Development Pipeline Progress Status

Status of regulatory filing for approval in Japan, US and Europe

As of October 30, 2025

Filed | Approved | Met PE

OPDIVO | Other than OPDIVO

DCC-3014（ROMVIMZA）
〔TGCT〕
2024/07⇒2025/09

DCC-3014（ROMVIMZA）
〔TGCT〕
2024/08⇒2025/02

〔1L-Hepatocellular carcinoma〕
with YERVOY
CheckMate-9DW
2024/08⇒2025/06

〔1L- Colorectal cancer (MSI-H)〕
with YERVOY
CheckMate-8HW
2024/09⇒2025/08

BRAFTOVI
〔1L-BRAF-mutant Colorectal cancer〕
with Cetuximab and FOLFOX
2024/12

ONO-4059（VELEXBRU）
〔2L-PCNSL〕

ONO-2017
〔Partial-onset seizures〕
2025/09

〔Neoadjuvant, Adjuvant - NSCLC〕
with Chemo
CheckMate-77T

〔Neoadjuvant, Adjuvant - Bladder cancer〕
with Chemo
ONO-4538-86

〔Adjuvant Hepatocellular carcinoma〕
CheckMate-9DX

FY2024 (results) | FY2025 | FY2026

PE : Primary endpoint

Development status of OPDIVO

As of October 30, 2025

- Approval or filed/awaiting approval in the past year
- Ongoing key clinical trials for approval

Target disease	Treatment Line	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Non-small cell lung cancer	Neo-adjuvant・Adjuvant	with Chemo	Ⅲ	Ⅲ	Ⅲ	Approved	Approved
Colorectal cancer	MSI-H／dMMR (1st)	with Ipi	Approved	–	–	Approved	Approved
Hepatocellular carcinoma	Adjuvant	Monotherapy	Ⅲ	Ⅲ	Ⅲ	Ⅲ	Ⅲ
	1st	with Ipi	Approved	Approved	Approved	Approved	Approved
Urothelial cancer / Bladder cancer	Neo-adjuvant ・Adjuvant	with Chemo	Ⅲ	Ⅲ	Ⅲ	Ⅲ	Ⅲ
Rhabdoid tumor	2nd	Monotherapy	Ⅱ	–	–	–	–
Richter transformation	2nd	Monotherapy	Ⅱ	–	–	–	–
Solid tumor	–	ONO-4538HSC (Comibination with vorhyaluronidase alfa)	Ⅰ	–	–	Approved	Approved

※Red: Update after announcement of FY 2024 financial result in May 2025
※Red: Update after Q1 FY2025 in August

Development pipeline (Oncology) ①

As of October 30, 2025

Code (Generic name)MOA, Modality	Target Indication	PI	PI/II	PII	PIII	F	A	Status	Area	ID
BRAFTOVI Capsule (Encorafenib) BRAF inhibitor	BRAF-mutant thyroid cancer	■	■	■	■	■		FY2024.12 Filing accepted	JP, US, EU, KR, TW and others★	NCT04607421
QINLOCK (ripretinib) KIT inhibitor	Gastrointestinal Stromal Tumor 2L KIT Exon 11+17/18 (GIST)	■	■	■	■			FY2025 Primary Completion	US, EU, KR, TW and others	NCT05734105
ONO-4059 (tirabrutinib) BTK inhibitor	Primary central nervous system lymphoma (PCNSL) ≥2L	■	■	■	■			FY2027 Primary Completion	US	NCT07104032
	Primary central nervous system lymphoma (PCNSL) 1L, ≥2L	■	■	■				FY2025 Primary Completion (Part A) (Actual)	US	NCT04947319
ONO-4578 PG receptor (EP4) antagonist	Gastric cancer*	■	■	■				FY2025 Primary Completion (Actual)	JP, KR, TW	NCT06256328
	Colorectal cancer*	■	■	■				FY2027 Primary Completion	JP, US, EU and others	NCT06948448
	Non-small cell lung cancer*	■						FY2026 Primary Completion	JP	NCT06542731
	Hormone receptor-positive, HER2-negative breast cancer	■						FY2026 Primary Completion	JP	NCT06570031
ONO-0530（sapablursen） Antisense oligonucleotide targeting TMPRSS6	Polycythemia Vera	■	■	■				FY2025 Primary Completion	US, EU and others	NCT05143957
ONO-4482 (relatlimab) Anti-LAG-3 antibody	Melanoma*	■	■					FY2024 Primary Completion (Actual)	JP, US, EU and others	NCT01968109
ONO-7427 Anti-CCR8 antibody	Solid tumor*	■	■					FY2025 Primary Completion	JP, US, EU and others	NCT04895709
DCC-3116（inlexisertib）ULK inhibitor	Advanced Malignancies (with ripretinib)	■	■					FY2026 Primary Completion	US	NCT05957367

