

Material Issue 2

Pipeline Expansion

Management of Priority Issues

Reason for being a priority issue	Our pipeline is the source of our sustainable growth. We continue enriching our pipeline to constantly provide innovative drugs to patients.
Vision over the medium to long term	The speed and accuracy of establishing PoC* for new drug candidates are improving, and the pipeline is enriched through licensing activities. <small>* PoC (Proof of Concept): PoC studies are an early stage of clinical drug development to confirm whether the drug candidates demonstrate the clinical safety and efficacy expected during the drug discovery phase.</small>
Indicators	<ul style="list-style-type: none"> The number of products in the clinical development stage The number of newly introduced products
Major initiatives	<ul style="list-style-type: none"> Establish PoC on multiple projects and conduct global clinical trials <ul style="list-style-type: none"> Continue system development for early establishment of PoC Further enhance activities for translational research (TR) and reverse translational research (rTR) Increase the speed and accuracy of establishing PoC by using state-of-the-art technologies and methodologies Strengthen licensing activities to obtain global rights

Early establishment of PoC

ONO is working to expedite clinical development and improve the success rate of drug candidates in order to fast-track the delivery of our in-house and in-licensed compounds to patients suffering from diseases around the world. We are flexibly utilizing our clinical development functions in Japan, the US and Europe to quickly establish PoC to expediently identify the potential product value of candidate compounds. To do this, we formulate appropriate clinical development plans, including target disease selection, propose study plans to accurately evaluate efficacy, and promote studies according to the plan. Also, while advancing the search for clinical markers through TR, we launch new discovery research projects using results obtained from clinical trials, creating an R&D virtuous cycle. We are also building a system to conduct global confirmatory studies after establishing PoC.

Licensing Activities

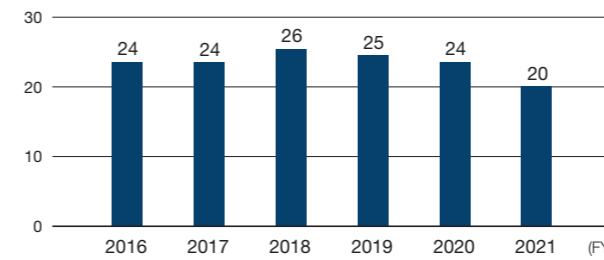
In addition to expanding our pipeline through in-house research, we are also actively pursuing licensing activities with the aim of in-licensing new candidates under development by pharmaceutical or bio-tech companies around the world. To do this, we are acquiring the global rights of new candidates with characteristics that can be of use to a global specialty pharmaceutical company, taking into consideration the areas targeted by our own products, with a view to global development in the U.S. and other countries.

Number of products in the clinical development stage

We are also proceeding with clinical development of existing products to maximize product value. For Opdivo, we are

conducting clinical trials aimed at expanding the range of cancer types, using the drug at earlier lines of treatment, and establishing combination therapies to enhance therapeutic efficacy. We are also focusing on expanding our pipeline beyond Opdivo, maintaining the number of products in the clinical development stage at more than 20 over the past several years. To improve the speed and quality of our clinical trials, we are digitizing our operations. We will continue to aggressively pursue clinical development not only in Japan but also worldwide for the benefit of patients awaiting new therapeutic agents.

Number of Products in the Clinical Development Stage



Global pipeline

Product (Development code)	Mechanism of Action	Target Disease	Development Stage (Japan)	Development Stage (Overseas)	In-house/In-licensing
VELEXBRU Tablets (ONO-4059)	BTK inhibitor	Primary central nervous system lymphoma	Launched	US: Phase 2	In-house
ONO-7475	Axl / Mer inhibitor	Acute leukemia	—	US: Phase 1/2	In-house
		EGFR-mutated non-small cell lung cancer	Phase 1	—	
		Solid tumors	Phase 1	—	
ONO-4685	PD-1×CD3 Bispecific antibody	Autoimmune disease	Phase 1	EU: Phase 1	In-house
		T-cell lymphoma	—	US: Phase 2	
ONO-2808	S1P5 receptor agonist	Neurodegenerative disease	Phase 1	EU: Phase 1	In-house
ONO-7684	FX1a inhibitor	Thrombosis	—	EU: Phase 1	In-house

In-licensed products (Phase 2 or later)

