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NovaBay’s Non-Antibiotic Anti-Infective Shows Efficacy In Impetigo Trial

NovaBay is a step closer to commercializing the first non-antibiotic for treating an infection typically treated with antibiotics, now that its topical gel yielded a 90 percent cure rate in a Phase IIa proof-of-concept trial against impetigo.

“While the market for impetigo is large on its own, NovaBay views impetigo as a gateway indication to other uncomplicated skin and skin structure infections,” CEO Ron Najafi said during an analyst call to announce the top-line results. Full data are to be presented at a conference later in the year.

If the investigational product, NVC-422, is successful, it should compete well against current impetigo therapies on both cure rate and on the new drug’s efficacy against both gram-positive and gram-negative bacteria, with little or no opportunity for the bacteria to develop antibiotic resistance.

NovaBay’s goal is to create products that meet or beat antibiotic performance, with a safe formulation that doesn’t give bacteria a chance to develop resistance, Najafi said in an interview. With products using NovaBay’s *Angiocide* platform technology, physicians won’t have to select the right topical antibiotic for the right bacteria because “one product covers all of the bacteria,” he said.

Bacteria Rendered Helpless, Not Destroyed

The key to NVC-422’s ability to cure broad spectrum infections without incurring resistance is in its mechanism of action, Najafi explained. The drug is extremely active against enzymes on the surface of bacteria, inactivating the enzymes and rendering the bacteria non-pathogenic without rupturing them and releasing toxic contents. The process happens so quickly the organisms can’t adapt.

The synthetic N-chlorinated antimicrobial molecules generated by NovaBay’s Aganocide platform mimic the chlorine mechanism white blood cells use to kill bacteria, but are engineered for sustained activity so they can have a shelf life up to 300 days.

Though reluctant to say “never,” Najafi said the company has put NVC-422 through every possible test of resistance and seen no indication the compound will encounter the same resistance that plagues antibiotics.

In the lab, NVC-422 has shown broad “pan-Staph” activity with no resistance after 15 passages (through 15 “generations”) treated with repeated sub-lethal doses, he said.

Early Evidence In Impetigo

NovaBay selected impetigo, a niche market for anti-infectives, as the initial field in which to prove its compound in dermatology. The randomized, double blind, dose-ranging study enrolled 129 children ages 2 to 12 with impetigo, including infections caused by *Staphylococcus aureus* or *S. pyogenes*, 117 of whom completed the trial. They were randomized to 0.1 percent, 0.5 percent and 1.5 percent concentrations of the drug. Clinical response rates were 85 percent, 87 percent and 92 percent, respectively. Side effects reported in roughly 5 percent of patients included redness and itching and were gone by follow-up.

The patients were treated three times a day for seven days, with examinations at the end of treatment and again a week later. Response was evaluated using the Skin Infection Rating Scale.

Of the 117 patients available for follow-up, 90 percent were infected by a single bacteria strain; of those, 80 percent were infected with *Staphylococcus aureus*. Ten patients were infected with methicillin-resistant *S. aureus* and in those patients, the cure rate was 100 percent.

Opportunity Tough To Measure, But It's Big

The top two products currently prescribed by physicians to treat the infection are mupirocin (GlaxoSmithKline's *Bactraban* and generics) and *Altabax* (retapamulin), for which GSK gained approval in 2007. Bactraban had a 71 percent success rate in impetigo when it was registered in the late 1980s, and Altabax had an 85 percent response rate in placebo-controlled trials, infectious disease consultant Catherine Hardalo said.

She noted that physicians are beginning to encounter mupirocin resistance and that the Centers for Disease Control and Prevention are just starting pilot projects to gauge the extent of that resistance in the U.S.

No consistent country to country data are available on the global prevalence of the skin infection itself, so NovaBay commissioned a physician survey and consulted 2009 IMS prescription data to give analysts an idea of the market opportunity, Roy Wu, senior VP for business development, said.