MOA : Mode of Action

＊： Combination with OPDIVO, ★: Development rights countries: JP, KR
Estimated study completion date shown in jRCT or ClinicaiTrials.gov

F : Filed, A : Approval
EU : European countries

※Red: Update after announcement of FY 2024 financial result in May 2025
※Red: Update after Q1 FY2025 in August

Development pipeline (Oncology) ②

As of October 30, 2025

Code (Generic name)MOA, Modality	Target Indication	PI	PI/II	PII	PIII	F	A	Status	Area	ID
DCC-3009　Pan-KIT inhibitor	Gastrointestinal Stromal Tumor							FY2028 Primary Completion	US	NCT06630234
ONO-7913 (magrolimab) Anti CD47 antibody	Pancreatic cancer*							FY2026 Primary Completion	JP	NCT06532344
	Colorectal cancer*							FY2027 Primary Completion	JP	NCT06540261
ONO-4685 PD-1 x CD3 bispecific antibody	T-cell lymphoma							FY2025 Primary Completion	US	NCT05079282
								FY2028 Primary Completion	JP	NCT06547528
ONO-8250 iPSC-derived HER2 CAR T-cell therapy	HER2-expressing Solid tumor							FY2029 Primary Completion	US	NCT06241456
ONO-7428 Anti-ONCOKINE-1 antibody	Solid tumor							FY2029 Primary Completion	JP	NCT06816108
DCC-2812　GCN2 Activator	Renal Cell Carcinoma, Urothelial Cancer, Castration-Resistant Prostate Cancer							FY2028 Primary Completion	US	NCT06966024

MOA : Mode of Action

＊： Combination with OPDIVO
Estimated study completion date shown in jRCT or ClinicaiTrials.gov

F : Filed, A : Approval

※Red: Update after announcement of FY 2024 financial result in May 2025
※Red: Update after Q1 FY2025 in August

Development pipeline (Non-oncology) ①

As of October 30, 2025

Code (Generic name)MOA, Modality	Target Indication	PI	PI/II	PII	PIII	F	A	Status	Area	ID
ROMVIMZA DCC-3014 (vimseltinib) CSF-1R inhibitor	Tenosynovial Giant Cell Tumor							FY2024 US: Approval FY2025 EU: Approval	US, EU and others	NCT05059262
	chronic Graft Versus Host Disease							FY2029 Primary Completion	US	NCT06619561
ONO-2017(cenobamate)Inhibition of voltage-gated sodium currents/positive allosteric modulator of GABAA ion channel	Partial-onset seizures							FY2025 JP : Filed	JP, KR and others★1	NCT04557085
	Primary generalized tonic-clonic seizures							FY2026 Primary Completion	JP	NCT06579573
VELEXBRU Tablet (ONO-4059：tirabrutinib) BTK inhibitor	Pemphigus							FY2027 Primary Completion	JP	NCT06696716
ONO-8531（povetacicept） BAFF/APRIL dual antagonist	IgA Nephropathy							FY2028 Primary Completion	JP, US, EU, KR, TW and others★2	NCT06564142
ONO-5532（Gel-One） Cross-linked hyaluronate	Knee osteoarthritis							FY2027 Completion	JP	jRCT2031240621
	Hip osteoarthritis							FY2027 Completion	JP	jRCT2061240110
ONO-2808 S1P5 receptor agonist	Multiple System Atrophy							FY2025 Primary Completion (Actual)	JP, US	NCT05923866

