

Initiating Coverage With A Buy Rating And \$22 PT

As An Antibiotic Biotech Investment AKAO Is AOK

- **Achaogen's lead drug in Phase III development is targeting a highly resistant pathogen with a mortality rate as high as 50% for bloodstream infections.** The pathogen is known as carbapenem-resistant enterobacteriaceae (CRE).
- **CRE rates are currently low from an overall numbers standpoint, but rates have been growing significantly.** It is classified as "Urgent" by the CDC. As a means of comparison, methicillin-resistant Staphylococcus aureus (MRSA) infections, which are always in mainstream headlines are classified one step lower as "Serious".
- **The FDA and BARDA (Biomedical Advanced Research And Development Authority) both see plazomicin as having strong merit given the \$103 million in guaranteed funding that has been awarded to Achaogen to date for the development of plazomicin.** Both the FDA and EMA have stated that one Phase III trial is all that is required for a regulatory submission. Achaogen is also eligible to receive an additional \$25 to \$30 million from BARDA. Investors would be buying into a name where the Phase III is significantly subsidized by government funding. Lack of clinical data for this indication is most likely a strong concern for investors, but we are focused on the preclinical data which often translates into clinical practice.
- **According to our physician survey results, CRE pathogens are one of the most concerning areas in antibiotic drug development.** The limited treatment options employed currently for CRE, colistin (generic) and tigecycline (Tygacil-PFE-Sell rated-\$29.95) are both associated with resistance and safety issues. While a small population currently on an absolute basis, we believe the rates of CRE will continue to grow.
- **The geographically disperse nature of the pathogen means a longer enrollment period.** Achaogen has stated that enrollment could take as long as two years to complete, but two interim analyses have been built-in to give investors data read-outs for both efficacy and safety. The first planned interim analysis will be in 2H15.
- **Controversy:** The belief that while the number of new infections is low now, it will remain so or the problem will be resolved. We believe this is a fallacy as MRSA was not a significant issue 10 to 15 years ago and now it is endemic in the hospital setting and continues to result in a significant mortality rate. With antibiotics, development time is key and we believe Achaogen's valuation is cheap when you analyze the market it is looking to address from a growth and pricing standpoint.
- **For a complete in-depth analysis of the antibiotic space, please refer to our white paper, The Big Bad Biotech Bug Book.**

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SEE PAGE 28 FOR REQUIRED DISCLOSURE INFORMATION

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Initiate Buy

Price Target: \$22.00

Price (Oct. 31, 2014)	\$10.62
52-Wk Range	\$18.95-\$8.00
Market Cap (\$M)	\$188
ADTV	60,403
Shares Out (M)	17.7
Short Interest Ratio/% Of Float	5.5%
Dividend/Yield	\$0.00/0.0%
TR to Target	107.2%

Cash Per Share	\$4.20
Total Debt	\$0.0
Long-Term Debt/Total Cap	0%
Cash And Equivalents (\$M)	\$74.5
Enterprise Value (\$M)	\$91.3
<i>Total Debt: Total long-term debt</i>	

2013A		2014E		2015E	
		Curr.	Prior	Curr.	Prior
EPS					
1Q	--	(\$1.00)A	--	(\$0.21)	--
2Q	--	(\$0.20)A	--	(\$0.21)	--
3Q	--	(\$0.20)	--	(\$0.20)	--
4Q	(\$0.58)	(\$0.19)	--	(\$0.19)	--
FY	(\$3.08)	(\$0.99)	--	(\$0.81)	--
P/E	NM	NM		NM	
Revenue (\$M)					
FY	\$19	\$25	--	\$28	--
EV/Sales	4.8x	3.7x		3.3x	
Consensus EPS					
FY	--	(\$1.11)	--	(\$1.12)	--
FYE Dec					

