Supplemental Information

New Drugs in Development

as of May 13, 2013

In our ongoing effort to create products that will promote the health of more people worldwide, Ono has many new drug formulations under development, including the following main drugs:

ONO-4164SC / BMS-188667SC (injection)

ONO-4164SC is a subcutaneous formulation of Orencia® which is under development for rheumatoid arthritis. ONO-4164SC is a biologic therapy that works by inhibiting the T cell activation and suppressing the production of pro-inflammatory cytokines, which leads to the amelioration of the inflammation in joints of patients.

Japan: J-NDA filed / rheumatoid arthritis (co-development with Bristol-Myers KK)
Overseas: Approved / rheumatoid arthritis (Bristol-Myers Squibb Company)

ONO-4164IV / BMS-188667IV (injection)

ONO-4164IV is an intravenous preparation of Orencia® and is marketed in Japan where it is indicated for use in patients of rheumatoid arthritis for whom other therapies have failed.

Japan: Phase III / juvenile idiopathic arthritis (additional indication) (co-development with Bristol-Myers KK), Phase III / lupus nephritis (additional indication) (being conducted as global clinical trial)
Overseas: Phase III / lupus nephritis (additional indication) (Co-development with Bristol-Myers Squibb Company)

Onoact® for Injection (ONO-1101)

Japan: J-NDA filed / tachyarrhythmia in low cardiac function

Glactiv® Tablets (ONO-5435 / MK-0431)

Japan: Phase III / combination therapy with a rapid-acting insulin secretagogue for type II diabetes (co-development with MSD K.K.)

Glactiv® and metformin Combination Tablets (ONO-5435A / MK-0431A)

Japan: Phase III / combination product with Glacitiv and biguanide for type II diabetes (co-development with MSD K.K.)

Proemend® Intravenous Infusion (ONO-7847 / MK-0517) (In-licensed from Merck & Co., Inc.)

Japan: Phase III / chemotherapy-induced nausea and vomiting in pediatric patients (additional indication)

Rivastach® Patch(ONO-2540 / ENA713D)

Japan: Phase III / alzheimer' disease (administration change) (co-development with Novartis Pharma KK)

ONO-4538 / BMS-936558 (injection)

ONO-4538, a fully human anti-PD-1 antibody, is expected to be a potential treatment for cancer etc. PD-1 is one of the receptors expressed on activated lymphocytes, and is involved in the negative regulatory system to suppress the activated lymphocytes. It has been reported that tumor cells utilize this system to escape from the host immune responses. It is anticipated that blockade of the negative regulatory signal mediated by PD-1 will promote the host's immune response, in which tumor cells and viruses are recognized as foreign and eliminated.

Japan: Phase III / renal cell cancer (being conducted as global clinical trial), Phase II / melanoma, Phase II / non-small cell lung cancer
Overseas: Phase III / melanoma (Bristol-Myers Squibb Company), Phase III / renal cell cancer (Bristol-Myers Squibb Company, global clinical trial),
US & Other Countries: Phase III / non-small cell lung cancer, Phase I /hematological cancer (Bristol-Myers Squibb Company)
US: Phase I / Hepatocellular carcinoma, Phase I / Hepatitis C (Bristol-Myers Squibb Company)

ONO-7165 / EMD531444 (injection) (In-licensed from Merck KGaA)

ONO-7165 is a liposome vaccine being developed for non-small cell lung cancer. ONO-7165 is a cancer immunotherapy targeting the tumor antigen, MUC-1. It is thought that an immune cell recognizes MUC-1 as tumor antigen, and then attacks cancer cells expressing MUC-1.

Japan: Phase II / non-small cell lung cancer (co-development with Merck KGaA)
Overseas: Phase III / non-small cell lung cancer (Merck KGaA)

ONO-4641 (tablet)

ONO-4641 is a sphingosine-1-phosphate (S1P) receptor agonist, being developed for the treatment of multiple sclerosis. ONO-4641 is a low molecular weight substance that keeps lymphocytes in lymph nodes and reduces the lymphocyte count in the blood, thereby inhibiting the infiltration of lymphocytes into lesions. ONO-4641 is therefore expected to be an innovative drug for the treatment of auto-immune diseases such as multiple sclerosis, which is regarded as an intractable disease.

Japan: Phase II / multiple sclerosis (being conducted as global clinical trial)
US and Europe: Phase II / multiple sclerosis (Merck KGaA, global clinical trial)

ONO-3849 / Methylnaltrexone bromide (injection)(In-licensed from Progenics Pharmaceuticals, Inc.)

