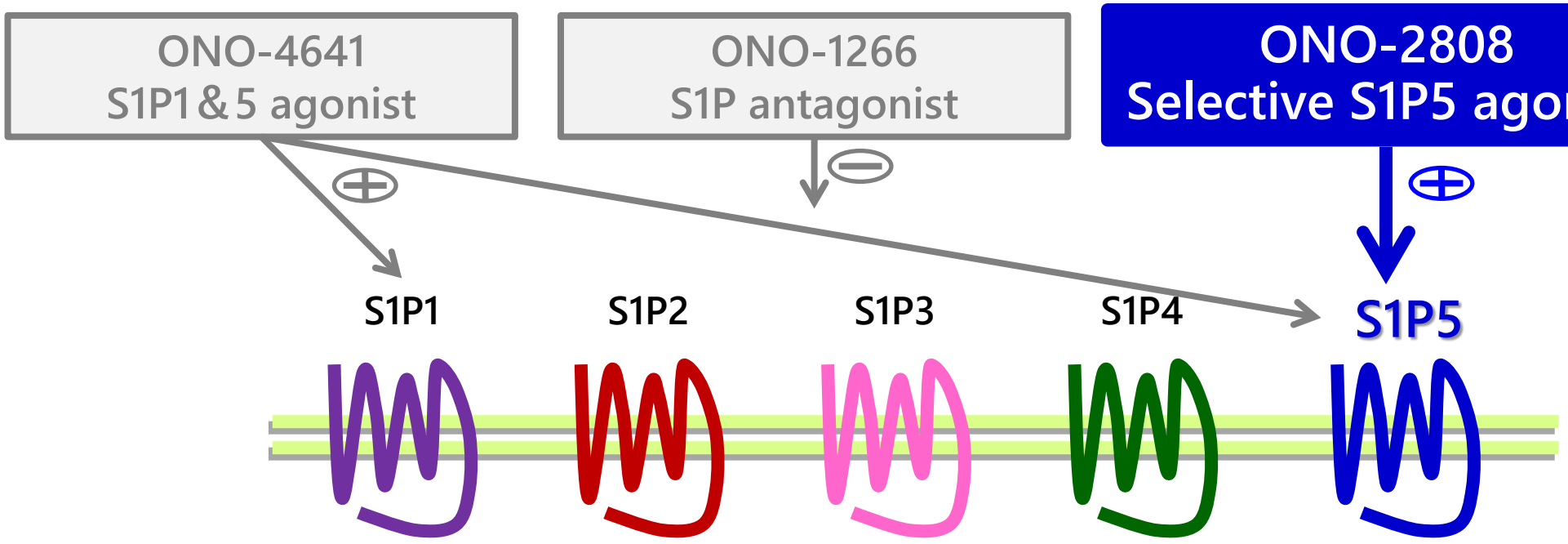
◆ ONO-2808：S1P5 Agonist (MSA)

◆ ONO-2020：Epigenetics Regulator
(AD, Agitation in AD)



Figure：BioRender

Lipid-targeted Drug Discovery (S1P Receptor Modulation)



- Drug discovery focusing on sphingosine-1-phosphate (S1P) function
- ONO-2808 focuses on its effects on oligodendrocytes and neurons

Ion Channel-targeted Drug Discovery

Utilizing Platform & Technology Through Open Innovation

- BioFocus (now Charles River)
- Evotec
- Vanderbilt University
- Xention (now Metrion Biosciences)

Experience in
Multiple Ion Channel Drug Discovery

- ◆ **$GABA_A\alpha5$ NAM** (cognitive impairment)
- ◆ **Channel A inhibitor** (pain)
- ◆ **Channel B modulator** (pain, cognitive impairment)

Focus on the action on extrasynaptic $GABA_A$ receptors

- ◆ **ONO-2017 (cenobamate, In-licensed from SK bio) : Voltage-gated Na^+ channel inhibition + $GABA_A$ activation** (epilepsy)

