**Annual Flash Report (unaudited)**
**Fiscal Year ended March 31, 2016**

Supplemental Information

# Status of Development Pipeline

as of May 9, 2016

## I. Main Pipelines Other than ONO-4538

### ⅰ. Developments Status in Japan

*Approved*

- **Proemend® for i.v. infusion (ONO-7847 / MK-0517)*1**
  - **Additional indication for pediatric use**
  - Chemotherapy-induced nausea and vomiting in pediatric patients [$NK_1$ receptor antagonist]
  - Injection
  - ***In-license (Merck & Co., Inc.)***

- **Orencia® SC (ONO-4164 / BMS-188667)*2**
  - **Additional formulation**
  - Orencia® SC 125 mg Auto-injector 1 mL
  - Injection
  - ***In-license (Bristol-Myers Squibb Company)***

*Filed*

- **ONO-7057 / Carfilzomib**
  - **New chemical entities**
  - Multiple Myeloma [Proteasome inhibitor]
  - Injection
  - ***In-license (Onyx Pharmaceuticals, Inc.)***
- **ONO-5163 / AMG-416 / Etelcalcetide Hydrochloride**
  - **New chemical entities**
  - Secondary hyperparathyroidism [Calcium sensing receptor agonist]
  - Injection
  - ***In-license (Amgen Inc.)***

*Ongoing clinical studies*

- **Orencia® IV (ONO-4164 / BMS-188667)**
  - **Additional indication**
  - Juvenile Rheumatoid Arthritis [T-cell activation inhibitor] / Phase III
  - Injection
  - ***In-license (Bristol-Myers Squibb Company)***
- **Orencia® IV (ONO-4164 / BMS-188667)**
  - **Additional indication**
  - Lupus nephritis[T-cell activation inhibitor] / Phase III
  - Injection
  - ***In-license (Bristol-Myers Squibb Company)***
- **Orencia® SC (ONO-4164 / BMS-188667)**
  - **Additional indication**
  - Rheumatoid Arthritis [T-cell activation inhibitor] / Phase III
  - Injection
  - ***In-license (Bristol-Myers Squibb Company)***
- **ONO-7057 / Carfilzomib**
  - **Additional Dosing Regimen and additional indication**
  - Multiple Myeloma [Proteasome inhibitor] / Phase III
  - Injection
  - ***In-license (Onyx Pharmaceuticals, Inc.)***
- **ONO-1162 / Ivabradine**
  - **New chemical entities**
  - Chronic heart failure [If channel inhibitor] / Phase III
  - Tablet
  - ***In-license (Les Laboratoires Servier)***
- **Onoact® Intravenous Infusion 50 mg / 150 mg (ONO-1101)**
  - **Additional indication for pediatric use**
  - Tachyarrhythmia in low cardiac function [Short acting beta 1 blocker] / Phase II/III
  - Injection
  - ***In-house***

*Ongoing clinical studies*

- **Onoact® Intravenous Infusion 50 mg / 150 mg (ONO-1101)**
  - **Additional indication**
  - Ventricular arrhythmia [Short acting beta 1 blocker] / Phase II/III
  - Injection
  - ***In-house***
- **ONO-7643 / RC-1291**
  - **New chemical entities**
  - Cancer anorexia/cachexia [Ghrelin mimetic] / Phase II
  - Tablet
  - ***In-license (Helsinn Healthcare, S.A.)***
- **ONO-6950**
  - **New chemical entities**
  - Bronchial asthma [LT receptor antagonist] / Phase II
  - Tablet
  - ***In-house***
- **ONO-2370 / Opicapone**
  - **New chemical entities**
  - Parkinson's disease [Long acting COMT inhibitor] / Phase II
  - Tablet
  - ***In-license (Bial)***
- **ONO-5371 / Metyrosine**
  - **New chemical entities**
  - Pheochromocytoma [Tyrosine hydroxylase inhibitor] / Phase I/II
  - Capsule
  - ***In-license (Valeant Pharmaceuticals North America LLC.)***
- **ONO-7268 MX1**
  - **New chemical entities**
  - Hepatocellular carcinoma [Therapeutic cancer peptide vaccines] / Phase I
  - Injection
  - ***In-license (OncoTherapy Science, Inc.)***
- **ONO-7268 MX2**
  - **New chemical entities**
  - Hepatocellular carcinoma [Therapeutic cancer peptide vaccines] / Phase I
  - Injection
  - ***In-license (OncoTherapy Science, Inc.)***
- **ONO-2160/CD**
  - **New chemical entities**
  - Parkinson's disease [levodopa pro-drug] / Phase I
  - Tablet
  - ***In-house***
- **ONO-4059**
  - **New chemical entities**
  - B cell lymphoma [Bruton's tyrosine kinase (Btk) inhibitor] / Phase I
  - Capsule
  - ***In-house***
- **ONO-8577*3**
  - **New chemical entities**
  - Overactive bladder [bladder smooth muscle relaxant] / Phase I
  - Tablet
  - ***In-house***