ONO-3849 is a peripherally acting mu-opioid receptor antagonist, and is developed for intractable opioid induced constipation. Opioid pain medications are often used for the treatment of pain in cancer and other advanced illnesses, but cause constipation in many of these patients. ONO-3849 is expected to decrease the constipating effects of opioid analgesics in the gastrointestinal tract without affecting their ability to relieve pain.

Japan: Phase II / opioid-induced constipation
Overseas: Marketed (Salix Pharmaceuticals, Inc.)

ONO-7643 / RC-1291 (tablet)(In-licensed from Helsinn Therapeutics (US), Inc.)

ONO-7643 is a small-molecule ghrelin mimetic being developed for cancer anorexia / cachexia. ONO-7643 has similar pharmacological actions to ghrelin, a circulating peptide hormone with multiple physiological actions, including appetite stimulation and muscle-building, and is therefore expected to be a breakthrough drug that improves quality of life (QOL) for patients impaired by a systemic wasting condition characterized by anorexia, lipolysis and muscle loss associated with the progression of cancer.

Japan: Phase II / cancer anorexia / cachexia
US & Other Countries: Phase III / cancer anorexia / cachexia (Helsinn Therapeutics (U.S.), Inc.)

ONO-2745 / CNS 7056 (injection)(In-licensed from PAION AG)

ONO-2745 is a $GABA_A$ receptor modulator, an innovative short-acting general anaesthetic and sedative, and is under clinical development as a sedative agent during the induction and maintenance of general anesthesia and during mechanical ventilation in the Intensive Care Unit (ICU). The sedative effects rapidly disappear after cessation of administration due to its metabolism by esterase enzymes, and therefore it is expected to be a drug with improved controllability and safety profile.

Japan: Phase II / III / general anesthesia,
Phase II / ICU sedation
US: Phase II / procedural sedation (PAION AG)

ONO-7057 / Carfilzomib (injection)(In-licensed from Onyx Pharmaceuticals, Inc.)

ONO-7057 is a proteasome inhibitor being developed for multiple myeloma, which is a cancer of plasma cells (one of blood cells). ONO-7057 is highly expected to be a new treatment option for poor prognosis multiple myeloma.

Japan: Phase I / II / multiple myeloma
Overseas: Approved under Accelerated Drug Approval Program in US / multiple myeloma (launched in August 2012)
Phase III in Europe/ multiple myeloma (Onyx Pharmaceuticals, Inc.).

ONO-5163 / AMG-416 (injection) (In-licensed from Amgen Inc.)

ONO-5163 is a calcium sensing receptor agonist currently being developed for the treatment of secondary hyperparathyroidism.

Japan: Phase I / II / secondary hyperparathyroidism
US: Phase III / secondary hyperparathyroidism (Amgen Inc.)

ONO-6950 (tablet)
ONO-6950 is a leukotriene receptor antagonist, and is under clinical development for bronchial asthma. It is expected to improve symptoms associated with the disease by inhibiting airway inflammation.

Japan: Phase I / bronchial asthma
US: Phase II / bronchial asthma

ONO-7056 / Salirasib (tablet) (In-licensed from Kadmon Pharmaceuticals, Inc.)
ONO-7056 is a Ras signal inhibitor which is expected to be effective in the cancers, such as pancreatic cancer, in which high RAS genetic mutation is found.

Japan: Phase I / solid tumor
US: Phase I / pancreatic cancer (Kadmon Pharmaceuticals, Inc.)

ONO-7268MX1 (injection) (In-licensed from OncoTherapy Science, Inc.)
ONO-7268 is a peptide vaccine and is expected to have effects on cancers such as hepatocarcinoma.

Japan: Phase I / hepatocarcinoma

ONO-1162 (tablet) (In-licensed from Servier)
ONO-1162 is an If channel blocker and is approved for the indication of chronic heart failure in addition to stable angina in Europe. It is under development in Japan for the indication of chronic heart failure.

Japan: Phase I / chronic heart failure
Overseas: Marketed / stable angina, chronic heart failure

ONO-2160/CD (tablet)
ONO-2160 is a combination product with levodopa pro-drug and carbidopa which is currently developed for Parkinson's disease.

Japan: Phase I / Parkinson's disease

ONO-4053 (tablet)
ONO-4053 is a PGD2 receptor antagonist and is under clinical development for allergic rhinitis. It is expected to improve particularly nasal congestion, one of the three major symptoms of allergic rhinitis such as nasal congestion, sneezing and nasal discharge.