According to IMS, in the U.S. there were 1.4 million prescriptions written in 2009 for impetigo as the main condition. In the five major countries of Europe, there were 2.3 million prescriptions written.

The survey of 120 dermatologists, pediatricians and primary care physicians revealed concerns about MRSA and a positive reaction to the possibility of a new non-antibiotic product, Wu said.

About half of those surveyed cited a significant need for a broad-spectrum antimicrobial agent with efficacy against MRSA and mupirocin-resistant organisms, while 75 percent confirmed mupirocin resistance is on the rise and 80 percent said they see community-acquired infections due to MRSA increasing, Wu said.

Next Steps For NVC-422 In Impetigo

The next step for NVC-422 in impetigo is a Phase IIb study expanded to the U.S. and possibly other countries, Najafi said. While FDA and other regulatory authorities were aware of the Phase IIa study, an IND was not required for the Dominican Republic, where impetigo is prevalent year-round, he explained, adding that an IND is in place for a six-week acne study. NovaBay plans to meet with FDA soon to plan the Phase IIb in impetigo, which Najafi said he expects to be placebo-controlled.

GSK had sought an indication for Altabax to treat uncomplicated skin structure infections due to *S. aureus* and *S. pyogenes*, but FDA narrowed its approval to impetigo and deemed the other indications "not approvable" (Pharmaceutical Approvals Monthly, September 2007). The Altabax review highlighted the ethics of using placebo controls in pediatric dermatology studies and found them permissible with adequate safety measures in place.

Uncomplicated skin infections account for almost 200 million physician visits in the U.S. annually, with treatment costs estimated at over \$300 million a year.

NovaBay Partnered With Galderma On Skin

Though NovaBay did the impetigo proof-of-concept on its own, it already has signed on with global dermatology specialist Galderma to take on larger segments. The firms entered into an exclusive development and commercialization agreement in 2009 for use of NovaBay's Aganocide compounds in

major dermatological conditions (EBI's Strategic Transactions Database, March 2009). Galderma, a 1981 joint venture between Nestle and L'Oreal, is developing NVC-422 for acne (in Phase II) and has an option to pick up the impetigo program, which Najafi said NovaBay hopes to see exercised by year-end.

Under their agreement, Galderma funds all development, excluding Japan. The agreement includes up to \$50 million in milestones and escalating double-digit royalties on marketed products, and reserves exclusive co-marketing rights for NovaBay in U.S. hospitals and health care institutions, as well as all rights in Asia and co-marketing rights in Japan.

NovaBay licensed its technology to Alcon in 2006 to develop treatments for eye, ear and sinus infections (EBI's Strategic Transactions Database, September 2006). The agreement involved a \$10 million upfront payment and up to \$70 million in potential milestones with all development funded. It also gives NovaBay royalties and co-marketing rights for otic and sinus applications in Asia.

A Phase IIb study of NVC-422 in viral conjunctivitis being conducted by Alcon is testing the drug's ability against viral infections. If successful, it will establish NovaBay's technology in another anti-infective arena, giving the firm proof-of-concept for its platform against antibiotics and antivirals.

In-House Program Aims At Biofilm In Catheters

The Emeryville, Calif., biopharma's top in-house priority is an NVC-422 irrigation solution for catheter-associated urinary tract infection, which is responsible for 40 percent of hospital-acquired infections, Najafi said. NovaBay reported positive Phase IIa results from the program in April and expects to start a second Phase II in spinal cord injury patients in the fourth quarter, with a PMA anticipated in 2012.

The key to NVC-422's efficacy in CAUTI is its ability to kill bacteria embedded in the protective slime matrix known as biofilm the colonies construct in hospitable environments, such as the inside of a catheter.

Encased in biofilm, bacteria are protected from white blood cells and enter a state in which they are also largely immune to antibiotics, according to NovaBay. The company's products, however, have exhibited the ability to both penetrate biofilm and attack the bacteria sheltered there.

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