

Achaogen, Inc.

Second-Quarter Financials Non-event; Phase III CARE Study Awaiting First Patient; Phase II Supportive Study Next

On Monday, August 11, after markets closed, Achaogen reported second quarter 2014 financial results (exhibit 1, on page 4). The company ended the second quarter with \$74.5 million in cash; we estimate the current cash, which includes cash resources from BARDA (Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services), should sustain operations through the data readout from the Phase III CARE study expected in first half 2017. Net loss for the quarter was \$3.6 million with a per share loss of \$0.20 versus our estimates of \$3.5 million and \$0.19, respectively. We updated our model as illustrated in exhibit 1.

Following certain operational setbacks experienced during the second quarter, Achaogen is ready to enroll the first patient for the Phase III CARE (Combating Antibiotic-Resistant Enterobacteriaceae) study, to be conducted throughout the United States, Europe, Asia, and South America. The top-line data is still expected during first half 2017, as previously guided. The Phase III CARE study will evaluate the company's lead asset, plazomicin, for the treatment of bloodstream infections and pneumonia caused by carbapenem-resistant Enterobacteriaceae (CRE). Although recruitment was originally planned to begin in the second quarter, issues arose with obtaining approvals for some clinical sites in the United States and Europe, and technical problems hindered the activation of testing laboratories employed to measure plazomicin concentration in patients' blood samples. By now the operational issues have been resolved. Management expects to make up for lost time during the enrollment period by setting up additional clinical sites and optimizing the activation process for testing laboratories; management also continues to anticipate all clinical and testing sites worldwide to be operational by first quarter 2015 and top-line data to be available by the previously stated first half 2017. An announcement will be made once the first patient has been enrolled.

This is the first pathogen-specific pivotal study that strives for superiority in overall survival as the primary endpoint. We believe that if such a label is obtained, plazomicin would be favored over other antibiotics against CRE and command premium pricing.

- Phase III CARE study design.** The 360-patient, randomized, open-label study compares efficacy and safety of plazomicin against colistin in patients with bloodstream infections (BSIs) or hospital-acquired pneumonia resulting from CRE versus standard of care. Patients who are infected with either presumed or confirmed pathogen who exhibit MIC of 4 µg/mL or greater against the broadest-spectrum carbapenems will be enrolled and randomized 1:1 to either the plazomicin- or colistin-based regimen. Patients are allowed one adjunctive antibiotic, either tigecycline or meropenem, at the time of randomization, at the discretion of the investigator. The treatment duration is 7 to 14 days. All-cause mortality, the primary endpoint, will be assessed at day 28, and late safety follow-up is planned at day 60. Secondary endpoints include time to death, microbiological and clinical responses, resolution of fever, and improvement in oxygenation for pneumonia patients, safety, and pharmacoeconomic assessments. The study includes two unblinded interim analyses of efficacy and futility; the two interim analyses are to occur when 33% and 67% of patients have reached day 28 (the end of the study), projected to occur at the end of 2015 and the end of 2016, respectively. Top-line data is expected in first half 2017.

Achaogen, a biopharmaceutical company based in South San Francisco, California, focuses its research-and-development efforts on novel antibacterials to treat multi-drug-resistant, Gram-negative infections.

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August 12, 2014

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: \$25.00

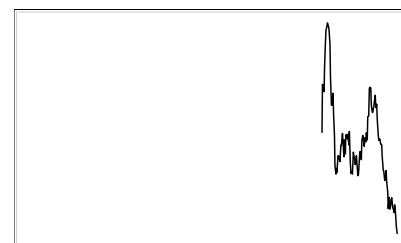
Symbol: AKAO (NASDAQ)
Price: \$10.14 (52-Wk.: \$9-\$20)
Market Value (mil.): \$179
Fiscal Year End: December
Long-Term EPS Growth Rate:
Dividend/Yield: None

