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Building value

Array picks Ono as partner in Japan, South Korea in potential $187.6M oncology deal

By Marie Powers, News Editor

With positive news flow on clinical development, Array Biopharma Inc. stayed busy on the partnering front, selecting Ono Pharmaceutical Co. Ltd. to license, develop and commercialize its late-stage oncology compounds, binimetinib and encorafenib, in Japan and South Korea. Array is set to receive $31.6 million (¥3.5 billion) up front and is entitled to another $156 million (¥17.3 billion) in development, regulatory and commercial milestone payments. The Boulder, Colo.-based company retained exclusive commercialization rights to the assets in the U.S., Canada and Israel.

Array also is eligible for tiered royalties on sales of binimetinib and encorafenib in Ono's territory that start at 22 percent and escalate to 25 percent when net sales exceed ¥10 billion.

Binimetinib, a MEK inhibitor, and encorafenib, a BRAF inhibitor, are in global phase III trials to treat patients with BRAF-mutant melanoma (COLUMBUS) and BRAF-mutant colorectal cancer (BEACON CRC). Earlier this month, the company reported top-line data from COLUMBUS part two, which showed that patients who took binimetinib, dosed at 45 mg twice daily, plus encorafenib, dosed at 300 mg daily, had a median progression-free survival of 12.9 months vs. 9.2 months for patients who received encorafenib 300 mg alone (p = 0.029). (See *BioWorld Today*, May 11, 2017.)

The company also disclosed that it completed a 30-patient run-in to the pivotal BEACON CRC trial examining its "triplet" – the binimetinib/encorafenib combo plus Erbitux (cetuximab) – which showed the safety profile was satisfactory and the combo was well-tolerated, with encouraging early signs of efficacy.

A portion of milestone payments from the agreement with Ono, of Osaka, Japan, is related to its future participation in BEACON CRC. Ono assumed responsibility to conduct trials of binimetinib and encorafenib in Japan and South Korea and gained the right to participate in future global development of the assets in return for contributing 12 percent of those development costs. Array will supply drug product for clinical studies conducted by Ono and may, at Ono's cost, provide commercial product supplies. The companies also agreed to devise a strategy to ensure the supply of companion diagnostics for use with binimetinib and encorafenib in certain indications in Ono's territory.

Although the Ono agreement isn't exactly a barn-burner for Array in melanoma – the company expects to file a new drug application (NDA) around midyear for the binimetinib/encorafenib combination in BRAF-mutant advanced, unresectable or metastatic melanoma – the Japanese market potential and economics around colorectal cancer could be compelling.

"We are about to file melanoma in the U.S. and other parts of the world, and while it is not the largest commercial driver for Japan, it's important to make the drugs available to Japanese patients with melanoma," Ron Squarer, Array's CEO, told *BioWorld Today*. "That sort of explains the timing, but we also wanted to make sure things were looking great with BRAF colorectal."

In November 2015, Array inked an agreement giving Pierre Fabre SA exclusive commercial rights to binimetinib and encorafenib in Europe, Latin America and most Asian markets in return for sharing global development costs along with $30 million up front and up to $425 million in additional milestones. (See *BioWorld Today*, Nov. 17, 2015.)

Japan was excluded from that deal because Pierre Fabre didn't have a major presence in the country, explained Andrew Robbins, Array's chief operating officer. Having the patience to forego a quick partnership in Japan gave Array the opportunity to structure a second deal with similar economics and a focus on the market's more important cancer indication.

Both the Pierre Fabre and Ono deals are focused geographically and the economics include large royalty arrangements – up to 35 percent in the Pierre Fabre tie-up. Another similarity is that both partners agreed to contribute to clinical development of the oncology candidates – at a rate of 40 percent, in the case of Pierre Fabre, "proportional to the value proposition," Squarer observed.

'Building potential value with MEK/BRAF franchise'

Less than a year before nailing down the Pierre Fabre partnership, Array regained control of its two molecules after an $85 million divorce settlement from Basel, Switzerland-based Novartis AG, which had received FDA approval in January 2014 for its own MEK/BRAF inhibitor combination – Mekinist (trametinib) and Tafinlar (dabrafenib) – to treat BRAF-mutated melanoma. (See *BioWorld Today*, Dec. 5, 2014, and Jan. 26, 2015.)

Array also lost some momentum while forced to sit on the sidelines during the ginormous asset swap between Novartis and London-based Glaxosmithkline plc (GSK). In 2014, Novartis paid $16 billion for GSK's marketed oncology portfolio, GSK acquired Novartis' vaccines arm for $5.25 billion and the two pooled their consumer health care businesses in a joint venture. (See *BioWorld Today*, April 23, 2014.)

Once back in the game, Array regained trajectory quickly, beginning with the Pierre Fabre pact.

"We have had interest in Japan for some time," Squarer said, noting that talks with multiple players put Array "in a very attractive position to choose a partner."

Ono rose to the top not only for its "tremendous commercial prowess" in Japan's oncology market – $1 billion in annual sales, Robbins said – but also for its leadership in immuno-oncology, including the development of Opdivo (nivolumab), licensed outside Japan to New York-based Bristol-Myers Squibb Co. (BMS).

Not coincidentally, a day earlier Array signed on with BMS to investigate the safety, tolerability and efficacy of binimetinib in combination with Opdivo and Opdivo plus Yervoy (ipilimumab) to treat metastatic colorectal cancer in patients with microsatellite stable tumors (MSS CRC). A phase I/II study is expected to establish recommended dose regimens for further study and explore preliminary antitumor activity, with results expected in the second half of 2017. Though specific terms were not disclosed, the companies are jointly supporting the phase I/II study, with Array serving as the sponsor.

Array also forged an agreement this month with Merck and Co. Inc., of Kenilworth, N.J., to investigate the safety and efficacy of binimetinib in combination with Keytruda (pembrolizumab) in MSS CRC.

"Those studies are very important, because there is evidence that adding a MEK to immunotherapy in most colorectal cancers can potentially turn a tumor that is cold to immunotherapy hot," Squarer said. "We're building potential value with our MEK/BRAF franchise in combinations – first in melanoma, then BRAF colorectal and then, potentially, the MEK with immunotherapy treating a large swath of colorectal, mostly outside of BRAF."

"One might imagine, based on the deal with Bristol-Myers – combining binimetinib with nivolumab in colorectal cancer – and Ono's specific interest now owning both of those products, there could be some synergies in future development surrounding that combination," Robbins added.

Array is comfortable navigating its portfolio of wholly owned assets – which includes ARRY-520 in multiple myeloma, ARRY-797 in lamin A/C-related dilated cardiomyopathy and ARRY-502 in asthma, according to Squarer, while partnerships do the heavy lifting on a dozen other candidates.

In a research note, Piper Jaffray analyst Edward Tenthoff said the Ono arrangement "delivers on a stated goal" while enabling the company to focus on its NDA filing of the binimetinib/encorafenib combo, followed by a marketing authorization application filing by partner Pierre Fabre. Meanwhile, the BEACON CRC study is expected to report preliminary data at a medical meeting this year.

"Including the Ono up-front, we estimate Array now holds pro forma cash of $238 million and has a $132 million convertible note due in 2020," Tenthoff wrote, reiterating an overweight rating on the stock and raising Array's price target to $14 from $12.

On Wednesday, Array's shares (NASDAQ:ARRY) closed at $7.58 for a loss of 28 cents, or 3.6 percent.