

ACHAAGEN

Achaogen Launches ZEMDRI™ (plazomicin), a Once-Daily Aminoglycoside for use in complicated Urinary Tract Infections (cUTI)

July 20, 2018

-- ZEMDRI now available for ordering in the U.S. --

-- ZEMDRI demonstrated *in vitro* microbiological activity against pathogens designated by the CDC as urgent and serious public health threats, including carbapenem-resistant (CRE) and extended spectrum beta-lactamase (ESBL)- producing Enterobacteriaceae --

SOUTH SAN FRANCISCO, Calif., July 20, 2018 (GLOBE NEWSWIRE) -- Achaogen, Inc. (NASDAQ:AKAO), a biopharmaceutical company developing and commercializing innovative antibacterial agents to address multi-drug resistant (MDR) gram-negative infections, today announced that ZEMDRI is now available for ordering. ZEMDRI is approved in the United States for the treatment of adults with cUTI, including pyelonephritis, due to certain Enterobacteriaceae. ZEMDRI was approved by the U.S. Food and Drug Administration on June 25, 2018.

"The challenge that healthcare providers face every day of addressing difficult-to-treat infections is significant and growing," said Blake Wise, Achaogen's Chief Executive Officer. "We are excited to launch ZEMDRI and partner with the infectious disease community in both the hospital and outpatient settings around the proper use, efficacy and safety of ZEMDRI, including its activity against certain MDR bacteria and its 30-minute, once-daily dosing regimen."

ZEMDRI for injection 500 mg/10 mL (50mg/mL) is supplied in single-use, clear glass vials (ten vials per carton). ZEMDRI dosing is based on patient weight and renal function; Achaogen expects that most patients receiving the standard dose will receive three vials per daily dose. ZEMDRI is available for purchase through specialty distributors such as ASD Healthcare, a company of AmerisourceBergen, Cardinal Health Specialty Distribution, FFF Enterprises and McKesson Plasma and Biologics.

The approval of ZEMDRI was supported in part by data from the EPIC (Evaluating Plazomicin In cUTI) clinical trial, which was the first randomized controlled study of once-daily aminoglycoside therapy for the treatment of cUTI, including pyelonephritis.

In the Phase 3 EPIC cUTI clinical trial, ZEMDRI demonstrated non-inferiority to meropenem for the co-primary efficacy endpoints of composite cure (clinical cure and microbiological eradication) in the microbiological modified intent-to-treat (mMITT; N=388) population at Day 5 and test-of-cure (TOC) visit (Day 17 + 2). Composite cure rates at Day 5 were 88.0% (168/191) for ZEMDRI vs. 91.4% (180/197) for meropenem (difference -3.4%, 95% CI, -10.0 to 3.1). Composite cure rates at TOC were 81.7% (156/191) for ZEMDRI vs. 70.1% (138/197) for meropenem (difference 11.6%, 95% CI, 2.7 to 20.3). Composite cure at the TOC visit in patients with concomitant bacteremia at baseline was achieved in 72.0% (18/25) of patients in the ZEMDRI group vs. 56.5% (13/23) in the meropenem group.¹ Relapse of clinical cUTI symptoms at late follow up (LFU, day 28 +/- 4) occurred in 1.6% (3/191) of ZEMDRI-treated patients compared with 7.1% (14/197) of meropenem-treated patients, and microbiological recurrence of the baseline uropathogens at LFU occurred in 3.7% (7/191) of ZEMDRI-treated patients compared with 8.1% (16/197) of meropenem-treated patients.² The most common side effects (≥1% of patients treated with ZEMDRI) are decreased renal function, diarrhea, hypertension, headache, nausea, vomiting, and hypotension.¹

About cUTI

cUTI is defined as a UTI occurring in a patient with an underlying complicating factor of the genitourinary tract, such as a structural or functional abnormality.³ Patients with pyelonephritis, regardless of underlying abnormalities of the urinary tract, are considered a subset of patients with cUTI.⁴ An estimated 3 million cases of cUTI are treated in the hospital setting in the U.S. each year.⁵ Enterobacteriaceae are the most common pathogens causing cUTIs⁶, and resistance within this family is a global concern. High rates of resistance to previous mainstays of therapy necessitate alternative treatment options. Ineffectively managed cUTI can lead to increased treatment failure rates, recurrence of infection, increased re-hospitalization, and increased morbidity and mortality. cUTI infections place an economic burden on hospitals and payers.^{6,7}

