

Initiation of Coverage October 30, 2014 BIOTECHNOLOGY

Equity Research

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# Achaogen, Inc. (AKAO-\$9.54)

**Rating: BUY** 

Target Price: \$13.00

# **Initiating Coverage with a BUY Rating and \$13 Price Target**

EPS	1Q	2Q	3Q	4Q
2013A	—	—	—	—
2014E	(1.00)A	(0.20)A	(0.17)E	(0.18)E
2015E	—	—	—	—
REV	1Q	2Q	3Q	4Q
2013A	—	—	-	—
2014E	6.0A	5.2A	5.5E	5.5E
2015E	—	—	-	—
FY	2013A	2014	E 20	015E
EPS	(33.83)A	(0.90		08)E
P/E	(0.3)x	(10.6		3.8)x
REV	18.5A	22.2F		0.0E
P/S	9.1x	7.6x		4x

We are initiating coverage of Achaogen (AKAO) with a BUY rating and a \$13 price target, based on Plazomicin's expected revenues of \$160M worldwide in 2025. AKAO has initiated a phase 3 trial to support approval in both pneumonia and bloodstream infection, which we expect to read out in 1H17. We forecast commercial launch of Plazomicin in 2018. Beyond Plazomicin, AKAO has preclinical assets, including an LpxC inhibitor, which we have not factored into our valuation but are a source of additional upside potential to our valuation.

- Gram-Negative Antibiotic, Plazomicin, meets a growing medical need. While the rise of MRSA has received attention from the press, the CDC reports that multidrug resistance in Gram negative bacteria, which are present in ~62% of all infections, is also growing among key members of the class. Plazomicin is a next generation aminoglycoside, designed to avoid the enzymatic modifications that are the primary cause of aminoglycoside resistance. Plazomicin has potency against multidrug resistant Gram-negative bacterial strains, which we expect to initially be reserved cases, and will likely be used empirically for bloodstream infections to generate, in our estimation, \$160M in 2025 worldwide sales.
- Plazomicin Synergizes with Other Antibiotics, Increasing the Appropriateness of Treatment. Infections are often treated empirically, and increasingly it is becoming common to use a combination of antibiotics to maximize both the bacterial and resistance spectra. Plazomicin has been shown to synergize with commonly used antibiotics (e.g., Inipenem and Cefepime), demonstrating bacteriacidal activity even at sub-MIC levels of both drugs. We believe this approach will both lower potential toxicities and increase the barrier to resistance development, by preventing evasion by only a single mutation.
- Robust Preclinical Pipeline of Novel Antibacterics. Antibiotic development has focused on modifying only a few known classes of drug in order to overcome resistance. In preclinical development, Acheogen has an antibacterial antibody and a LpxC inhibitor. Both these assets, we believe, have novel mechanisms of action, raising the hurdle for resistance, though they have also been untested in the clinic. Due to the early stage of these programs, they are not reflected in our valuation but are a source for potential upside.

#### **Current Statistics**

Market Cap (\$Mil)	\$169.0	
Avg. Daily Trading Volume (3 mo.):	61,215	
Shares Out (Mil):	17.710	

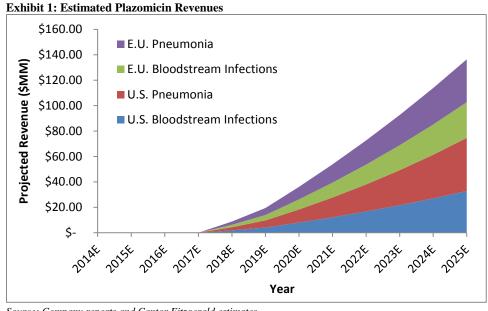


#### **Summary**

We are initiating coverage of Achaogen, Inc. (AKAO) with a BUY rating and \$13 price target.

Achaogen's Gram-Negative Antibiotic, Plazomicin, Meets a Growing Medical Need. A 2010 analysis by Hamad et al estimated that the worldwide antibiotic market is growing at 4% annually, with ~\$42 billion revenue in 2009. This revenue has been derived from heavy prescription levels, with the CDC reporting as many as 258 million scripts in the U.S. alone in 2012. This overprescribing often results in the unnecessary use of antibiotics, which has caused the rise of resistant bacteria. The CDC estimates that antibiotic-resistant pathogens caused >2,000,000 infections in 2013 and resulted in ~23,000 deaths in the United States. Gram-negative bacteria account for ~62% of all infections, and in the CDC's monitoring of the ICU infections, growing antibiotic resistance in key members of this class were observed (on average 13% of *E. coli* and *Klebsiella*, 17% of *P. aeruginosa*, and 74% of *A. baumannii* are multidrug-resistant). Plazomicin is a next-generation aminoglycocide with potency against multidrug-resistant, Gram-negative bacterial strains, which we expect to initially be reserved for cases that have failed other treatment.

Achaogen is developing Plazomicin to target treatment of blood stream infection and pneumonia, which we believe have a combined incidence of 110K patients in the United States and European Union. Treatment of infection is typically done empirically (i.e., prior to a firm diagnosis), with physicians prescribing a broad-spectrum antibiotic, as the delay involved in obtaining laboratory confirmation of the diagnosis could prove harmful to the patient. As with other bacterial infections, resistant bacteria have increased in prevalence in blood stream infection and with a mortality rate that can exceed 30%. The average weighted incremental cost of treating blood stream infections has been estimated at \$10-20K, with resistant infection potentially exceeding that range. Management has suggested that \$15,000 for a course of treatment would not be unreasonable, given the life threatening nature of bloodstream infections and pneumonia as well as the costs associated with these infections. We do not believe hospitals will be willing to routinely accept this high premium (newly approved Dalvance costs ~4,500/course) but expect the drug to be adopted as a drug of last resort and potentially generate sales of \$160M worldwide in 2025.



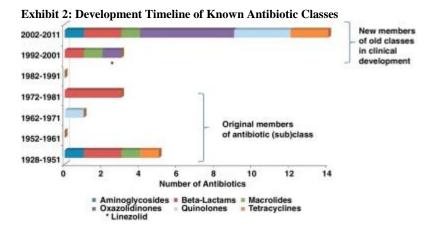


Plazomicin Synergizes with Other Antibiotics, Increasing the Appropriateness of Treatment. Bloodstream infections are a life-threatening condition with a mortality rate that exceeds 30%. Death occurs through development of sepsis and organ failure. Retrospective analysis suggest early and appropriate treatment can cut the mortality rate nearly in half, and physicians often place patients on drugs empirically rather than delay waiting for laboratory tests.

Patients tend to be given broad spectrum antibiotics empirically, to reduce the chance of inappropriate treatment being given. Patients can be cycled through sequential monotherapies with unresponsiveness, whether due to resistance or incorrect specificity. Treatment guidelines of the Infectious Disease Society of America recommend antibiotic combinations as a potential regimen, which we believe has advantages over monotherapy. In our opinion, combination treatment allows greater spectrum, lower individual dose of each drug, potentially lowering adverse events, and a higher bar to resistance development, requiring multiple escape mutations.

