ONO PHARMACEUTICAL CO.,LTD.

April 25, 2018

ONO Submits Applications for Manufacturing and Marketing Approval for Encorafenib, a BRAF Inhibitor and Binimetinib, a MEK Inhibitor for Indication of Unresectable BRAF-mutant Melanoma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that it submitted an application for the manufacturing and marketing approval of encorafenib (ONO-7702) ("encorafenib"), a BRAF inhibitor and binimetinib (ONO-7703) ("binimetinib"), a MEK inhibitor in Japan for the indication of unresectable BRAF-mutant melanoma.

This application is based on the result of a global randomized, open label Phase III study (COLUMBUS study) conducted in and outside Japan in patients with BRAF-mutant advanced, unresectable or metastatic melanoma. The result showed that the combination treatment with encorafenib 450 mg once daily and binimetinib 45 mg twice daily (COMBO450) demonstrated statistically significant extension of a median progression-free survival (mPFS) as assessed by a Blinded Independent Central Review (BICR) with a mPFS of 14.9 months, compared to vemurafenib, with 7.3 months (hazard ratio 0.54; 95% confidence interval: 0.41 - 0.71, P<0.0001).

In May 2017, ONO concluded a license agreement regarding encorafenib and binimetinib with the U.S.-based Array BioPharma Inc. ("Array"), and obtained exclusive rights to develop and commercialize both products in Japan and South Korea. Array retains exclusive rights to encorafenib and binimetinib in the U.S. and Canada. Array has granted Pierre Fabre exclusive rights to commercialize both products in all other countries, including Europe, Asia and Latin America.

About Melanoma

Melanoma is a form of skin cancer that develops from the pigment-producing cells (melanocytes) which are deeply related with the skin colour, and said to be the most metastatic and deadliest form of the disease. It is reported that the number of melanoma patients is about 4,000 patients [*1] with about 700 deaths [*2] due to melanoma per year in Japan.

*1: CANCER STATISTICS IN JAPAN 2013, Patient Survey (Basic Disease Classification), Ministry of Health, Labour and Welfare 2011

*2: Vital Statistics, Ministry of Health, Labour and Welfare 2012

About Encorafenib and Binimetinib

Encorafenib is a low molecule BRAF inhibitor and binimetinib is a low molecule MEK inhibitor. BRAF and MEK are key protein kinases in the MAPK signalling pathway (RAS-RAF-MEK-ERK). Research has shown this pathway regulates several key cellular activities including proliferation, differentiation, survival and angiogenesis. Inappropriate activation of proteins in this pathway has been shown to occur in many cancers including melanoma and colorectal cancer. Encorafenib and binimetinib target key enzymes in this pathway. Encorafenib and binimetinib are being studied in

clinical studies, including the global Phase III BEACON CRC study evaluating the efficacy and safety of encorafenib in combination with cetuximab with or without binimetinib compared to cetuximab and irinotecan-based therapy. In addition, New Drug Applications (NDA) and Marketing Authorization Applications (MAA) for combination therapy of encorafenib and binimetinib are under review for the treatment of patients with BRAF-mutant melanoma by the U.S. FDA (Food and Drug Administration) and EMA (European Medicines Agency), respectively. Encorafenib and binimetinib are investigational medicines and are not currently approved in any country.

About COLUMBUS study

The COLUMBUS study (NCT01909453), is a two-part, global, randomized, open-label Phase 3 study evaluating the efficacy and safety of combination therapy of encorafenib and binimetinib compared to vemurafenib and encorafenib monotherapy in 921 patients with locally advanced, unresectable or metastatic melanoma with $BRAF^{V600}$ mutation. Over 200 sites across North America, Europe, South America, Africa, Asia and Australia participated in the study. Patients were randomized into two parts:

- In Part 1, 577 patients were randomized 1:1:1 to receive COMBO450, encorafenib 300 mg daily (ENCO300), or vemurafenib 960 mg twice daily alone. A higher dose of encorafenib was possible due to improved tolerability when combined with binimetinib. Therefore, the dose of encorafenib in the combination arm is set up at 50% higher than the single agent maximum tolerated dose of 300 mg. The primary endpoint for the COLUMBUS study was a mPFS comparison of the COMBO450 arm versus vemurafenib. mPFS is determined based on tumor assessment (RECIST version 1.1 criteria) by a Blinded Independent Central Review (BICR). Secondary endpoints include a comparison of the mPFS of ENCO300 to that of the COMBO450 arm and a comparison of overall survival (OS) of the COMBO450 arm to that of vemurafenib alone.

- In Part 2, 344 patients were randomized 3:1 to receive encorafenib 300 mg once daily plus binimetinib 45 mg twice daily (COMBO300) or ENCO300. Part 2 was designed to provide additional data to help evaluate the contribution of binimetinib to the combination of encorafenib and binimetinib.

About Array BioPharma

Array BioPharma Inc. is a biopharmaceutical company focused on the discovery, development and commercialization of targeted small molecule drugs to treat patients afflicted with cancer and other conditions. Ten registration studies are currently advancing related to eight Array-owned or partnered drugs: encorafenib (LGX818), binimetinib (MEK162), ARRY-797, selumetinib (partnered with AstraZeneca), danoprevir (partnered with Roche), ipatasertib (partnered with Genentech), larotrectinib (partnered with Loxo Oncology) and tucatinib (partnered with Seattle Genetics). For more information on Array, please go to www.arraybiopharma.com.

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