Development Pipeline Progress Status (Summary)
for 2nd Quarter of Fiscal Year Ended March 31, 2016

Main development status of OPDIVO

2nd line or later therapy of melanoma
OPDIVO has been already launched for this indication in Japan, the USA and EU. In Korea, the product has been approved. In Taiwan, an NDA was filed.

1st line therapy (mono-therapy) of melanoma
OPDIVO has been approved in EU in June 2015. An application for additional indication was accepted in the US in May, and it was submitted in Japan in July 2015. In addition, a supplemental application was filed in Korea.

1st line therapy of melanoma (Combination therapy with ipilimumab)
OPDIVO has been approved in the USA under the accelerated approval system. In EU, an application was accepted in July 2015. Phase II clinical study is ongoing in Japan.

2nd line or later therapy of non-small cell lung cancer (NSCLC)
In the USA, following an approval for the treatment of squamous NSCLC in March 2015, OPDIVO has been approved for non-squamous NSCLC in October 2015. In EU, it has been approved for squamous NSCLC in July 2015, with an application for non-squamous NSCLC being accepted in the same month. In Japan, an application for squamous NSCLC was submitted in April 2015, and an application for NSCLC including squamous NSCLC was submitted in July 2015. In Korea, the same applications were filed, while an application only for squamous NSCLC was filed in Taiwan.

1st line therapy of NSCLC
Phase III clinical study for the treatment of NSCLC is ongoing smoothly as a global collaborative study in EU and the USA including Japan, Korea and Taiwan.

2nd line or later therapy of renal cell cancer (RCC)
Phase III clinical study for the treatment of RCC, which was conducted as a global collaborative study in EU and the USA including Japan, was stopped early in July 2015 because it was concluded that the study met its endpoint.

1st line therapy of RCC (combination therapy with ipilimumab)
Phase III clinical study of OPDIVO in combination with ipilimumab is ongoing for the

indication of the 1st-line treatment as a global collaborative study in EU and the USA including Japan.

Head and neck carcinoma

Phase III clinical study is ongoing as a global collaborative study in EU and the USA including Japan, Korea and Taiwan.

Gastric cancer

As for gastric cancer which occurs with relatively high incidence in Asia, Phase III clinical study is being conducted in Japan, Korea and Taiwan ahead of EU and the USA where Phase I/II clinical study is ongoing as another study.

Small cell lung cancer

Phase III clinical study was started in Japan, Korea and Taiwan, together with EU and the USA.

Esophageal cancer

A good result was obtained in Phase II clinical study in Japan. The result was presented in the 53th Annual Meeting of Japan Society of Clinical Oncology. Phase III clinical study was started in Japan, Korea and Taiwan.

Glioblastoma

Phase III clinical study is ongoing in EU and the USA for the treatment of glioblastoma which is refractory and a type of cerebral tumor. In Japan, Phase II clinical study was started in June 2015 to bridge the study with Phase III clinical study which is conducted in EU and the USA.

Ovarian cancer

An investigator initiated clinical study was conducted for ovarian cancer in the Kyoto University. Based on the study result, Phase II clinical study was started in August 2015.

Urothelial cancer

Phase II clinical study has already been started in EU and the USA. It was also started in Japan in May 2015.

Virus positive, negative solid tumor

Phase I/II clinical study was started in EU, the USA, Japan, Korea and Taiwan.

Bile duct carcinoma
Phase I clinical study was started in Japan.

Hepatocellular carcinoma
Phase I clinical study is being conducted in Japan, EU and the USA. Data showing an efficacy of the product was obtained.

Others (cancers at a relative early stage)
It is expected that an early approval for Hodgkin lymphoma will be granted because data showing a significantly high efficacy of the product was obtained while it is still in a small scale, and because the FDA granted Breakthrough Therapy designation for this indication last year. In Japan, another Phase II clinical study is conducted for the treatment of Hodgkin lymphoma.
As for two types of non-Hodgkin lymphoma (diffuse large B cell lymphoma and follicular lymphoma), Phase II clinical studies are ongoing in EU and the USA.
For colon cancer, Phase I/II clinical studies are ongoing in EU and the USA.
In addition, an exploratory Phase I/II clinical studies are ongoing in EU and the USA for the treatment of pancreatic cancer, gastric cancer, small cell lung cancer, triple-negative breast cancer, etc.

Combination study with OPDIVO and other immune checkpoint inhibitors

ONO entered into a new collaboration agreement with Bristol-Myers Squibb (BMS) covering Japan, Korea and Taiwan last year. Under this agreement, both companies will jointly co-develop a total of 5 compounds, namely OPDIVO, ipilimumab (anti-CT-LA4 antibody), anti-KIR antibody, anti-LAG-3 antibody and CD137 receptor agonist.

The following clinical studies were started in Japan in May 2015 or thereafter.

- Phase III clinical study for the treatment of NSCLC in combination with OPDIVO and ipilimumab
- Phase I clinical study for solid tumors in combination with OPDIVO and BMS-986016 (anti-LAG-3 antibody)
- Phase I/II clinical study for solid tumors and non-Hodgkin lymphoma in combination with OPDIVO and Urelumab (CD137 receptor agonist)

In addition, a collaboration agreement was concluded with Kyowa Hakko Kirin Co., Ltd. (KHK) regarding a KHK's anti-CCR4 antibody, mogamulizumab (which has been approved in Japan for the treatment of blood cancer) at the end of last year. Phase I clinical study is

ongoing for solid tumors in combination with OPDIVO and mogamulizumab.

Global development project (besides OPDIVO)

In the project pipeline other than OPDIVO, nine projects are currently ongoing on a global basis, that is, ONO-6950 (bronchial asthma), ONO-2952 (irritable bowel syndrome), ONO-9054 (glaucoma and ocular hypertension), ONO-4059 (B-cell lymphoma), ONO-8055 (underactive bladder), ONO-2160 (Parkinson's disease), ONO-1266 (Portal hypertension), ONO-4232 (Acute heart failure) and ONO-4474 (osteoarthrosis).

Development pipeline in Japan

The ongoing development pipeline in Japan is described as follows in order of late (advanced) development stage of the compounds. The following is a progress situation made in May 2015 or thereafter:

In addition to the currently approved dose and dosage of Rivastach Patch for the treatment of Alzheimer's disease, a supplemental application for the dose and dosage to increase to 18 mg (maintenance dose) by one step (4 weeks) was approved, resulting in higher convenience.

An application of ONO-7057 (carfilzomib), a proteasome inhibitor for manufacturing and marketing approval for the indication of relapsed and refractory multiple myeloma was submitted. ONO expects to bring this product to the patients as soon as possible.

For Orencia subcutaneous infusion, Phase III clinical trial was started in September 2015 in patients with rheumatoid arthritis who have not been treated with anti-rheumatoid drugs, in order to obtain the data relating to prevention of destruction of cartilage.

Phases III clinical study with ONO-1162 (ivabradine), an If channel inhibitor, was started in August 2015 in patients with chronic heart failure.

The development of ONO-7056 (salirashib), a Ras signal inhibitor under Phase I clinical study in patients with solid tumors was discontinued because the compound didn't demonstrate an expected efficacy.