MOA : Mode of Action

★1 : Development rights country: JP, ★2 : Development rights countries: JP, KR
Estimated study completion date shown in jRCT or ClinicaiTrials.gov

F : Filed, A : Approval
EU : European countries

※Red: Update after announcement of FY 2024 financial result in May 2025
※Red: Update after Q1 FY2025 in August

Development pipeline (Non-oncology) ②

As of October 30, 2025

Code (Generic name)MOA, Modality	Target Indication	PI	PI/II	PII	PIII	F	A	Status	Area	ID
ONO-1110 Endocannabinoid regulation	Postherpetic Neuralgia							FY2026 Primary Completion	JP	NCT06708416
	Fibromyalgia							FY2026 Primary Completion	JP	NCT06752590
	Hunner Type Interstitial Cystitis							FY2026 Primary Completion	JP	NCT06752603
	Major Depressive Disorder							FY2026 Primary Completion	JP	NCT06792136
	Social Anxiety Disorder							FY2026 Primary Completion	JP	NCT06805565
ONO-2020 Epigenetic regulation	Alzheimer's Disease							FY2026 Primary Completion	JP, US	NCT06881836
	Agitation Associated with Dementia Due to Alzheimer's Disease							FY2026 Primary Completion	JP	NCT06803823
ONO-4685 PD-1 x CD3 bispecific antibody	Autoimmune disease							FY2024 Completion (jRCT)	JP	jRCT2071220081
								FY2024 Primary Completion(Actual)	EU	NCT05332704
ONO-4915 PD-1 x CD19 bispecific antibody	Autoimmune disease							FY2026 Completion (jRCT)	JP	jRCT2071240056

MOA : Mode of Action

Estimated study completion date shown in jRCT or ClinicaiTrials.gov
Shaded boxes indicate studies on healthy volunteers.

F : Filed, A : Approval
EU : European countries

※Red: Update after announcement of FY 2024 financial result in May 2025
※Red: Update after Q1 FY2025 in August

ONO-4578-08 study

EP4 antagonist / Gastric Cancer, 1L

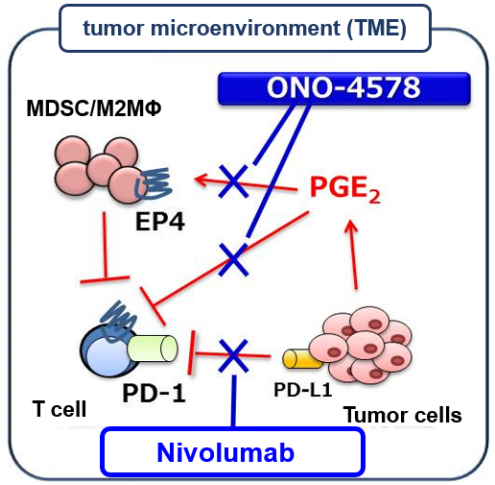
ONO-4578 overview

Compound information

Compound	ONO-4578
Originator	Ono Pharmaceutical Co., Ltd.
Mechanism	Prostaglandin receptor (EP4) antagonist
Formulation	Tablet
Target indication	Solid tumor
Development status	Phase II : gastric cancer 1L (JP, KR, TW) : colorectal cancer 1L (JP, US, EU, etc) Phase I : non-small cell lung cancer (JP) : hormone receptor-positive, HER2-negative breast cancer (JP)

