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Previous Release | Next Release

Achaogen Announces Positive Results in Phase 3 cUTI and CRE Clinical Trials of Plazomicin

-- EPIC registration trial successfully achieves FDA primary endpoints in patients with complicated urinary tract infections (cUTI) --

-- EPIC demonstrates superiority on EMA primary endpoints --

-- CARE descriptive trial shows 71 percent relative reduction in Day 28 all-cause mortality compared with colistin in patients with serious CRE infections --

-- Plazomicin well tolerated in both trials and shows improved overall safety compared with colistin in CARE trial --

-- Company plans to proceed with regulatory submissions in the U.S. and Europe --

-- Company to host a conference call and webcast today at 8:30 a.m. EST --

SOUTH SAN FRANCISCO, Calif., Dec. 12, 2016 (GLOBE NEWSWIRE) -- Achaogen, Inc. (NASDAQ:AKAO), a clinical-stage biopharmaceutical company developing novel antibacterials addressing multi-drug resistant (MDR) gram-negative infections, today announced that its lead product candidate, plazomicin, met the objective of non-inferiority compared to meropenem for the U.S. Food and Drug Administration (FDA) and achieved superiority for the European Medicines Agency (EMA) primary efficacy endpoints in the Phase 3 EPIC registration trial in patients with complicated urinary tract infections (cUTI) and acute pyelonephritis (AP). In addition, in the Phase 3 CARE trial in patients with serious infections due to carbapenem-resistant Enterobacteriaceae (CRE) a lower rate of mortality or serious disease-related complications was observed for plazomicin compared with colistin therapy, one of the few remaining antibiotics for treatment of infections due to CRE.

"We are thrilled with the outcome of both the EPIC and CARE clinical trials and the potential opportunity for plazomicin to address many of the multi-drug resistant bacterial infections occurring every day," said Kenneth Hillan, M.B. Ch.B., Achaogen's Chief Executive Officer. "We are grateful to the patients and investigators who were involved in both of these studies, and we look forward to seeking plazomicin's approval from FDA and EMA. We believe that, if approved, plazomicin will provide an important new option in treating MDR infections, including those caused by CRE."

Achaogen plans to submit a New Drug Application (NDA), which will include

EPIC and CARE data, to the FDA in the second half of 2017. The Company also plans to submit a Marketing Authorization Application (MAA) to the EMA in 2018. In addition, Achaogen plans to publicly present detailed results from both the EPIC and CARE trials in 2017.

"These data are exceptional and better than I would have expected - plazomicin's superiority in microbiologic cure for patients with cUTI at the test-of-cure visit compared to meropenem, a gold standard for treating MDR infections, is impressive. Importantly, the safety profile of the drug looks favorable," said James A. McKinnell, Assistant Professor of Medicine at the David Geffen School of Medicine and LA Biomed at Harbor-UCLA. "The data from the CARE trial provides compelling evidence for plazomicin as a treatment option for serious infections due to CRE. The sample size for the CARE study was small, but the data show a clear trend in favor of plazomicin in terms of efficacy and overall safety compared to colistin. CRE infections cause serious morbidity and mortality and seem to be on the rise. Based on these data, plazomicin would be a valuable addition to my short list of available treatment options for both empiric and directed treatment of patients, and as a single agent or in combination with other antibiotics."

In the EPIC trial, plazomicin successfully met the objective of non-inferiority compared to meropenem for the FDA-specified primary efficacy endpoints, and achieved superiority for the EMA-specified primary efficacy endpoints.