During in vitro studies of Plazomicin in combination with other known antibiotic classes, it acted synergistically against both MRSA and Pseudomonas, and we believe Plazomicin will be readily adopted for bloodstream infections as part of treatment cocktails.

Robust Preclinical Pipeline of Novel Antibacterialseve. Drug developers and bacteria are locked in an eternal dance, with a constant need for new antibiotics to reach the market as bacteria develop resistance to the current drugs. The development of antibiotics though has been dominated by only six classes since the discovery of penicillin in 1928 by Alexander Flemming ushered in the antibiotic age. These drugs tend to be very complex, requiring the core structure be produced by fermentation with only limited potential semisynthetic modificiation. We believe the only incremental changes made during each generation of development are easily surmounted by incremental mutation in existing resistance mechanisms and new drugs with truly novel mechanisms of action are needed.



Source: current opinions in Pharmacology

Achaogen has two assets in preclinical development, which we believe have novel mechanisms. The first of these is a monoclonal antibody, which normally acts by either opsinizing the invading bacteria for more efficient phagocytosis or neutralization of the toxins produced by the bacteria. Achaogen is attempting to generate antibodies which will exert antibiotic-like properties. The second asset is an inhibitor of the LpxC enzyme, which is vital for the second and committed step in lipid A biosynthesis. In Gram negative bacteria, lipid A provides the anchor outer membrane lipopolysaccharide. While not conserved across all Gram-negative bacteria, the structure of LpxC does shared enough homology that these inhibitors show broad potentcy, and we believe will expand the armamentarium with a new class of antibiotic.



### **Industry Overview**

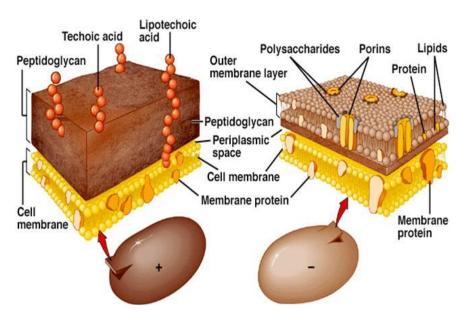
#### **Antibiotic Development and Resistance**

In the course of our lives, we coexist with countless bacteria, many of which are beneficial to us. Our microbiome is kept in check by both the interaction of component organisms and our immune systems. When these checks break down and bacteria invade tissue, this is considered an infection, and is classified according to the tissues affected, as well as the severity. While the invading bacteria may produce toxins, which cause tissue necrosis, many of the symptoms associated with infection are the result of one's body mounting an active immune response, namely coughing and sneezing, fever, inflammation, vomiting, diarrhea, fatigue, and cramping. If not treated, the infection can spread to other tissues and, by causing a cytokine storm, possibly result in multiple organ failure and death.

In the human gut alone, greater than 1,000 species of bacteria have been identified, and it is these enteric organisms which often are responsible for infection of the intestinal tract or hepatobiliary tree (i.e., intra-abdominal infection), kidneys, bladder, ureter, or urethra (i.e., urinary tract infection). At the very top level, bacteria can be divided into two classes: Gram-positive and Gram-negative, based their ability to bind crystal violet dye—the former retains the dye due to the presence of a high percentage of peptidoglycans in the cell wall. Antibiotics such as vancomycin, which inhibit peptidoglycan synthesis, cause bacteriostasis in Gram-positive strains by substantially weakening the cell wall, but Gram-negative bacteria have far less peptidoglycan in their cell walls, rendering them far less susceptible.

Exhibit 3: Difference in Bacterial Membranes

Gram Positive Gram Negative



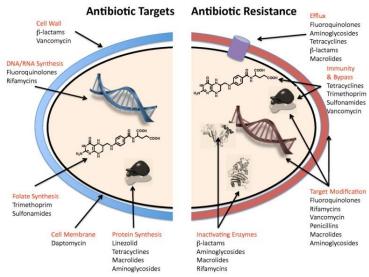
Source: Medimoon

Bacterial peptidoglycan synthesis is not the only pathway targeted—other classes of antibiotics target replication, protein synthesis, and cell membrane integrity. Some targets, such as inhibition of the ribosome to prevent protein synthesis, are common between Gram-positive and Gram-negative strains, and these agents are considered broad spectrum. Other targets, predominantly associated with the cell wall, are only active in a single bacterial strain or class of bacteria, making them narrow spectrum. In general, the in vivo efficacy of an antibiotic is strongly correlated with the in vitro potency and, if the drug shows a favorable tissue distribution, human trials are conducted largely to demonstrate safety.



Drug developers and bacteria are locked in an eternal dance, with a constant need for new antibiotics to reach the market as bacteria develop resistance to the current drugs. Inappropriate use of antibiotics might hasten the increase in prevalence of resistant strains, but selective pressure caused by the use of any antibiotic will produce resistance. Bacterial resistance can arise through three principal mechanisms: 1) mutation of the target can reduce the efficacy of a drug by preventing physical binding, 2) upregulation of efflux pumps lowers intracellular concentrations below the inhibitory levels, or 3) detoxification of the drug through covalent modification by intracellular enzymes. These mechanisms can arise spontaneously though random mutation, but bacteria are also able to transfer genetic material in the form of plasmids, which allows resistance, once established, to spread rapidly between strains.

**Exhibit 4: Antibiotic Targets and Resistance** 



Source: BMC Biology

#### **Commercial Landscape**

The serendipitous discovery of penicillin by Alexander Fleming ushered in the modern era of antibiotic treatment, which in 2009 had reached ~\$42 billion in worldwide sales, with blockbusters such as Zyvox recording annual revenues >\$1 billion worldwide. Only half of the antibiotics approved during the last 15 years have efficacy against Gram-negative bacteria, and the majority of those have been either fluoroquinolones or carbapenems, which have growing resistant populations.

