Development Pipeline Progress Status

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

As of April 23, 2025

Filed | Approved | Met PE

OPDIVO | Other than OPDIVO

FY2024 (results)

- DCC-3014（ROMVIMZA）〔TGCT〕 July 2024
- DCC-3014（ROMVIMZA）〔TGCT〕 August 2024
- 〔1L-Hepatocellular carcinoma〕 with YERVOY CheckMate-9DW August 2024
- 〔1L- Colorectal cancer (MSI-H)〕 with YERVOY CheckMate-8HW September 2024
- BRAFTOVI 〔1L-BRAF-mutant Colorectal cancer〕 with Cetuximab and FOLFOX December 2024

FY2025

- ONO-4059（VELEXBRU）〔2L-PCNSL〕
- 〔Neoadjuvant, Adjuvant - Bladder cancer〕 with Chemo ONO-4538-86
- 〔Adjuvant Hepatocellular carcinoma〕 CheckMate-9DX
- ONO-2017 〔 Partial-onset seizures 〕
- 〔 Neoadjuvant, Adjuvant - NSCLC〕 with Chemo CheckMate-77T

FY2026

- 〔1L-Gastric cancer〕 with YERVOY and Chemo ONO-4538-113

PE : Primary endpoint

Development status of OPDIVO

As of April 23, 2025

- Approval in FY2024 or filed/awaiting approval
- 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	Filed
Gastric cancer	1st	with Ipi/Chemo	Ⅲ	Ⅲ	Ⅲ	–	–
Colorectal cancer	MSI-H／dMMR (1st)	with Ipi	Filed	–	–	Approved	Approved
Hepatocellular carcinoma	Adjuvant	Monotherapy	Ⅲ	Ⅲ	Ⅲ	Ⅲ	Ⅲ
	1st	with Ipi	Filed	Ⅲ	Ⅲ	Approved	Approved
Urothelial cancer / Bladder cancer	Neo-adjuvant ・Adjuvant	with Chemo	Ⅲ	Ⅲ	Ⅲ	Ⅲ	Ⅲ
	1st	with Chemo	Approved	Approved	Approved	Approved	Approved
Rhabdoid tumor	2nd	Monotherapy	Ⅱ	–	–	–	–
Richter transformation	2nd	Monotherapy	Ⅱ	–	–	–	–
Solid tumor	–	ONO-4538HSC (Comibination with vorhyaluronidase alfa)	Ⅰ	–	–	Approved	Filed

※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

Development pipeline (Oncology) ①

As of April 23, 2025

Code (Generic name)MOA, Modality	ID/Area	Target Indication	PI	PI/II	PII	PIII	Filed	Approval
BRAFTOVI Capsule (Encorafenib) BRAF inhibitor	jRCT2011200018/JP	BRAF-mutant thyroid cancer	FY2024.5 Approval					
MEKTOVI Tablet (Binimetinib) MEK inhibitor	jRCT2011200018/JP	BRAF-mutant thyroid cancer	FY2024.5 Approval					
BRAFTOVI Capsule (Encorafenib) BRAF inhibitor	NCT04607421/JP, KR and others	1L BRAF-mutant colorectal cancer Combination with Cetuximab and FOLFOX	FY2024.12 Filing accepted					
QINLOCK (ripretinib) KIT inhibitor	NCT05734105/NA, SA, EU, AU, KR, TW	Gastrointestinal Stromal Tumor 2L KIT Exon 11+17/18	FY2025 Primary Completion					
ONO-4059 (tirabrutinib) BTK inhibitor	NCT04947319/US	Primary central nervous system lymphoma	FY2025 Primary Completion (Part A)					
ONO-4578 PG receptor (EP4) antagonist	NCT06256328/JP, KR, TW	Gastric cancer*	FY2025 Primary Completion					
	—/US	Colorectal cancer*	FY2027 Primary Completion					
	NCT06542731/JP	Non-small cell lung cancer*	FY2026 Primary Completion					
	NCT06570031/JP	Hormone receptor-positive, HER2-negative breast cancer	FY2025 Primary Completion					
ONO-0530（sapablursen） Antisense oligonucleotide targeting TMPRSS6	NCT05143957/US, EU and others	Polycythemia Vera	FY2025 Primary Completion					
ONO-4482 (relatlimab) Anti-LAG-3 antibody	NCT01968109/JP, US, EU	Melanoma*	FY2024 Primary Completion (Actual)					
ONO-7427 Anti-CCR8 antibody	NCT04895709/JP, US, EU	Solid tumor*	FY2025 Primary Completion					
DCC-3116　ULK inhibitor	NCT04892017/US	Solid tumor (with sotorasib)	FY2027 Primary Completion					
	NCT05957367/US	Advanced Malignancies (with ripretinib)	FY2026 Primary Completion					