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*1: Approval for a partial change in approved items of the manufacturing and marketing authorization of Proemend® for intravenous infusion was obtained in Japan for the treatment of chemotherapy-induced nausea and vomiting for pediatric patients.
*2: Orencia® SC was obtained in Japan for the manufacturing and marketing approval of subcutaneous injection 125 mg Auto-injector 1 mL.
*3: Phase I of ONO-8577 (bladder smooth muscle relaxant) was initiated for overactive bladder.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

## ⅱ. Developments Status outside Japan

### *Ongoing clinical studies*

- **ONO-6950**
  - **New chemical entities**
  - Bronchial asthma [LT receptor antagonist] / Phase II
  - Tablet
  - USA
  - ***In-house***
- **ONO-2952**
  - **New chemical entities**
  - Irritable bowel syndrome [TSPO antagonist] / Phase II
  - Tablet
  - USA
  - ***In-house***
- **ONO-9054*4**
  - **New chemical entities**
  - Glaucoma, ocular hypertension [PG receptor (FP / EP3) agonist] / Phase II
  - Eye drop
  - USA
  - ***Out-license (Santen Pharmaceutical Co., Ltd.)***
- **ONO-4059**
  - **New chemical entities**
  - B cell lymphoma [Bruton's tyrosine kinase (Btk) inhibitor] / Phase I
  - Capsule
  - USA & Europe
  - ***Out-license (Gilead Sciences, Inc.)***
- **ONO-8055**
  - **New chemical entities**
  - Underactive bladder [PG receptor (EP2 / EP3) agonist] / Phase I
  - Tablet
  - Europe
  - ***In-house***
- **ONO-1266**
  - **New chemical entities**
  - Portal hypertension [S1P receptor antagonist] / Phase I
  - Capsule
  - USA
  - ***In-house***
- **ONO-4232**
  - **New chemical entities**
  - Acute heart failure [PG receptor (EP4) agonist] / Phase I
  - Injection
  - USA
  - ***In-house***
- **ONO-4474**
  - **New chemical entities**
  - Osteoarthritis [Tropomyosin receptor kinase (Trk) inhibitor] / Phase I
  - Capsule
  - Europe
  - ***In-house***

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*4: A licensing agreement was entered with Santen Pharmaceutical Co., Ltd. to grant Santen exclusive right to manufacture, develop and commercialize globally ONO-9054, an FP and EP3 dual receptor agonist.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

## II. Main Pipelines ONO-4538 etc

### ⅰ. Developments Status in Japan, South Korea, and Taiwan

*Approved*

| Product Name / Development Code | Development Indications | Area | In-house / In-license |
|---|---|---|---|
| Opdivo® Intravenous Infusion (ONO-4538) /BMS-936558 | Non-small cell lung cancer*1 | South Korea | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Melanoma*2 | Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Non-small cell lung cancer (Squamous)*2 | Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*1: Approval for the partial change in approved items of the manufacturing and marketing approval for Opdivo® Intravenous Infusion was obtained in South Korea for the additional indication of locally advanced or metastatic non-small cell lung cancer refractory to existing chemotherapy.
*2: The manufacturing and marketing approval for Opdivo® Intravenous Infusion was obtained in Taiwan for the treatment of unresectable or metastatic melanoma and metastatic squamous non-small cell lung cancer.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

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| Product Name / Development Code | Development Indications | Area | In-house / In-license |
|---|---|---|---|
| Opdivo® Intravenous Infusion (ONO-4538) /BMS-936558 | Non-small cell lung cancer (Non- Squamous) | Taiwan*3 | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Renal cell carcinoma | Japan<br>Taiwan*3 | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Hodgkin's lymphoma*4 | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*3: A supplemental application for approval for the additional indication of Opdivo® Intravenous Infusion was filed in Taiwan for the treatment of unresectable or metastatic renal cell carcinoma and previously treated non-squamous non-small cell lung cancer.
*4: A supplemental application for approval for the additional indication of Opdivo® Intravenous Infusion was filed in Japan for the treatment of relapsed or refractory Hodgkin's lymphoma.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

