

# Development Pipeline Progress Status

**May 10, 2019**

# Development status of OPDIVO (nivolumab) (1)

Target disease	JAPAN	US/EU	KR/TW
Melanoma (1 <sup>st</sup> )	Approved	Approved	Approved
Melanoma (Adjuvant Therapy)	Approved	Approved (US) Approved(EU)	III
Non-small cell lung cancer (2 <sup>nd</sup> ~)	Approved	Approved	Approved
Non-small cell lung cancer (1 <sup>st</sup> )	III	III(US) Filing(EU)	III
Renal cell carcinoma (2 <sup>nd</sup> ~)	Approved	Approved	Approved
Renal cell carcinoma (1 <sup>st</sup> )	Approved	Approved (US) Approved(EU)	Approved
Hodgkin lymphoma	Approved	Approved	Approved
Head and neck carcinoma	Approved	Approved	Approved
Gastric cancer	Approved	III	Approved
Malignant pleural mesothelioma	Approved	III	-
Colorectal cancer	Filing	Approved (US) II/III(EU)	-
Esophageal cancer	III	III	III
Gastro-esophageal junction cancer and esophageal cancer	III	III	III
Small cell lung cancer	III	Approved (US) III (EU)	III
Hepatocellular carcinoma	III	Approved (US) III (EU)	III(KR) Approved (TW)

\*Red : Change from the announcement in May 2018



# Development status of OPDIVO (nivolumab) (2)

Target disease	JAPAN	US/EU	KR/TW
Glioblastoma	Ⅲ	Ⅲ	-
Urothelial cancer	Ⅲ	Approved	Approved
Ovarian cancer	Ⅲ	Ⅲ	-
Bladder cancer	Ⅲ	Ⅲ	Ⅲ
Cervix carcinoma, Uterine body cancer, Soft tissue sarcoma	Ⅱ	-	-
Central nervous system lymphoma, Primary Testicular Lymphoma	Ⅱ	Ⅱ	-
Pancreatic cancer	Ⅱ	Ⅱ	Ⅱ
Virus positive/negative solid carcinoma	I / Ⅱ	I / Ⅱ	I / Ⅱ
Biliary tract cancer	I	-	-
Multiple myeloma	-	Ⅲ	-
Diffuse large B cell lymphoma (Non-Hodgkin lymphoma)	-	Ⅱ	-
Follicular lymphoma (Non-Hodgkin lymphoma)	-	Ⅱ	-
Prostate cancer	-	Ⅱ	-
Pancreatic cancer, Triple negative breast cancer (CheckMate-032 study)	-	I / Ⅱ	-
Blood cancer (T-cell lymphoma, Multiple myeloma, Chronic leukemia, etc. )			
Chronic myeloid leukemia	-	I	-

\*Red : Change from the announcement in May 2018



# Clinical trials in combination therapy

## OPDIVO (nivolumab) & other I-O compounds (1)

Combination therapy	Cancer type	Japan	US/EU	KR/TW
Nivolumab + Ipilimumab	Melanoma	Approved	Approved	Approved
	Renal cell carcinoma	Approved	Approved(US) Approved(EU)	Approved
	Non-small cell lung cancer	III	III(US) Filing(EU)	III
	Small cell lung cancer	III	III	III
	Head and neck cancer	III	III	III
	Gastric cancer	III	III	III
	Malignant pleural mesothelioma	III	III	-
	Esophageal cancer	III	III	III
	Urothelial cancer	III	III	III
	Colorectal cancer	-	Approved(US) II (EU)	-
	Ovarian cancer	-	I / II	-
	Virus positive/negative solid carcinoma	I / II	I / II	I / II

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# Clinical trials in combination therapy

## OPDIVO (nivolumab) & other I-O compounds (2)

Development code/ Generic name (Pharmacological action)	Cancer type	Japan	US/EU	KR/TW
ONO-7701 (IDO1 inhibitor)	Melanoma	III	III	-
	Bladder cancer	III	III	III
ONO-4687 / Cabiralizumab (Anti-CSF-1R antibody)	Pancreatic cancer	II	II	II
ONO-4686 (Anti-TIGIT antibody)	Solid tumor	I / II	I / II	-
ONO-7807 (Anti-TIM-3 antibody)	Solid tumor	I / II	I / II	-
ONO-4482 / Relatlimab (Anti-LAG-3 antibody)	Melanoma	I / II	II / III	-
ONO-4483 / Lirilumab (Anti-KIR antibody)	Solid tumor	I	I / II	-
ONO-4481 / Urelumab (CD137 receptor agonist)	Solid tumor	I	I / II	-
ONO-7475 (Axl/Mer inhibitor)	Solid tumor	I	-	-

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# Development pipeline in Japan (Oncology, other than OPDIVO) (1)

Product name/ Development code (Generic name)	Target indication	Pharmacological action
<b>【Approved/Launch】</b>		
<b>Braftovi (Encorafenib)</b>	<b>Melanoma</b>	<b>BRAF inhibitor</b>
<b>Mektovi (Binimetinib)</b>	<b>Melanoma</b>	<b>MEK inhibitor</b>
<b>Demser (Metyrosine)</b>	<b>Pheochromocytoma</b>	<b>Tyrosine hydroxylase inhibitor</b>
<b>【Filing】</b>		
<b>ONO-7643 (Anamorelin)</b>	<b>Cancer cachexia (in all types of cancer)</b>	<b>Ghrelin mimetic</b>
<b>KYPROLIS &lt;Change in dosage and administration&gt;</b>	<b>Multiple myeloma</b>	<b>Proteasome inhibitor</b>
<b>【Phase III】</b>		
<b>Braftovi (Encorafenib)</b>	<b>Colorectal cancer</b>	<b>BRAF inhibitor</b>
<b>Mektovi (Binimetinib)</b>	<b>Colorectal cancer</b>	<b>MEK inhibitor</b>
<b>ONO-7701 / BMS-986205</b>	<b>Melanoma</b>	<b>IDO1 inhibitor</b>
	<b>Bladder cancer</b>	<b>IDO1 inhibitor</b>

