Array BioPharma Announces Presentation of Updated Overall Survival from the Phase 3 COLUMBUS Trial of BRAFTOVI + MEKTOVI in advanced BRAF-mutant Melanoma at 2019 ASCO Annual Meeting

May 29, 2019

- Consistent with prior readouts, BRAFTOVI + MEKTOVI demonstrates 33.6 months median overall survival with longer median follow up over 48 months -

- Landmark analysis estimates 47% and 39% of patients alive at 3 and 4 years, respectively -

- Oral poster presentation June 3, 2019 -

BOULDER, Colo., May 29, 2019 /PRNewswire/ -- Array BioPharma Inc. (Nasdaq: ARRY) announced that that it will present data from the Phase 3 COLUMBUS Trial of BRAFTOVI + MEKTOVI in advanced *BRAF*-mutant melanoma in an oral poster discussion on June 3, 2019, at the 55th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois. Landmark overall survival (OS) and progression-free survival (PFS), as well as subgroup analyses and updated safety and tolerability, will be presented.

"We are pleased to report a 4-year landmark analysis of the long-term benefit of BRAFTOVI + MEKTOVI from the COLUMBUS trial," said Ron Squarer, Chief Executive Officer. "Both the overall survival and progression-free survival data remain consistent with prior reports and continue to represent new benchmarks for BRAF + MEK inhibitor combinations in the treatment of $BRAF^{V600}$-mutant advanced melanoma. We remain steadfastly committed to developing products that treat cancers in dire need of effective therapies."

Across arms, median follow-up for OS was 48.6 months, with a median OS of 33.6 months (95% CI, 24.4–39.2) for BRAFTOVI, 450 mg daily + MEKTOVI, 45 mg twice daily, compared to 16.9 months (95% CI, 14.0–24.5) for vemurafenib, consistent with prior readouts. Compared to vemurafenib, BRAFTOVI, 450 mg daily + MEKTOVI, 45 mg twice daily, decreased the risk of death by 39% (HR, 0.61 [95% CI, 0.48–0.79]).

Updated median progression-free survival (PFS) also remained consistent and was 14.9 months (95% CI, 11.0–20.2) with BRAFTOVI, 450 mg daily + MEKTOVI, 45 mg twice daily, compared to 7.3 months (95% CI, 5.6–8.2) with vemurafenib (HR, 0.52 [95% CI, 0.40–0.67]).

Poster Discussion

Title:	Update on Overall Survival in COLUMBUS: A Randomized Phase 3 Trial of Encorafenib (ENCO) Plus Binimetinib (BINI) versus Vemurafenib (VEM) or ENCO in Patients with *BRAF* V600–Mutant Melanoma
Presenter:	Paolo Ascierto, M.D., Director, Unit of Melanoma, Cancer Immunotherapy and Innovative Therapy at the National Tumor Institute Fondazione G. Pascale, Naples, Italy.
Abstract:	Abstract #9512
Session:	Melanoma/Skin Cancers
Date:	Monday, June 3, 2019
Poster session:	1:15 – 4:15 PM Central Time
Poster discussion:	4:30 PM – 6:00 PM Central Time
Location:	Hall A

The abstracts can be accessed through the ASCO website, http://abstract.asco.org/. Following the poster presentation on Monday, June 3, 2019, the poster will be available as a PDF on Array's website at www.arraybiopharma.com.

About *BRAF*-mutant Metastatic Melanoma

Melanoma develops when unrepaired DNA damage to skin cells triggers mutations that may lead them to multiply and form malignant tumors. Metastatic melanoma is the most serious and life-threatening type of skin cancer and is associated with low survival rates. [1,2] There are a variety of gene mutations that can lead to metastatic melanoma. The most common genetic mutation in metastatic melanoma is *BRAF*. There are about 200,000 new cases of melanoma diagnosed worldwide each year, approximately half of which have *BRAF* mutations, a key target in the treatment of metastatic melanoma. [1-5]

About COLUMBUS

The COLUMBUS trial (NCT01909453) is a two-part, international, randomized, open label Phase 3 trial evaluating the efficacy and safety of BRAFTOVI (encorafenib) in combination with MEKTOVI (binimetinib) compared to vemurafenib and encorafenib monotherapy in 921 patients with locally advanced, unresectable or metastatic melanoma with $BRAF^{V600}$ mutation. All secondary efficacy analyses, including overall survival, are descriptive in nature. Over 200 sites across North America, Europe, South America, Africa, Asia and Australia participated in the trial.