Mechanism of Action

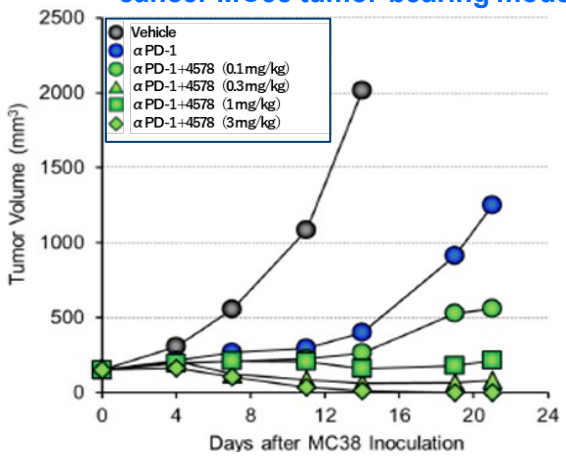
- Prostaglandin E_2 (PGE_2) is a bioactive lipid produced by the cyclooxygenase (COX) pathway and exerts various actions via its receptors (EP1-EP4).
- COX-2 is overexpressed in solid tumor[1]. PGE_2 has been reported to induce myeloid-derived suppressor cells (MDSC) and M2 macrophages in the tumor microenvironment 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 PGE_2 constructs via EP4.



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

Non-clinical data

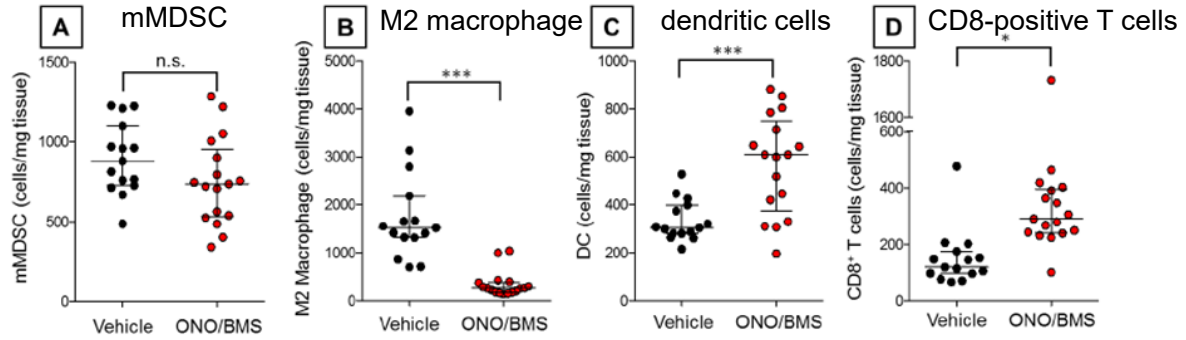
Fig 1. Time course of median tumor volume in syngeneic mouse colorectal cancer MC38 tumor-bearing model



- In syngeneic mouse tumor-bearing model, ONO-4578 improved immunosuppressive tumor microenvironment and showed antitumor effects (Figs. 1 and 2).
- Furthermore, ONO-4578 enhanced its antitumor effect by co-administration with anti-mouse PD-1 antibody (αPD-1) (Fig. 1).

Fig 2. Effect of ONO-4578 on intra-tumoral immune cells in syngeneic mouse colorectal cancer MC38 tumor-bearing model

