New Studies Highlight Activity of XERAVA™ Against Gram-Negative and Gram-Positive Clinical Isolates, Including Multidrug-Resistant Pathogens

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Additional Data Points to Potential of XERAVA to Treat Carbapenem-Resistant, Multidrug-Resistant Escherichia Coli

TP-6076 Demonstrates In Vivo Efficacy in Murine Lung and Thigh Infection Models with Acinetobacter Baumannii

WATERTOWN, Mass.--(BUSINESS WIRE)--Jun. 24, 2019-- Tetraphase Pharmaceuticals, Inc. (NASDAQ:TTPH), a biopharmaceutical company focused on commercializing novel tetracyclines to treat serious and life-threatening conditions, announced the presentation of new data on XERAVA ™(eravacycline), a novel, fully synthetic fluorocycline approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency for the treatment of complicated intra-abdominal infections (cIAI) in adults, and TP-6076, a clinical-stage candidate targeting multidrug-resistant (MDR) infections, at the American Society for Microbiology (ASM) Microbe 2019 Annual Meeting held June 20-24 in San Francisco.

"The data presented at ASM Microbe underscore the broad potential of XERAVA as a potent antibiotic against gram-negative and gram-positive clinical isolates, including MDR pathogens," said Larry Edwards, current Chief Operating Officer of Tetraphase and recently named President and Chief Executive Officer, effective August 1, 2019. "As we now focus our efforts squarely on the commercial success of XERAVA in complicated intra-abdominal infections, we continue to be encouraged by studies that highlight its validity as a new treatment option for serious, life-threatening infections. Additionally, as recently announced, we are looking to outlicense our early-stage pipeline, and we believe that the pharmacokinetic and efficacy data of TP-6076 strengthens this asset as an attractive outlicensing candidate."

Studies Continue to Demonstrate the Potent *In Vitro* Activity of Eravacycline Against Gram-Negative and Gram-Positive Clinical Isolates, Including Multidrug-Resistant Pathogens

Carbapenem resistance is emerging in *E. coli*, including its MDR lineage. New agents, including XERAVA, have distinctive mechanisms that inhibit or kill many carbapenem-resistant organisms. Accordingly, Johnson *et al.* tested these antibiotics against clinical *E. coli* isolates, including those that are carbapenem resistant, from surveillance systems encompassing multiple sites across the U.S. The minimum inhibitory concentrations (MIC) of 179 U.S. clinical *E. coli* isolates, which were non-susceptible to one or more carbapenems, were determined with cefiderocol, ceftazidime-avibactam and XERAVA; three carbapenems (meropenem,*imipenem*, ertapenem); and eight non-carbapenem comparators. Using FDA/Clinical and Laboratory Standards Institute (CLSI) breakpoint interpretations, the percent susceptible isolates was higher for cefiderocol (96%), ceftazidime-avibactam (92%), and XERAVA (97%) than for any carbapenem (meropenem, 75%; imipenem, 46%; ertapenem, 3%) and for all other comparators except tigecycline (98%) and colistin (99%). These data demonstrated that cefiderocol, ceftazidime-avibactam and XERAVA were highly active overall among the carbapenem-resistant *E. coli* clinical isolates, notwithstanding variation by phylogroup, clonal group, *New Delhi metallo-beta-lactamase* genotype and geographical region. Given these results, XERAVA may be a promising new treatment option for infections caused by carbapenem-resistant, multidrug-resistant *E. coli*.

In a large, ongoing surveillance study of XERAVA, researchers evaluated the *in vitro* activity of the drug against Gram-negative and Gram-positive global isolates collected in 2017, including MDR pathogens. A total of 7,084 bacterial isolates were collected from different geographic regions, including Europe (n=3,539), the U.S. (n=2,381) and Asia/Pacific (n=1,164). Overall, XERAVA exhibited potent *in vitro* activity against *Enterobacteriaceae*, *A. baumannii* and clinically important Gram-positive organisms, including resistant pathogens. The MICs of XERAVA against all *Enterobacteriaceae* (n=3,250) were generally two- to four-fold lower than tigecycline, including for MDR isolates.

