

September 24, 2003

Theravance Announces Promising Results From Multiple Research And Clinical Studies With the Investigational Antibiotic TD-6424

Phase 2 Trials Underway For Serious Infections Caused by Gram-Positive Bacteria

SOUTH SAN FRANCISCO, CA

Date: September 24, 2003

Theravance, Inc., today announced that results from a series of eleven in vitro, in vivo, and human clinical studies with the investigational antibiotic TD-6424 were presented at the 43rd annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Chicago. ICAAC, organized by the American Society for Microbiology, is the world's premier meeting on infectious diseases and antimicrobial agents.

TD-6424, a rapidly bactericidal injectable antibiotic with multiple mechanisms of action, was discovered at Theravance through the application of multivalent drug design in a research program dedicated to finding new antibiotics for serious infections due to *Staphylococcus aureus* (including multi-drug resistant strains) and other Gram-positive pathogens. TD-6424 is currently in Phase 2 clinical trials.

Among the highlights of the TD-6424 studies presented at ICAAC were:

- An in vivo study in which TD-6424 was compared to vancomycin in a rabbit model of aortic valve endocarditis caused by methicillin-resistant or vancomycin-intermediate-susceptibility *Staphylococcus aureus*. In this model of severe infections, only TD-6424 produced significant reductions in valve vegetation titers against each of the bacterial strains.
- A series of in vivo studies demonstrating that TD-6424 is more potent than vancomycin, linezolid and nafcillin in animal models of infection in both immunocompetent and immunocompromised hosts. Moreover, the in vivo efficacy of TD-6424 was less affected by the immune status of the animals - a finding consistent with the bactericidal properties of TD 6424.
- A study demonstrating the potential utility of TD-6424 in staphylococcal infections that can occur with indwelling medical devices (i.e., pacemakers or intracardiac defibrillators). Experiments using an in vitro model of these biofilm-associated infections, found that TD 6424 caused more consistent and extensive bactericidal effects than vancomycin, teicoplanin, linezolid, or moxifloxacin.
- Results of a Phase 1 clinical study demonstrating that the pharmacokinetics of TD-6424 are linear and predictable with plasma concentrations of TD-6424 remaining well above the minimum inhibitory concentrations for Gram-positive pathogens during the full 24-hour period following once-a-day dosing. Safety results from this study are supportive of further development for the treatment of serious infections.
- Results of mechanistic experiments demonstrating that, unlike vancomycin and other early members of the glycopeptide class, TD-6424 acts through a combination of mechanisms.
- In vitro studies demonstrating potent activity versus streptococci (including penicillin-resistant *Streptococcus pneumoniae*), enterococci (including vancomycin-resistant *Enterococcus* spp.), and anaerobic Gram-positive species and corynebacteria. These results complement presentations at earlier scientific meetings that described the potent activity of TD-6424 versus *Staphylococcus aureus* (including methicillin-resistant strains and strains with intermediate susceptibility or frank resistance to vancomycin).
- In vitro time-kill studies showing that TD-6424 is more rapidly bactericidal than vancomycin or linezolid against penicillin-resistant *Streptococcus pneumoniae* and bactericidal against strains of enterococci for which vancomycin is either ineffective or only bacteriostatic. In another in vitro study, serum was shown to have no detrimental effect on the bactericidal activity of TD-6424 against methicillin-resistant *Staphylococcus aureus* despite the relatively high level of protein binding seen with TD-6424.
- An in vitro study demonstrating a low frequency of spontaneous resistance to TD-6424 and delayed resistance selection among both staphylococci and enterococci. The lack of TD 6424-resistant isolates of *Staphylococcus aureus* in this study may be due to the multiple mechanisms of action against this important pathogen.

Theravance is a privately-held pharmaceutical company dedicated to utilizing its proprietary multivalent technology to discover, develop and market best-in-class medicines for a wide variety of serious medical conditions. Since its inception, Theravance has implemented an integrated model of drug discovery and exploratory development and applied its multivalent approach to create an impressive pipeline of clinical and pre-clinical compounds across diverse therapeutic areas. For more information, please visit the company's web site at www.theravance.com.

THERAVANCE™ and the THERAVANCE™ LOGO are trademarks of Theravance, Inc.