**Exhibit 5: Antibiotics Approved Within the Last 15 Years** 

Drug	Comon name	Class	Company	Bacteria type	Dosing	Effect	Approval	
Priftin	Rifapentine	Rifamycin	Sanofi	TB	Oral	Bactericidal	1998	
Synercid	Quinupristin/dalfopristin	Combination	Pfizer	G+ve	IV only	Bactericidal	1999	
Avelox	Moxifloxacin	Fluoroquinolone	Bayer	G+ve/G-ve	IV/Oral	Bacteriostatic	1999	
Tequin	Gatifloxacin	Fluoroquinolone	BMY	G+ve/G-ve	IV/Oral	Bacteriostatic	1999 (withdrawn)	
Zyvox	Linezolid	Oxazolidinone	Pfizer	G+ve	IV/Oral	Bacteriostatic	2000	
Spectracef	Cefditoren pivoxil	Chephalosporin	Cornerstone	G+ve/G-ve	Oral Bacteriosta		2001	
Invanz	Ertapenem	Carbapenem	Merck	G+ve/G-ve	IV only	Bacteriostatic	2001	
Factive	Gemifloxacin	Fluoroquinolone	Oscient	G+ve/G-ve	IV/Oral	Bacteriostatic	2003	
Cubicin	Daptomycin	Lipopeptide	Cubist	G+ve	IV only	Bactericidal	2003	
Ketek	Telithromycin	macrolide	Sanofi	G+ve/G-ve	Oral	Bactericidal	2004	
Tygacil	Tigecycline	Tetracycline	Merck	G+ve/G-ve	IV only	Bacteriostatic	2005	
Altabax	Retapamulin	Pleuromutilin	GSK	G+ve	Topical	Bacteriostatic	2007	
Doribax	Doripenem	Carbapenem	JNJ	G+ve/G-ve	IV only	Bactericidal	2007	
Vibativ	Telavancin	Glycopeptide	Theravance	G+ve	IV only	Bactericidal	2009	
Dificid	Fidaxomicin	Tiacumicin	Cubist	G+ve	Oral	Bactericidal	2011	

Source: Journal of Antibiotics



New drugs constantly need to reach market, as the development of resistant strains renders approved drugs ineffective. Developmental pipelines have dried up, however, and there are currently only four assets in development for Gram-negative infections. Two of these clinical assets—Cubist's ceftolozane/tazobactam and AstraZeneca's ceftazidime/avibactam—utilize a cocktail comprised of a cephalosporin and a beta-lactamase inhibitor, reducing the number of distinct classes being developed. Eravacycline, we believe, is unique within the pipeline, being the only asset with an oral dosing option. Aminoglycocides are often synergistic with other classes of antibiotics such as  $\beta$ -lactam or tetracycline, and we expect plazomicin to not compete with these other assets in development but rather to be used in combination with these other assets.

**Exhibit 6: Late-Stage Gram Negative Antibiotics** 

	0 0			
Company	Tetraphase Cubist		Actavis/ AstraZeneca	Achaogen
Drug	Eravacycline	Ceftolzane/ tazobactam	Ceftazidime/ avibactam	plazomicim
Drug Class	Tetracycline	Cephalosporin/ β-lactamase inhibitor	Cephalosporin/ β-lactamase inhibitor	Aminoglycoside
Dosing	BID oral/IV	TID IV	TID IV	IV
Clinical phase	Phase 3	Phase 3	Phase 3	Phase 3

Source: Company reports

### **Company Overview**

Achaogen, Inc., a clinical-stage biopharmaceutical company, is developing novel antibiotics for Gramnegative bacterial infections. The company's lead product is plazomicin, which has initiated phase 3 clinical trials for treatment of Multidrug resistant blood stream and pneumonia infections, including carbapenem-resistant Enterobacteriaceae. The company also has novel classes of antibiotics in preclinical development, including antipseudomonal drugs. The company, which was founded in 2002, is based in South San Francisco, CA and has 43 employees.

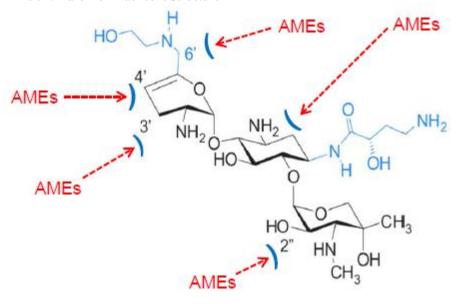
Achaogen currently has no source of revenue from the sale of any products, but will receive up to \$103M in contract revenue from BARDA. Plazomicin is a development-stage drug candidate and represents the company's first potential commercial asset. For the year ended December 31, 2013, Achaogen's net loss was approximately \$13.1M, and the company's cumulative net loss since inception through June 30, 2014, was \$135.7 million. We forecast that Achaogen will experience a loss of \$14.5M during FY:14. We expect AKAO to spend an additional \$92M in operating expenses through 2020, when we forecast AKAO will become profitable. Achaogen currently owns 100% of the commercialization rights to Plazomicin, which offers another potential source of financing through partnership.

#### **Plazomicin**

Aminoglycosides have been in use since 1943, when Streptomycin was isolated from the broth of Streptomyces. On a commercial basis, the full synthesis of the molecule is not viable and discovery of novel aminoglycosides has progressed though semi-synthesis, where the basic trisaccharide backbone structure is isolated from fermentation broth. Plazomicin is derived from sisomicin but 2 bulky side chains have been added to ring 1 and ring 2 to prevent the access of aminoglycoside modifying enzymes (AMEs) within the bacteria, which by covalently modifying the drug and altering its target binding, are the primary resistance mechanism.



**Exhibit 7: Plazomicin Backbone Structure** 



Source: Company reports

Achaogen licensed plazomicin from Isis in 2006 and is initially developing it for bloodstream infections and pneumonia, which we believe have incidence of 4.7M in the U.S. and E.U. Physicians typically initiate treatment of serious infections empirically, utilizing a broad spectrum antibiotic immediately before lab tests are able to characterize the pathogen. Aminoglycosides are often proscribed in cases of septicemia and with the higher resistance hurdle as well as synergy with existing antibiotic classes, we believe Plazomicin will enter the armamentarium as a drug of last resort, generating peak, 2025 revenues of \$160M worldwide.

We believe that for an antibiotic to be successfully developed, it needs to have high in vitro potency, pharmacokinetics allowing efficacious concentrations within the infected tissue, and a robust safety profile. Plazomicin has been tested against clinical isolates of Gram-negative and Gram-positive bacterial strains. Included in the panel were strains with known multidrug resistant S. aureus strains, which are of growing concern in the hospital setting. These preclinical studies compared plazomicin to approved aminoglycoside antibiotics. For the most part, plazomicin had similar or higher potency in this panel than the comparators. Despite P. aeruginosa being a notable example of plazomicin having reduced potency, we believe this profile suggests potential clinical efficacy as a monotherapy and the ability to be used interchangeably with any other aminoglycoside.