NA : North America, SA : South America, AU : Australia, EU : European countries
* : Combination with OPDIVO
Estimated study completion date shown in jRCT or ClinicaiTrials.gov

※Red: Update after announcement of FY 2023 financial result in May 2024
※Red: Update after Q3 FY2024 in February
MOA : Mode of Action

Development pipeline (Oncology) ②

As of April 23, 2025

Code (Generic name)MOA, Modality	ID/Area	Target Indication	PI	PI/II	PII	PIII	Filed	Approval
DCC-3084 Pan-RAF inhibitor	NCT06287463/US	Advanced Malignancies	→ FY2026 Primary Completion					
DCC-3009 Pan-KIT inhibitor	NCT06630234/US	Gastrointestinal Stromal Tumor	→ FY2028 Primary Completion					
ONO-7475 (tamnorzatinib) Axl/Mer inhibitor	NCT06525246/JP	EGFR-mutated non-small cell lung cancer	→ FY2025 Primary Completion					
ONO-7913 (magrolimab) Anti CD47 antibody	NCT06532344/JP	Pancreatic cancer*	→ FY2026 Primary Completion					
	NCT06540261/JP	Colorectal cancer*	→ FY2027 Primary Completion					
ONO-4685 PD-1 x CD3 bispecific antibody	NCT05079282/US	T-cell lymphoma	→ FY2025 Primary Completion					
	NCT06547528/JP		→ FY2028 Primary Completion					
ONO-8250 iPSC-derived HER2 CAR T-cell therapy	NCT06241456/US	HER2-expressing Solid tumor	→ FY2029 Primary Completion					
ONO-7428 Anti-ONCOKINE-1 antibody	NCT06816108/JP	Solid tumor	→ FY2029 Primary Completion					

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

MOA : Mode of Action ※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

Development pipeline (Non-oncology)

As of April 23, 2025

Code （Generic name）MOA, Modality	ID/Area	Target Indication	PI	PI/II	PII	PIII	Filed	Approval
ROMVIMZA DCC-3014 (vimseltinib) CSF-1R inhibitor	NCT05059262/NA, EU	Tenosynovial Giant Cell Tumor			FY2024 FDA: Approval EMA: Filing accepted			
ONO-2017(cenobamate)Inhibition of voltage-gated sodium currents/positive allosteric modulator of $GABA_A$ ion channel	NCT06579573/JP	Primary generalized tonic-clonic seizures				FY2026 Primary Completion		
	NCT04557085/JP	Partial-onset seizures				FY2024 Primary Completion(Actual)		
VELEXBRU Tablet (ONO-4059：tirabrutinib) BTK inhibitor	NCT06696716/JP	Pemphigus				FY2027 Primary Completion		
ONO-2808 S1P5 receptor agonist	NCT05923866/JP, US	Multiple System Atrophy			FY2025 Primary Completion			
ROMVIMZA DCC-3014 (vimseltinib) CSF-1R inhibitor	NCT06619561/US	chronic Graft Versus Host Disease				FY2029 Primary Completion		
ONO-1110 Endocannabinoid regulation	NCT06708416/JP	Postherpetic Neuralgia				FY2026 Primary Completion		
	NCT06752590/JP	Fibromyalgia				FY2026 Primary Completion		
	NCT06752603/JP	Hunner Type Interstitial Cystitis				FY2026 Primary Completion		
	NCT06792136/JP	Major Depressive Disorder				FY2026 Primary Completion		
	NCT06805565/JP	Social Anxiety Disorder				FY2026 Primary Completion		
ONO-2020 Epigenetic Regulation	NCT06881836/JP, US	Alzheimer's Disease				FY2026 Primary Completion		
	NCT06803823/JP	Agitation Associated with Dementia Due to Alzheimer's Disease				FY2026 Primary Completion		
ONO-4685 PD-1 x CD3 bispecific antibody	jRCT2071220081/JP	Autoimmune disease		FY2024 Completion (jRCT)				
	NCT05332704/EU				FY2024 Primary Completion(Actual)			
ONO-4915 PD-1 x CD19 bispecific antibody	jRCT2071240056/JP	Autoimmune disease		FY2026 Completion (jRCT)				

NA : North America,
EU : European countries

Estimated study completion date shown in jRCT or ClinicaiTrials.gov. Dashed lines indicate studies on healthy adults.