Results for FDA pre-specified composite endpoint of clinical cure and microbiological eradication in the microbiological modified intent-to-treat (mMITT) population were as follows:

- Day 5: 88.0% plazomicin vs. 91.4% meropenem (difference -3.4%, 95% CI: -10.0, 3.1%), indicating statistical non-inferiority
- Test-of-Cure: 81.7% plazomicin vs. 70.1% meropenem (difference 11.6%, 95% CI: 2.7, 20.3%), indicating statistical superiority

Results for EMA-specified endpoints of microbiological eradication at the test-of-cure visit were as follows:

- mMITT: 87.4% plazomicin vs. 72.1% meropenem (difference 15.4%, 95% CI: 7.5, 23.2%), indicating statistical superiority
- ME: 90.5% plazomicin vs. 76.6% meropenem (difference 13.9%, 95% CI: 6.3, 21.7%), indicating statistical superiority

Phase 3 EPIC Trial in Patients with cUTI: Summary of FDA and EMA Primary Efficacy Endpoints
(* indicates statistical superiority)

	Plazomicin n/N (%)	Meropenem n/N (%)	Difference (%)[a] (95% CI)
Composite endpoint at Day 5, mMITT (FDA)	168/191 (88.0%)	180/197 (91.4%)	-3.4% (-10.0, 3.1%)
Composite endpoint at TOC, mMITT (FDA)	156/191 (81.7%)	138/197 (70.1%)	11.6% (2.7, 20.3%)*
Microbiological eradication at TOC, mMITT (EMA)	167/191 (87.4%)	142/197 (72.1%)	15.4% (7.5, 23.2%)*
Microbiological eradication at TOC, ME (EMA)	162/179 (90.5%)	134/175 (76.6%)	13.9% (6.3, 21.7%)*

CI: confidence interval; ME: microbiologically evaluable; mMITT: microbiological modified intent-to-treat; TOC: test-of-cure;[a] Difference = plazomicin minus meropenem

Plazomicin was well tolerated with no new safety concerns identified in the EPIC trial. Total treatment emergent adverse events (TEAEs) related to renal function were reported in 3.6% and 1.3% of patients in the plazomicin and meropenem groups, respectively. TEAEs related to cochlear or vestibular function were reported in a single patient in each of the plazomicin and meropenem treatment groups. Both events were considered mild and resolved completely.

In the Phase 3 CARE trial in patients with serious infections due to CRE a lower rate of mortality or serious disease-related complications was observed for plazomicin compared with colistin therapy.

Results from the CARE trial were as follows:

- Day 28 all-cause mortality or significant disease related complications (primary endpoint); 23.5% plazomicin vs. 50.0% colistin (difference 26.5%, 90% CI: -0.7, 51.2%)
- Day 28 all-cause mortality; 11.8% plazomicin vs. 40.0% colistin (difference 28.2%, 90% CI: 0.7, 52.5%)

Phase 3 CARE Trial in Patients with BSI or HABP/VABP due to CRE
(Cohort 1 mMITT population)

	Plazomicin n/N (%)	Colistin n/N (%)	Difference[a] (90% CI)	Relative Reduction
Day 28 all-cause mortality or significant disease-related complications	4/17 (23.5%)	10/20 (50.0%)	26.5% (-0.7, 51.2%)	53.0%
Day 28 all-cause mortality	2/17 (11.8%)	8/20 (40.0%)	28.2% (0.7, 52.5%)	70.5%

[a] Difference = colistin minus plazomicin

The safety profile of plazomicin was favorable to that of colistin in critically ill patients in the CARE trial. Study drug-related TEAEs related to renal function were reported in 16.7% and 38.1% of patients in the plazomicin and colistin groups, respectively. No TEAEs related to cochlear or vestibular function were reported in either group.

About the EPIC Trial
EPIC (**E**valuating **p**lazomicin **i**n **c**UTI) was a multinational, randomized, controlled, double-blind clinical trial in adult patients with complicated urinary tract infections (cUTI) and acute pyelonephritis (AP). The trial enrolled 609 patients who were randomized 1:1 to receive plazomicin 15 mg/kg as a once daily 30-minute intravenous (IV) infusion or meropenem 1.0 gram every 8 hours as a 30 minute IV infusion. After a minimum of 4 days of IV therapy, patients who met protocol-defined criteria for improvement were allowed to step-down to oral levofloxacin to complete a total of 7 to 10 days of therapy (IV plus oral).