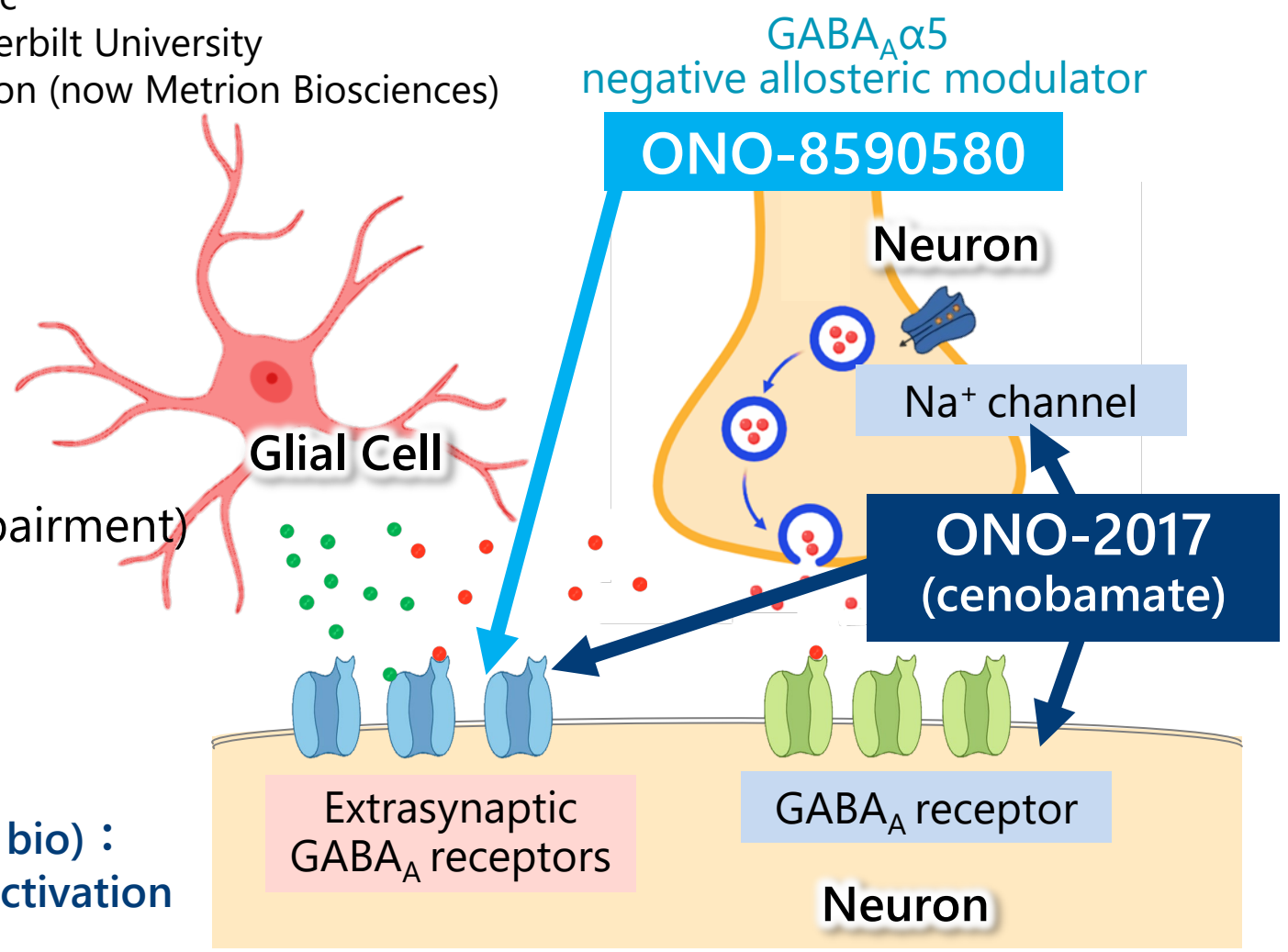
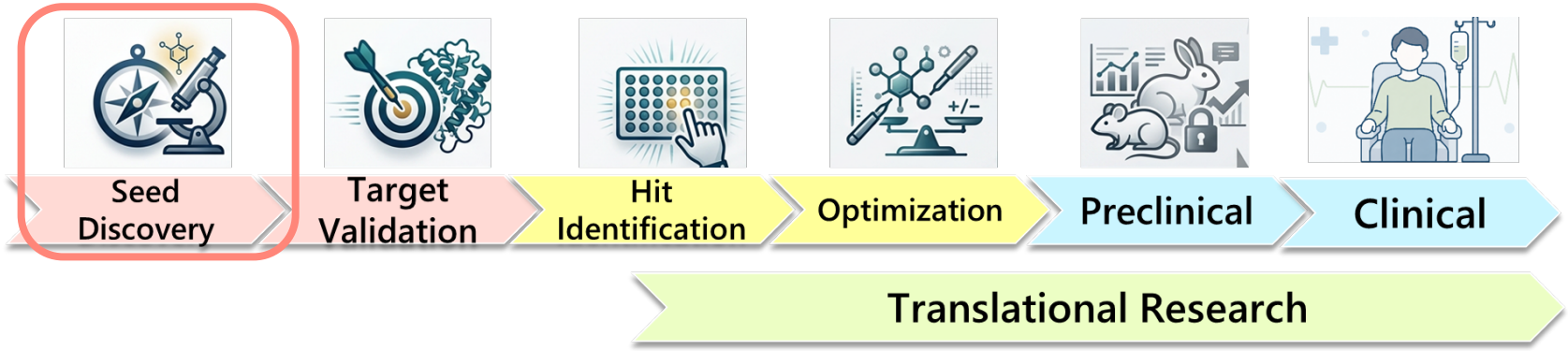