Achaogen STRH / Bull / Bear Scenarios

Bull Case	Bear Case	STRH Case
<ul style="list-style-type: none"> Price target \$26, 145% upside; 20% probability Achaogen completes Phase III clinical development and launches plazomicin in the U.S. following the same timeline that we assume in the STRH scenario. Plazomicin achieves a faster uptake and penetrates 28% of the targeted U.S. market in 2025. Achaogen books peak U.S. sales of \$465 million in that year Plazomicin is priced at a 10% discount in the EU due to limited alternative treatment options. We project 24% market penetration in 2025 with Achaogen receiving \$86 million royalties from total sales of \$430 million 	<ul style="list-style-type: none"> Price target \$13, 22% upside; 20% probability Achaogen experiences a half-year delay in enrollment for plazomicin and subsequent product launch in the U.S. The market penetration in 2025 is 18% and peak revenues are \$299 million We assume the same EU pricing as in the STRH scenario. We project 15% market penetration in 2025 with Achaogen receiving \$42 million in royalties from total sales of \$209 million 	<ul style="list-style-type: none"> Price target \$22, 107% upside; 60% probability The ongoing Phase III clinical trial reports top-line data in 1H17, following the timeline that management has provided. Achaogen submits the NDA in 2H17 and plazomicin receives priority review from the FDA based on the significant unmet medical need that the antibiotic addresses. FDA approval is granted in 1H18 and Achaogen launches in the U.S. mid-year 2018. Plazomicin also receives EMA approval and Achaogen enters into a partnership for commercialization in the EU, receiving tiered royalties ranging from 15% to 25%. Plazomicin achieves rapid uptake in the U.S. upon launch, penetrating 8% of the targeted market in 2019, the first full year of commercialization, and 25% of that market in 2025, the out year of our model. In 2025, we project plazomicin to generate peak U.S. sales revenue of approximately \$415 million. We estimate plazomicin to price at a 30% discount in the EU due to the pricing pressure in that market. We project EU market penetration to be slightly lower than that in the U.S., with plazomicin garnering 20% market share in 2025 and generating \$279 million in sales revenue. We model Achaogen to book \$56 million in royalties from EU plazomicin sales

Source: SunTrust Robinson Humphrey

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ACHAOGEN, INC.

Achaogen is a biotechnology company focused on the discovery and development of antibacterials to treat multi-drug resistant (MDR), gram-negative infections. The company is developing plazomicin, in Phase III development, for the treatment of serious bacterial infections due to MDR *Enterobacteriaceae*, including carbapenem-resistant *Enterobacteriaceae*, or CRE. Achaogen's pipeline includes two programs that specifically target infections caused by *Pseudomonas aeruginosa*.

NASDAQ: AKAO
South San Francisco, CA

Senior Management

Kenneth Hillan, M.B., Ch.B.	Chief Executive Officer
Derek J. Bertocci	SVP & Chief Financial Officer
Ian R. Friedland, M.D.	Chief Medical Officer

Drug Candidate	Phase	Indication
Plazomicin	III	Carbapenem Resistant Enterobacteriaceae (CRE)
LpxC Inhibitors	Preclinical	Pseudomonal Infections

Capitalization	
Long-Term Debt (MM):	\$0.0
Market Value of Equity (MM):	\$188.1
Cash (MM):	\$74.5
Technology Value (MM):	\$113.6

Source: SunTrust Robinson Humphrey

Investment Thesis

Achaogen's Plazomicin Targets The Worst Of The Worst

Achaogen's plazomicin is an antibiotic that is the first of its generation in the aminoglycoside class. Plazomicin is currently in Phase III development and actively enrolling patients for the treatment of multi-drug resistant (MDR) Gram-negative bacterial pathogens collectively referred to as carbapenem-resistant *Enterobacteriaceae* (CRE). The bacteria within this group are resistant to the majority of currently available antibiotics that are typically the last-line of defense in the treatment of these very difficult to treat strains. The ongoing Phase III clinical trial is evaluating the safety and efficacy of plazomicin for the treatment of serious infections caused by CRE. Carbapenems are a sub-class of antibiotics within the larger β -lactam class and are typically used as the "last resort" for bacterial infections because of their broad spectrum and strong potency against both Gram-positive and Gram-negative strains.