Europe: Phase II / allergic rhinitis

ONO-2952 (tablet)
ONO-2952 is an antagonist of translocator protein (TSPO) that is involved in neurosteroid production mainly in central nervous system, and is under clinical development for irritable bowel syndrome. It is expected to improve various symptoms of the disease by blocking the mechanism eliciting abnormality of brain-gut interactions under stress.

US: Phase II / IBS

ONO-7746 (capsule) (In-licensed from Nissan Chemical Industries, Ltd.)
ONO-7746 is an orally active low molecule compound which may increase platelet count by activating a receptor of thrombopoietin, which is a hematopoietic factor to accelerate platelet production. It is therefore expected to be developed as a new drug which may reduce the risk of bleeding in various diseases with thrombocytopenia and overcome the risk of infection associated with platelet transfusion. Nissan Chemical is participating in co-development by process development and manufacture of the drug substance.

US: Phase I / thrombocytopenia

ONO-9054 (eye drop)
ONO-9054 is a prostaglandin receptor (FP/EP3) agonist being developed for glaucoma and ocular hypertension.

US: Phase I / glaucoma and ocular hypertension

ONO-4059 (tablet)
ONO-4059 is a Btk inhibitor being developed for the treatment of B cell lymphoma.

Europe: Phase I / B cell lymphoma

ONO-8539 (tablet)
ONO-8539 is a prostaglandin receptor (EP1) antagonist being developed for the treatment of gastroesophageal reflux disease (GERD).

Europe: Phase I /GERD

ONO-8055 (tablet)
ONO-8055 is a prostaglandin receptor (EP2/EP3) agonist being developed for the treatment of underactive bladder.

Europe: Phase I / underactive bladder

- **ONO-6950 (tablet)**
  Bronchial asthma (Phase II) [LT receptor antagonist]
- **ONO-4053 (tablet)**
  Allergic rhinitis (Phase II) [PGD2 receptor antagonist]
- **ONO-2952 (tablet) *5**
  Irritable bowel syndrome (Phase II) [TSPO antagonist]
- **ONO-8539 (tablet)**
  Gastroesophageal reflux disease (GERD) (Phase I) [PG receptor (EP1) antagonist]
- **ONO-4538 / BMS-936558 (injection)**
  (Out-licensed to Bristol-Myers Squibb Company)
  Hepatitis C (Phase I) [Fully human anti-PD-1 antibody]
- **ONO-7746 (capsule)**
  (In-licensed from Nissan Chemical Industries, Ltd.)
  Thrombocytopenia (Phase I) [TPO receptor agonist]
- **ONO-9054 (eye drop)**
  Glaucoma, ocular hypertension (Phase I) [PG receptor (FP / EP3) agonist]
- **ONO-4059 (tablet)**
  B cell lymphoma (Phase I) [Bruton's tyrosine kinase (Btk) inhibitor]
- **ONO-8055 (tablet)**
  Underactive bladder (Phase I) [PG receptor (EP2 / EP3) agonist]
- **ONO-4538 / BMS-936558 (injection) *6**
  (Out-licensed to Bristol-Myers Squibb Company)
  Hematological cancer (Phase I) [Fully human anti-PD-1 antibody]
- **ONO-4538 / BMS-936558 (injection) *7**
  (Out-licensed to Bristol-Myers Squibb Company)
  Hepatocellular carcinoma (Phase I) [Fully human anti-PD-1 antibody]

Changes from Third Quarter Flash Report for the Fiscal Year ending March 2013 announced on February 4, 2013

- *1: J-NDA of Onoact® 50 for Injection was filed for additional indication of tachyarrhythmia in low cardiac function.
- *2:Phase I clinical study of ONO-2160, levodopa pro-drug was commenced for Parkinson's disease.
- *3: Phase III clinical study of Orencia IV® IV, RA therapeutic agent was commenced for juvenile rheumatoid arthritis.
- *4: Phase III clinical study of Orencia IV® IV, RA therapeutic agent was commenced for lupus nephritis.
- *5: Phase II clinical study of ONO-2952, TSPO (translocator protein) antagonist was commenced for IBS.
- *6: Phase I clinical study of ONO-4538, fully human anti-PD-1 antibody was commenced for hematological cancer.
- *7: Phase I clinical study of ONO-4538, fully human anti-PD-1 antibody was commenced for hepatocellular carcinoma.
- *: Further development of ONO-3951 for irritable bowel syndrome was discontinued because expected efficacy was not confirmed in Phase II clinical study.