**Exhibit 8: In Vitro Plazomicin Potency** 

Organism	Isolates			MIC90	(μg/ml)		
Organism	เรบเลเตร	Plazomicin	Gentamicin	Tobramycin	Amikacin	Ciprofoxacin	Ceftazidime
E. coli	320	1	32	8	4	>16	1
K. Pneumoniae	108	0.5	≤0.5	≤0.5	≤1	0.25	0.5
E. cloacae	52	0.5	32	4	2	4	>32
S. marcescens	25	0.5	1	2	4	1	1
P. mirabilis	27	0.5	2	2	4	2	≤0.5
K. oxytoca	28	0.5	≤0.5	1	2	0.12	0.5
E. aerogenes	20	0.5	≤0.5	1	2	0.5	>32
P. aeruginosa	174	16	8	2	16	4	32
S. maltophilia	39	>64	>32	>32	>64	>16	>32
A. baumannii	5	0.5	0.5	0.5	1	0.25	8
S. aureus	367	1	≤0.5	1	4	2	16
MRSA	85	1	≤0.5	>64	32	>16	>32
S. epidermidis	33	8	>32	>32	16	>16	>32
E. faecalis	83	>64	>32	>64	>64	>16	>32

Source: Company reports

Physicians typically treat life threatening infections empirically, initiating treatment before lab tests confirm the nature of the infection. In a retrospective analysis of patients with blood stream infections, those treated early with appropriate antibiotics had a 20% mortality rate compared to 34% when inappropriate treatment was given. Use of antibiotic cocktails can broaden the active spectrum, increasing the likelihood of an appropriate treatment. Plazomicin, like other aminoglycides, synergizes well with existing classes of antibiotics in both multidrug resistant strains and also in Pseudomonas. We believe a combination drug strategy, in which plazomicin is a component, has many benefits over monotherapy, including lower individual drug levels, broader activity, and a potentially higher hurdle to resistance.

Exhibit 9: In Vitro Synergies of Plazomicin Against Pseudomonas

Exhibit 9: In Vitro Synergies of Plazomicin Against Pseudomonas											
	3 hr	6 hr	12 hr	24 hr							
		Cefepime	9								
Synergy	20%	72%	88%	80%							
Indifference	80%	28%	12%	20%							
Antagonism	0%	0%	0%	0%							
		Doripener	n								
Synergy	12%	72%	84%	80%							
Indifference	88%	28%	16%	20%							
Antagonism	0%	0%	0%	0%							
		Inipenem	1								
Synergy	44%	72%	80%	68%							
Indifference	56%	28%	20%	32%							
Antagonism	0%	0%	0%	0%							
	Pe	peracillin-tazo	obactam								
Synergy	24%	76%	84%	92%							
Indifference	76%	24%	16%	8%							
Antagonism	0%	0%	0%	0%							

Source: antimicrobial Agents and Chemotherapy



### cUTI Phase 2 Clinical Study:

Achaogen completed a phase 2 trial of plazomicin, testing two dosing regimens in complicated urinary tract infection (NCT01096849). The trial was a double-blind, active-comparator controlled, international study, randomizing patients to 10 mg/kg or 15 mg/kg QD IV plazomicin or 750 mg levofloxacin QD IV for 5 days. Specimens were collected and bacterial strains were isolated to determine the baseline characteristics. The primary endpoint of the study was microbiological eradication in both intent to treat and microbiologically evaluable population. Secondary endpoint will be investigator assessed clinical cure.

This phase 2 study demonstrated that plazomicin is at least as efficacious as levofloxacin in the treatment of cUTI. Urinary tract infections are predominately caused by Gram-negative bacteria (75-95% at baseline); however, often an infection is caused by multiple strains. Plazomicin and levofloxacin were used empirically, with plazomicin administered at either 10 mg/kg QD or 15 mg/kg QD IV. Both dose levels achieved rates of clinical cure equivalent to or greater than the active comparator (86%, 89%, and 81% for 10 mg/kg, 15 mg/kg plazomicin, and levofoxacin, respectively). We believe these data suggest broad efficacy, and—as aminoglycocides are not affected by extended spectrum beta-lactamases, which deactivate the penicillin, cephem, carbapenem, penem, and monobactam classes—has potential utility when resistant bacteria are suspected.

Exhibit 10: Phase 2 cUTI Trial Results

	Plaz	omicin	Levofloxacin							
	10mg/kg	15mg/kg	750mg							
MITT Population										
N	12.00	51.00	29.00							
Eradication	50%	61%	59%							
Non-eradication	8%	10%	14%							
Indeterminate	42%	29%	28%							
	ME Pop	ulation								
N	7	35	21							
Eradication	86%	89%	81%							
Non-eradication	14%	11%	19%							

Source: Company reports

Plazomicin is an aminoglycocide-class antibiotic and, as such, may cause adverse events common to this class, such as nephrotoxicity and odotoxicity. Overall, plazomicin is very well tolerated during the study, with GI and nervous system events being the most commonly cited. Both these nephrotoxicity and odotoxicity are related to duration as well as exposure, and by instituting a therapeutic drug management program, Achaogen believes they minimized this risk. In the phase 2 study of 96 patients dosed with plazomicin, mild tinnitus and dizziness was reported in two patients, which would be consistent with odotoxicity. While a future safety signal cannot be ruled out due to the small number of patients treated, we believe plazomicin is a safe and tolerable alternative to the currently used therapies.



Exhibit 11: Adverse Events Experienced by Plazomicin

Adverse event	Plazor	micin	Levofloxacin
Adverse event	10mg/kg (n=22)	15mg/kg (n=74)	750mg (n=44)
Any TEAE	31.8%	35.1%	47.7%
GI Disorders	18.2%	17.6%	11.4%
Diarrhea	0.0%	5.4%	4.5%
Nausea	0.0%	5.4%	0.0%
Vomiting	0.0%	5.4%	2.3%
General disorders	9.1%	1.4%	11.4%
Infections	0.0%	2.7%	13.6%
Metabolic disorders	0.0%	5.4%	4.5%
Nervous system disorders	9.1%	12.2%	13.6%
Dizziness	1.0%	5.4%	0.0%
Headache	9.1%	8.1%	6.8%
Respiratory disorders	9.1%	2.7%	2.3%
Skin disorders	9.1%	1.4%	4.5%

Source: Company reports

#### Phase 3 Study in Bloodstream and Pneumonia Infections.

Achaogen will also be conducting a phase 3 study in bloodstream infection or pneumonia (NCT01970371). This two arm, randomized, double blinded phase 3 trial will be conducted globally to assess the efficacy of plazomicin compared to a colistin-based regimen in patients suspected of being carbapenem-resistant. This study will enroll 360 total patients. This is a non-interiority study and the primary endpoints for this study will be all cause mortality at 28 days. Other secondary endpoints will be clinical response, PK, Safety and time to death. This study has not begun enrollment, and topline data is expected in 1H:17.

Exhibit 12: Design of Plazomicin Phase 3 Trial



Source: Company reports

## LpxC Inhibitor

In vitro potency is a strong predictor of in vivo efficacy for antibiotics. ACHN-975 has been tested against bioterror pathogens, where it demonstrated potency in some cases than currently used antibiotics. A phase 1 study of ACHN-975 was begun, but was discontinued due to Thrombophabitis at the injection site. Achaogen is performing preclinical studies on additional back up compounds to ACHN-975 and plans to move one of these leads into clinical development during 2015.



