Targanta Therapeutics

TARGANTA PRESENTS STUDY RESULTS AT ICAAC SHOWING BROAD POTENTIAL OF ORITAVANCIN AGAINST GRAM-POSITIVE PATHOGENS

Novel Antibiotic Acts Quickly to Kill Bacteria, Inhibit Biofilm Growth, and is Active Against All Resistant Strains Tested

SAN FRANCISCO, Calif. – September 28, 2006 – Targanta Therapeutics today announced that *in vitro* studies of its antibiotic, oritavancin, showed a broad spectrum of activity against antibiotic-resistant pathogens that cause life-threatening infections. These findings were presented at the 46th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC).

Oritavancin, a novel glycopeptide antibiotic, is Targanta's lead product currently in post-Phase III clinical development. With the emergence of glycopeptide resistance among enterococci and staphylococci, knowledge regarding the level of activity of any new compound in development against such bacteria is critical to halting the spread of resistance. According to the Centers for Disease Control and Prevention, over the last 30 years the percentage of staphylococcal bacteria resistant to traditional antibiotics rose by more than 50 percent in U.S. hospitals.

"This novel therapy, in advanced stages of development, shows significant promise in combating a critical public health issue," said Thomas Parr, Ph.D., Chief Scientific Officer, Targanta Therapeutics. "We are encouraged by these results and other research showing how oritavancin may offer significant benefits in treating serious gram-positive infections."

The following research was presented at the ICAAC meeting:

- **Comparative *In Vitro* Potency of Oritavancin (ORI), Teicoplanin (TEI), and Vancomycin (VAN) against Glycopeptide-Susceptible and –Resistant Gram-Positive Organisms.** (ICAAC06-A-1859-ASM)
  Researchers analyzed the *in vitro* potency of oritavancin (ORI) compared to that of other currently available glycopeptides, teicoplanin (TEI) and vancomycin (VAN). They determined that ORI, VAN and TEI have comparable potency against VAN-susceptible bacteria, but against VAN-resistant bacteria, only ORI maintained a high level of activity. Researchers tested the relative potency of the three agents in the laboratory against hundreds of enterococcal clinical isolates and against two strains of VAN-resistant *Staphylococcus aureus* (VRSA). Results indicated that ORI maintained superior efficacy compared with the other glycopeptides against both the VAN-resistant enterococci and the two VRSA strains studied.

- **Oritavancin Kills *Staphylococcus aureus* in Slow-growing Planktonic and Biofilm States** (ICAAC06-A-2348-ASM)

Infections caused by *Staphylococcus aureus* bacteria that are slow-growing or have formed a biofilm, also known as slime, are common. Their resistance to current therapies poses a serious clinical challenge. Researchers tested ORI in the laboratory against *Staphylococcus aureus* growing in these states and determined that it maintained rapid anti-bacterial activity *in vitro*. Studies of the ability of ORI and comparator glycopeptides to kill cells over time were performed on slow-growing bacteria that were challenged with various concentrations of ORI, VAN and TEI over the course of 24 hours. Repeated sampling of the bacterial cultures allowed the researchers to determine that that extent of cell killing by ORI was unparalleled by VAN or TEI. In the biofilm experiments, plates were washed of the drugs after 24 hours of their exposure to the adherent cells and checked again for bacterial growth 48 hours later. ORI inhibited the growth of the bacteria in the biofilm over the course of 24 hours, while VAN lacked activity against the bacteria. Furthermore, ORI sterilized the *in vitro* biofilm, as no bacteria regrew within 48 hours whereas bacterial regrowth occurred within 24 hours even at the highest concentrations of all other antibiotics tested. Under the conditions tested, ORI acts more rapidly and completely than other antibiotics in its class *in vitro* against *Staphylococcus aureus* in both slow-growing and biofilm states.

- **Pharmacokinetic-Pharmacodynamic Profiling of Oritavancin in the Rat Granuloma Pouch Model** (ICAAC06-A-2495-ASM)
  Complicated skin and skin structure infections caused by *Staphylococcus aureus* remain some of the most serious infections facing hospital patients. To determine whether ORI could show activity against these infections, researchers tested it in rats whose tissue had been treated with a mixture of air and oil to form a granuloma pouch, which replicates the inflamed tissue most susceptible to infection. The pouches were inoculated with methicillin-sensitive *S. aureus.* Two hours later, the rats received ORI intravenously in seven different doses ranging from 0.25 to 30 mg/kg. A group of rats received VAN at 100 mg/kg subcutaneously to compare; another group received no treatment. Samples of fluid inside the pouch were taken at various time points during therapy to determine bacterial counts, thereby determining whether the treatments were effective in reducing the bacterial load. Results showed clearly that ORI acted more quickly than VAN against the bacteria in the granuloma pouch and that ORI delayed regrowth of bacteria more than three times longer than VAN. The longer duration of ORI activity against bacteria correlated well with its long (about 70 hours) presence in the granuloma pouch. These studies suggest that infrequent dosing of ORI may be applicable in treating infections caused by gram-positive bacteria.

- **Oritavancin Disrupts Transmembrane Potential and Membrane Integrity Concomitantly With Cell Killing in *Staphylococcus aureus* and**

Vancomycin-Resistant Enterococci. (ICAAC06-A-2459-ASM)
ORI is a potent antibacterial agent active against most gram-positive bacteria including VAN-resistant *S. aureus* and enterococci. Researchers conducted studies to understand whether its mechanism of action could explain its enhanced *in vitro* activity relative to vancomycin and other glycopeptides. They found that ORI's ability to kill bacteria was tightly linked with its ability to disrupt bacterial cell membranes thereby drastically altering membrane energy processes critical to bacterial cell survival. The higher the concentration of ORI and the longer it was exposed to the bacteria, the more effectively it disrupted the cell membrane. These findings help to explain the basis for ORI's enhanced activities when compared with other glycopeptides.

About Oritavancin

Oritavancin, Targanta's lead product candidate, is a once-daily, semi-synthetic glycopeptide antibiotic with rapid bactericidal activity against all studied clinically relevant serious gram-positive pathogens, including multi-resistant strains. Oritavancin's multiple targets and mechanisms of action work against the development of resistant strains, which is important when treating serious gram-positive infections. To date, 1,566 individuals have received Oritavancin in clinical trials, including two large multicenter Phase III studies. Targanta expects to file a new drug application for oritavancin with the U.S. Food and Drug Administration in 2007.

About Targanta Therapeutics

Targanta Therapeutics is a privately held biopharmaceutical company developing and commercializing antibacterial drugs to treat serious infections in the hospital setting. Its pipeline includes an array of antibacterial agents in various stages of development. The company is headquartered in Indianapolis, Ind. For further information about Targanta, visit the company website, www.targanta.com.

Disclaimer

All forward-looking statements and other information included in this press release are based on information available to Targanta as of the date hereof, and Targanta assumes no obligation to update any such forward-looking statements or information. Targanta's actual results could differ materially from those described in Targanta's forward-looking statements.

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