	2013A	2014E	2015E
Estimates			
EPS Q1	NA	A\$-1.00	NA
Q2	NA	A\$-0.20	NA
Q3	NA	\$-0.20	NA
Q4	NA	\$-0.21	NA
FY	\$-1.36	\$-1.00	\$-0.68
CY		\$-1.00	\$-0.68
Sales (mil.)	NA	22	24
Valuation			
FY P/E	NM	NM	NM
CY P/E		NM	NM

Trading Data (FactSet)	
Shares Outstanding (mil.)	3
Float (mil.)	6
Average Daily Volume	101,239

Financial Data (FactSet)	
Long-Term Debt/Total Capital (MRQ)	0.0
Book Value Per Share (MRQ)	4.5
Return on Equity (TTM)	0.0

Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

Next event: Initiation of the supportive Phase II study; top-line results expected by late 2015 could act as significant catalyst for plazomicin program, in our opinion. Management plans to initiate two additional confirmatory studies for plazomicin over the next 18 months. The first study will be a single-arm, open-label study investigating the effects of plazomicin on CRE infections in 50 patients. The study will provide additional safety and efficacy support based on clinical and microbiological outcomes, but not survival endpoints. The study will begin in late 2014 with top-line data expected in fourth quarter 2015. We believe the goals of the study are several: 1) the 50 patients will constitute part of plazomicin's overall safety database; 2) the study plans to enroll a broader CRE patient population, including patients with cUTI, cIAI (complicated intra-abdominal infections), and colistin-resistant infections in addition to the BSI and pneumonia eligible for the Phase III study, so as to gain broader experience of plazomicin in various CRE infections; 3) successful data in late 2015 could generate excitement, boost confidence, and help accelerate enrollment in the Phase III CARE study; and 4) successful data could also serve as potential supportive data should Achaogen request Breakthrough Therapy designation for plazomicin for the treatment of CRE. As a result, we believe results from the Phase II supportive study are a significant catalyst for the plazomicin program in late 2015.

Key catalysts spread out in the coming years should continue to drive awareness of plazomicin. Achaogen has devised an efficient registrational strategy to quickly push plazomicin to market. Top-line data from the Phase III CARE study are expected in 2017; however, two interim analyses expected in second half 2015 and second half 2016 will act as key catalysts over the next several years along with top-line data from the Phase II supportive study by the end of 2015. Regulatory filing for plazomicin is expected in second half 2017, and we anticipate U.S. approval by the FDA during second half 2018. We illustrate plazomicin's development timeline in exhibit 3, on page 5.

We maintain our Outperform rating and \$25 price target (exhibit 2, on page 4). Our Outperform rating is centered on our belief that Achaogen's lead asset, plazomicin, will become the standard of care for the treatment of BSIs and pneumonia caused by CRE infection, and could generate peak worldwide sales of \$370 million by 2028. In our probability-adjusted NPV model, we expect plazomicin to reach the market by 2018 and become the market leader in the treatment of CRE infections. We assume peak penetration of plazomicin at about 70%, both in the United States and in Europe, based on our expectation that plazomicin obtains a favorable label regarding superiority in survival benefit for the indication. We assume plazomicin will be priced at \$16,000 and \$14,000 per course of therapy at launch in the United States and Europe, respectively. We therefore derive U.S. peak sales of about \$290 million in 2031 and about \$100 million in Europe in 2028, with peak worldwide sales of roughly \$370 million in 2028. We assign plazomicin \$22 per share in valuation, with \$16 associated with its commercial prospects in the United States and \$6 in Europe. Combining our valuation for plazomicin with net cash of approximately \$4 per share at the end of 2014, we derive our 12-month price target of \$25.

Potential sources of upside to our revenue estimates include: 1) empirical use of plazomicin, which could add an additional \$100 million in sales in 2028; 2) upside to net U.S. pricing; and 3) sales of plazomicin in territories outside the United States and Europe.