Exhibit 13: Activity of ACHN-975 Against Biothreats in vitro

B. mallei	ACHN-975	Azithromycin
MIC Range (μg/ml)	0.12 - 2	0.12 – 1
MIC <sub>50</sub>	0.5	0.5
MICon	1	1
B. pseudomallei	ACHN-975	Ceftazidime
MIC Range (µg/ml)	0.12 - 4	1 – ≥64
MIC <sub>50</sub>	1	2
MICon	2	4
F. tularensis	ACHN-975	Ciprofloxacin
MIC Range (μg/ml)	0.25 – ≥16	0.06 - 0.12
MIC <sub>50</sub>	0.5	0.008
MICon	2	0.25
Y. pestis	ACHN-975	Ciprofloxacin
MIC Range (μg/ml)	0.03 - 0.5	0.004 - 0.03
MIC <sub>50</sub>	0.25	0.015
MICon	0.5	0.015

Source: Company reports

### **Pipeline**

**Exhibit 14: Status of Achaogen's Clinical Programs** 

Preclinical Phase 1 Phase 2 Phase 3

Target: Carbapenem-Resistant Enterobacteriaceae (CRE)

# **Plazomicin**

Target: Pseudomonas Aeruginosa

**LpxC Inhibitors** 

Antibacterial Antibody

Target: Gram-negative bacteria

Discovery Engine

Source: Company reports



# Milestones

**Exhibit 15: Upcoming AKAO Milestones** 

Plazomicin	Indication/Setting	Comment	Timing
Phase 3 first Interim	BSI/Pneumonia	360 patients, Plazomicin vs.colistin, 28 day all cause mortality.	2H:15
Phase 3 second Interim	BSI/Pneumonia	360 patients, Plazomicin vs.colistin, 28 day all cause mortality.	2H:16
Phase 3 Top Line	BSI/Pneumonia	360 patients, Plazomicin vs.colistin, 28 day all cause mortality.	1H:17
File NDA	BSI/Pneumonia	Single submission for both indication	Mid:2017
Other Programs	Indication/Setting	Comment	Timing
Antibody or LpxC	Gram-Negative Infection	Forward at least one clinical program	2015



## Management

**Exhibit 16: Brief Biographies of Achaogen Management** 

Name	Position	Company Management Biography
Kenneth J. Hillan M.B. Ch.B.	CEO	Dr. Hillan joined Achaogen in April 2011 as Chief Medical Officer and became CEO and a member of its board of directors in October 2011. Prior to joining Achaogen, he served at Genentech, Inc. He has an M.B. Ch.B. degree from the Faculty of Medicine at the University of Glasgow, U.K. and is a Fellow of the Royal College of Surgeons, and a Fellow of the Royal College of Pathologists.
Derek A. Bertocci	CFO and SVP	Mr. Bertocci joined Achaogen in February 2014 as Senior Vice President and Chief Financial Officer. Prior to joining Achaogen, Mr. Bertocci was Chief Financial Officer for numerous companies including Accuray, BioForm, and Laserscope. He holds a B.A. from Stanford University and an M.B.A. from the University of Southern California. He is also a Certified Public Accountant.
lan R. Friedland, MD	СМО	Dr. Friedland joined Achaogen in 2014 as Chief Medical Officer. Prior to joining Achaogen, he served at numerous companies, including Cubist, Calixa and Merck & Co.

Source: Company reports

## Valuation

We assign Achaogen a BUY rating based on a \$13 price target. This rating is in turn, based on a net income NPV model, which we believe is the most appropriate method with which to value AKAO shares. We model risk net income out to 2025; this assumes the primary driver of cash flow is plazomicin sales, which we believe will become generic in 2031 at the end of patent exclusivity. Based on these assumptions and a weighted average cost of capital of 12.5%, our NPV valuation indicates a target price for AKAO at \$13.

Exhibit 17: Net Income NPV Valuation of Achaogen

Achaogen																							
Net Income NPV																							
Dan Brims, 212.294.7729																							
Fiscal year ends December 3	1			2014E	2015E		2016E	2017E	20	018E		2019E	2020E	- 2	2021E	2	022E		2023E	2024E	2025E	Ter	minal
Total Product Revenue			\$	22	\$ 20	\$	20	\$ 2	\$	9	\$	19	\$ 36	\$	54	\$	73	\$	93	\$ 114	\$ 136	\$	584
Operating Margin (ex non-cash	ехр	enses)		-62%	-84%		-86%	-1677%	-1	10%		-11%	33%		40%		46%		46%	46%	46%		46%
Tax Rate				0%	0%		0%	0%		0%		0%	12%		17%		25%		32%	32%	32%		32%
Net Income			\$	(14.52)	\$ (17.75)	\$	(19.12)	\$(35.38)	\$ (14	4.60)	\$	(3.21)	\$ 15.65	\$ 2	26.52	\$ 3	6.99	\$	42.54	\$ 52.02	\$ 61.98	\$ 18	32.55
Discount rate		12.5%								1						Disco	ount ra	te					
Terminal growth		3%													7.5%	10	0.0%		12.5%	15.0%	17.5%		
Terminal value (Eravacycline)	\$	44										-	-2.5%		32.54	2	20.41		11.63	5.24	0.56		
NPV	\$	45										rate	0.0%		33.89	- 2	21.33		12.27	5.69	0.87		
Shares outstanding		3.46										₹	2.5%		35.32	2	22.31		12.95	6.16	1.20		
DCF per share	\$	13										Growth 1	5.0%		36.85	2	23.36		13.67	6.66	1.55		
-													7.5%		9.56	2	24.47		14.44	7.19	1.92		



#### Risks

**Clinical trial risk.** Pre-clinical studies and Phase I/II clinical trials of plazomicin may not be predictive of success in subsequent larger clinical studies or in clinical studies in new disease settings. Also, efficacy against infection in one tissue type is not predictive of efficacy in other tissues.

**Regulatory risk.** Commercialization of plazomicin is dependent on FDA approval in the United States and/or approval by comparable regulatory agencies in Europe and other countries. There can be no assurance that Achaogen's ongoing and planned trials for plazomicin, even if successful by some measure, will be adequate to satisfy FDA or foreign regulatory approval standards for approval.

**Commercialization risk.** Achaogen will need to develop a sales force to commercialize plazomicin in the United States. Currently, Achaogen does not have the ability to co-promote or co-commercialize plazomicin in any country outside the United States.

**Pipeline risk.** While plazomicin represents only one of Achaogen's drug development assets, and the company presently has other compounds in clinical development, we believe it will be the primary driver for Achaogen's stock. The failure of plazomicin to achieve successful clinical trial endpoints, delays in clinical or development of plazomicin, unanticipated adverse side effects related to plazomicin, or any other adverse developments or information related to plazomicin would significantly negatively impact the company's common stock.