AACR 2020: Poster #4443



Phase I results

Efficacy in patients pre-treated with OPDIVO

ESMO 2023: Poster #1546

One prior therapy

OPDIVO
Non-PD in best response

3rd line

PD

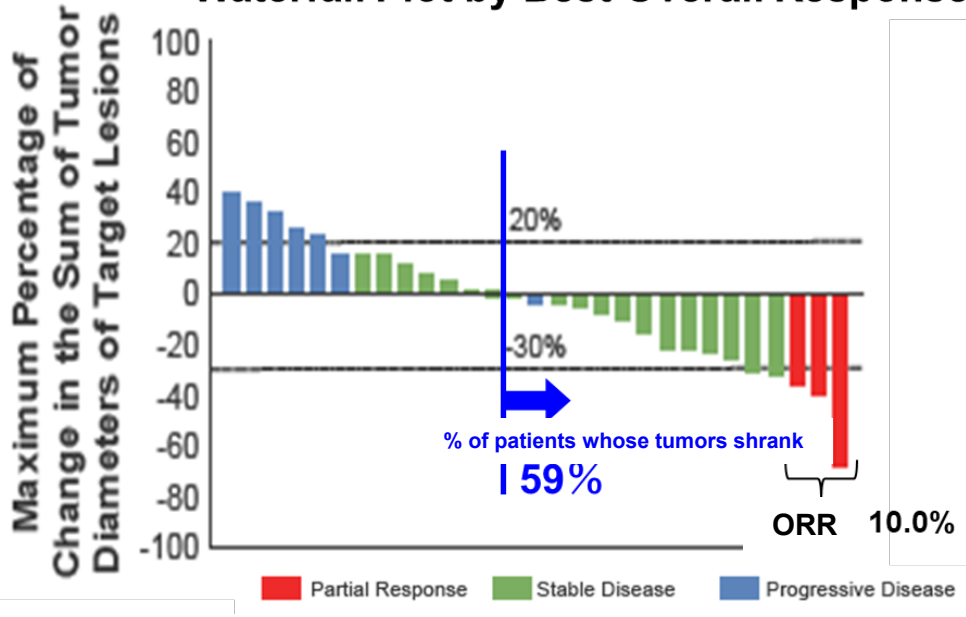
progressive disease

Study treatment

ONO-4578 + OPDIVO

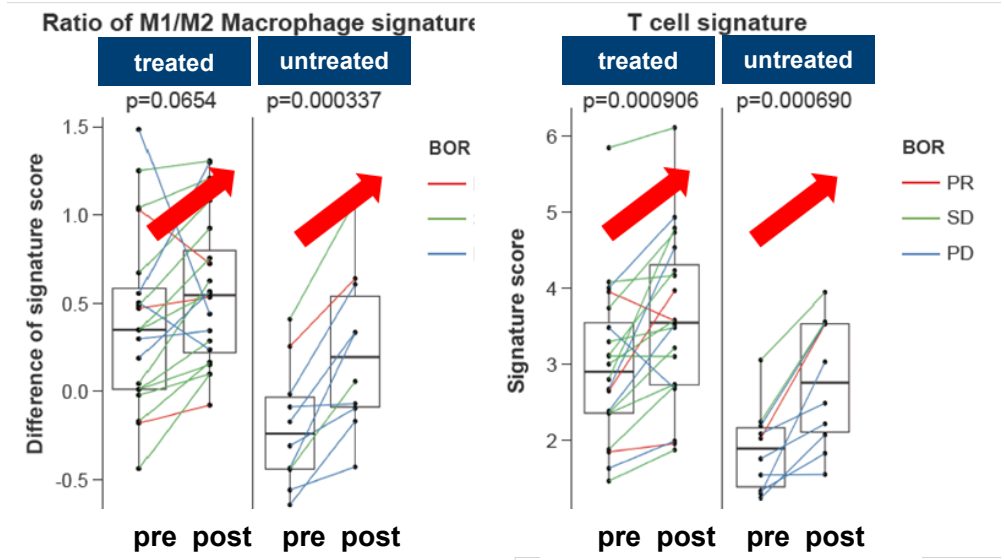
4th line

Waterfall Plot by Best Overall Response



Tumor shrinkage was observed in more than half of the patients who had previously achieved clinical benefit with OPDIVO and then worsened.