*Ongoing clinical studies*

| Product Name / Development Code | Development Indications | Clinical Stage | Area | In-house / In-license |
|---|---|---|---|---|
| Opdivo®Intravenous Infusion (ONO-4538) /BMS-936558 | Head and neck cancer | Phase III | Japan<br>South Korea<br>Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Gastric cancer | Phase III | Japan<br>South Korea<br>Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |

*Ongoing clinical studies*

| Product Name / Development Code | Development Indications | Clinical Stage | Area | In-house / In-license |
|---|---|---|---|---|
| Opdivo®Intravenous Infusion (ONO-4538) /BMS-936558 | Esophageal cancer | Phase III | Japan South Korea Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Small cell lung cancer | Phase III | Japan South Korea Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Hepatocellular carcinoma | Phase III | Japan South Korea Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Glioblastoma | Phase III | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Urothelial cancer*5 | Phase III | Japan South Korea Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Ovarian cancer | Phase II | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Solid tumor*6 (Cervical cancer, Endometrial cancer, Soft tissue sarcoma) | Phase II | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Malignant pleural mesothelioma*7 | Phase II | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Virus-positive/negative solid tumor | Phase I/II | Japan South Korea Taiwan | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Biliary tract cancer | Phase I | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |
| Urelumab (ONO-4481) /BMS-663513 | Solid tumor | Phase I | Japan | In-house (Co-development with Bristol-Myers Squibb Company) |

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*5: Phase III of Opdivo® Intravenous Infusion was initiated for the treatment of Urothelial cancer.
*6: Phase II of Opdivo® Intravenous Infusion was initiated for the treatment of Solid tumor (Cervical cancer, Endometrial cancer, and Soft tissue sarcoma).
*7: Phase II of Opdivo® Intravenous Infusion was initiated for the treatment of Malignant pleural mesothelioma.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

## ⅱ. Developments Status in Europe and the United States

### *Approved*

| Product Name / Development Code | Development Indications | Area | In-house / In-license |
|---|---|---|---|
| Opdivo® Intravenous Infusion (ONO-4538) / BMS-936558 | Renal cell carcinoma *8 | Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Non-small cell lung cancer (Non-squamous) *9 | Europe | In-house (Co-development with Bristol-Myers Squibb Company) |

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*8: Approval for the partial change in approved items of the manufacturing and marketing approval for Opdivo® Intravenous Infusion was obtained in Europe for the additional indication of previously treated advanced renal cell carcinoma.
*9: Approval for the partial change in approved items of the manufacturing and marketing approval for Opdivo® Intravenous Infusion was obtained in Europe for the additional indication of locally advanced or metastatic non-squamous non-small cell lung cancer after prior chemotherapy.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

### *Filed*

| Product Name / Development Code | Development Indications | Area | In-house / In-license |
|---|---|---|---|
| Opdivo® Intravenous Infusion (ONO-4538) /BMS-936558 | Hodgkin's lymphoma*10 | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2016 announced on February 2, 2016
*10: A supplemental application for approval for the additional indication of Opdivo® Intravenous Infusion was filed in USA and Europe for the treatment of previously treated classical Hodgkin lymphoma.

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.

### *Ongoing clinical studies*

| Product Name / Development Code | Development Indications | Clinical Stage | Area | In-house / In-license |
|---|---|---|---|---|
| Opdivo®Intravenous Infusion (ONO-4538) / BMS-936558 | Head and neck cancer | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Glioblastoma | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Small cell lung cancer | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Urothelial cancer | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Hepatocellular carcinoma | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Esophageal cancer | Phase III | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |

*Ongoing clinical studies*

| Product Name / Development Code | Development Indications | Clinical Stage | Area | In-house / In-license |
|---|---|---|---|---|
| Opdivo® Intravenous Infusion (ONO-4538) / BMS-936558 | Diffuse large B cell lymphoma | Phase II | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Follicular lymphoma | Phase II | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Colon cancer | Phase I/II | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Solid tumors (triple negative breast cancer, gastric cancer, pancreatic cancer, small cell lung cancer, urothelial cancer, ovarian cancer) | Phase I/II | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Virus-positive/negative solid tumor | Phase I/II | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Hematologic cancer (T-cell lymphoma, multiple myeloma, chronic leukemia, etc.) | Phase I | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Chronic myeloid leukemia | Phase I | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |
| | Hepatitis C | Phase I | USA Europe | In-house (Co-development with Bristol-Myers Squibb Company) |

**Note**: "In-house" compounds include a compound generated from collaborative research.
In the case of clinical development of the anticancer compound in the same indication, the most advanced clinical phase is described.