The development of resistance to the carbapenems poses a serious issue for physicians, patients and public health officials alike as there are currently no alternative treatment strategies that are fully effective in combating CRE.

Achaogen has received a contract from the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response within the U.S. Department of Health and Human Services for the Phase III development of plazomicin.

1. The contract was awarded in August 2010 with an initial funding of **\$27.6 million** for the first two years.
2. In September 2012, BARDA exercised a contract option for an additional **\$15.8 million** towards the development of plazomicin.
3. In April 2013, Achaogen received an additional **\$60.4 million** from BARDA for the pivotal Phase III clinical trial of plazomicin. The contract option was issued under BARDA's Broad Spectrum Antimicrobials (BSA) program.

The total value of the contract is **\$103.8 million**. Moreover, the BARDA contract contains an unexercised option for additional funding to support plazomicin's registration studies, including an

additional study that Achaogen plans to initiate in 2015 to help further boost the total number of patients that are to be contained in the safety database for an NDA filing.

Exhibit 1: BARDA Contracts Awarded To Achaogen

Date	Contract (\$MM)	Cumulative Total (\$MM)	Terms
August 2010	27.6	27.6	Effective through June 2014
September 2012	15.8	43.4	Effective through September 2014
April 2013	60.4	103.8	To support the plazomicin Phase III clinical trial

Source: SunTrust Robinson Humphrey and Corporate Documents

The BARDA funding, similar to what Cemptra has received, is just one of several means by which government agencies are willing to provide to assist in the development of much needed antibiotics. We believe the monies received from BARDA as well as the funds raised from Achaogen's IPO are sufficient to get the company through the current Phase III development plans for plazomicin.

Investment Risks

- Patient enrollment in the ongoing pivotal Phase III clinical trial could be slower than expected and there are no significant near-term catalysts to drive the stock.** Although the prevalence of CRE is increasing rapidly, the absolute number of patients is still small. Additionally, Achaogen will need to screen for the most appropriate patients to demonstrate a survival benefit in the Phase III study. This will further limit the number of patients eligible for the enrollment criteria. The timeline of the planned supportive efficacy study is still unclear and the first interim analysis is scheduled for 2H15, likely in the 4Q by our estimates.
- Plazomicin has not been evaluated in previous clinical studies for CRE.** The completed Phase II clinical trial was for a different type of infection caused by Gram-negative pathogens. Although plazomicin has demonstrated strong potency against CRE pathogens in *in vitro* studies and animal infection models, there is no guarantee that the same treatment outcome can be replicated in humans. The design of the Phase III clinical trial is partially based on a meta-analysis from patients who received carbapenems for the treatment of bacterial infections. The correlation between carbapenam *in vitro* potency and treatment effects may not apply to plazomicin, which belongs to a different class of antibiotic.
- A premium pricing for plazomicin may receive pushback from payers.** Although we believe the pricing of \$15,000 per treatment cycle that we assume in our model is well justified should plazomicin meet the primary endpoint of the Phase III clinical trial by demonstrating a superior survival benefit as compared to a currently available antibiotic, the number is significantly higher when compared to other branded antibiotics. Payer push back will negatively affect hospital adoption and plazomicin's revenue potential.
- Strong execution will be essential for commercial success.** We model Achaogen to market plazomicin independently in the U.S. Although a small specialty sales force should be sufficient based on the in-hospital setting and the geographic concentration of CRE prevalence, independent commercialization will still be a big challenge for a company of Achaogen's size.

Carbapenem-Resistant Enterobacteriaceae (CRE): WHEN, WHERE And WHAT?

WHEN Did Carbapenem Resistance Arrive In The U.S. And WHERE Is It Found Today?

CRE is relatively new to the U.S., but as most new strains do, this strain can spread quickly and go from being relatively rare in occurrence in the U.S. to becoming an endemic issue. CRE first popped up in the U.S. according to the Centers for Disease Control (CDC) in 2001 in a North Carolina hospital. Since that time it has found its way to 41 states in total. Carbapenem-resistant bacteria are typically found in patients who have been admitted into acute healthcare settings, such as intensive care units (ICUs), and are suffering from nosocomial infections (hospital-based). These patients typically have compromised immune systems. CRE has a high mortality associated with infection. The mortality rate can be as high as 50% in patients with bloodstream infections commonly referred to as sepsis.