About ZEMDRI

ZEMDRI is an aminoglycoside administered as a once-daily, 30-minute intravenous (IV) infusion that has activity against certain Enterobacteriaceae. Achaogen's EPIC clinical trial successfully evaluated the safety and efficacy of ZEMDRI in adult patients with cUTI, including pyelonephritis. ZEMDRI was engineered to overcome aminoglycoside-modifying enzymes, the most common aminoglycoside-resistance mechanism in Enterobacteriaceae, and has *in vitro* activity against ESBL- producing, aminoglycoside- resistant, and carbapenem- resistant isolates. The Centers for Disease Control and Prevention (CDC) has characterized ESBL- producing Enterobacteriaceae as a "serious threat" and CRE as "nightmare bacteria" which is an immediate public health threat that requires urgent and aggressive action.

Indications & Usage

ZEMDRI (plazomicin) is indicated in patients 18 years of age or older for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by the following susceptible microorganism(s): *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae*.

As only limited clinical safety and efficacy data for ZEMDRI are currently available, reserve ZEMDRI for use in cUTI patients who have limited or no alternative treatment options.

To reduce the development of drug-resistant bacteria and maintain effectiveness of ZEMDRI and other antibacterial drugs, ZEMDRI should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible microorganisms.

Important Safety Information

BOXED WARNINGS: NEPHROTOXICITY, OTOTOXICITY, NEUROMUSCULAR BLOCKADE AND FETAL HARM

- **Nephrotoxicity has been reported with ZEMDRI.** The risk of nephrotoxicity is greater in patients with impaired renal function, the elderly, and in those receiving concomitant nephrotoxic medications. Assess creatinine clearance in all patients prior to initiating therapy and daily during therapy. Therapeutic Drug Monitoring (TDM) is recommended for complicated urinary tract infection (cUTI) patients with CLcr less than 90 mL/min to avoid potentially toxic levels.
- **Ototoxicity, manifested as hearing loss, tinnitus, and/or vertigo, has been reported with ZEMDRI.** Symptoms of aminoglycoside-associated ototoxicity may be irreversible and may not become evident until after completion of therapy. Aminoglycoside-associated ototoxicity has been observed primarily in patients with a family history of hearing loss, patients with renal impairment, and in patients receiving higher doses and/or longer durations of therapy than recommended.
- **Aminoglycosides have been associated with neuromuscular blockade.** During therapy with ZEMDRI, monitor for adverse reactions associated with neuromuscular blockade particularly in high-risk patients, such as patients with underlying neuromuscular disorders (including myasthenia gravis) or in patients concomitantly receiving neuromuscular blocking agents.
- **Aminoglycosides, including ZEMDRI, can cause fetal harm when administered to a pregnant woman.**

Contraindications: ZEMDRI is contraindicated in patients with known hypersensitivity to any aminoglycoside.

