



Array BioPharma Announces Positive Top-Line Results from Part 2 of the Phase 3 COLUMBUS Study of Binimetinib and Encorafenib for BRAF-Mutant Melanoma

May 9, 2017

- Median PFS for patients on combination of binimetinib (45mg) plus encorafenib (300mg) was 12.9 months versus 9.2 months for patients on encorafenib (300mg) -
- Generally well-tolerated and safety profile consistent with COLUMBUS Part 1 results -
- New Drug Application filing on track for June or July 2017 -

BOULDER, Colo., May 9, 2017 /PRNewswire/ -- Array BioPharma (Nasdaq: ARRY) today announced top-line results from Part 2 of the Phase 3 COLUMBUS study evaluating binimetinib, a MEK inhibitor, and encorafenib, a BRAF inhibitor, in patients with *BRAF*-mutant advanced, unresectable or metastatic melanoma. The primary analysis of Part 2 compared progression free survival (PFS) in patients treated with binimetinib 45mg twice daily plus encorafenib 300mg daily (COMBO300) to patients treated with encorafenib 300mg daily as a single agent. The median PFS for patients treated with COMBO300 was 12.9 months compared to 9.2 months for patients treated with single agent encorafenib, with HR of 0.77 [95% CI 0.61-0.97, p=0.029]. COMBO300 was generally well-tolerated and reported dose intensity and adverse events were consistent with COMBO450 results in COLUMBUS Part 1. Part 2 was designed specifically to assess the contribution of binimetinib to the combination of binimetinib and encorafenib by reducing the dose of encorafenib to 300mg in the combination arm to allow for a comparison of equal doses across arms. Further results from Part 2 will be presented at a medical meeting during the second half of 2017.



"The totality of the COLUMBUS results, including estimated progression free survival, objective response rate, dose intensity and tolerability of the combination, provide a strong and consistent theme across multiple endpoints, underscoring the promise of binimetinib plus encorafenib as an attractive treatment option for patients diagnosed with *BRAF*-mutant melanoma," said Keith T. Flaherty, M.D., Director of the Termeer Center for Targeted Therapy, Massachusetts General Hospital and Professor of Medicine, Harvard Medical School.

Ron Squarer, Chief Executive Officer at Array BioPharma noted: "The robust PFS benefit and tolerability observed with binimetinib plus encorafenib in COLUMBUS Part 2 once again demonstrates the combination represents a potentially important addition to the MEK/BRAF treatment landscape for patients with *BRAF*-mutant melanoma. The results of Part 2 confirm the contribution of binimetinib to the combination."

Based on the strength of data from Part 1 and Part 2, Array is on track to file an NDA for COLUMBUS in June or July 2017.

About the Phase 3 COLUMBUS Study

The COLUMBUS trial, (NCT01909453), is a two-part, international, randomized, open label Phase 3 study evaluating the efficacy and safety of the combination of binimetinib plus encorafenib 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 study. Patients were randomized into two parts:

- In Part 1, 577 patients were randomized 1:1:1 to receive 45mg binimetinib plus 450mg encorafenib (COMBO450), 300mg encorafenib alone, or 960mg vemurafenib alone. The dose of encorafenib in the combination arm is 50% higher than the single agent maximum tolerated dose of 300mg. A higher dose of encorafenib was possible due to improved tolerability when combined with binimetinib. The primary endpoint for the COLUMBUS trial was a PFS comparison of COMBO450 versus vemurafenib. PFS 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 PFS of encorafenib monotherapy to that of COMBO450 and a comparison of overall survival (OS) for COMBO450 to that of vemurafenib alone.

In November 2016, results from Part 1 were presented at the Society for Melanoma Research Annual Congress. The study met its primary endpoint, with COMBO450 significantly improving PFS compared with vemurafenib alone. In the analysis of the primary endpoint, the mPFS for patients treated with COMBO450 was 14.9 months versus 7.3 months for patients treated with vemurafenib; hazard ratio (HR) 0.54, (95% CI 0.41-0.71, P<0.001). As part of the trial design, the primary analysis was based on a BICR of patient scans, while results by local review at the investigative site were also analyzed. The chart below outlines the mPFS results, as determined by both assessments, for COMBO450 versus vemurafenib, COMBO450 versus encorafenib, and encorafenib versus vemurafenib:

	mPFS BICR		mPFS Local Review	
COMBO450 vs. Vemurafenib	COMBO450	Vemurafenib	COMBO450	Vemurafenib
	14.9 months	7.3 months	14.8 months	7.3 months
	HR (95% CI): 0.54 (0.41-0.71); P<0.001		HR (95% CI): 0.49 (0.37-0.64); P<0.001	
COMBO450 vs. Encorafenib	COMBO450	Encorafenib	COMBO450	Encorafenib
	14.9 months	9.6 months	14.8 months	9.2 months
	HR (95% CI): 0.75 (0.56-1.00); P=0.051		HR (95% CI): 0.68 (0.52-0.90); P=0.006	