Figure : BioRender

Challenges and Strategies in Neurological Drug Discovery

Challenges	Strategies
Target Validation ● Understanding disease pathology ● Access to brain tissue and cerebrospinal fluid ● Appropriate disease models	✓ Research collaboration for target discovery ✓ Utilizing disease models and evaluation systems from academia that recapitulate disease pathology
Drug Discovery ● Identification of high-quality hits ● CNS penetration	✓ Leveraging drug discovery platforms through biotech collaboration ✓ Leveraging computational science capabilities from academia and biotech
Translational Research ● Prediction of clinical efficacy ● Appropriate clinical trial assessment	✓ Identifying and utilizing biomarkers from early stages of drug discovery ✓ Biomarker discovery through clinical research

Challenges and Strategies in Neurological Drug Discovery

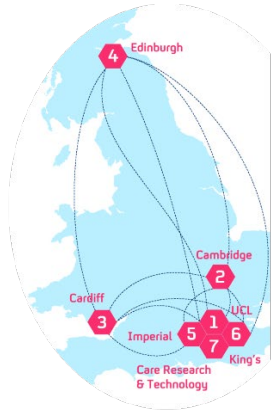


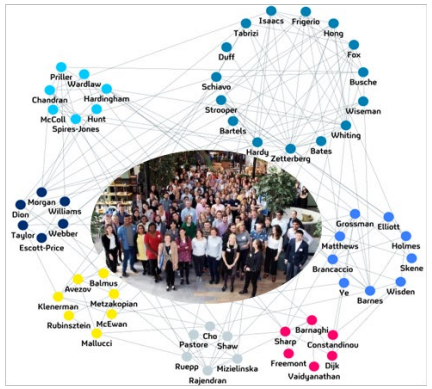
The Tohoku University Tohoku Medical Megabank Organization (ToMMo)

- Conducting community-based cohort study and three-generation cohort study launched in 2013
- Performing large-scale whole genome sequencing of the general population with follow-up capability
- Completing whole genome sequence of 100,000 Japanese individuals in June 2024 (one of the world's largest)
- Ono has participated in the Consortium for Integrated Analysis of Whole Genome Information and Medical/Health Information since March 2021.