In an additional XERAVA study, up to 15 hospitals submitted pathogens collected from 2014-2018 from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units as part of CANWARD, an ongoing national Health Canada and Canadian Antimicrobial Resistance Alliance (CARA) partnered surveillance program in Canadian hospitals. The *in vitro* activity of XERAVA was compared to a variety of other antibiotics against a total of 15,887 Gram-negative and Gram-positive pathogens and showed that XERAVA was more active than meropenem and piperacillin-tazobactam against methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus faecalis, Enterococcus faecium,* vancomycin-resistant enterococci (VRE), *Stenotrophomonas maltophilia* and *Acinetobacter baumannii*.

Additional posters highlighted ways to evaluate XERAVA using the Beckman Coulter MicroScan Dried Gram-Negative MIC Panels and the bioMérieux ETEST®. The ETEST strip and the MicroScan Dried Gram-Negative MIC panel containing XERAVA were each shown to correlate well with MICs obtained by broth microdilution reference method (BMD). Both methods could represent a valuable tool for XERAVA susceptibility testing and an alternative to the BMD reference method.

New Data on the Pharmacokinetics and Efficacy of TP-6076 in the Murine Lung and Thigh Infection Models with *A. baumannii*

In addition to the XERAVA findings, new data on TP-6076, Tetraphase's Phase 2 ready candidate for MDR Gram-negative bacteria, such as carbapenem-resistant *Enterobacteriaceae* and carbapenem-resistant *Acinetobacter baumanii*, were presented. These resistant organisms, particularly MDR *A.* baumannii, are of increasing concern in association with ventilator-associated pneumonia with high morbidity and mortality rates, especially in immunocompromised patients.

Studies were performed to evaluate the efficacy of TP-6076 in murine lung infection and murine thigh infection models against MDR *A. baumannii* clinical isolates. TP-6076 demonstrated high potency against MDR *A. baumannii* clinical isolates that were used in these *in vitro* models, with MICs that ranged from <0.008 - 0.25 ug/mL (MIC 90 = 0.0625 ug/mL).

Results of the first study indicated TP-6076's ability to penetrate the lung. Single IV doses of TP-6076 (0.25 – 40 mg/kg) were administered to neutropenic (or immunocompromised) mice, and epithelial-lining fluid (ELF) was subsequently evaluated. TP-6076 resulted in statistically significant

reductions in bacterial lung titers in the murine lung infection model, with *A. baumannii* lung colony forming units (CFU) decreasing by 2.4 – 6.2 $\log_{10}$ CFU when compared to the untreated control group. In comparison, tigecycline resulted in a 0.2 – 4.2 $\log_{10}$ CFU reduction in mean lung titers.

TP-6076's *in vivo* efficacy was also demonstrated in an immunocompromised murine thigh infection model with *A. baumannii*. Female neutropenic mice were infected intramuscularly with MDR *A. baumannii* clinical isolates into their right hind-limb thighs. TP-6076 doses resulted in a statistically significant reduction ($p<0.0001$) in mean thigh CFU to 3.0 – 3.8 $\log_{10}$ CFU, compared to the untreated controls. Doses of tigecycline resulted in less than a 2 $\log_{10}$ CFU reduction observed for most isolates, which was not statistically significant.

The results of these studies demonstrated *in vitro* activity of TP-6076 against MDR *A. baumannii* isolates with statistically significant reductions in bacterial tissue titers in the murine thigh and lung infection models and suggest that TP-6076 has the potential to treat life-threatening multi-drug resistant *A. baumannii* infections, including ventilator-associated pneumonia.