Exhibit 18: Achaogen Income Statement (in millions, except per share data)

# Achaogen INCOME STATEMENT

Cantor Fitzgerald & Co Dan Brims, 212.294.7729

Fiscal Period: ends Dec. 31		2013		1Q		2Q		3QE		4QE		2014E		2015E		2016E	2017	:	2018E		2019E		2020E		2021E	$\overline{}$	2022E	$\overline{}$	2023E	_	2024E		2025E
riscarrenoa. enas bec. or		2010		100		200		UQL		TQL		ZVITE		20101		20102	20171	+	ZUIUL		20132		ZUZUL		ZVZIL	╁	ZVZZL		ZUZUL	_	ZVZ-TL		ZUZUL
Plazomicin	\$	-	\$	-	\$	-	\$	-	\$	-	\$	-	\$	-	\$	-	\$ -	\$	8.8	\$	19.4	\$	36.1	\$	53.8	\$	72.6	\$	92.6	\$	113.8	\$	136.4
Product sales, net		-										-		<del></del>		•		-	13.3		29.2		53.9		79.9	H	107.2		136.0	_	166.3		198.2
Collaboration and Contract Revenue	\$	18.5		6.0		5.2		5.5		5.5	\$	22.2		20.0		20.0	2.1		_		-						_		-	ı	-		-
Other Revenue	\$	-									\$	-		-		-	-		_		-						_		-	ı	-		-
Total Revenue	\$	18.5	\$	6.0	\$	5.2	\$	5.5	\$	5.5	\$	22.2	\$	20.0	\$	20.0	\$ 2.1	\$	13.3	\$	29.2	\$	53.9	\$	79.9	\$	107.2	\$	136.0	\$	166.3	\$	198.2
Cost of product sales		_		-		_		_		-		_		- '		-	-	'	2.26		4.38		6.47	Ċ	9.59	'	12.87		16.32		19.95		23.78
Gross Profit		18.5		6.0		5.2		5.5		5.5		22.2		20.0		20.0	2.1		11.0		24.8		47.4		70.3		94.4		119.7	ı	146.3		174.4
Research and development	\$	23.5		6.6		6.2		6.5		6.7	\$	26.0	\$	26.8	\$	27.05	\$ 27.32	\$	15.27	\$	16.92	\$	17.78	\$	20.77	\$	21.45	\$	27.20	\$	33.26	\$	39.63
Selling, general and administrative	\$	7.0		2.6		2.3		2.4		2.5	\$	9.9	\$			10.07	\$ 10.17				11.09		11.86		17.57		23.59		-		36.58	\$	43.60
Other Expenses	\$	-									\$	-	\$	-	\$	-	\$ -	\$		\$	-	\$	-	\$	-	\$	-	\$	-	\$	-	\$	-
Total operating expense (including COGS)	Ť	30.5		9.2		8.5		8.9		9.2	,	35.9	,	36.8	,	37.1	37.5	,	27.9	Ť	32.4	*	36.1	,	47.9	,	57.9	,	73.4	1	89.8	Ť	107.0
Operating Income		(12.0)		(3.2)		(3.3)		(3.4)		(3.7)		(13.7)		(16.8)		(17.1)	(35.4)		(14.6)		(3.2)		17.8		32.0	<u> </u>	49.3		62.6		76.5		91.2
Interest Income				(0.2)		-		-		-				110.07			(00.1	+	(1-1.0)		- (0.2)				-	<u> </u>	-		-				
Interest expense	\$	(1.3)		(0.2)		(0.2)		(0.2)		(0.2)	\$	(0.8)	\$	(1.0)	\$	(2.0)	\$ -	\$	_	\$	_	\$	_	\$	_	\$	_	\$	_	\$	_	\$	_
Other Income/ Expense	\$	0.2		(0.2)		(0.2)		(0.2)		(0.2)	ŝ	-	\$	- (1.0)	\$	(2.0)	\$ -	\$	_	\$	_	\$	_	\$	_	\$	_	\$	_	ı \$	_	\$	_
Loss on extinguishment of debt	\$	-									\$		\$		\$		\$ -	\$	_	\$		\$		\$		\$	_	\$		ı ¢		\$	
Net Income Before Taxes	Ψ	(13.1)		(3.5)		(3.6)		(3.6)		(3.9)	Ψ	(14.5)	Ψ	(17.8)	Ψ	(19.1)	(35.4)	\ <del>\</del>	(14.6)	Ψ	(3.2)	Ψ	17.8	Ψ	32.0	Ψ	49.3	Ψ.	62.6	<u> </u>	76.5	Ψ	91.2
Provision for Income Taxes		(10.1)		(0.0)		-		(0.0)		(0.0)		(14.0)		111.0		(13.1)	(00.4)	+	(14.0)		(0.2)		2.1		5.4	╁	12.3	$\vdash$	20.0	_	24.5		29.2
Net Income After Taxes	e	(13.1)	\$	(3.5)	e	(3.6)	\$	(3.6)	e	(3.9)	٠	(14.5)		(17.8)	e	(10.1)	\$ (35.4)	ء ا	(14.6)	\$	(3.2)	\$	15.6	\$	26.5	\$		e	42.5	e	52.0		62.0
Net Illcome Alter Taxes	Ţ	(13.1)	Ą	(3.3)	φ	(3.0)	φ	(3.0)	Ÿ	(3.3)	φ	(14.3)	P	(17.0)	Ţ	(13.1)	\$ (33.4	ų ų	(14.0)	φ	(3.2)	φ	13.0	φ	20.3	Ţ	37.0	<u> </u>	42.3	<u> </u>	JZ.0	Ą	02.0
Basic Weighted Average Shares		0.4		3.5		17.7		21.8		21.9		16.2		16.4		16.6	16.8		17.0		17.2		17.4		17.6		17.8		18.0	ı	18.2		18.4
Diluted Weighted Average Shares		0.4		3.5		17.7 17.7		21.0 21.8		21.9	-	16.2		16.4		16.6	16.8		17.0		17.2		17.4		17.6		17.8		18.0	ı	18.2		18.4
Diluted Weighted Average Shares		0.4		3.5		17.7		21.0		21.9		10.2		10.4		10.0	10.0		17.0		17.2		17.4		17.0		17.0		10.0	ı	10.2		10.4
Diluted EPS as-reported (GAAP)		(22 02)		(4.00)	e ((	201	e /	0 17\	e .	(0.40)	ę.	(0.00)	ė	(4 00)		(4.45)	\$ (2.11)	ء ا	(0.96)		(0.19)	\$	0.90	\$	1.51		2.08		2.36	\$	2.86	e	3.37
Diluted Er3 as-reported (GAAP)	Ð,	(33.63)	Ą	(1.00)	<b>\$</b> (0	J.ZU)	<b>Ф</b> (	0.17)	ą	(0.16)	Ą	(0.90)	Ą	(1.00)	Ą	(1.13)	⇒ (Z.11)	Į Į	(0.00)	Ą	(0.19)	Ą	0.50	Ą	1.31	Þ	2.00	à	2.30	<u> </u>	2.00	Ą	3.31
Add of district on the Case	_	(40.4)	_	(0.5)	•	(0.0)	_	(0.0)	•	(0.C)	_	(4.4.5)		(47.0)	_	(40.4)	A (05.5)	+	(44.6)	_	(0.0)	•	45.0	_	00.5	<u>_</u>	07.0	_	40.5	•	FO C	_	
Adjusted Net Income (non-GAAP)	\$	(13.1)	\$	(3.5)	\$	(3.6)	\$	(3.6)	\$	(3.9)	\$	(14.5)	\$	(17.8)	\$	(19.1)	\$ (35.4)	\$	(14.6)	\$	(3.2)	\$	15.6	\$	26.5	\$	37.0	\$	42.5	\$	52.0	\$	62.0
A	١.		١.	(4.00)								(0.05)		(4.05)	١.	(4.45)			(0.00)	١.	(0.40)					١.						١.	
Adjusted fully diluted EPS (non-GAAP)	\$ (	(33.83)	\$	(1.00)	\$ ((	J.20)	\$ (	U.17)	\$	(0.18)	\$	(0.90)	\$	(1.08)	\$	(1.15)	\$ (2.11)	)   \$	(0.86)	\$	(0.19)	\$	0.90	\$	1.51	\$	2.08	\$	2.36	\$	2.86	\$	3.37
Cook and Emiliate		44						74 5			•	70		C4		40	6 67				40	•			0.5		400		404		244		272
Cash and Equivalents	\$	11					\$	14.5			\$	76	\$	61	\$	46	\$ 67	\$	50	\$	46	\$	60	\$	85	\$	120	þ	161	\$	211	\$	272