Validating target relevance using global-scale genome analysis data

Collaboration with UK Dementia Research Institute

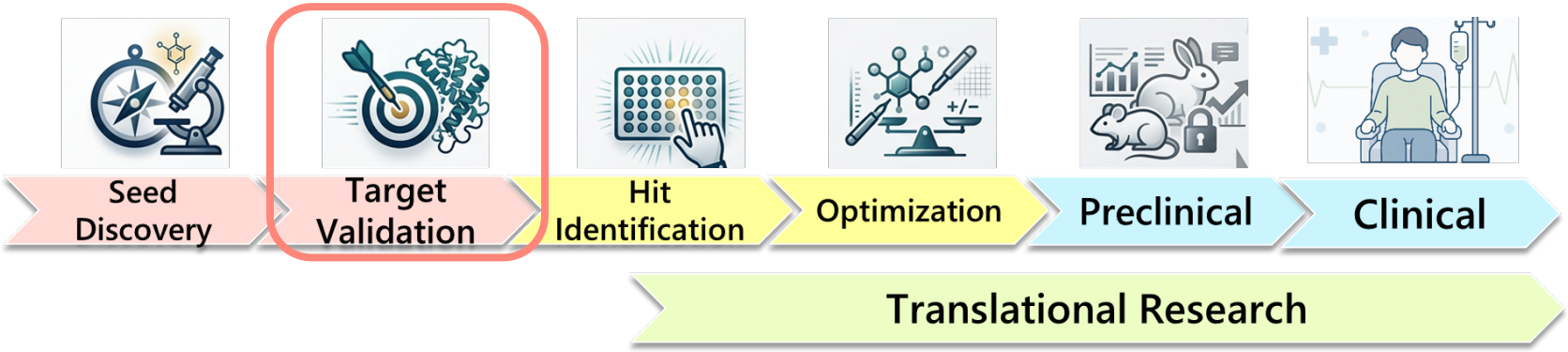




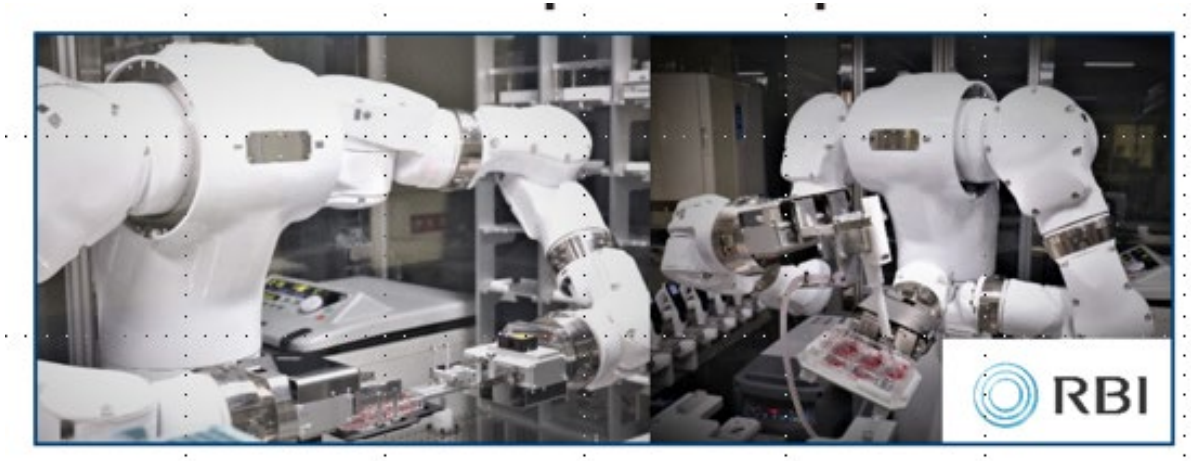
University College London | University of Cambridge | Cardiff University | University of Edinburgh | Imperial College London | King's College London

Identifying of new drug targets through research networks and strong research capabilities in the UK