Key risks to our Outperform rating and price target include: 1) Phase III study assumptions are based on a meta-analysis of mortality in patients with carbapenemase-producing Enterobacteriaceae (CPE) in addition to in vitro and in vivo animal studies; 2) no prior study has been conducted on the effects of plazomicin in patients with CRE-related BSIs or pneumonia; 3) serious adverse events may increase with exposure; 4) enrollment is hard to track and estimate because the target population is rare; 5) the CRE market may be smaller than expected and may be difficult to penetrate; 6) a companion diagnostic from ARK Diagnostics is required that must also receive regulatory approval; 7) if highly priced, reimbursement may be difficult or hindered; and 8) financing risk exists.

Review of Key Points From Phase III CARE Study

While we believe plazomicin is a viable antibiotic for the treatment of CRE, several arguments must be taken into consideration when assessing its overall likelihood of success. Several of our rationales for assigning the program a 70% probability of success include:

- ***The potency of plazomicin in CRE is based on in vivo and in vitro studies, as discussed above; translation to humans is predicted but needs to be demonstrated.*** While plazomicin is comparable with levofloxacin for safety and efficacy in cUTIs, there are no prior dedicated studies investigating the effects of plazomicin in CRE. Although we are relatively confident that efficacy of antibacterials generally translates from in vivo models to the clinic, it still needs to be demonstrated in this case. We note that Achaogen will initiate a supporting single-arm Phase II study in CRE in late 2014 and data should read out in late 2015. This study should provide the first data on plazomicin's activity in CRE and, if successful, should create heightened excitement and confidence in the ongoing Phase III CARE study.

- **Phase III enrollment is projected to take three years, but the emerging epidemiology is a moving target.** The incidence of CRE has been increasing over the past few years, especially in certain hotspot areas; however, the exact timeline of enrollment is difficult to predict as the epidemiology data is still developing.
- **The statistical assumptions for the Phase III study are based on a meta-analysis of three observational studies.** There is limited data in literature on mortality rates from CRE and as discussed in detail herein, the Phase III study is based on a meta-analysis describing mortality outcomes from 309 patients infected with carbapenemase-producing Enterobacteriaceae. The meta-analysis classified outcomes of these patients into two groups: resistant or sensitive to carbapenems, and observed that the absolute mortality difference between the two groups was 21% (60% relative difference). Based on such data, the underlying assumption for the CARE study is that plazomicin treatment should afford patients a similar mortality benefit to those in the sensitive group in the meta-analysis, which is a 21% absolute mortality reduction from the current standard of care.
- **Although the Phase III study is based on a meta-analysis, a margin of safety is built in, thereby increasing the probability of success, in our opinion.** The Phase III study is powered at 70% to detect an absolute reduction in mortality of 12% (35% relative reduction). This assumption appears conservative as compared with the observed mortality reduction of 21% (60% relative reduction) demonstrated by the meta-analysis. This difference allows for a reasonable margin of safety, thus increasing the probability of success, in our opinion.
- **Interim analyses are built in to provide a potential opportunity to adjust sample size if necessary, ensuring power of the study.** There will be two unblinded interim analyses occurring when 33% and 67% of the patients in the study have reached day 28 (the end of the study). A data monitoring committee will review the data and determine if the study should be stopped based on efficacy or futility. These interim analyses might also help determine whether more patients will need to be enrolled to ensure power of the study.
- **A companion diagnostic will be employed to ensure plazomicin plasma and lung concentration reaches bactericidal levels, thereby ensuring maximum efficacy in every patient.** Since plazomicin is renally excreted, dosing will be individually optimized using a diagnostic to ensure sufficient drug plasma and lung concentration to combat infections. Pharmacometric modeling developed at Achaogen predicts that 92% of patients should be able to achieve sufficient drug levels in the blood or the lung that are effective against their CRE infection.
- **Phase III study is enriched with patients who will most likely see a mortality benefit from plazomicin treatment.** To better assess mortality in terms of disease severity, all patients will be evaluated using the APACHE II score, which ranges from 0 to 71, with 71 being most severe. Enrolled patients will have APACHE II scores ranging from 15 to 30. We highlight this because it ensures that enrolled patients are neither too healthy nor too sick, increasing the odds of demonstrating a mortality benefit.
- **The safety profile remains to be evaluated when used for a longer duration of treatment in a sicker patient population.** While the Phase II study in cUTI demonstrated a safe and tolerable profile for 5 days of treatment, the safety profile needs to be further evaluation in the Phase III study where treatment duration is increased to 7-14 days, and the patient population is much sicker. Undoubtedly, the risk/benefit profile will be different in this sicker population, with patients and regulators willing to accept greater risk if a significant mortality benefit is demonstrated.
- **High risk, high reward: The primary endpoint of mortality is bold and novel to antibiotics.** Unlike other antibiotics, the registrational trial will strive for superiority in survival. Should such a label be obtained, plazomicin should be preferentially used in the labeled indication, and command premium pricing, in our opinion.