MOA : Mode of Action ※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

Sapablursen (ONO-0530)

- **Anti-sense oligonucleotide targeting TMPRSS6[1)]**
- **Ongoing Phase II study for adult polycythemia vera (PV) patients is expected to be completed in 2025**

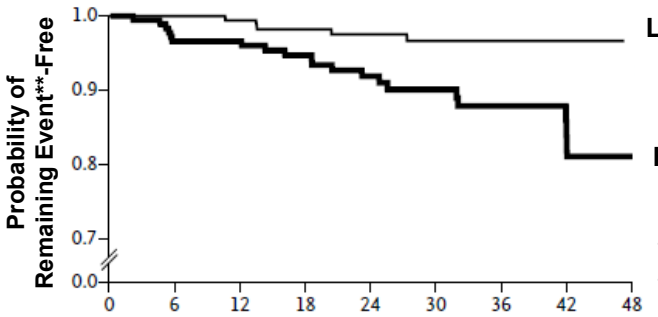
【Polycythemia vera (PV)】

- More than 95% PV patients have a *JAK2* gene mutation, leading to the overproduction of red blood cells.
- PV is a rare and potentially life-threatening hematologic disease with an incidence rate of approximately 2 cases per 100,000 population[2)] and a total of 75,000 patients on treatment in the US[3)]
- In the PV patients with high hematocrit (HCT) have a 3.91 times higher risk of cardiovascular death or thrombotic events compared to patients with low HCT.[4)]
- Quality of life (QOL) is impaired due to symptoms such as headaches, dizziness, and fatigue.
- Standard of care includes phlebotomy, low-dose aspirin and cytoreductive therapy (CRT) to maintain HCT <45% and prevent thrombotic events.
- Patients with high frequent phlebotomy present with iron deficiency. CRT increases the risks of infections and secondary cancers.

【Hypothetical Mechanism of Action】

- Hepcidin is the key regulator of iron homeostasis.
- Sapablursen (ONO-0530) increases hepcidin production through suppressing the TMPRSS6 gene expression, thereby reducing red blood cells in PV patients.

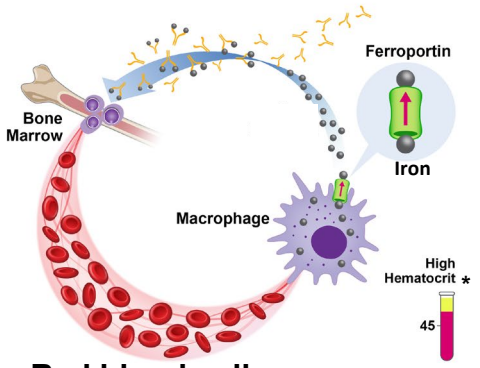
Increase in the risk of cardiovascular death and thrombotic events by PV



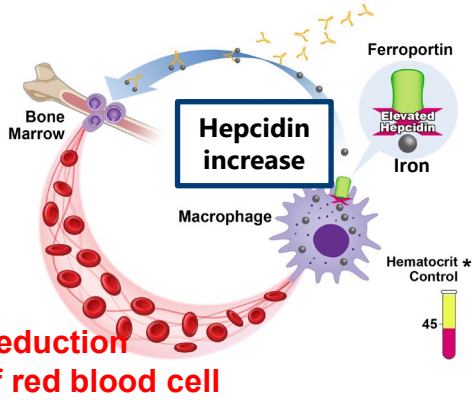
*HCT: Percentage of red blood cells in the blood
**Event: cardiovascular death and major thrombosis

Adapted from Marchioli R, et al. N Engl J Med. 2013;368:22-33.