Challenges and Strategies in Neurological Drug Discovery



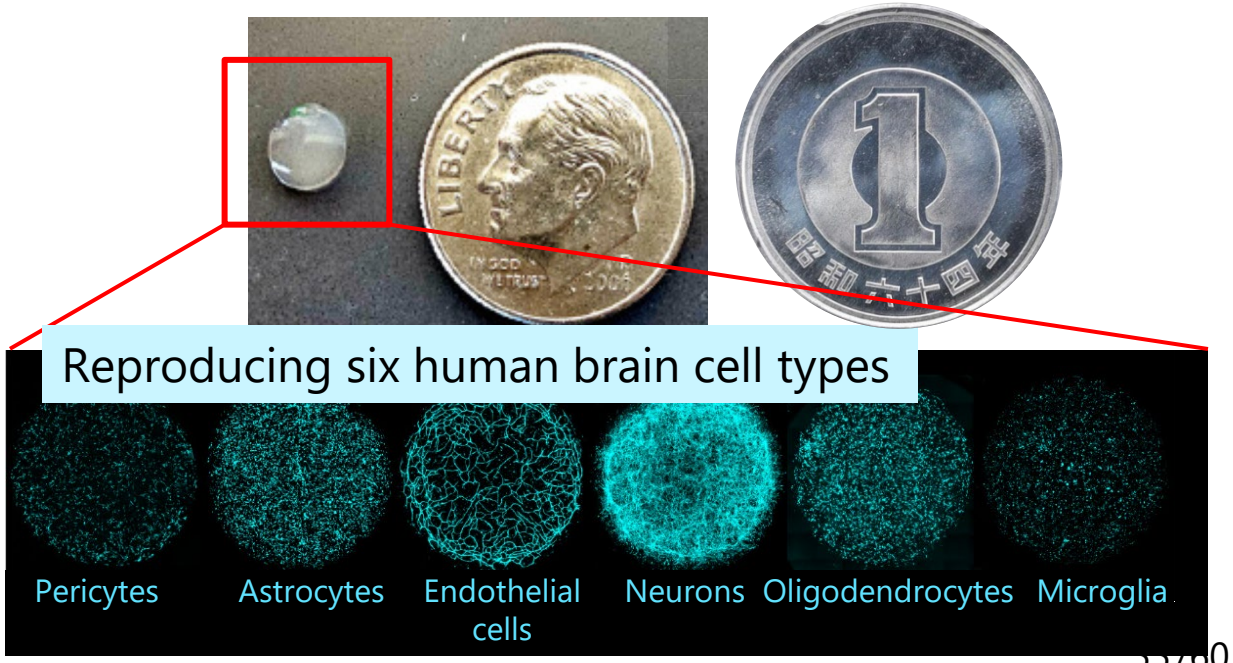
Introduction of Mahoro robots



Stably culturing iPS cells to support drug discovery projects

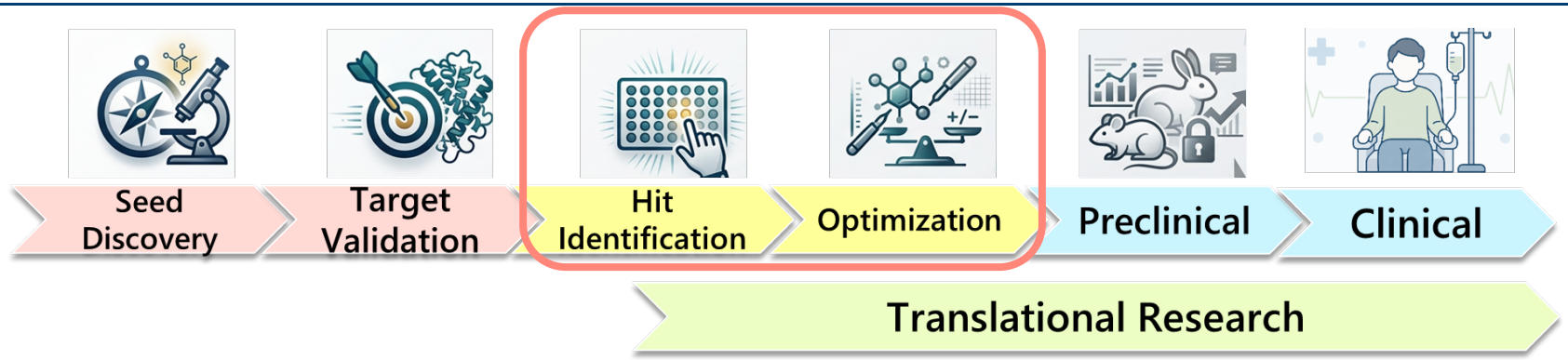
Brain organoid model using iPS cells

Organoid 10-cent coin 1-yen coin

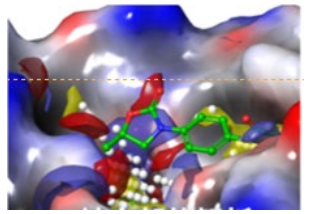


Proc Natl Acad Sci USA. 2025 Oct 21;122(42):e2511596122.

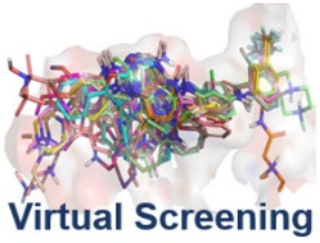
Challenges and Strategies in Neurological Drug Discovery



AI-driven drug discovery with Tokyo-1



Binding Site Analysis



Rapidly processing and analyzing large chemical and biochemical data to identify high-quality hit compounds

Drug discovery partnership with Vanderbilt University

December 10, 2015

Vanderbilt, Ono Pharmaceutical sign drug discovery agreement

Vanderbilt University Medical Center and Ono Pharmaceutical Group, an international company based in Japan, have signed a drug discovery agreement.

https://news.vumc.org/2015/12/10/vanderbilt-ono-pharmaceutical-sign-drug-discovery-agreement/

