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Watch Your Back, Actemra

Yeastward Ho! Alder's Antibody Method Nets Jumbo BMS Deal

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Alder Biopharmaceuticals Inc.'s yeast-based way of making a fast follower – or eventual follower – to the FDA-stalled rheumatoid arthritis candidate Actemra helped the firm pull down a whopper deal with Bristol-Myers Squibb Co., which is shelling out \$85 million up front for what could become a rival to Roche's FDA-stalled therapy, already cleared in Europe.

"It depends on how long their delay is at the FDA, which we don't know at this point," said Randall C. Schatzman, president and CEO of Bothell, Wash.-based Alder. "But I suspect they will launch in 2010, and we'll be several years behind that."

ALD518 shows the potential for dosing three or four times per year rather than once monthly, like Actemra, and could be given at about one-tenth the dose.

The latter's half-life is about six days, ALD518's about a month. "And this will be a much better molecule than Actemra," Schatzman pledged, and should beat the latter's safety as well as efficacy.

BMS, of New York, apparently believes it. The firm is buying exclusive rights to develop and commercialize the drug for everything except cancer, for which Alder keeps rights while giving BMS an option to co-develop and commercialize outside the U.S. Anemia and fatigue are cancer indications at which Alder is taking aim.

Up to \$764 million in milestone payments based on progress across various indications come with the BMS collaboration, along with sales-based rewards that could pass \$200 million.

Royalties are part of the deal, and Alder has an option to require that BMS make an equity investment of up to \$20 million if Alder goes public.

Alder's manufacturing approach means the firm can make drugs more quickly and cheaper with fewer immune reactions at less frequent dosing.

Development happens faster, too: Generating a commercial antibody strain using mammalian cell cultures takes about a year, on average. Alder's yeast-based cultures take about five weeks.

"We're able to save six-month intervals in multiple

places," noted John A. Latham, chief scientific officer. Interleukin-6-targeting ALD518 went from disease antigen to first dose in humans in 18 months. "We knew we needed a molecule that displayed much higher potency, and we wanted to get into the landscape much more quickly," he said.

BMS – nontypically among big pharma, lately busying themselves with mergers and acquisitions to build their companies – has taken aim at specific compounds to beef up its pipeline. "They're going to take this as a franchise opportunity," said Mark J. Litton, Alder's chief business officer.

With IL-6, "the nice thing is the broad-based biology," Schatzman said, ideal for the plan. "Where the guys at BMS want to take this immediately is farther in RA," he added. After that, "the first on their list is probably Crohn's [disease]."

ALD518 has finished one Phase II RA trial and will enter another dose-finding study next year in "several hundred patients," Schatzman said. Results from the first experiment will be disclosed in the coming months at a scientific meeting or in a journal.

Roche Holding AG, of Basel, Switzerland, submitted its biologics license application for mammalian-made Actemra (tocilizumab) about two years ago, and said in December 2008 that the FDA wanted more animal data plus a risk evaluation and mitigation strategy.

An advisory panel in the summer of 2008 blessed Actemra with a 10-1 vote in favor of approval for RA, and European regulators let the drug onto the market as RoActemra in January. (See *BioWorld Today*, July 30, 2008.)

Already Actemra is fondly looked upon by rheumatologists, according to a recent Decision Resources poll. Ninety-eight percent of specialists surveyed said they would prescribe the drug, with 60 percent pointing to the drug's efficacy, proven comparable to anti-TNF blockbusters Enbrel (etanercept), from Thousand Oaks, Calif.-based Amgen, and Humira (adalimumab), from Abbott, of Abbott Park, Ill.

ALD518, if it works better and proves safer, "has the potential to take the market by storm," Schatzman said.

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As for reimbursement, 75 percent of managed care organizations said they would likely cover Actemra, while 80 percent said they would cover anti-CD20 competitor Arzerra (ofatumumab) from Copenhagen, Denmark-based Genmab A/S, and 85 percent liked same-class ocrelizumab, from Biogen Idec Inc., of Cambridge, Mass.

Arzerra, not yet approved in RA, recently won the FDA's nod in chronic lymphocytic leukemia, and is made by Genmab partner GlaxoSmithKline plc, of London. Genmab this summer reported positive results from a Phase III trial in RA, but said next steps were still under discussion with GSK. (See *BioWorld Today*, July 31, 2009, and Oct. 28, 2009.)

Genmab's study with Arzerra in TNF-alpha refractory RA patients is not expected to yield data until next year, and analysts suspect the focus has shifted to development of a subcutaneous formulation, with a Phase I study due to complete by the end of this year.

The idea is to differentiate the product from chimeric antibody Rituxan (rituximab) and its humanized successor ocrelizumab, in Phase III trials.

Both are given intravenously.

With ALD518, Alder and partner BMS also are mulling a subcutaneous RA therapy that patients could self-administer once per month, Schatzman said. ■