Polycythemia vera (PV)



Reduction of red blood cells through increased hepcidin production in PV



*HCT: Percentage of red blood cells in the blood

1) Ono Entered into License Agreement with Ionis Pharmaceuticals for Sapablursen for the Treatment of Polycythemia Vera in March 2025
2) Blood Cancer Journal (2020) 10:22, 3) Nat Rev Dis Primers. 2025 Apr 17;11(1):26. 4) N Engl J Med. 2013;368:22-33.,

Appendix

OPDIVO Approval Track Record (1)

As of April 23, 2025

Target disease	Treatment Line	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Melanoma	Adjuvant・1st・2nd	Monotherapy, with Ipi (1st only)	Approved	Approved	Approved	Approved	Approved
	1st	Combination drug★ (relatlimab)	–	–	–	Approved	Approved
Non-small cell lung cancer	Neo-adjuvant	with Chemo	Approved	Approved	Approved	Approved	Approved
	1st	with Ipi	Approved	Approved	Approved	Approved	–
		with Ipi/Chemo	Approved	Approved	Approved	Approved	Approved
		with Chemo	Approved	–	–	–	–
		with Chemo (NSQ)	Revision of labeling	Approved	Approved	–	–
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Hodgkin's lymphoma	Relapsed /Refractory	Monotherapy	Approved	Approved	Approved	Approved	Approved
Head and neck cancer	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Malignant pleural mesothelioma	1st	with Ipi	Approved	Approved	Approved	Approved	Approved
	2nd	Monotherapy	Approved	–	–	–	–
Malignant mesothelioma (Excluding Pleura)	1st	Monotherapy	Approved				

★Combination drug (Relatlimab) : ONO-7121(Opdivo+Relatlimab (ONO-4482)

※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

OPDIVO Approval Track Record(2)

As of April 23, 2025

Target disease	Treatment Line	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Gastric cancer	1st	with Chemo	Approved	Approved	Approved	Approved	Approved
	3rd	Monotherapy	Approved	Approved	Approved	–	–
Esophageal cancer	Adjuvant	Monotherapy	Approved	Approved	Approved	Approved	Approved
	1st	with Ipi, with Chemo	Approved	Approved	Approved	Approved	Approved
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Colorectal cancer	MSI-H／dMMR (3rd)	Monotherapy	Approved	–	Approved	Approved	–
		with Ipi	Approved	Approved	Approved	Approved	Approved★★
Hepatocellular carcinoma	2nd	with Ipi	–	–	Approved	Approved	–

★★2nd Line

※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

OPDIVO Approval Track Record(3)

As of April 23, 2025

Target disease	Treatment Line	Treatment	Phase				
			Japan	Korea	Taiwan	US	EU
Renal cell carcinoma	1st	with Ipi	Approved	Approved	Approved	Approved	Approved
		with TKI	Approved	Approved	Approved	Approved	Approved
	2nd	Monotherapy	Approved	Approved	Approved	Approved	Approved
Urothelial cancer / Bladder cancer	Adjuvant	Monotherapy	Approved	Approved	Approved	Approved	Approved
	2nd	Monotherapy	–	Approved	Approved	Approved	Approved
Cancer of unknown primary	–	Monotherapy	Approved	–	–	–	–
Epithelial skin malignancies	1st	Monotherapy	Approved	–	–	–	–
Flat dose	240 mg (every 2 weeks)		Approved	Approved	Approved	Approved	Approved
	360 mg (every 3 weeks)		Approved	Approved	Approved	Approved	Approved
	480 mg (every 4 weeks)		Approved	Approved	Approved	Approved	Approved

※Red: Update after announcement of FY 2023 financial result in May 2024 ※Red: Update after Q3 FY2024 in February

Key milestones in FY2024 Q4 (FY ending March 2025)

As of April 23, 2025

(Development pipeline)