Additional Warnings and Precautions

- **Nephrotoxicity:** Reported with the use of ZEMDRI. Most serum creatinine increases were ≤ 1 mg/dL above baseline and reversible. Assess CLcr in all patients prior to initiating therapy and daily during therapy with ZEMDRI, particularly in those at increased risk of nephrotoxicity, such as those with renal impairment, the elderly and those receiving concomitant potentially nephrotoxic medications. In the setting of worsening renal function, the benefit of continuing ZEMDRI should be assessed. Adjust the initial dosage regimen in cUTI patients with CLcr ≥ 15 mL/min and < 60 mL/min. For subsequent doses, TDM is recommended for patients with CLcr ≥ 15 mL/min and < 90 mL/min.
- **Ototoxicity:** Reported with ZEMDRI (manifested as hearing loss, tinnitus, and/or vertigo). Symptoms of aminoglycoside-associated ototoxicity may be irreversible and may not become evident until after completion of therapy. Aminoglycoside-associated ototoxicity has been observed primarily in patients with a family history of hearing loss (excluding age-related hearing loss), patients with renal impairment, and in patients receiving higher doses and/or for longer periods than recommended. The benefit-risk of ZEMDRI therapy should be considered in these patients.
- **Neuromuscular Blockade:** Aminoglycosides have been associated with exacerbation of muscle weakness in patients with underlying neuromuscular disorders, or delay in recovery of neuromuscular function in patients receiving concomitant neuromuscular blocking agents. During therapy with ZEMDRI, monitor for adverse reactions associated with neuromuscular blockade, particularly in high-risk patients, such as patients with underlying neuromuscular disorders (including myasthenia gravis) or those patients concomitantly receiving neuromuscular blocking agents.
- **Fetal Harm:** Aminoglycosides, including ZEMDRI, can cause fetal harm when administered to a pregnant woman. Patients who use ZEMDRI during pregnancy, or become pregnant while taking ZEMDRI should be apprised of the potential hazard to the fetus.
- **Hypersensitivity Reactions:** Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving aminoglycoside antibacterial drugs. Before therapy with ZEMDRI is instituted, careful inquiry about previous hypersensitivity reactions to other aminoglycosides should be made. Discontinue ZEMDRI if an allergic reaction occurs.
- **Clostridium difficile-Associated Diarrhea (CDAD):** Reported for nearly all systemic antibacterial drugs and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial drugs alters the normal flora of the colon and may permit overgrowth of *C. difficile*. Careful medical history is necessary. If CDAD is suspected or confirmed, antibacterial drugs not directed against *C. difficile* may need to be discontinued.
- **Development of Drug-Resistant Bacteria:** Prescribing ZEMDRI in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Please click [here](#) to see the full Prescribing Information, including BOXED WARNINGS, for additional Important Safety Information.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Achaogen at (833) AKAO-402.

About Achaogen

Achaogen is a biopharmaceutical company passionately committed to the discovery, development, and commercialization of innovative antibacterial treatments for MDR gram-negative infections. Achaogen's first commercial product is ZEMDRI, for the treatment of adults with complicated urinary tract infections (cUTI), including pyelonephritis. The Achaogen ZEMDRI program has been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, under Contract No. HHSO100201000046C. The Company is also developing C-Scape, an orally-administered beta-lactam/beta-lactamase inhibitor combination, which is also supported by BARDA. Achaogen has other programs in early and late preclinical stages focused on other MDR gram-negative infections and additional disease areas. All product candidates are investigational, have not been determined to be safe or efficacious, and have not been approved for commercialization. For more information, visit the Achaogen website at www.achaogen.com.

Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical facts contained herein are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, Achaogen expectations regarding the timing of commercial availability of ZEMDRI, the potential uses and advantages of ZEMDRI, Achaogen commercial objectives and the Achaogen pipeline of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties, and other important factors that may cause Achaogen's actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the risks and uncertainties of the regulatory approval process; market size and growth; timing of activities, including launch dates of products; statements about the efficacy, safety and tolerability of ZEMDRI; the risks and uncertainties of product sales; the risk of when bacteria will evolve resistance to ZEMDRI; Achaogen's reliance on third-party contract manufacturing organizations for manufacture and supply, including sources of certain raw materials; risk of third party claims alleging infringement of patents and proprietary rights or seeking to invalidate Achaogen's patents or proprietary rights; and the risk that Achaogen's proprietary rights may be insufficient to protect its technologies and product candidates. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the Achaogen business in general, see Achaogen current and future reports filed with the Securities and Exchange Commission, including its Annual Report on Form 10-K filed on February 27, 2018, and its Quarterly Report on Form 10-Q filed on May 7, 2018. Achaogen does not plan to publicly update or revise any forward-looking statements contained in this press release, whether as a result of any new information, future events, changed circumstances, or otherwise.

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¹ ZEMDRI [package insert]. South San Francisco, CA: Achaogen, Inc.; 2018.

² Achaogen data on file.

³ Nicolle LE. J Infect Dis. 2001;183(Suppl 1):S5-8.

⁴ U.S. Food & Drug. Complicated Urinary Tract Infections: Developing Drugs for Treatment Guidance for Industry. <https://www.fda.gov/downloads/Drugs/Guidances/ucm070981.pdf>. Accessed June 25, 2018.

⁵ Decision Resources Disease Landscape & Forecast, Hospital-Treated Gram-Negative Infections, September 2017; data on file.

⁶ Bader MS et al. Postgrad Med. 2010;122(6):7-15.

⁷ Turner RM et al. Clin Ther. 2015;37(9):2037-2047.

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