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TOP-LINE IN HAND, RSV COULD BE KEY

On cusPIDD of a win? Adma's phase III results have teeth, final next year

By Randy Osborne, Staff Writer

Taking what CEO Adam Grossman called "a different spin on intravenous immunoglobulin [IVIG]" while "trying to provide a product that's very targeted, niche-focused, and is going to provide an advantage to a subset" of the patient population, Adma Biologics Inc. reported positive top-line phase III results in primary immune deficiency diseases (PIDD) with lead compound RI-002.

A plasma-derived, polyclonal, intravenous immune globulin, RI-002 contains naturally occurring polyclonal antibodies such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, cytomegalovirus, measles, tetanus, etc., as well as standardized, high levels of antibodies to respiratory syncytial virus (RSV). The compound met its primary endpoint in the 59-patient, year-long study of preventing serious bacterial infections such as bacterial pneumonia, osteomyelitis and bacterial sepsis in PIDD patients.

PIDD comprises "about 150 different types of genetic defects that affect certain aspects of the immune system," Grossman told *BioWorld Today*. In the U.S., about 250,000 patients have one or more forms of PIDD, with half requiring monthly infusions of IVIG to support their systems.

"There is a subset of the PIDD population that has combined immune deficiency, meaning that they have both B and T cell dysfunction," Grossman said. "We're providing a product that has a unique antibody profile in that it has higher levels of antibodies against all respiratory viruses over regular IVIG. We think there's a subset of about 8,000 to 20,000 patients currently receiving IVIG who we believe clinicians would feel our product would provide more protection at certain times of the year," such as winter.

Adma enters a field dominated by such plasma players as Deerfield, Ill.-based Baxter International Inc., CSL Behring Ltd., of King of Prussia, Pa., and Barcelona's Grifols SA, which collectively boast a market cap of more than $110 billion. For immune globulin products, the market is $3.5 billion to $4 billion in the U.S., and Adma seeks a slice of that pie. Most companies in the space simply collect plasma from healthy volunteers, which is "not enriched or enhanced for any specific additional antibody," Grossman said. "We test all of our plasma donors and individually select which donors had elevated levels of antibodies against RSV. Then we pool all that plasma together," formulating each batch to rigid standards.

"There are about six labeled uses for IVIG, [but] Medicare reimburses for over 40 different unlabeled, evidence based uses," Grossman said. "Of that $3.5 billion to $4 billion total market size, about half of that is used in an evidence-based way and reimbursed. [The indications are] outside of the label, but the general consensus is that immune globulins provide benefits in this area."

This means, since IVIGs are "used very widely in bone marrow transplant, solid organ transplant, high dose chemotherapy and radiation, there may also be an opportunity for Adma to expand our label and expand our market penetration, once we're a commercial company, by doing additional studies in this transplant and chemotherapy population," Grossman said.

Meanwhile, "RSV, in particular, is a severe problem in the immunocompromised bone marrow/solid organ transplant population," with an incident rate of 10 percent to 15 percent in the winter, Grossman said. "There are no FDA approved RSV treatments for adults. They use aerosolized ribavirin, which is toxic and its efficacy is questionable. They sometimes use Synagis [palivizumab, Medimmune Inc., part of London-based Astrazeneca plc], which is a very expensive monoclonal. And they use regular IVIG."

Grossman previously worked at Medimmune, where he served on the marketing teams for RSV and cytomegalovirus immunoglobulins. Synagis' precursor was Respigam, and with Adma, he is "bringing to market a product that meets all the criteria for the FDA for IVIG, plus we're enhancing it with that Respigam-like component, ensuring we have standardized high levels of neutralizing titers against RSV," with antibodies against other infections as well. (See *BioWorld Today*, June 22, 1998.)

Jerry Isaacson, analyst with Lifesci Capital, wrote in a research report last month that RI-002 has "a clear regulatory pathway. According to published FDA Guidance for Industry June 2008, 'A statistical demonstration of a serious infection rate per person-year less than 1.0 [as Adma's trial is designed to who] is adequate to provide substantial evidence of efficacy.' As a basis for comparison, PIDD patients who require but do not receive IVIG, often experience four or more serious acute bacterial infections per year, while PIDD patients who receive IVIG typically experience less than 0.6 serious acute bacterial infections per year." Lifesci Capital is affiliated with Lifesci Advisors, of which Adma is a client.

ADMA: WE'LL DO THE MARKETING

Adma's stock (NASDAQ:ADMA) closed Wednesday at $10.60, down $1.31, or 11 percent. "There's nothing in the data that should cause any concern, especially since it's very much just top-line," Isaacson told *BioWorld Today*. "It's kind of hard to tell, it's definitely a tough day [on Wall Street]. But also Adma is a stock that has been under the radar screen, and maybe this is the first time people are seeing it today, because of the news. It's just taking the market a little time to digest what's going on here."

Not long ago, ADMA, founded with a series A round from Aisling Capital in 2007, completed up-listing its shares to trade on the Nasdaq Capital Market, and trading began Nov. 10. According to a sample set of data from Nasdaq, companies up-listing in 2014 experienced a mean increase of 33 percent in market capitalization and 125 percent in trading volume. Companies up-listing in 2013 saw an average 100 percent increase in market capitalization and a 552 percent hike in trading volume. "While these trends are not predictive, up-listing to Nasdaq should positively impact the marketability of Adma shares, especially in terms of volume and liquidity," Isaacson predicted. Better times may lie ahead, as the company plans to unveil full phase III data in the first quarter of next year.

Matt Duffy, managing director at Lifesci Capital and Lifesci Advisors, also came from Medimmune, where he was in charge of marketing for Respigam. "That was my baby," he told *BioWorld Today*. "I don't there's an expectation that Adma's going to jump in and take the entire market," but the efficacy against particular infections should give RI-002 an edge in IVIG, he said.

CEO Grossman said Adma likely will handle its own marketing. "My standard answer is, we would love to commercialize this [ourselves]," he said. "We think we can do a very good job. We have a Rolodex of the top clinicians who set the protocols and see these types of patients. It's not a wide market. There are probably 300 to 500 institutions in the U.S. that see these patients." At the same time, the firm is "always open to business development discussions and partnership opportunities," he said.

Outside the U.S., Adma has an agreement with Biotest AG, of Dreieich, Germany, which is also the contract manufacturer in the U.S. as part of a deal that included up-front payments and potential milestone rewards for Adma. Biotest holds rights in the European Union, North Africa, and select territories in the Middle East.

Adma went public in October 2013. "So far, I've hit every milestone that I've set for the company," Grossman said. "We're very pleased with the progress."