	Product/ Code(Generic name)	Target indication/Study name	Progress
Product to be approved	ROMVIMZA (vimseltinib)	chronic Graft Versus Host Disease	Approved in US (Feb.2025)
	OPDIVO	MSI-H Colorectal cancer (1st with Ipi) /CheckMate-8HW	Approved in US (Apr.2025)
		Hepatocellular carcinoma(1st with Ipi) /CheckMate-9DW	Approved in EU (Mar.2025), US(Apr.2025)
P2		Richter transformation	Started in JP (Jan.2025)
	ONO-2020	Alzheimer's disease	Started in JP (Jan.2025)
	ONO-4578	Colorectal cancer (with OPDIVO)	Started in US (Feb.2025)
P1		Pancreatic cancer	Discontinued (Jan.2025)
	ONO-4482	Hepatocellular carcinoma(with OPDIVO)	Discontinued (Feb.2025)
	ONO-7914	Solid tumor(with OPDIVO)	Discontinued (Feb.2025)
	ONO-7475	Pancreatic cancer(with OPDIVO)	Discontinued (Mar.2025)
	ONO-7018	Non-Hodgkin lymphoma, Chronic lymphocytic leukemia	Discontinued (Apr.2025)

Key milestones in FY2024 Q4 (FY ending March 2025)

As of April 23, 2025

(Drug discovery partnerships & Research collaborations/Licensing & Co-promotion)

Title	Progress
Ono Enters into License Agreement with Ionis Pharmaceuticals for Sapablursen for the Treatment of Polycythemia Vera	License-in (2025.3)
Ono Enters into a Basic Agreement with Seikagaku for Co-development and Marketing Collaboration on Gel-One for the treatment of Osteoarthritis in Japan	License-in (2025.4)
Ono Enters into Drug Discovery Collaboration Agreement with Reborna Biosciences to Generate RNA-Targeting Novel Small Molecule in the Central Nervous System Area	Started
Ono Commences Research Collaboration with Jorna Therapeutics to Generate Novel RNA Editing Therapeutics	
Ono Enters into a Research Collaboration Agreement with InveniAI to Identify Novel Therapeutic Targets	Discontinued
ONO Announces a Strategic Drug Discovery Alliance Agreement with Cancer Research UK and LifeArc for Cancer Immunotherapy	
Ono Enters a Drug Discovery Collaboration Agreement with Memo Therapeutics to Discover and Develop Antibody Drugs in the Immuno-oncology Field	
Ono Enters into a Collaboration and Option Agreement with Cue Biopharma for CUE-401, a Bispecific Protein	
Ono Enters into Research Collaboration Agreement with Healx Limited	

Status of approval of OPDIVO (i.v. and s.c.) in the US

As of January 24, 2025

Indication	Line	TREATMENTS ADMINISTERED	i.v.	s.c.
Melanoma	Adjuvant	Monotherapy	Approval	Approval
	1L	Monotherapy	Approval	Approval
		With YERVOY	Approval	(monotherapy after combination therapy)
	2L	Monotherapy	Approval	Approval
Non-small cell lung cancer	Neoadjuvant	With chemotherapy	Approval	Approval
	Neo-adjuvant /Adjuvant	With chemotherapy	Approval	Approval
	1L	With YERVOY	Approval	
		With YERVOY or with chemotherapy	Approval	
	2L	Monotherapy	Approval	Approval
Hodgkin's lymphoma	Relapsed/refractory	Monotherapy	Approval	
Head and neck cancer	2L	Monotherapy	Approval	Approval
Malignant pleural mesothelioma	1L	With YERVOY	Approval	
Gastric cancer	1L	With chemotherapy	Approval	Approval

Indication	Line	TREATMENTS ADMINISTERED	i.v.	s.c.
Esophageal cancer	Adjuvant	Monotherapy	Approval	Approval
	1L	With YERVOY	Approval	
		With chemotherapy	Approval	Approval
	2L	Monotherapy	Approval	Approval
Colorectal cancer	MSI-H/dMMR (3rd line)	Monotherapy	Approval	Approval
		With YERVOY	Approval	(Following combination therapy monotherapy)
Hepatocellular carcinoma	2L	With YERVOY	Approval	(Following combination therapy monotherapy)
Renal cell carcinoma	1L	With YERVOY	Approval	(Following combination therapy monotherapy)
		With TKI	Approval	Approval
	2L	Monotherapy	Approval	Approval
Urothelial carcinoma/ Bladder cancer	Adjuvant	Monotherapy	Approval	Approval
	1L	With chemotherapy	Approval	Approval
	2L	Monotherapy	Approval	Approval

OPDIVO Qvantig™
nivolumab + hyaluronidase-nvhy
SUBCUTANEOUS INJECTION | 120 mg + 2,000 units / mL