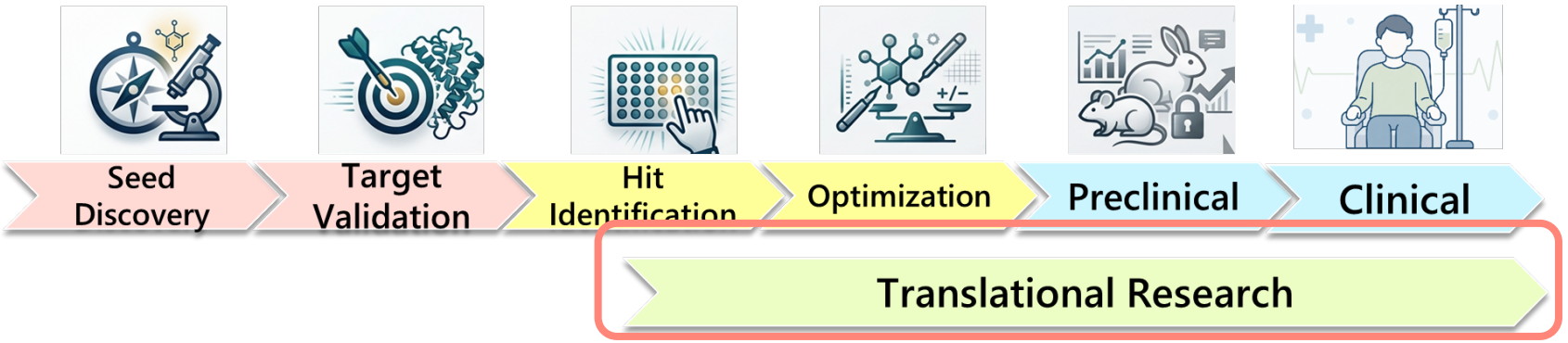
Lindsley Lab

WARREN CENTER FOR NEUROSCIENCE DRUG DISCOVERY

https://lab.vanderbilt.edu/lindsleylab/

Leveraging Vanderbilt's ion channel drug discovery expertise to rapidly optimize compounds

Challenges and Strategies in Neurological Drug Discovery



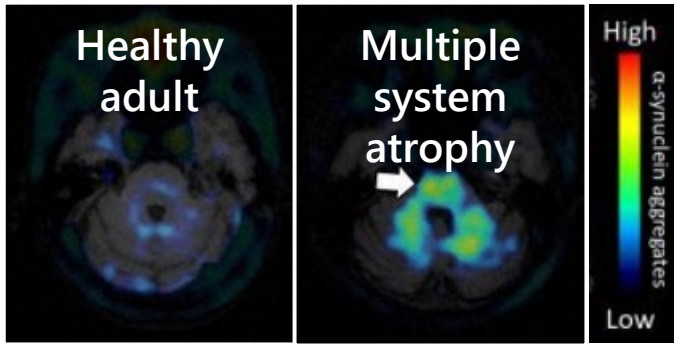
Co-development of brain PET ligands (CNS drug discovery alliance)

Co-development of α-synuclein pathology PET

調和ある多様性の創造 国立研究開発法人 QST 量子科学技術研究開発機構 National Institutes for Quantum Science and Technology

Eisai ONO Takeda

Successful imaging of α-synuclein pathology in the human brain (world's first)



'22/8/31 QST PR (https://www.qst.go.jp/site/news/20220831.html)

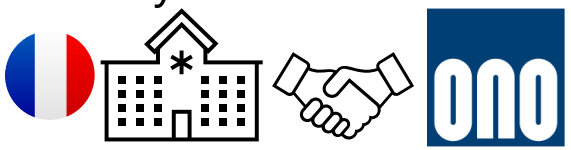
Longitudinal clinical study of the disease (investigator-initiated observational study)

Disease Progression in Multiple System Atrophy: The ASPIRE Multi-Modal Biomarker Study

Margherita Fabbri, X,[1,2,3†] Natalia del Campo,[1†] Wassilios G. Meissner,[4,5] Vanessa Rousseau,[6] Agnès Sommet,[6] Pierre Payoux,[3] Pierre Gantet,[7] Amel Drif,[8] Hélène Catalá,[8] Claire Thalamas,[8] Christine Tranchant,[9] Franck Durif,[10] Ana Marques,[10] Alexandre Eusebio,[11] Luc Defebvre,[12] Jean-Christophe Corvol,[13] Stéphane Thobois,[14,15,16] Anthime Flaus,[15,17] Anne-Gaelle Corbille,[18] Solène Frismand,[19] Beverley Patterson,[20,21] Alexandra Foubert-Samier,[4,5] Anne Pavy-Le Traon,[1,2] Germain Arribarat,[3] Patrice Péran, PhD,[3‡] and Olivier Rascol, MD, PhD,[1,2,3‡] for the ASPIRE Study Group

Ann Neurol. 2026 Jan;99(1):96-113.