Exhibit 1
Achaogen, Inc.
Income Statement
(dollars in thousands)

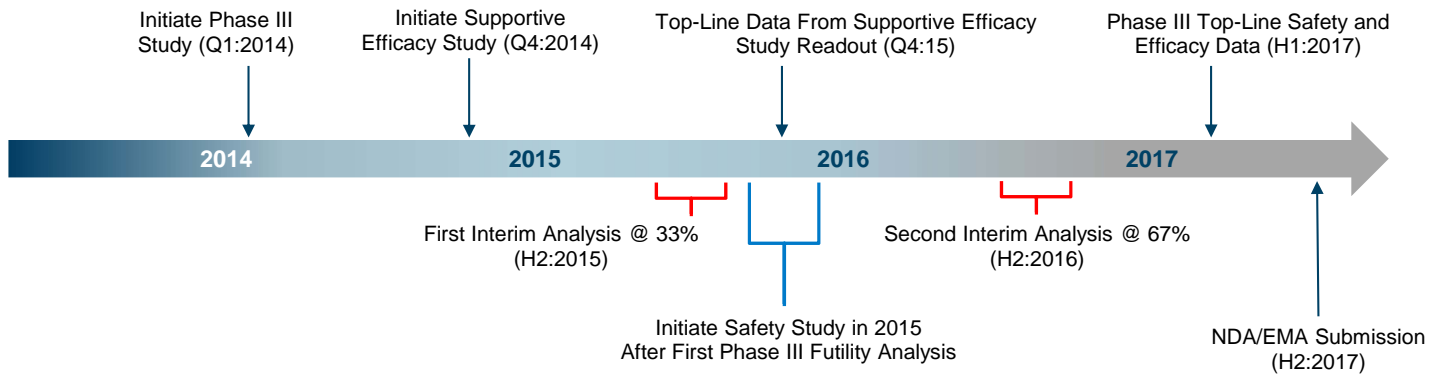
	2012A FY:12A	2013A FY:13A	2014E					2015E	2016E
			Q1A	Q2A	Q3E	Q4E	FY:14E	FY:15E	FY:16E
Revenues									
Plazomicin US revenues	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Plazomicin OUS royalties	-	-	-	-	-	-	-	-	-
Collaboration and licensing revenue	-	-	-	-	-	-	-	-	-
Contract and grant revenue	17,941	18,512	5,988	5,203	5,203	5,203	21,597	24,000	24,000
Total Revenues	17,941	18,512	5,988	5,203	5,203	5,203	21,597	24,000	24,000
Expenses									
COGS	-	-	-	-	-	-	-	-	-
R&D expense	26,581	23,484	6,605	6,195	6,257	6,320	25,376	26,042	27,097
SG&A expense	7,349	6,992	2,617	2,346	2,369	2,393	9,726	10,203	11,038
Total Operating Expenses	33,930	30,476	9,222	8,541	8,626	8,713	35,102	36,245	38,135
Operating Income	(15,989)	(\$11,964)	(3,234)	(3,338)	(3,423)	(3,510)	(13,505)	(12,245)	(14,135)
Interest income	51	193	-	-	74	71	146	256	389
Interest expense, net	(2,427)	(1,341)	(221)	(217)	(217)	(217)	(872)	(231)	-
Other (expense) income, net	-	-	-	-	-	-	-	-	-
Total Other Income (Expense)	(18,365)	(13,112)	(3,455)	(3,555)	(3,566)	(3,656)	(14,231)	(12,220)	(13,746)
Pretax income/(loss)	(18,365)	(13,112)	(3,455)	(3,555)	(3,566)	(3,656)	(14,231)	(12,220)	(13,746)
Other comprehensive gain/(loss)	-	-	-	-	-	-	-	-	-
Provision for income taxes/(income)	-	-	-	-	-	-	-	-	-
Net Income/(Loss)	(\$18,365)	(\$13,112)	(\$3,455)	(\$3,555)	(\$3,566)	(\$3,656)	(\$14,231)	(\$12,220)	(\$13,746)
GAAP EPS		(\$1.36)	(\$1.00)	(\$0.20)	(\$0.20)	(\$0.21)	(\$1.00)	(\$0.68)	(\$0.66)
Weighted average shares outstanding, diluted		9,673	3,456	17,691	17,741	17,791	14,170	17,978	20,966