T-cell Gene Signature and M1/M2 Macrophage Gene Signature in Tumor Biopsies

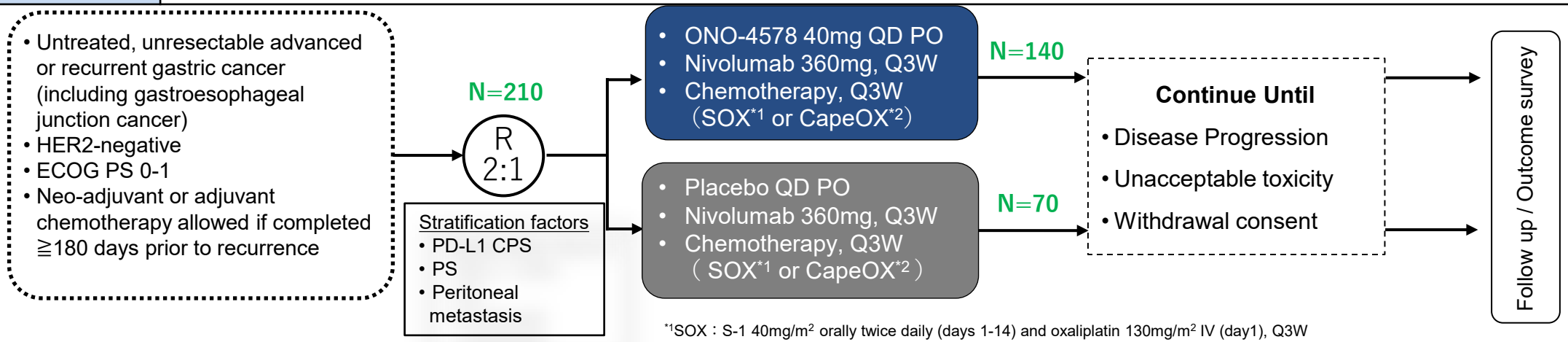


After administration, increases both in the M1/M2 macrophage ratio and in the T cell signature score were confirmed.

Signature score was calculated as mean of log-transformed expression value BOR, best overall response; PD, progressive disease; PR, partial response; SD, stable disease Scr, Screening period; C2D15, Cycle2 Day15 (1 Cycle=4 Weeks)

ONO-4578-08 Study Design

Objective	This clinical trial was conducted in patients with previously untreated, HER2-negative unresectable advanced or recurrent gastric cancer or gastroesophageal junction cancer. ONO-4578 in combination with nivolumab and fluoropyrimidine-based and platinum-based chemotherapy which is one of the standard treatments in this setting was compared with placebo in combination with nivolumab and chemotherapy. The primary endpoint of this trial is progression-free survival (PFS).
Target population	Previously untreated, HER2-negative unresectable advanced or recurrent gastric cancer (including gastroesophageal junction cancer)
Study design	A multicenter, double-blind, randomized controlled Phase 2 clinical trial
Usage・Dosage	ONO-4578 group：ONO-4578 40mg QD／nivolumab 360mg Q3W／Chemotherapy (SOX[*1] or CapeOX[*2]) Q3W Placebo group：Placebo QD／nivolumab 360mg Q3W／Chemotherapy (SOX[*1] or CapeOX[*2]) Q3W
Endpoint	Primary endpoint：progression-free survival（PFS） Secondary endpoint：overall survival（OS）, objective response rate（ORR）, duration of response（DOR）, safety, etc
Target enrollment	210 patients［Japan, South Korea and Taiwan］



*1SOX：S-1 40mg/m² orally twice daily (days 1-14) and oxaliplatin 130mg/m² IV (day1), Q3W
*2CapeOX： capecitabine 1000mg/m² orally twice daily (day1-14) and oxaliplatin 130mg/m² IV (day1), Q3W

Annual Number of Gastric Cancer Patients (Japan)

Gastric Cancer Prevalence

- Approximately 126,000 patients per year[1]

Unresectable, Advanced, or Recurrent Gastric Cancer (Eligible for Chemotherapy)

- Approximately 27,000 patients per year[2]
  - HER2-negative: Approximately 22,000 patients per year[2]

Reference[2]

- US : Estimated 11,000 patients (HER2-negative: 9,000)
- EU : Estimated 26,000 patients (HER2-negative: 22,000)
- anti-PD-1 antibody + chemotherapy (HER2-negative, Claudin-negative) : approx. 50%

1) Globocan 2022: Stomach Cancer, Japan, World Health Organization Available at: https://gco.iarc.who.int/media/globocan/factsheets/populations/392-japan-fact-sheet.pdf
2) Ono internal estimates