Exhibit 19: Achaogen Balance Sheet (in millions, except per share data)

# Achaogen BALANCE SHEET

Cantor Fitzgerald & Co Dan Brims, 212.294.7729

Fiscal year ends June 30		201	2	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025
All \$MM unless noted																
Cash, equivalents and investments		\$ 7.07	\$	10.74	\$ 76.10 \$	61.00 \$	46.44 \$	66.91 \$	50.34 \$	46.26 \$	59.51 \$	84.50 \$	119.55 \$	160.75 \$	211.34 \$	271.8
Accounts receivable		4.26		7.23	6.66	6.00	4.00	0.32	1.99	4.38	8.08	11.98	16.08	20.40	24.94	29.7
Inventory		-		-	-	-	-	-	0.18	0.35	0.52	0.77	1.03	1.31	1.60	1.9
Prepaid expenses and other current	*	0.40		1.87	2.44	2.00	0.80	0.04	0.27	0.58	1.08	1.60	2.14	2.72	3.33	3.9
Total current assets	·-	11.73		19.84	85.20	69.00	51.24	67.27	52.78	51.58	69.19	98.85	138.81	185.18	241.21	307.3
Property and equipment, net		1.34		0.74	1.21	1.11	1.03	0.95	0.88	0.89	0.91	0.92	0.94	0.92	0.92	0.9
Goodwill and Intangibles		-		-	-	-	-	-	-	-	-	-	-	-	-	-
Restricted cash		0.13		0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.1
Other assets		0.07		0.05	3.77	3.40	2.50	0.21	1.33	2.92	5.39	7.99	10.72	13.60	16.63	19.8
Total assets		\$ 13.27	\$	20.76	\$ 90.31 \$	73.64 \$	54.89 \$	68.55 \$	55.11 \$	55.52 \$	75.62 \$	107.89 \$	150.60 \$	199.83 \$	258.89 \$	328.2
Accounts payable		\$ 2.91	\$	2.92	\$ 2.15 \$	2.21 \$	2.23 \$	2.25 \$	1.67 \$	1.94 \$	2.17 \$	2.88 \$	3.47 \$	4.41 \$	5.39 \$	6.4
Accrued liabilities		1.57		3.00	2.51	2.76	2.78	2.81	2.09	2.43	2.71	3.59	4.34	5.51	6.73	8.0
Deferred revenue		-		-	-	-	-	-	-	-	-	-	-	_	-	-
Current portion of debt		7.22		4.99	4.99	-	-	-	-	-	-	-	-	_	-	-
Other current liabilities	*	0.33		0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.0
Total current liabilities	•	12.03		10.99	9.73	5.03	5.08	5.13	3.84	4.45	4.95	6.54	7.89	9.99	12.20	14.5
Accrued interest on debt		-		-	-	-	-	-	-	-	-	-	-	-	-	-
Long Term Debt		11.75		1.70	1.70	1.70	1.70	-	-	-	-	-	-	-	-	-
Other long-term liabilities		1.70	1	0.37	1.08	1.10	1.11	1.12	0.84	0.97	1.08	1.44	1.74	2.20	2.69	3.2
Total liabilities	-	25.49		13.06	12.50	7.84	7.90	6.26	4.67	5.42	6.03	7.98	9.63	12.19	14.89	17.7
Total stockholders' equity		(12.22	2)	7.70	77.81	65.81	47.00	62.29	50.44	50.10	69.59	99.91	140.97	187.64	244.00	310.
Total equity and liabilities	_	\$ 13.27	\$	20.76	\$ 90.31 \$	73.64 \$	54.89 \$	68.55 \$	55.11 \$	55.52 \$	75.62 \$	107.89 \$	150.60 \$	199.83 \$	258.89 \$	328.2



Exhibit 20: Achaogen Statement of Cash Flows (in millions, except per share data)