About BRAFTOVI + MEKTOVI

BRAFTOVI is an oral small molecule BRAF kinase inhibitor and MEKTOVI is an oral small molecule MEK inhibitor which target key enzymes in the MAPK signaling pathway (RAS-RAF-MEK-ERK). Inappropriate activation of proteins in this pathway has been shown to occur in many cancers including melanoma, colorectal cancer, non-small cell lung cancer and others. In the U.S., BRAFTOVI + MEKTOVI are approved for the treatment of unresectable or metastatic melanoma with a $BRAF^{V600E}$ or $BRAF^{V600K}$ mutation, as detected by an FDA-approved test. BRAFTOVI is not indicated for treatment of patients with wild-type *BRAF* melanoma. In Europe, the combination is approved for adult patients with unresectable or metastatic melanoma with a $BRAF^{V600}$ mutation, as detected by a validated test. In Japan, the combination is approved for unresectable melanoma with a *BRAF* mutation.

Array has exclusive rights to BRAFTOVI and MEKTOVI in the U.S. and Canada. Array has granted Ono Pharmaceutical Co. Ltd., exclusive rights to commercialize both products in Japan and South Korea, Medison exclusive rights to commercialize both products in Israel and Pierre Fabre exclusive rights to commercialize both products in all other countries, including Europe, Latin American and Asia (excluding Japan and South Korea).

BRAFTOVI + MEKTOVI have received regulatory approval in the United States, European Union, Australia and Japan. The Swiss Medicines Agency (Swissmedic) is currently reviewing the Marketing Authorization Applications for BRAFTOVI and MEKTOVI submitted by Pierre Fabre.

Indications and Usage

BRAFTOVI® (encorafenib) and MEKTOVI® (binimetinib) are kinase inhibitors indicated for use in combination for the treatment of patients with unresectable or metastatic melanoma with a *BRAF*^{V600E} or *BRAF*^{V600K} mutation, as detected by an FDA-approved test.

Limitations of Use: BRAFTOVI is not indicated for the treatment of patients with wild-type BRAF melanoma.

BRAFTOVI + MEKTOVI Important Safety Information

The information below applies to the safety of the combination of BRAFTOVI and MEKTOVI unless otherwise noted. See full Prescribing Information for BRAFTOVI and for MEKTOVI for dose modifications for adverse reactions.

Warnings and Precautions

New Primary Malignancies: Cutaneous and non-cutaneous malignancies can occur. In the COLUMBUS trial, cutaneous squamous cell carcinoma, including keratoacanthoma, occurred in 2.6% and basal cell carcinoma occurred in 1.6% of patients. Perform dermatologic evaluations prior to initiating treatment, every 2 months during treatment, and for up to 6 months following discontinuation of treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Dose modification is not recommended for new primary cutaneous malignancies. Based on its mechanism of action, BRAFTOVI may promote malignancies associated with activation of RAS through mutation or other mechanisms. Monitor patients receiving BRAFTOVI for signs and symptoms of non-cutaneous malignancies. Discontinue BRAFTOVI for RAS mutation-positive non-cutaneous malignancies.

Tumor Promotion in BRAF Wild-Type Tumors: Confirm evidence of BRAF^{V600E} or ^{V600K} mutation prior to initiating BRAFTOVI.