About XERAVA ™

XERAVA(eravacycline for injection) is a tetracycline class antibacterial indicated for the treatment of complicated intra-abdominal infections (cIAI) in patients 18 years of age and older. XERAVA was investigated for the treatment of cIAI as part of the Company's IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline) Phase 3 program. In the first pivotal Phase 3 trial in patients with cIAI, twice-daily intravenous (IV) XERAVA met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to ertapenem and was well-tolerated. In the second Phase 3 clinical trial in patients with cIAI, twice-daily IV XERAVA met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to meropenem and was well-tolerated. In both trials, XERAVA achieved high cure rates in patients with Gram-negative pathogens, including resistant isolates.

Indications and Usage

XERAVA is indicated for the treatment of complicated intra-abdominal infections (cIAI) caused by susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca, Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus, Streptococcus anginosus* group, *Clostridium perfringens, Bacteroides* species, and *Parabacteroides distasonis* in patients 18 years or older.

Limitations of Use

XERAVA is not indicated for the treatment of complicated urinary tract infections (cUTI).

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of XERAVA and other antibacterial drugs, XERAVA should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Important Safety Information

XERAVA is contraindicated for use in patients with known hypersensitivity to eravacycline, tetracycline-class antibacterial drugs, or to any of the excipients. Life-threatening hypersensitivity (anaphylactic) reactions have been reported with XERAVA.

The use of XERAVA during tooth development (last half of pregnancy, infancy and childhood to the age of eight years) may cause permanent discoloration of the teeth (yellow-gray-brown) and enamel hypoplasia.

The use of XERAVA during the second and third trimester of pregnancy, infancy and childhood up to the age of eight years may cause reversible inhibition of bone growth.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis.

The most common adverse reactions observed in clinical trials (incidence ≥3%) were infusion site reactions (7.7%), nausea (6.5%), and vomiting (3.7%).

XERAVA is structurally similar to tetracycline-class antibacterial drugs and may have similar adverse reactions. Adverse reactions including photosensitivity, pseudotumor cerebri, and anti-anabolic action which has led to increased BUN, azotemia, acidosis, hyperphosphatemia, pancreatitis, and abnormal liver function tests, have been reported for other tetracycline-class antibacterial drugs, and may occur with XERAVA. Discontinue XERAVA if any of these adverse reactions are suspected.

To report SUSPECTED ADVERSE REACTIONS, contact Tetraphase Pharmaceuticals Inc., at 1-833-7-XERAVA (1-833-793-7282) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for XERAVA at www.XERAVA.com.

About Tetraphase Pharmaceuticals, Inc.

Tetraphase Pharmaceuticals, Inc., is a biopharmaceutical company using its proprietary chemistry technology to create novel tetracyclines for serious and life-threatening conditions, including infections caused by many of the multidrug-resistant bacteria highlighted as urgent public health threats by the World Health Organization and the Centers for Disease Control and Prevention. The Company has created more than 3,000 novel tetracycline compounds using its proprietary technology platform. Tetraphase's lead product XERAVA™ is approved for the treatment of complicated intra-abdominal infections by the U.S. Food and Drug Administration and the European Medicines Agency. The Company's pipeline also includes TP-271 and TP-6076, which are Phase 2 ready, and TP-2846, which is in preclinical testing for acute myeloid leukemia. The Company intends to outlicense its pipeline candidates. Please visit www.tphase.com for more company information.

Forward-Looking Statements

Any statements in this press release about our future expectations, plans and prospects, including statements regarding our strategy, future operations, prospects, plans and objectives, and other statements containing the words "anticipates," "believes," "expects," "plans," "will" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether preclinical data is indicative of expected clinical data; our cash resources and the expected revenue will be sufficient to fund our operations in the future; our product candidates will succeed in clinical trials; even if such clinical trials are successful, whether we may ever achieve regulatory approval of such product candidates; and other clinical, regulatory and commercial risk factors discussed in the "Risk Factors" section of our quarterly report on Form 10-Q for the period ended March 31, 2019, filed with the Securities and Exchange Commission on May 8, 2019. In addition, the forward-looking statements included in this press release represent our views as of June 24, 2019. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so.

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