Partnership with University of Toulouse in France



Identification of clinical biomarkers for multiple system atrophy

▼

Utilized in the clinical trial for ONO-2808

Development Pipeline (Neurology)

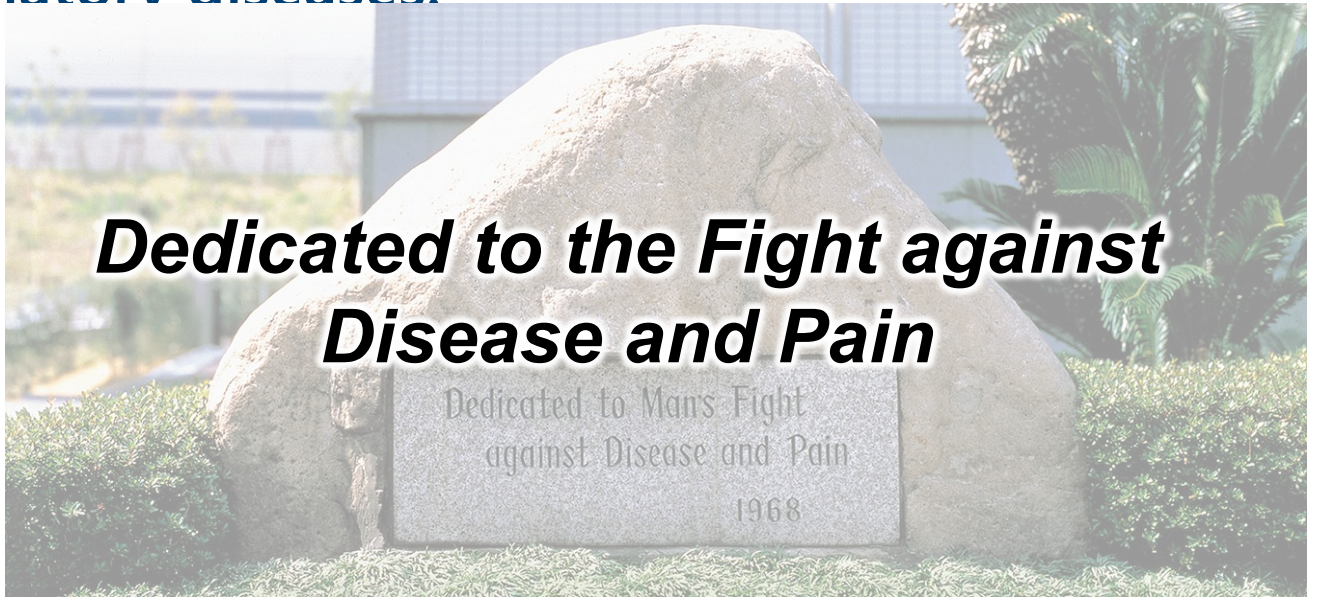
Code	Target Indication	P Ⅰ	P Ⅱ	P Ⅲ	Filed	Approval
ONO-2017	Partial-onset seizures	■	■	■	■	
	Partial-onset seizures (pediatric)	■	■	■		
	Primary generalized tonic-clonic seizures	■	■	■		
ONO-2808	Mutiple system atrophy	■	■			
ONO-1110	Postherpetic neuralgia	■	■			
	Fibromyalgia	■	■			
	Hunner-type interstitial cystitis	■	■			
	Major depressive disorder	■	■			
	Social anxiety disorder	■	■			
ONO-2020	Alzheimer's disease (AD)	■	■			
	Agitation associated with dementia due to AD	■	■			
ONO-2416	Psychiatric disorders	■				

⋮ Coming soon

Summary

- Ono is strengthening our pipeline by integrating internal and external expertise across the stage of the drug discovery process.

- Ono leverages cutting-edge technologies and open innovation to deliver innovative new drugs as quickly as possible to patients worldwide, addressing unmet medical needs not only in neurology but also in oncology, immunology,
and inflammatory diseases.



ONO PHARMA

Dedicated to the Fight against Disease and Pain