Cardiomyopathy, manifesting as left ventricular dysfunction associated with symptomatic or asymptomatic decreases in ejection fraction, has been reported in patients. In the COLUMBUS trial, cardiomyopathy occurred in 7% and Grade 3 left ventricular dysfunction occurred in 1.6% of patients. Cardiomyopathy resolved in 87% of patients. Assess left ventricular ejection fraction by echocardiogram or MUGA scan prior to initiating treatment, 1 month after initiating treatment, and then every 2 to 3 months during treatment. Safety has not been established in patients with a baseline ejection fraction that is either below 50% or below the institutional lower limit of normal. Patients with cardiovascular risk factors should be monitored closely.

Venous Thromboembolism (VTE): In the COLUMBUS trial, VTE occurred in 6% of patients, including 3.1% of patients who developed pulmonary embolism.

Hemorrhage: In the COLUMBUS trial, hemorrhage occurred in 19% of patients and ≥ Grade 3 hemorrhage occurred in 3.2% of patients. Fatal intracranial hemorrhage in the setting of new or progressive brain metastases occurred in 1.6% of patients. The most frequent hemorrhagic events were gastrointestinal, including rectal hemorrhage (4.2%), hematochezia (3.1%), and hemorrhoidal hemorrhage (1%).

Ocular Toxicities: In the COLUMBUS trial, serous retinopathy occurred in 20% of patients; 8% were retinal detachment and 6% were macular edema. Symptomatic serous retinopathy occurred in 8% of patients with no cases of blindness. RVO is a known class-related adverse reaction of MEK inhibitors and may occur in patients treated with MEKTOVI in combination with encorafenib. In patients with *BRAF* mutation-positive melanoma across multiple clinical trials, 0.1% of patients experienced retinal vein occlusion (RVO). The safety of MEKTOVI has not been established in patients with a history of RVO or current risk factors for RVO including uncontrolled glaucoma or a history of hyperviscosity or hypercoagulability syndromes. Perform ophthalmological evaluation for patient-reported acute vision loss or other visual disturbance within 24 hours. Permanently discontinue MEKTOVI in patients with documented RVO. In COLUMBUS, uveitis, including iritis and iridocyclitis was reported in 4% of patients. Assess for visual symptoms at each visit. Perform ophthalmological evaluation at regular intervals and for any visual disturbances, and to follow new or persistent ophthalmologic findings.

Interstitial Lung Disease (ILD): ILD, including pneumonitis occurred in 0.3% of patients with *BRAF* mutation-positive melanoma across multiple clinical trials. Assess new or progressive unexplained pulmonary symptoms or findings for possible ILD.

Hepatotoxicity: In the COLUMBUS trial, the incidence of Grade 3 or 4 increases in liver function laboratory tests was 6% for alanine aminotransferase (ALT) and 2.6% for aspartate aminotransferase (AST), and 0.5% for alkaline phosphatase. Monitor liver laboratory tests before and during treatment and as clinically indicated.

Rhabdomyolysis: In the COLUMBUS trial, elevation of laboratory values of serum creatine phosphokinase (CPK) occurred in 58% of patients. Rhabdomyolysis was reported in 0.1% of patients with *BRAF* mutation-positive melanoma across multiple clinical trials. Monitor CPK and creatinine levels prior to initiating MEKTOVI, periodically during treatment, and as clinically indicated.

QTc Prolongation: BRAFTOVI is associated with dose-dependent QTc interval prolongation in some patients. In the COLUMBUS trial, an increase in QTcF to > 500 ms was measured in 0.5% (1/192) of patients. Monitor patients who already have or who are at significant risk of developing QTc prolongation. Correct hypokalemia and hypomagnesemia prior to and during BRAFTOVI administration. Withhold, reduce dose, or permanently discontinue for QTc > 500 ms.

Embryo-Fetal Toxicity: BRAFTOVI or MEKTOVI can cause fetal harm when administered to pregnant women. BRAFTOVI can render hormonal contraceptives ineffective. Non-hormonal contraceptives should be used during treatment and for at least 30 days after the final dose for patients taking BRAFTOVI + MEKTOVI.

Adverse Reactions

The most common adverse reactions (≥20%, all Grades, in the COLUMBUS trial): were fatigue, nausea, diarrhea, vomiting, abdominal pain, arthralgia, myopathy, hyperkeratosis, rash, headache, constipation, visual impairment, serous retinopathy.

