Achaogen Inc
Form 8-K
June 26, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 26, 2018

ACHAOGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-36323**	**68-0533693**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification Number)**

1 Tower Place, Suite 300

South San Francisco, CA 94080

(Address of principal executive offices, including Zip Code)

Registrant s telephone number, including area code: (650) 800-3636

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging Growth Company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financing accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 8.01 Other Events.

On June 26, 2018, Achaogen, Inc. (the Company) announced that the U.S. Food and Drug Administration (FDA) approved ZEMDRI (plazomicin) for adults with complicated urinary tract infections (cUTI), including pyelonephritis, caused by certain Enterobacteriaceae in patients who have limited or no alternative treatment options. ZEMDRI is an intravenous infusion, administered once daily.

Regarding the potential indication for plazomicin for the treatment of bloodstream infection (BSI), the FDA issued a Complete Response Letter (CRL) stating that the CARE study does not provide substantial evidence of effectiveness of plazomicin for the treatment of BSI. The Company intends to meet with the FDA to determine whether there is a feasible resolution to address the CRL.

ZEMDRI Phase 3 Clinical Results

The approval of ZEMDRI is 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 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 and 56.5% (13/23) of patients in the meropenem group. The most common side effects (³1% of patients treated with ZEMDRI) were decreased kidney function, diarrhea, hypertension, headache, nausea, vomiting, and hypotension.[1]

The FDA approved a breakpoint of <= 2 mcg/mL; greater than 99% of *Escherichia coli*, *Klebsiella pneumoniae* and *Enterobacter cloacae* in U.S. surveillance are susceptible to ZEMDRI when applying this breakpoint.[2]

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 cUTIs[6], 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 with once-daily dosing that has activity against certain Enterobacteriaceae, including CRE and ESBL- producing 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 ³ 15 mL/min and < 60 mL/min. For subsequent doses, TDM is recommended for patients with CLcr ³ 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.

[1] ZEMDRI [package insert]. South San Francisco, CA: Achaogen, Inc.; 2018.
[2] Castanheira M. Antimicrob Agents Chemother. 2018. doi: 10.1128/AAC.00313-18. [Epub ahead of print]
[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.

Forward-Looking Statements

This report 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 and Achaogen commercial objectives. 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 Achaogen s business in general, see Achaogen s 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ACHAOGEN, INC.

Date: June 26, 2018

By: /s/ Gary Loeb
Gary Loeb
General Counsel