Encorafenib vs. Vemurafenib	Encorafenib	Vemurafenib	Encorafenib	Vemurafenib
	9.6 months	7.3 months	9.2 months	7.3 months
	HR (95% CI): 0.68 (0.52-0.90); P=0.007		HR (95% CI): 0.70 (0.54-0.91); P=0.008	

COMBO450 was generally well-tolerated and reported adverse events (AEs) were overall consistent with previous bini/enco combination clinical trial results in BRAF-mutant melanoma patients. Grade 3/4 AEs which occurred in more than 5 percent of patients receiving COMBO450 included increased gamma-glutamyltransferase (GGT), increased blood creatine phosphokinase (CK), and hypertension. The incidence of AEs of special interest (toxicities commonly associated with commercially available MEK+BRAF-inhibitor treatments), for patients receiving COMBO450 included: rash (23 percent), pyrexia (18 percent), retinal pigment epithelial detachment (13 percent) and photosensitivity (5 percent).

- In Part 2, 344 patients were randomized 3:1 to receive 45mg binimetinib plus 300mg encorafenib or 300mg encorafenib alone. Part 2 is designed to provide additional data to help evaluate the contribution of binimetinib to the combination of binimetinib and encorafenib. As the comparison of COMBO450 to encorafenib in Part 1 did not achieve statistical significance, the statistical analysis conducted in Part 2 is descriptive.

About BRAF-Mutant Melanoma

Melanoma is the fifth most common cancer among men and the sixth most common cancer among women in the United States, with more than 87,000 new cases and over 9,700 deaths from the disease expected in 2017. Up to 50 percent of patients with metastatic melanoma have activating BRAF mutations, the most common gene mutation in this patient population. Current marketed MEK/BRAF combination agents have a run rate approaching \$1 billion in annual worldwide sales.

About Binimetinib & Encorafenib

MEK and BRAF 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, such as melanoma, colorectal and thyroid cancers. Binimetinib is a late-stage small molecule MEK inhibitor and encorafenib is a late-stage small molecule BRAF inhibitor, both of which target key enzymes in this pathway. Binimetinib and encorafenib are being studied in clinical trials in advanced cancer patients, including the Phase 3 BEACON CRC trial with encorafenib in combination with cetuximab with or without binimetinib in patients with *BRAF V600E*-mutant colorectal cancer.

Binimetinib and encorafenib are investigational medicines and are not currently approved in any country. Array BioPharma retains exclusive rights to binimetinib and encorafenib in key markets including the U.S., Japan, Canada, Korea and Israel. Pierre Fabre will have exclusive rights to commercialize both products in all other countries, including Europe, Asia and Latin America.

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. Seven registration studies are currently advancing related to seven drugs: binimetinib (MEK162), encorafenib (LGX818), selumetinib (partnered with AstraZeneca), danoprevir (partnered with Roche), larotrectinib (partnered with Loxo Oncology), tucatinib (partnered with Cascadian Therapeutics) and ipatasertib (partnered with Genentech).

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 binimetinib and encorafenib, and the timing of the announcement of further results of clinical trials for binimetinib and encorafenib; expectations regarding the timing of regulatory filings for binimetinib and encorafenib and regarding approval of binimetinib and encorafenib for *BRAF*-mutant melanoma; expectations that events will occur that will result in greater value for Array; and the potential for the results of current and further clinical trials to support regulatory approval or the marketing success of binimetinib and encorafenib. 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 that results from clinical trials are not sufficient to support registration or marketing approval of binimetinib and encorafenib; 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 within and outside the United States; 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 May 9, 2017. 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.

CONTACTS: Tricia Haugeto
(303) 386-1193
thaugeto@arraybiopharma.com

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