ONO-2808-03 study

S1P5 Receptor Agonist

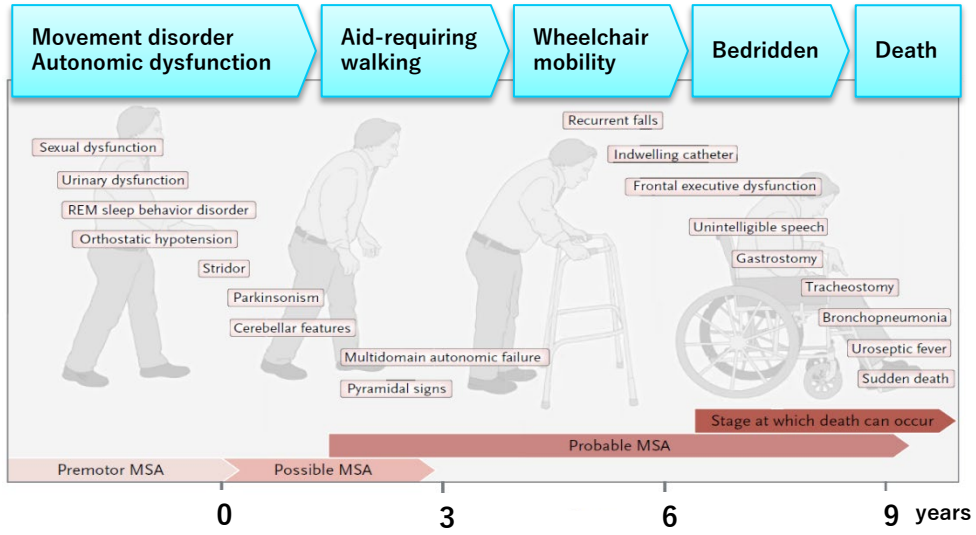
MSA；Multiple System Atrophy

ONO-2808 and MSA

Compound information

Compound	ONO-2808
Originator	ONO Pharmaceutical Co., Ltd.
Mechanism	S1P5 receptor agonist
Formulation	Oral
Target indication	MSA (Multiple System Atrophy)
Development status	Phase II (US, Japan)

Multiple System Atrophy

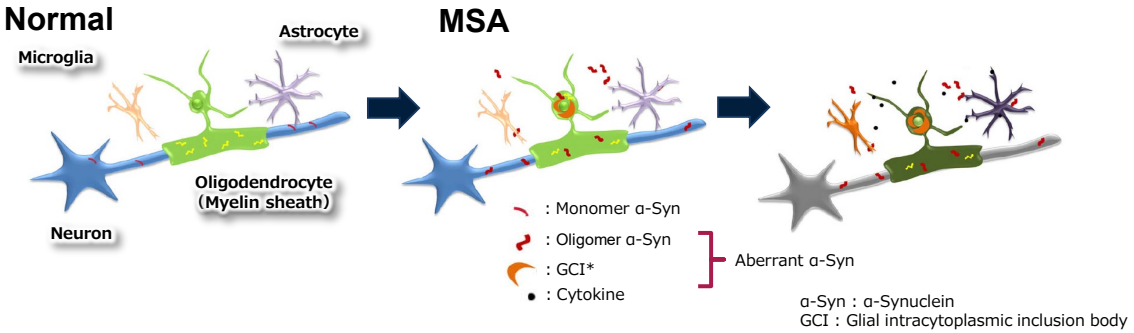


Gregor K. Wenning, N Engl J Med 2015; 372(3)

