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Bristol Pays \$85 Million Upfront To Acquire Rheumatoid Arthritis Compound From Alder

Paying \$85 million upfront, Bristol-Myers Squibb entered into a global agreement to develop and commercialize a Phase II antibody from Alder Biotherapeutics in rheumatoid arthritis. And potential milestones make the transaction potentially worth more than \$1 billion for Alder.

Bristol obtains exclusive rights to ALD518 except in cancer indications, which Alder will continue to develop. Should ‘518 reach the market in a cancer indication, Bristol would have the option to co-develop and commercialize the drug outside the U.S.

In RA, ‘518, an interleukin-6 inhibitor, will likely compete in the market with Roche’s *Actemra* (tocilizumab), an IL-6 receptor antagonist, which has been launched in eight EU markets plus Japan, Brazil and India. The Roche drug, however, is tied up at FDA due to a September 2008 “complete response” letter that requested additional information on manufacturing and labeling (‘The Pink Sheet’ DAILY, Dec. 5, 2008). Roche refiled its NDA this past July and received a priority review from FDA.

In an interview, Alder chief executive Randy Schatzman said ‘518 should enjoy several advantages over Actemra, helping to drive the high upfront price for a molecule that just completed Phase IIa. These include the fact that ‘518 inhibits IL-6 itself, rather than the IL-6 receptor, and a production process that should allow for quick scale-up.

“In developing ‘518, we felt that going after IL-6 itself, as opposed to the receptor, was going to be an important aspect of addressing the biology,” Schatzman said. “IL-6 is about 1,000-fold lower than the receptor in terms of the disease antigen load. What that means is we have to get a lot less antibody on board to neutralize the biology than Actemra does with the receptor.”

Using its proprietary Antibody Selection technology, Alder also was able to create a more potent molecule than Actemra, Schatzman claimed. “We’re about 1,000-fold higher affinity for our disease antigen as Roche is for theirs,” he said. “What that allows us to do, again, is get less antibody on board and it also determines that the antibody that we have has a much faster onset of action than Actemra does. So our patients see relief within days of getting this drug, whereas other agents like Actemra can require weeks or months to really see the important disease-relief activity.”

Quick manufacturing process called an advantage over Actemra

Alder’s antibody also should have a cleaner safety profile than Actemra, he added, due to less cell cytotoxicity. In addition, the biotech’s yeast-based production system can produce the monoclonal antibodies much more quickly than the typical mammalian Chinese hamster ovary cell-based technology used by other companies, Schatzman said.

"Yeast divides in about 90 minutes, whereas a mammalian CHO cell ... takes 24 to 36 hours to double," he explained, adding that this results in manufacturing process that takes days rather than weeks or months.

Bristol described the transaction as the latest in its "string of pearls" in-licensing strategy. "This transaction provides Bristol-Myers Squibb with the opportunity to strengthen our immunoscience pipeline and leverage our company's experience in developing and delivering novel biologics to help patients prevail over rheumatoid arthritis and, potentially, other autoimmune diseases," said Brian Daniels, senior VP, global development and medical affairs, in a release.

Mark Litton, Alder's chief business officer, says Bristol was selected out of significant competition in part because of its plans to develop '518 in inflammation indications beyond RA. The Bothell, Wash., biotech would share in the revenues if Bristol gets '518 approved in other indications.

"One of the things we liked about BMS was their approach not only to RA, but they wanted to, in parallel, do several other indications as well," Litton said. "So we really saw this as a franchise opportunity with them."

Bristol will take over development of '518 in RA and other autoimmune indications, while Alder will continue advancing the antibody in cancer. In June, Alder unveiled Phase I data from a study in non-small cell lung cancer that showed the drug relieved symptoms of cancer cachexia in patients with advanced disease.

Under the deal, Alder also will provide clinical supplies of '518 for both trials it runs, as well trials run by Bristol. Upon commercialization, Bristol will be responsible for manufacturing the drug, but will do so using Alder's proprietary *Mab Xpress* technology, Litton said.

Big bio-bucks plus equity investment requirement should IPO occur

In addition to the generous upfront payment, the deal also could pay Alder up to \$674 million in development and regulatory-based milestones across a range of indications, sales-based milestones that could exceed \$200 million, and royalties on net sales. Litton would not specify the royalty percentage other than to call it "significant."

One unique aspect to the deal is a requirement that Bristol make an equity investment of up to \$20 million should Alder attempt to go public. Alder has been through three venture funding rounds since its inception, raising more than \$67 million, including a \$40 million Series C in early 2008 (Elsevier's Strategic Transactions Database, January 2008).

Citing still iffy market conditions, Schatzman said Alder has no short-term plans to file an IPO, but asserted it would be in Bristol's best interests to invest in such an offering to help its partner remain strong and grow.

-Joseph Haas (j.haas@elsevier.com)

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