About the CARE Trial

CARE (**C**ombating **A**ntibiotic **R**esistant **E**nterobacteriaceae) was a multinational, open label, Phase 3 clinical trial evaluating the efficacy and safety of plazomicin in patients with serious bacterial infections due to CRE. The study included two cohorts of patients. Cohort 1 (N=39) was a randomized, comparator-controlled cohort to compare plazomicin with colistin (either in combination with meropenem or tigecycline) for the treatment of bloodstream infection (BSI), hospital acquired bacterial pneumonia (HABP) or ventilator associated bacterial pneumonia (VABP) due to CRE. Cohort 1 enrolled 30 patients with BSI and 9 patients with HABP/VABP. Cohort 2 (N=30) was a single-arm expanded access cohort to evaluate plazomicin-based therapy in patients with BSI, HABP/VABP or cUTI due to CRE who were not eligible for enrollment in Cohort 1.

The primary analysis for Cohort 1 was conducted in the mMITT population (patients with confirmed CRE infection) and was defined as all-cause mortality at Day 28 or significant disease related complications. Due to limitations of the small sample size, no formal statistical hypothesis testing was performed, but a two-sided 90% exact confidence interval is provided to describe the degree of variability around the observed differences.

Conference Call
The Company will host a conference call today, December 12, 2016 at 8:30 a.m. EST/5:30 a.m. PST. To participate by telephone, please dial 888-857-6929 (domestic) or 719-325-2328 (international). The conference ID number is 1600601. A live and archived audio webcast can be accessed through the Investors section of the Company's website at www.achaogen.com. The archived audio webcast will remain available on the Company's website for 30 days following the conference call.

About Achaogen
Achaogen is a clinical-stage biopharmaceutical company passionately committed to the discovery, development, and commercialization of novel antibacterials to treat MDR gram-negative infections. Achaogen is developing plazomicin, Achaogen's lead product candidate, for the treatment of serious bacterial infections due to MDR Enterobacteriaceae, including carbapenem-resistant Enterobacteriaceae. Achaogen's plazomicin program is funded in part with Federal funds from the Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, under Contract No. HHSO100201000046C. Plazomicin is the first clinical candidate from Achaogen's gram-negative antibiotic discovery engine. Achaogen has other programs in early and late preclinical stages focused on other MDR gram-negative infections, including LpxC inhibitors for the treatment of serious bacterial infections including MDR gram-negative bacteria. Achaogen's LpxC inhibitor program has been funded in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN272201500009C. LpxC inhibitors are the second class of molecules from Achaogen's gram-negative antibiotic discovery engine. For more information, please visit 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's plan to submit an NDA to the FDA in the second half of 2017, Achaogen's plans to submit an MAA to the EMA in 2018, Achaogen's expectations regarding whether the full CARE trial results will be submitted as supportive data with the plazomicin NDA submission and Achaogen's plan to publicly present detailed results from both the EPIC and CARE trials in 2017. 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 uncertainties inherent in the preclinical and clinical development process; the risk of failure to successfully validate, develop and obtain regulatory clearance or approval for an *in vitro* diagnostic (IVD) assay for plazomicin; the risks and uncertainties of the regulatory approval process; the risks and uncertainties of commercialization and gaining market acceptance; the risk that bacteria may evolve resistance to plazomicin; risks and uncertainties as to Achaogen's ability to raise additional capital to support the development and potential commercialization of plazomicin and its other programs; uncertainties regarding the availability of adequate third-party coverage and reimbursement for newly approved products; Achaogen's reliance on third parties to conduct certain preclinical studies and all of its clinical trials; Achaogen's reliance on third-party contract manufacturing organizations to manufacture and supply its product candidates and certain raw materials used in the production thereof; Achaogen's dependence on its President and Chief Executive Officer; risks and uncertainties related to the acceptance of government funding for certain of Achaogen's programs, including the risk that BARDA could terminate Achaogen's contract for the funding of the plazomicin development program; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, and its Annual Report on Form 10-K for the fiscal year ended December 31, 2015. 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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