

Development Pipeline Progress Status

August 1, 2019

Development status of OPDIVO (nivolumab) (1)

| Target disease | JAPAN | US/EU | KR/TW |
|--|---------------|---------------------------|------------------------|
| Melanoma (1 st) | Approved | Approved | Approved |
| Melanoma (Adjuvant Therapy) | Approved | Approved | Ⅲ(KR) Approved (TW) |
| Non-small cell lung cancer (2 nd ~) | Approved | Approved | Approved |
| Non-small cell lung cancer (1 st) | Ⅲ | Ⅲ(US) Filing(EU) | Ⅲ |
| Renal cell carcinoma (2 nd ~) | Approved | Approved | Approved |
| Renal cell carcinoma (1 st) | Approved | Approved | 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 (MSI-H) | Filing | Approved (US) Ⅱ /Ⅲ(EU) | Approved(TW) |
| Esophageal cancer | Filing | 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) |

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*Red : Change from the announcement in May 2019



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 | - | I / II | - |
| Blood cancer (T-cell lymphoma, Multiple myeloma, Chronic leukemia, etc.) | - | I | - |
| Chronic myeloid leukemia | - | I | - |

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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 | 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 (MSI-H) | - | Approved(US) II(EU) | Approved(TW) |
| | 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) | 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-7475 (Axl/Mer inhibitor) | Solid tumor | I | - | - |
| ONO-7911 (PEGylated IL-2) | 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 |
|--|--|------------------------|
| 【Filing】 | | |
| ONO-7643 (Anamorelin) | Cancer cachexia (in all types of cancer) | Ghrelin mimetic |
| KYPROLIS <Change in dosage and administration> | Multiple myeloma | Proteasome inhibitor |
| 【Phase III】 | | |
| Braftovi (Encorafenib) | Colorectal cancer | BRAF inhibitor |
| Mektovi (Binimetinib) | Colorectal cancer | MEK inhibitor |
| ONO-7701 / BMS-986205 | Bladder cancer | IDO1 inhibitor |
| 【Phase II】 | | |
| ONO-4687 (Cabiralizumab) | Pancreatic cancer | Anti-CSF-1R antibody |
| ONO-4059 (Tirabrutinib) | Primary macroglobulinemia, Lymphoplasmacytic lymphoma | Btk inhibitor |

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

| Development code (Generic name) | Target indication | Pharmacological action |
|------------------------------------|---------------------------------|------------------------|
| 【Phase I / II】 | | |
| 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 |

| | | |
|----------------------|--|------------------------------|
| 【Phase I】 | | |
| ONO-4483 (Lirilumab) | Solid tumor | Anti-KIR antibody |
| ONO-4578 | Solid tumor | PG receptor (EP4) antagonist |
| ONO-7705 | Multiple myeloma, Non-Hodgkin lymphoma | XPO1 inhibitor |
| ONO-7475 | Solid tumor | Axl / Mer inhibitor |
| ONO-7911 | Solid tumor | PEGylated IL-2 |

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

| Product name/ Development code (Generic name) | Target indication | Pharmacological action |
|--|-----------------------|----------------------------|
| 【Filing】 | | |
| ONO-1162 (Ivabradine) | Chronic heart failure | HCN channel inhibitor |
| ONO-2370 (Opicapone) | Parkinson's disease | Long acting COMT inhibitor |

| | | |
|------------------------------------|--------------------------------|-----------------------------|
| 【Phase III】 | | |
| 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 |
|---------------------------------|---|---------------------------------------|
| 【Phase II / III】 | | |
| Onoact <Pediatric> | Tachyarrhythmia in low cardiac function | β_1 blocker (short acting) |
| Onoact <Additional indication> | Tachyarrhythmia upon sepsis | β_1 blocker (short acting) |
| 【Phase II】 | | |
| ONO-5704 / SI-613 | Enthesopathy | Hyaluronic acid-NSAID |
| ONO-4059 (Tirabrutinib) | Pemphigus | Btk inhibitor |
| 【Phase I】 | | |
| ONO-7269 | Cerebral infarction | FXIa inhibitor |
| ONO-4685 | Autoimmune disease | PD-1 × CD3 Bispecific antibody |

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Global development projects (Other than OPDIVO)

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

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