Achaogen CASHFLOW Canbr Fitzgerald & Co Dan Brims, 212.294.7729															
Fiscal year ends June 30	20	012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
All \$MM unless noted															
Net income (loss) GAAP			(13.11) \$	(14.52) \$	(17.75) \$	(19.12) \$	(35.38) \$	(14.60) \$	(3.21) \$	15.65 \$	26.52 \$	36.99 \$	42.54 \$	52.02 \$	61.98
Stock-based compensation	0.	83	1.05	1.11	1.16	1.22	1.28	1.34	1.41	1.48	1.56	1.63	1.72	1.80	1.89
Depreciation and amortization	0.	57	0.51	0.13	0.12	0.11	0.10	0.10	0.09	0.10	0.10	0.10	0.10	0.10	0.10
Disposal of PP&E	-		0.01	-	-	-	-	-	-	-	-	-	-	-	-
Warrant and Stock adjustments	-		-	-	-	-	-	-	-	-	-	-	-	-	-
Loan Interest.	1.	77	0.67	-	-	-	-	-	-	-	-	-	-	-	-
Changes in Working Capital															
Inventories	-		-	-	-	-	-	(0.18)	(0.17)	(0.17)	(0.25)	(0.26)	(0.28)	(0.29)	(0.31)
Accounts recievable	0.	63	(2.97)	0.57	0.66	2.00	3.68	(1.67)	(2.39)	(3.71)	(3.90)	(4.10)	(4.32)	(4.54)	(4.78)
Prepaid Expenses and Other current	0.	10	(1.46)	(0.57)	0.44	1.20	0.76	(0.22)	(0.32)	(0.49)	(0.52)	(0.55)	(0.58)	(0.61)	(0.64)
Deferred revenue	-		-	- 1	-	-	-	- '	- '	-	- 1	-	- '	-	-
Accounts payable	(1.	91)	1.45	(0.77)	0.05	0.02	0.02	(0.58)	0.27	0.22	0.71	0.60	0.93	0.98	1.03
Accrued liabilities	(0.	38)	(0.20)	(0.49)	0.25	0.03	0.03	(0.72)	0.34	0.28	0.89	0.75	1.17	1.23	1.29
Other adjustments		,	0.20					•							
Net operating cash flow	\$ (16.	76) \$ (*	(13.85) \$	(14.54) \$	(15.07) \$	(14.54) \$	(29.51) \$	(16.54) \$	(3.97) \$	13.36 \$	25.10 \$	35.16 \$	41.29 \$	50.68 \$	60.57
Capital expenditures	\$ (0.	57) \$	(0.11) \$	(0.09) \$	(0.03) \$	(0.03) \$	(0.03) \$	(0.03) \$	(0.11) \$	(0.11) \$	(0.11) \$	(0.11) \$	(0.08) \$	(0.10) \$	(0.11)
Investment-related transactions			-												
Other adjustments	0.	ე4	-												
Net cash from investing	\$ (0.	53) \$	(0.11) \$	(0.09) \$	(0.03) \$	(0.03) \$	(0.03) \$	(0.03) \$	(0.11) \$	(0.11) \$	(0.11) \$	(0.11) \$	(0.08) \$	(0.10) \$	(0.11)
Equity related transactions			22.20 \$	80.00 \$	-	\$	50.00								
Debt-related transactions	6.	71	(4.57)	-	-		-	-	-	-	-	-	-	-	-
Other transactions															
Net cash from financing	\$ 11.	84 \$ '	17.63 \$	80.00 \$	- \$	- \$	50.00 \$	- \$	- \$	- \$	- \$	- \$	- \$	- \$	-
Foreign currency effect															
Net change in cash	\$ (5.	46) \$	3.67 \$	65.36 \$	(15.10) \$	(14.56) \$	20.47 \$	(16.57) \$	(4.08) \$	13.25 \$	24.99 \$	35.05 \$	41.20 \$	50.59 \$	60.46
Cash and equivalents, at start	\$ 12.		7.07 \$	10.74 \$	76.10 \$	61.00 \$	46.44 \$	66.91 \$	50.34 \$	46.26 \$	59.51 \$	84.50 \$	119.55 \$	160.75 \$	211.34
Cash and equivalents, at end	7.	07	10.74	76.10	61.00	46.44	66.91	50.34	46.26	59.51	84.50	119.55	160.75	211.34	271.81
Investments, at start	\$(	0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Investments, at end	\$0		\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Cash and investments, at end			10.74 \$	76.10 \$	61.00 \$	46.44 \$	66.91 \$	50.34 \$	46.26 \$	59.51 \$	84.50 \$	119.55 \$	160.75 \$	211.34 \$	271.81



## **Company Description**

Achaogen, Inc., a clinical-stage biopharmaceutical company, developing novel antibiotics for Gram-negative bacterial infections. The company's lead product is plazomicin, which has initiated phase 3 clinical trials for treatment of Multidrug resistant blood stream and pneumonia infections. including carbapenem-resistant Enterobacteriaceae. The company also has novel classes of antibiotics in preclinical development, including antipseudomonal drugs. The company, which was founded in 2002, is based in South San Francisco, CA and has 43 employees.

# **Companies Mentioned:**

Actavis, Inc. (ACT - NYSE): NC
AstraZeneca PLC (AZN - NYSE): NC
Bayer AG (BAYRY - OTC): NC
Bristol-Myers Squibb Company (BMY - NYSE): NC

Cornerstone Therapeutics Inc. (CRTX - NASDAQ): NC Cubist Pharmaceuticals, Inc. (CBST - NASDAQ): HOLD

Cubist Pharmaceuticais, Inc. (CBST - NASDAQ): HOLD

GlaxoSmithKline plc (GSK - NYSE): NC Isis Pharmaceuticals, Inc. (ISIS - NASDAQ): NC

Johnson & Johnson (JNJ - NYSE): NC Merck & Co., Inc. (MRK - NYSE): NC

Pfizer Inc. (PFE - NYSE): NC Sanofi (SNY - NYSE): NC

Tetraphase Pharmaceuticals, Inc. (TTPH - NASDAQ): BUY

Theravance Inc. (THRX - NASDAQ): NC

# Disclosures Appendix Analyst Certification

The analyst primarily responsible for this research report, and whose name appears on the front cover, certifies that: (i) all of the views expressed in this research report accurately reflects his or her personal views about any and all of the subject securities or issuers featured in this report; and (ii) no part of any of the research analyst's compensation was, is, or will be, directly or indirectly related to the specific recommendations or views expressed by the research analyst in this report.

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# Cantor Fitzgerald's rating system

**BUY:** We have a positive outlook on the stock based on our expected 12 month return relative to its risk. The expected return is based on our view of the company and industry fundamentals, catalysts, and valuation. We recommend investors add to their position.

**HOLD:** We have a neutral outlook on the stock based on our expected 12 month return relative to its risk. The expected return is based on our view of the company and industry fundamentals, catalysts, and valuation.

**SELL:** We have a negative outlook on the stock based on our expected 12 month return relative to its risk. The expected return is based on our view of the company and industry fundamentals, catalysts, and valuation. We recommend investors reduce their position.

NC: Not Covered. Cantor Fitzgerald does not provide an investment opinion or does not provide research coverage on this stock.

Prior to September 12, 2006, Cantor Fitzgerald had the below ratings:

BUY - denotes stocks that we expect will provide a total return (price appreciation plus yield) of 15% or more over a 12-month period. a BUY rated stock is expected to outperform the total average return of analyst's industry coverage universe on a risk adjusted basis.

HOLD - denotes stocks that we suggest will provide a total return or total negative return of up to 15% over 12-month period. A HOLD rated stock is expected to perform in-line with the total average return of the analyst's industry coverage universe on a risk adjusted basis.



SELL - denotes stocks that we expect to provide a total negative return of more than 15% over a 12 month period. A SELL rated stock is expected to underperform the total average return of the analyst's industry coverage universe on a risk adjusted basis.

NC - Not Covered. Cantor Fitzgerald does not provide research coverage on this company.

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# Distribution of Ratings/Investment Banking Services (IB) as of 10/30/14 Cantor

			IB Serv	./Past 12 Mos.
Rating	Count	Percent	Count	Percent
BUY [B]	88	61.11	20	22.73
HOLD [H]	48	33.33	10	20.83
SELL [S]	8	5.56	1	12.50