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# Development pipeline in Japan (Oncology, other than OPDIVO) (2)

Development code (Generic name)	Target indication	Pharmacological action
<b>【Phase II】</b>		
<b>ONO-4687 (Cabiralizumab)</b>	<b>Pancreatic cancer</b>	<b>Anti-CSF-1R antibody</b>
<b>ONO-4059 (Tirabrutinib)</b>	<b>Primary macroglobulinemia, Lymphoplasmacytic lymphoma</b>	<b>Btk inhibitor</b>
<b>【Phase I / II】</b>		
ONO-4686 / BMS-986207	Solid tumor	Anti-TIGIT antibody
ONO-4059 (Tirabrutinib)	Central nervous system lymphoma	Btk inhibitor
ONO-4482 (Relatlimab)	Melanoma	Anti-LAG-3 antibody
ONO-7807 / BMS-986258	Solid tumor	Anti-TIM-3 antibody
<b>【Phase I】</b>		
ONO-4481 (Urelumab)	Solid tumor	Anti-CD137 antibody
ONO-4483 (Lirilumab)	Solid tumor	Anti-KIR antibody
ONO-4578	Solid tumor	PG receptor (EP4) antagonist
<b>ONO-7705</b>	<b>Multiple myeloma, Non-Hodgkin lymphoma</b>	<b>XPO1 inhibitor</b>
<b>ONO-7475</b>	<b>Solid tumor</b>	<b>Axl / Mer inhibitor</b>
<b>ONO-7911</b>	<b>Solid tumor</b>	<b>PEGylated IL-2</b>

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# Development pipeline in Japan (Non-oncology) (1)

Product name/ Development code (Generic name)	Target indication	Pharmacological action
<b>【Approved】</b>		
Rivastach Patch <Change of formulation>	Alzheimer's disease	acetylcholinesterase inhibitor
Onoact <Additional indication>	Ventricular arrhythmia	$\beta_1$ blocker (short acting)
<b>【Filing】</b>		
ONO-1162 (Ivabradine)	Chronic heart failure	HCN channel inhibitor
ONO-2370 (Opicapone)	Parkinson's disease	Long acting COMT inhibitor
<b>【Phase III】</b>		
Orencia SC <Additional indication>	Untreated rheumatoid arthritis	T-cell activation inhibitor
Orencia SC <Additional indication>	Primary Sjögrens syndrome	T-cell activation inhibitor
Orencia SC <Additional indication>	Polymyositis/Dermatomyositis	T-cell activation inhibitor
ONO-5704 / SI-613	Osteoarthritis	Hyaluronic acid-NSAID

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# Development pipeline in Japan (Non-oncology) (2)

Development code (Generic name)	Target indication	Pharmacological action
<b>【Phase II / III】</b>		
Onoact <Pediatric>	Tachyarrhythmia in low cardiac function	$\beta_1$ blocker (short acting)
Onoact <Additional indication>	Tachyarrhythmia upon sepsis	$\beta_1$ blocker (short acting)

<b>【Phase II】</b>		
ONO-5704 / SI-613	Enthesopathy	Hyaluronic acid-NSAID
<b>ONO-4059 (Tirabrutinib)</b>	<b>Pemphigus</b>	<b>Btk inhibitor</b>

<b>【Phase I】</b>		
<b>ONO-7269</b>	<b>Cerebral infarction</b>	<b>FXIa inhibitor</b>

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# Global development projects (Other than OPDIVO)

Development code (Generic name)	Target indication	Pharmacological action	Area
<b>【Phase III】</b>			
ONO-7702 (Encorafenib)	Colorectal cancer	BRAF inhibitor	KR
	Melanoma		KR
ONO-7703 (Binimetinib)	Colorectal cancer	MEK inhibitor	KR
	Melanoma		KR
<b>ONO-7701 / BMS-986205</b>	<b>Bladder cancer</b>	<b>IDO1 inhibitor</b>	<b>KR/TW</b>
<b>【Phase II】</b>			
ONO-4059 (Tirabrutinib)	B cell lymphoma	Btk inhibitor	EU
	Sjögrens syndrome		US/EU
<b>ONO-4687 (Cabiralizumab)</b>	<b>Pancreatic cancer</b>	<b>Anti-CSF-1R antibody</b>	<b>KR/TW</b>
<b>【Phase I / II】</b>			
<b>ONO-4578</b>	<b>Solid tumor</b>	<b>PG receptor (EP4) antagonist</b>	<b>US/EU</b>
<b>【Phase I】</b>			
ONO-4059 (Tirabrutinib)	B cell lymphoma	Btk inhibitor	US
ONO-7475	Acute leukemia	Axl / Mer inhibitor	US
<b>ONO-5788</b>	<b>Acromegaly</b>	<b>Growth hormone secretion inhibitor</b>	<b>US</b>
<b>ONO-7684</b>	<b>Thrombosis</b>	<b>FXIa inhibitor</b>	<b>EU</b>

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