Sources: Achaogen, Inc. and William Blair & Company, L.L.C. estimates

Exhibit 2
Achaogen, Inc.
Sum-of-the-Parts Fair Value
(dollars in thousands, except shares)

Drug	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value per Share	Percentage of Fair Value
Plazomicin—United States	\$289,456	Phase III	H2:2018	70%	100%	\$285,934	\$15.94	63.0%
Plazomicin—Europe	\$99,128	Phase III	H1:2019	70%	30% Royalty	\$109,419	\$6.10	24.1%
Subtotal						\$395,353	\$22.04	87.0%
Net Cash at Mid-year 2015						\$63,866	\$3.56	14.1%
Net Present Value of additional Gain (Loss)*						(\$5,000)	(\$0.28)	(1.1%)
Sum-of-Parts Fair Value						\$454,219	\$25.32	100.0%

Exhibit 3
Achaogen, Inc.
Plazomicin Development Timeline



Sources: Achaogen, Inc. and William Blair & Company, L.L.C.

William Blair & Company, L.L.C.

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William Blair is a market maker in the security of Achaogen, Inc. and may have a long or short position.

William Blair intends to seek investment banking compensation in the next three months from Achaogen, Inc.

Within the past 12 months William Blair has provided or is providing investment banking services to or has an investment services relationship with Achaogen, Inc.

Additional information is available upon request.

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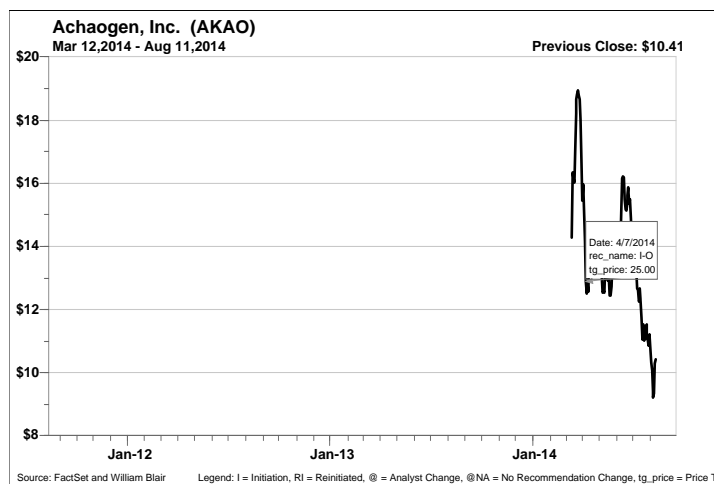
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DOW JONES: 16,569.98

S&P 500: 1,936.92

NASDAQ: 4,401.33



Current Rating Distribution (as of 07/31/14)

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	66	Outperform (Buy)	16
Market Perform (Hold)	31	Market Perform (Hold)	3
Underperform (Sell)	1	Underperform (Sell)	0

*Percentage of companies in each rating category that are investment banking clients, defined as companies for which William Blair has received compensation for investment banking services within the past 12 months.

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