Tetraphase Pharmaceuticals Announces New XERAVA™ (eravacycline) Data at the 39th Annual Surgical Infection Society Meeting

June 10, 2019

-Study Examines Microbiology and Hospitalization Outcomes Among Complicated Intra-Abdominal Infection Patients-

-Data Underscore XERAVA's Role as an Empiric Treatment Option for Patients With Complicated Intra-Abdominal Infections-

WATERTOWN, Mass.--(BUSINESS WIRE)--Jun. 10, 2019-- Tetraphase Pharmaceuticals, Inc. (NASDAQ:TTPH), a biopharmaceutical company focused on developing and commercializing novel tetracyclines to treat serious and life-threatening conditions, today announced the presentation of positive data from three studies further evaluating its lead compound, XERAVA™ (eravacycline), a novel, fully-synthetic fluorocycline, approved by the U.S. Food and Drug Administration and the European Medicines Agency for the treatment of complicated intra-abdominal infections (cIAI), as well as data from a retrospective study of hospital-based outcomes in cIAI. These data were presented at the 39th Annual Surgical Infection Society (SIS) Meeting, held June 5-8, 2019 in Coronado, Calif.

"Data continue to demonstrate that cIAI represents a significant threat to patients that is exacerbated by growing resistance to many of the antibiotics commonly used to treat these infections," said Larry Tsai, M.D., Chief Medical Officer of Tetraphase Pharmaceuticals. "A retrospective study that collected multi-year data from patients with cIAI and positive cultures at approximately 180 hospitals showed a hospital mortality rate of 7.6%, and a 30-day rehospitalization rate of 11.2%, underscoring the need for more effective empiric treatments for these life-threatening infections."

Dr. Tsai added, "The data presented at SIS continue to reinforce the clinical utility of XERAVA in the treatment of cIAI. With the versatility to treat both confirmed and empiric cIAI and demonstrated activity against a broad range of Gram-negative, Gram-positive and anaerobic bacteria, XERAVA represents an important option in the cIAI treatment landscape."

Microbiology and Outcomes of Hospitalization With Intra-Abdominal Infections in the U.S.: A Retrospective Cohort Study

To better understand the microbiology and outcomes of hospitalization due to cIAIs, researchers performed a multicenter retrospective cohort study in the Premier database of approximately 180 hospitals from 2013-2017. All adult patients hospitalized with cIAI and a positive blood or abdominal culture were identified.

Among 4,453 patients with cIAI and positive cultures, 3,771 (84.7%) had a Gram-negative and 1,782 (40.0%) had a Gram-positive organism identified. The majority of cases (n=2,941; 66.0%) were monomicrobial. Among patients with a polymicrobial infection, 1,118 (25.1%) had two organisms while 394 (8.8%) had three or more pathogens. Notably, resistance to third-generation cephalosporins occurred in 7.6% of all Gram-negative pathogens. The most common Gram-negative pathogens were *E. coli* (2,624; 58.9%) and *K. pneumoniae* (774; 17.4%).

Beyond microbiology, this retrospective study analyzed hospitalization outcomes. Findings showed that hospital mortality due to cIAI was 7.6%, and 11.2% of patients were readmitted within 30 days of discharge. The median (interquartile range) length of stay was 6 (3, 12) days, and median total cost was $21,148 ($12,051, $43,637). These results highlight the significant morbidity and mortality associated with cIAI hospitalizations, as well as the substantial cost burden.

Efficacy of Eravacycline in Non-Appendiceal Complicated Intra-Abdominal Infections: An Analysis of Two Phase 3 Trials

Compared to complicated appendicitis, cIAIs of non-appendiceal etiology carry a higher risk for initial treatment failure, prolonged treatment duration, and increased mortality.[1] Researchers hypothesized that patients with non-appendiceal cIAIs treated with XERAVA would have similar clinical outcomes when compared to those treated with carbapenems. A post-hoc analysis of patients diagnosed with cIAI of non-appendiceal origin from two Phase 3 studies, IGNITE1 and IGNITE4, was performed to determine clinical outcomes. Clinical cure rates in patients diagnosed with complicated appendicitis were 89.0% and 88.6% in patients treated with XERAVA and comparators, respectively. In patients with non-appendiceal cIAIs treated with XERAVA and comparators, clinical cure rates were 88.8% and 89.7%, respectively. Across the non-appendiceal subgroups, clinical outcomes between XERAVA and comparators were similar.

This pooled analysis suggests that XERAVA is an effective empiric treatment option for patients with cIAI, including those with specific higher-risk diagnoses such as peritonitis and intestinal perforation.

2017 Global Surveillance of the In Vitro Activity of Eravacycline Against Clinical Isolates From Gastrointestinal Infections

In a subset of data from a 2017 global surveillance study, 2,005 non-duplicate, non-consecutive, single-patient gastrointestinal isolates were analyzed to determine the Minimum Inhibitory Concentration (MIC) required to inhibit the growth of 50% and 90% of organisms, respectively, for XERAVA and comparators. Results demonstrated potent *in vitro* activity against *Enterobacteriaceae* with an MIC_{90} value of 1 mg/L compared to 4 mg/L for tigecycline. XERAVA demonstrated two- to eight-fold greater potency than tigecycline against ***Escherichia coli*, *Klebsiella* spp.** and *Acinetobacter baumannii*,including against pathogens expressing extended spectrum beta-lactamases (ESBL). In addition, XERAVA had two- to four-fold greater potency than tigecycline versus clinically important Gram-positive pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Enterococcus spp.*

These data support that XERAVA is a treatment option for cIAI in patients who harbor or are at risk for infections due to resistant *Enterobacteriaceae*.

Factors That Impact Duration of Antibiotic Therapy From Phase 3 Studies of Eravacycline for Intra-Abdominal Infection

A post-hoc analysis of two pooled Phase 3 studies (IGNITE1 and IGNITE4) of XERAVA examined the impact of certain patient-specific variables on

duration of treatment. Researchers sought to determine whether variables associated with duration of treatment differed in patients based on the type of cIAI – complicated appendicitis or non-appendiceal infections. Patients with cIAI from both Phase 3 studies were randomized (1:1) to receive XERAVA or a carbapenem. Duration of therapy was discretionary up to 14 days. Groups were categorized by the following durations: ≤5 days, 6-8 days and >8 days.

Results showed that among all patients, those who received longer treatment were older (p=0.004), sicker (p<0.001), more likely to have non-appendiceal infections (p<0.001) and to have undergone open surgery for infection source control (p<0.001). For patients with complicated appendicitis, open surgery and polymicrobial infection were associated with longer treatment (p<0.001), whereas patients with non-appendiceal infections who had longer length of therapy were more likely to be ill (p=0.029), to have undergone open surgery (p=0.001) and to have received prior antibiotics (p=0.001). Further analysis to quantify the impact of various factors in terms of days of therapy showed that patients who had laparoscopic surgery for source control had approximately one day less of therapy, while patients who had a multidrug-resistant Enterococcus pathogen received 1.3 additional days of therapy.

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 in Phase 1 clinical trials, and TP-2846, which is in preclinical testing for acute myeloid leukemia. 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, including our key milestones for 2019 and our anticipated cash runway, 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 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 10, 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.

[i] Mazsuki JE et al. *Surg Infect*. 2017; 18(1):1-76.

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Source: Tetraphase Pharmaceuticals, Inc.

Jennifer Viera
jviera@tphase.com
617-600-7040