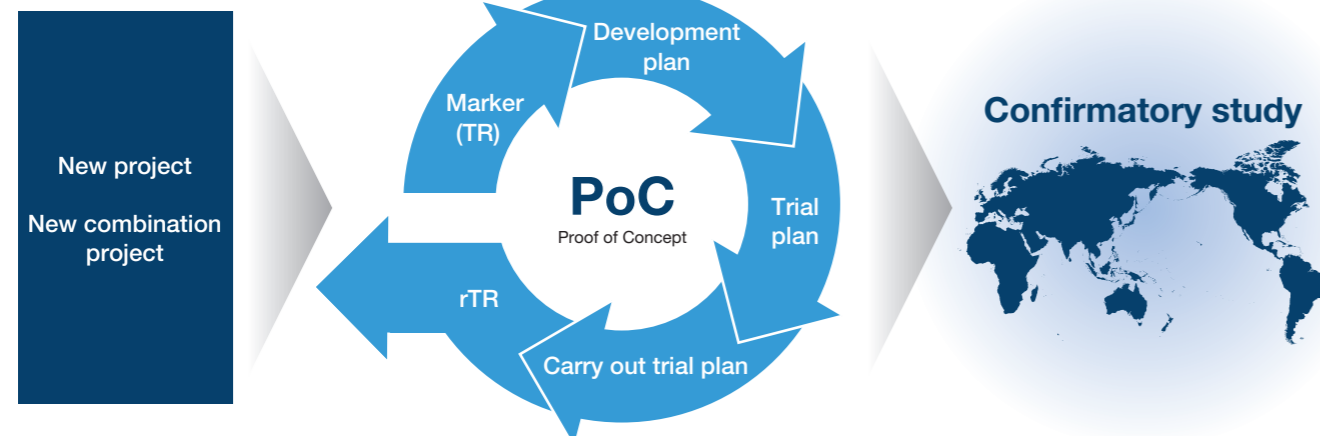
Product (Development code)	Mechanism of Action	Target Disease	Development Stage (Japan)	In-licensing
ONO-7913	Anti-CD47 antibody	TP53-mutated acute myeloid leukemia	Phase 3	Gilead Sciences, Inc.
ONO-2017	Inhibition of voltage-gated sodium currents / positive allosteric modulator of GABA _A ion channel	Primary generalized tonic-clonic seizures	Phase 3	SK Biopharmaceuticals
		Partial-onset seizures	Phase 3	
Braftovi Capsules	BRAF inhibitor	Thyroid cancer	Phase 2	Pfizer Inc.
Mektovi Tablets	MEK inhibitor	Thyroid cancer	Phase 2	Pfizer Inc.

Global Pipeline and In-licensed Products

Among new in-house drug candidates that we are developing globally are VELEXBRU Tablets (BTK inhibitor) that are already marketed in Japan, as well as ONO-7475 (Axl / Mer inhibitor), ONO-4685 (PD-1×CD3 bispecific antibody), ONO-2808 (S1P5 receptor agonist), and ONO-7684 (FX1a inhibitor). The in-licensed product ONO-7018 (MALT1 inhibitor: in-licensed from Cordia), for which we obtained global development and marketing rights, is being prepared for overseas development. In addition, ONO-7913 (anti-CD47 antibody) and ONO-2017 (voltage-dependent sodium current inhibition/GABA_A ion channel function enhancer), which are in late-stage development and were obtained through licensing activities, are being developed for approval (launch) in Japan.

In the future, we will further promote our own drug discovery as well as licensing activities to acquire global rights and engage in further enrichment of our pipeline.

The R&D Cycle



Message from the Director in Charge

To Deliver Innovative New Drugs to Patients Around the World

We continue increasing the number of new drug candidates by reinforcement of our in-house research and licensing activities, and we will quickly confirm whether these compounds demonstrate the expected clinical safety and efficacy (establish PoC). To this end, we use the data we have accumulated to date and the results of translational research to improve the accuracy of efficacy and safety prediction. Furthermore, we take a broad view of potential indications and determine the potential value of compounds as early as possible by conducting clinical trials for multiple target diseases. We conduct clinical trials flexibly in Japan, the U.S. and Europe, and are in the process of establishing a system to obtain approval on our own to deliver as many innovative new drugs as possible to patients around the world as early as possible.



