TAXIS PHARMACEUTICALS DEMONSTRATES CLINICAL POTENTIAL OF TXA709 IN COMBATING ANTIBIOTIC RESISTANCE

Poster Presentation at ECCMID 2015 Highlights
Unique Mechanism of Action and Potent Bactericidal Activity against MRSA Strains

NORTH BRUNSWICK, N.J., April 27, 2015 – TAXIS Pharmaceuticals, a drug-discovery company focused on developing a new class of antibiotic agents to treat life-threatening, multidrug-resistant bacterial infections, today announced the presentation of data demonstrating the promise of its lead clinical candidate, TXA709, in combating antibiotic resistance. In a poster presentation at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Copenhagen, Denmark, researchers presented pre-clinical data highlighting the unique mechanism of action and potent bactericidal activity of TXA709 against *Staphylococcus aureus* isolates that are resistant to current standard-of-care antibiotics including vancomycin, daptomycin and linezolid.

TXA709 inhibits the bacterial protein FtsZ, which plays an essential role in bacterial cell division. The inhibition of FtsZ is considered a novel mechanism of action, making TXA709 an appealing product candidate as researchers work to develop antibacterial agents to address the public health crisis stemming from the growing frequency of antibiotic resistance.

“Methicillin-resistant *Staphylococcus aureus*, or MRSA, is a major contributor to the global antibiotic resistance problem. Our research shows that TXA709, which the body converts into a benzamide compound called TXA707, offers superior *in vivo* efficacy against MRSA and other resistant *Staphylococcus aureus* strains, compared to standard-of-care antibiotic agents,” explained Edmond J. LaVoie, Ph.D., lead author of the poster, professor and chair, Department of Medicinal Chemistry, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, and a co-founder of TAXIS Pharmaceuticals. “Its unique inhibition of the FtsZ protein translates into potent bactericidal activity, enhanced metabolic stability and improved pharmacokinetic properties, making TXA709 a potentially valuable tool in the global struggle against antibiotic resistance.”

Dr. LaVoie and colleagues reported on a series of antibiotic challenge studies in which TXA707, the metabolite of TXA709, maintained potent bactericidal activity against *S. aureus* isolates with documented resistance or non-sensitivity to methicillin, vancomycin, daptomycin, and linezolid. They also presented an analysis of antistaphylococcal efficacy in a mouse peritonitis model of systemic infection, in which TXA709 was associated with enhanced (two- to four-fold greater) *in vivo* efficacy against both methicillin-sensitive *S. aureus* (MSSA) and MRSA strains, compared to another TAXIS compound with a similar mechanism of action.

“The antibacterial activity of TXA709 and the disruption of bacterial cell division by its metabolite, TXA707, show that we are on the right track in targeting FtsZ,” noted Daniel S. Pilch, Ph.D., associate professor, Department of Pharmacology, Rutgers Robert Wood Johnson Medical School, co-author of the poster and a co-founder of TAXIS Pharmaceuticals.

A second-generation FtsZ inhibitor, TXA709 is a prodrug (a biologically inactive compound that can be metabolized in the body to produce a drug) of TXA707, a derivative of benzoic acid that disrupts the form and function of FtsZ. In the presence of TXA707, FtsZ does not function properly, resulting in bacterial cell death that is achieved more rapidly than that observed with standard antibiotics such as vancomycin.

“There is an urgent need for drugs to stem the tide of antibiotic resistance,” commented Gregory Mario, president and chief executive officer of TAXIS Pharmaceuticals. “Our latest findings, which we hope to validate in ongoing research, highlight TXA709 as a potential weapon in that fight, and we are committed to bringing it, along with other novel, potentially life-saving antibiotic agents, to the clinic.”

Dr. Pilch and colleagues also reported on experiments that validate FtsZ as the bactericidal target of TXA707, which induces the overstimulation of FtsZ polymerization, the process by which FtsZ forms a ring-like structure (called the Z-ring) at the middle of the bacterial cell that serves as a scaffold for the recruitment and organization of other critical components of cellular synthesis, septum formation, and cell division. The extent of this stimulation depends on the TXA707 concentration, he noted. TXA707 disrupts Z-ring formation in bacteria by inducing a filamentous phenotype, as well as mislocalization of FtsZ from the septal Z-ring at midcell to multiple punctate sites (areas marked with points or punctures) throughout the cell. The mislocalization of septal biosynthesis away from midcell results in disrupted cell division and, ultimately, cell death in *S. aureus*.

A pharmacokinetic analysis showed that TXA707 is eliminated approximately six times less rapidly and is associated with superior oral bioavailability relative to PC190723, the metabolite of a first-generation FtsZ inhibitor known as TXY541. Additionally, the volume of distribution of TXA707 was found to be roughly three times greater than that of normal body water in the mouse (0.7 L/kg), indicating that the compound distributes well into the tissue.

“With its enhanced potency against multidrug-resistant strains, favorable pharmacokinetics, and greater stability, TXA709 clearly stands apart from other antibiotic agents,” stated Mr. Mario. “TXA709 thus represents a new class of antibiotics, one that works where other drugs fail. We are currently scaling up for IND-enabling studies of TXA709, and look forward to characterizing the activity of this agent more fully in ongoing and future research as we continue to confront the deadly scourge of multidrug resistance.”

About TAXIS

TAXIS Pharmaceuticals is a privately held biopharmaceutical company dedicated to developing novel antibiotics to combat the growing threat of multidrug-resistant bacteria. To date, TAXIS has identified and patented twelve (12) new classes of proprietary antibiotic agents that exploit a novel mechanism of bactericidal action distinct from any other antibiotic in clinical use today. The company is currently advancing its lead clinical candidate, TXA709, which is designed to disrupt the division of bacterial cells. The company's goal is to improve the treatment of multidrug-resistant bacterial infections such as methicillin-resistant *Stapylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA), vancomycin-resistant *Enterococci* (VRE), *Clostridium difficile* (C-diff), *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.

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Media Contact:
Sean Hudgins
SmithSolve LLC
Tel: 973-442-1555 x113
Email: sean.hudgins@smithsolve.com