In the COLUMBUS trial, the most common laboratory abnormalities (≥20%, all Grades): included increased creatinine, increased CPK, increased gamma glutamyl transferase, anemia, increased ALT, hyperglycemia, increased AST, and increased alkaline phosphatase.

Drug Interactions

Avoid concomitant use of strong or moderate CYP3A4 inhibitors or inducers and sensitive CYP3A4 substrates with BRAFTOVI. Modify BRAFTOVI dose if concomitant use of strong or moderate CYP3A4 inhibitors cannot be avoided. Avoid co-administration of BRAFTOVI with medicinal products with a known potential to prolong QT/QTc interval.

Please see full Prescribing Information for BRAFTOVI and full Prescribing Information for MEKTOVI for additional information. [6,7] You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Array at 1-844-Rx-Array (1-844-792-7729).

About Array BioPharma
Array BioPharma Inc. is a fully integrated biopharmaceutical company focused on the discovery, development and commercialization of transformative and well-tolerated targeted small molecule drugs to treat patients afflicted with cancer and other high-burden diseases. Array markets BRAFTOVI® (encorafenib) capsules in combination with MEKTOVI® (binimetinib) tablets for the treatment of patients with unresectable or metastatic melanoma with a *BRAF*^{V600E} or *BRAF*^{V600K} mutation in the United States and with partners in other major worldwide markets. Array's lead clinical programs, encorafenib and binimetinib, are being investigated in over 30 clinical trials across a number of solid tumor indications, including a Phase 3 trial in *BRAF*-mutant metastatic colorectal cancer. Array's pipeline includes several additional programs being advanced by Array or current license-holders, including the following programs currently in registration trials: selumetinib (partnered with AstraZeneca), LOXO-292 (partnered with Eli Lilly), ipatasertib (partnered with Genentech), tucatinib (partnered with Seattle Genetics) and ARRY-797. Vitrakvi® (larotrectinib, partnered with Bayer AG) is approved in the United States and Ganovo® (danoprevir, partnered with Roche) is approved in China. For more information on Array, please visit www.arraybiopharma.com or follow @arraybiopharma on Twitter and LinkedIn.

References
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[4] Klein O, et al. *Eur J Cancer*, 2013.
[5] American Cancer Society. What Causes Melanoma Skin Cancer? 2016. https://www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/what-causes.html. Accessed April 11, 2018.
[6] BRAFTOVI ™ (encorafenib) Prescribing Information. Array BioPharma Inc., June 2018
[7] MEKTOVI® (binimetinib) Prescribing Information. Array BioPharma Inc., June 2018

Forward-Looking Statement
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, among others, statements about the future development plans of encorafenib and binimetinib; expectations that events will occur that will create greater value for Array; and the potential for the results of current and future clinical trials to support regulatory approval or the marketing success of encorafenib and binimetinib. Because these statements reflect our current expectations concerning future events and involve significant risks and uncertainties, our actual results could differ materially from those anticipated in these forward-looking statements as a result of many factors. These factors include, but are not limited to, our ability to effectively and timely conduct clinical trials in light of increasing costs and difficulties in locating appropriate trial sites and in enrolling patients who meet the criteria for certain clinical trials; risks associated with our dependence on third-party service providers to successfully conduct clinical trials and to manufacture drug substance and product within and outside the U.S.; our ability to grow and successfully develop commercialization capabilities; our ability to achieve and maintain profitability and maintain sufficient cash resources; and our ability to attract and retain experienced scientists and management. Additional information concerning these and other risk factors can be found in our most recent annual report filed on Form 10-K, in our quarterly reports filed on Form 10-Q, and in other reports filed by Array with the Securities and Exchange Commission. We are providing this information as of May 29, 2019. We undertake no duty to update any forward-looking statements to reflect the occurrence of events or circumstances after the date of such statements or of anticipated or unanticipated events that alter any assumptions underlying such statements**.**

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