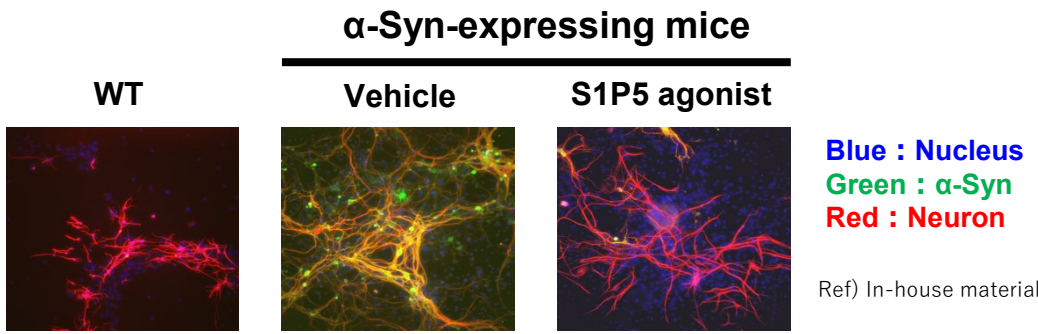
<Features>

- Progressive neurodegenerative disease with cerebellar atrophy
- Average onset age: 55–60 years
- Severe and rapidly progressive
- Currently symptomatic treatment with limited efficacy
- Estimated patients
  US [1), 2)]: 15,000～50,000, Japan [3)] : 10,000

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



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



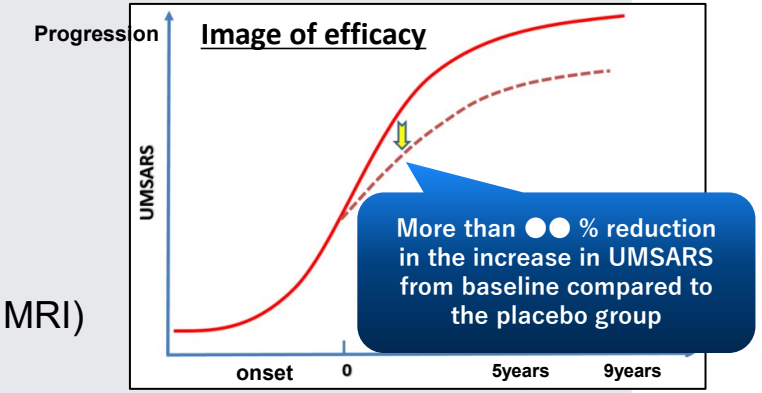
Ref) In-house material

S1P5 agonist suppressed α-Syn accumulation in neuronal axons

1) National Institutes of Health: https://www.ninds.nih.gov/health-information/disorders/multiple-system-atrophy, 2) Kaplan S, et al. Parkinsonism Relat Disord. 2023;117:105920. 3) https://www.nanbyou.or.jp/entry/59

Outline of the global phase II ONO-2808-03 study

ONO-2808-03 study	
Objective	To investigate the safety, tolerability, and pharmacokinetics of repeated-dose oral administration of ONO-2808 in patients with MSA.
Study design	Placebo-controlled, double-blind, randomized, parallel-group study
Target criteria	• Patients 30 to 80 years of age diagnosed with MSA • Patients defined as a maximum of 5 years since the onset of symptoms such as parkinsonism, ataxia, orthostatic hypotension and urinary dysfunction • Patients with an anticipated survival of at least 3 years
Endpoint	**Primary endpoint** • **Safety, tolerability** Secondary endpoint • PK、concentration in cerebrospinal fluid (CSF) Exploratory Endpoints • **UMSARS (Historical Review, Motor Examination)** • MSA-QoL、MoCA(Montreal Cognitive Assessment), COMPASS-31* • Brain volume(MRI：Brain stem, Cerebellum), White matter(Diffusion MRI) • Plasma BM(Neurofilament Light Chain, α-Syn, proteomics, etc.)
Dosage	**Double-blind phase：Placebo, low dose, medium dose, high dose** Extension phase：Maintain dose level(P group switches to low dose after completion of the transition period)
Duration	**Double-blind phase：6 months** Extension phase: 14months(Transition period for 2 months, extension phase for 12 months)
Enrollment	**20 patients per group, 80 in total**
Trial countries	US, Japan



COMPASS-31* : **Autonomic Examination**