Kiyooki Idemitsu
Member of the Board of Directors,
Corporate Executive Officer
Executive Director,
Clinical Development

Status of Development Pipeline

(As of July 29, 2022)

Main Status of Development Pipelines (Oncology)

Product Name or Development Code (Generic Name)	Mechanism of Action, etc.	Target Disease	Development Stage				Area	In-house / In-license
			I	II	III	Filed		
OPDIVO Intravenous Infusion (Nivolumab)	Anti-PD-1 antibody	Hepatocellular carcinoma	→				JP-KR	In-house (Co-development with Bristol-Myers Squibb)
		Ovarian cancer	→				JP-KR-TW	
		Bladder cancer	→				JP-KR-TW	
		Prostate cancer	→				JP-KR-TW	
		Pancreatic cancer	→				JP-KR-TW	
		Virus positive / negative solid carcinoma	→				JP-KR-TW	
YERVOY Injection* (Ipilimumab)	Anti-CTLA-4 antibody	Gastric cancer	→				JP-KR-TW	Co-development with Bristol-Myers Squibb
		Urothelial carcinoma	→				JP-KR-TW	
		Hepatocellular carcinoma	→				JP-KR-TW	
		Virus positive / negative solid carcinoma	→				JP-KR-TW	
		Esophageal cancer	→				KR	
ONO-7913 (Magrolimab)	Anti-CD47 antibody	TP53-mutant acute myeloid leukemia	→				JP	Gilead Sciences
		Pancreatic cancer*	→				JP	
		Colorectal cancer*	→				JP	
		Solid tumor	→				JP	
		Myelodysplastic syndrome	→				JP	
BRAFTOVI Capsules (Encorafenib)	BRAF inhibitor	Thyroid cancer	→				JP	Pfizer
		Thyroid cancer	→				JP	
MEKTOVI Tablets (Binimetinib)	MEK inhibitor	Thyroid cancer	→				JP	Pfizer
ONO-4686*	Anti-TIGIT antibody	Solid tumor	→				JP	Co-development with Bristol-Myers Squibb
ONO-4482* (Relatlimab)	Anti-LAG-3 antibody	Melanoma	→				JP	Co-development with Bristol-Myers Squibb
ONO-7475	Axl / Mer inhibitor	Solid tumor*	→				JP	In-house
		EGFR-mutated non-small cell lung cancer	→				JP	
		Acute leukemia	→				US	

Product Name or Development Code (Generic Name)	Mechanism of Action, etc.	Target Disease	Development Stage				Area	In-house / In-license
			I	II	III	Filed		
ONO-4059 (Tirabrutinib Hydrochloride)	Bruton's tyrosine kinase (BTK) inhibitor	Primary central nervous system lymphoma	→				US	In-house
ONO-4578	PG receptor (EP4) antagonist	Colorectal cancer*	→				JP	In-house
		Pancreatic cancer*	→				JP	
		Non-small cell lung cancer*	→				JP	
		Solid tumor, Gastric cancer*	→				JP	
		Hormone receptor-positive, HER2-negative breast cancer	→				JP	
ONO-7119* (Atamparib)	PARP7 inhibitor	Solid tumor	→				JP	Ribon
ONO-7122*	TGF-β inhibitor	Solid tumor	→				JP	Co-development with Bristol-Myers Squibb
ONO-7914*	STING agonist	Solid tumor	→				JP	In-house
ONO-4685	PD-1×CD3 bispecific antibody	T-cell lymphoma	→				US	In-house

* In combination with OPDIVO.

Main Status of Development Pipelines (Other than Oncology)

Product Name or Development Code (Generic Name)	Mechanism of Action, etc.	Target Disease	Development Stage				Area	In-house / In-license
			I	II	III	Filed		
Onoact for Intravenous Infusion (Landiolol Hydrochloride)	Short-active selective β ₁ blocker	Tachyarrhythmia in low cardiac function (Pediatric)	→				JP	In-house
Velexbru Tablets (Tirabrutinib Hydrochloride)	Bruton's tyrosine kinase (BTK) inhibitor	Pemphigus	→				JP	In-house
		Generalized scleroderma	→				JP	
ONO-2017 (Cenobamate)	Inhibition of voltage-gated sodium currents/positive allosteric modulator of GABA _A ion channel	Primary generalized tonic-clonic seizures	→				JP	SKBP
		Partial-onset seizures	→				JP	
ONO-2910	Schwann cell differentiation promoter	Diabetic polyneuropathy	→				JP	In-house
ONO-2808	S1P5 receptor agonist	Neurodegenerative disease	→				JP-EU	In-house
ONO-4685	PD-1×CD3 bispecific antibody	Autoimmune disease	→				JP-EU	In-house
ONO-2909	PG receptor (DP1) antagonist	Narcolepsy	→				JP	In-house
ONO-7684	FXIa inhibitor	Thrombosis	→				EU	In-house
ONO-2020	Epigenetic Regulation	Neurodegenerative disease	→				US	In-house