Array BioPharma Announces Publication of Detailed Phase 3 COLUMBUS Trial Data of Encorafenib and Binimetinib in Melanoma Patients in The Lancet Oncology

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- Trial Demonstrated a Median Progression-Free Survival of 14.9 Months Using Encorafenib and Binimetinib Combination -

BOULDER, Colo., March 22, 2018 /PRNewswire/ -- Array BioPharma Inc. (Nasdaq: ARRY) today announced that detailed results of its pivotal Phase 3 COLUMBUS trial for the treatment of patients with *BRAF*-mutant advanced, unresectable or metastatic melanoma were published in *The Lancet Oncology*. In the analysis of the primary endpoint, the median progression-free survival (mPFS) for patients treated with the combination of encorafenib, 450 mg daily, plus binimetinib, 45 mg twice daily (COMBO450) was 14.9 months versus 7.3 months for patients treated with vemurafenib, 960 mg twice daily [hazard ratio (HR) 0.54, 95% CI 0.41–0.71; p<0.0001].

The manuscript entitled "Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with *BRAF*-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial," was published online on March 21, 2018. Array previously announced top line results from this study in September 2016.

"A median progression-free survival of nearly 15 months with the combination of encorafenib and binimetinib is clinically meaningful for patients with advanced *BRAF*-mutant metastatic melanoma," said Keith T. Flaherty, M.D., Director of the Termeer Center for Targeted Therapy, Massachusetts General Hospital Cancer Center and Professor of Medicine, Harvard Medical School. "Further, a median overall survival of 33.6 months, compared to 16.9 months with vemurafenib monotherapy (HR of 0.61, 95% CI 0.47-0.79, p<0.001), a secondary endpoint not included in this publication, was recently announced. This further supplements the published data and shows that the combination of encorafenib and binimetinib may become a promising new therapy for patients with advanced *BRAF*-mutant metastatic melanoma."

As previously reported, the combination of encorafenib and binimetinib was generally well-tolerated. The median duration of treatment was 51.2 weeks (27.1-79.7) for encorafenib and 50.6 weeks (26.1-79.7) for binimetinib. The median dose intensity was 100% (93-100) of planned doses of encorafenib and 99.6% (80-100) of planned doses of binimetinib. The most common Grade 3/4 adverse events (AEs) seen in more than 5% of patients were increased gamma-glutamyltransferase (GGT) 9% (18/192 patients), increased creatine phosphokinase 7% (13), and hypertension 6% (11) in the encorafenib plus binimetinib group.

The U.S. Food and Drug Administration (FDA) is currently reviewing the New Drug Applications to support use of the combination of encorafenib and binimetinib for the treatment of patients with *BRAF*-mutant advanced, unresectable or metastatic melanoma. The FDA set a target action date under the Prescription Drug User Fee Act (PDUFA) of June 30, 2018 for both applications. In addition, the European Medicines Agency (EMA), as well as the Swiss Medicines Agency (Swissmedic) and the Australian Therapeutic Goods Administration (TGA), are reviewing the Marketing Authorization Applications for encorafenib and binimetinib.

An update from the COLUMBUS trial will be presented at an upcoming medical congress.

About Melanoma

Metastatic melanoma is the most serious and life-threatening type of skin cancer and is associated with low survival rates. [1, 2] 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, 3, 4]

About COLUMBUS

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

- In Part 1, 577 patients were randomized 1:1:1 to receive COMBO450, encorafenib, 300 mg daily (ENCO 300), or vemurafenib, 960 mg twice daily alone. The dose of encorafenib in the combination arm is 50% higher than the single agent maximum tolerated dose of 300 mg. A higher dose of encorafenib was possible due to improved tolerability when combined with binimetinib. The primary endpoint for the COLUMBUS trial was an 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 COMBO450 arm to that of ENCO300 and a comparison of overall survival (OS) in patients treated in the COMBO450 arm to that of vemurafenib alone. Results from Part 1 of the COLUMBUS trial previously presented at the 2016 Society for Melanoma Research Annual Congress, showed that COMBO450 more than doubled mPFS in patients with advanced *BRAF*-mutant melanoma, with a mPFS of 14.9 months compared with 7.3 months observed with vemurafenib [HR 0.54, (95% CI 0.41-0.71, p<0.0001)]. In the secondary mPFS comparison of COMBO450 to ENCO300, ENCO300 demonstrated a mPFS of 9.6 months [HR 0.75, (95% CI 0.56-1.00, p=0.051)].
- In Part 2, 344 patients were randomized 3:1 to receive encorafenib 300 mg 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.

As the secondary endpoint comparison of mPFS between the COMBO450 arm and ENCO300 arm in Part 1 did not achieve statistical significance, the

protocol specified analysis of OS is descriptive.

About Encorafenib and Binimetinib
BRAF and MEK are key protein kinases in the MAPK signaling 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 is a late-stage small molecule BRAF inhibitor and binimetinib is a late-stage small molecule MEK inhibitor, both of which target key enzymes in this pathway. Encorafenib and binimetinib are being studied in clinical trials in advanced cancer patients, including the Phase 3 BEACON CRC trial and the Phase 3 COLUMBUS trial.

Array BioPharma has exclusive rights to encorafenib and binimetinib in the U.S. and Canada. Array has granted Ono Pharmaceutical exclusive rights to commercialize both products in Japan and South Korea and Pierre Fabre exclusive rights to commercialize both products in all other countries, including Europe, Asia and Latin America. Encorafenib and binimetinib are investigational medicines and are not currently approved in any country.

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.

References
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[3] Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx. Accessed January 2018.
[4] Klein O, et al. *Eur J Cancer*, 2013.

Array BioPharma Forward-Looking Statement
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements about the future development plans of encorafenib and binimetinib; expectations regarding approval of encorafenib and binimetinib for *BRAF*-mutant melanoma and timing of such approvals; expectations that events will occur that will result in 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. Specifically, there is no assurance that results from the BEACON CRC and COLUMBUS trials will satisfy the requirements of regulatory authorities necessary for approval. These statements involve significant risks and uncertainties, including those discussed 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. Because these statements reflect our current expectations concerning future events, 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, the determination by the FDA, EMA or other regulatory agencies that results from clinical trials are not sufficient to support registration or marketing approval of encorafenib and binimetinib; 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. We are providing this information as of March 22, 2018. 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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