Achaogen Announces Publication of Plazomicin Phase 3 CARE Study Results in the New England Journal of Medicine

February 21, 2019

SOUTH SAN FRANCISCO, Calif., Feb. 21, 2019 (GLOBE NEWSWIRE) -- Achaogen, Inc. (Nasdaq: AKAO), a biopharmaceutical company discovering, developing and commercializing innovative antibacterial agents to address multi-drug resistant (MDR) gram-negative infections, today announced that the *New England Journal of Medicine*has published the results from the Phase 3 CARE (Combating Antibiotic Resistant Enterobacteriaceae) study of plazomicin in a Letter to the Editor. In this published study, the efficacy and safety of plazomicin versus colistin was evaluated in patients with serious bloodstream infections or hospital-acquired/ventilator-associated bacterial pneumonia caused by carbapenem-resistant Enterobacteriaceae (CRE). Full study results are published in a Letter to the Editor and Supplementary Appendix in the February 21, 2019 issue of the Journal.

About ZEMDRI

ZEMDRI® (plazomicin) is an aminoglycoside administered as a once-daily, 30-minute intravenous (IV) infusion that has activity against certain Enterobacteriaceae. Achaogen's EPIC (Evaluating Plazomicin In cUTI) 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.

ZEMDRI was approved by the U.S. Food and Drug Administration on June 25, 2018 for the treatment of adults with cUTI, including pyelonephritis, due to certain Enterobacteriaceae. The approval of ZEMDRI was supported in part by data from the EPIC clinical trial, which was the first randomized controlled study of once-daily aminoglycoside therapy for the treatment of cUTI, including pyelonephritis.

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.

The most common adverse reactions (≥ 1% of patients treated with ZEMDRI) are decreased renal function, diarrhea, hypertension, headache, nausea, vomiting and hypotension.

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® (plazomicin), for the treatment of adults with complicated urinary tract infections (cUTI), including [acute] pyelonephritis. The Achaogen plazomicin program was funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), Office of the Assistant Secretary for Preparedness and Response. The Company is currently developing C-Scape, an orally-administered beta-lactam/beta-lactamase inhibitor combination, which is also supported by BARDA. C-Scape is investigational, has not been determined to be safe or efficacious, and has 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, the potential uses and advantages of ZEMDRI, Achaogen’s 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 and product candidates; the risks and uncertainties of product sales; the risk of when bacteria will evolve resistance to ZEMDRI and product candidates; 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 or about August 6, 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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