Exhibit 2: FDA Approved Carbapenems

Drug	Approval Date	Initial U.S. Launch
Imipenem	1985	Merck
Meropenem	1996	AstraZeneca
Ertapenem	2001	Merck
Doripenem	2007	Johnson & Johnson

Source: SunTrust Robinson Humphrey

According to the National Nosocomial Infection Surveillance (NNIS) report, the U.S. prevalence of CRE in the U.S. was low prior to 1990, with approximately 2.3% of 1,825 *Enterobacter* isolates resistant to imipenem. However, among isolates reported to the National Healthcare Safety Network (NHSN) in 2006 and 2007, up to 4.0% of *Escherichia coli* and 10.8% of *Klebsiella pneumoniae* isolates that were associated with certain device-related infections had gained carbapenem resistance. In the meropenem Yearly Susceptibility Test Information Collection Program, meropenem resistance increased from 0.6% in 2004 to 5.6% in 2008.

According to the CDC, approximately 18% of long-term acute care hospitals and approximately 4% of short-stay hospitals in the U.S. detected at least one case of CRE infection during the first half of 2012.

The healthcare industry is especially concerned with the recent increase in the number of cases of *Klebsiella pneumoniae* that are resistant to carbapenems and 3rd generation cephalosporins.

Moreover, many CRE cases may have evaded recognition, since it is not yet mandatory to report CRE cases to the CDC and many cases present in the community hospitals where these infections often go undetected. Proper epidemiology is very difficult to ascertain as very few States actively track CRE infections and as a result there is most likely significant under-reporting occurring.

Exhibit 3: Prevalence Numbers Are Hard To Come By As Surveillance Is In Its Infancy

Prevalence Assumptions (infections included in case/death estimates)	Healthcare-associated infections (HAIs) caused by <i>Klebsiella</i> and <i>E. coli</i> with onset in hospitalized patients
Infections not included in prevalence assumption	<ul style="list-style-type: none">• Infections occurring outside of acute care hospitals (e.g., nursing homes)• Infections acquired in acute care hospitals but not diagnosed until after discharge• Infections caused by Enterobacteriaceae other than <i>Klebsiella</i> and <i>E. coli</i> (e.g., <i>Enterobacter</i> spp.)

Source: SunTrust Robinson Humphrey and CDC

Of great concern is the speed by which carbapenem resistance can spread. As mentioned above the prevalence rate in the U.S. has increased significantly over the past decade. Our physician consultants have previously mentioned and have again highlighted the fact that some hospitals in heavily-affected geographic areas such as New York have identified approximately 50% of the hospital isolates to be carbapenem resistant.

WHAT Exactly Are Enterobacteriaceae Besides Being A Spelling Bee Challenge Word?

Enterobacteriaceae are bacteria that include safe and healthy strains that are found naturally in the gut of humans and they are also comprised of strains that are disease causing to varying degrees. There are three species of *Enterobacteriaceae* that comprise the majority (80% to 95%) of strains found in the clinical setting:

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Proteus mirabilis*

Carbapenem-resistant *Enterobacteriaceae* (CRE) specifically refers to bacteria resistant to the carbapenem class of antibiotics, which are normally considered the antibiotic class of last resort for the treatment of bacterial infections.

Due to the high level of resistance found in almost all classes of currently available antibiotics, CRE has a much higher mortality rate than other bacterial infections caused by carbapenem-susceptible strains. In a clinical study comparing patients with bloodstream infections caused by CRE, extended-spectrum β -lactamase (ESBL) producing *Enterobacteriaceae*, or susceptible *Klebsiella pneumoniae*, it was found that the infection-related mortality rate was 48% for CRE, 22% for ESBL producers and 17% for susceptible *Klebsiella pneumoniae*, respectively (Ben-David et al., Clin. Microbiol. Infect 2012).

CRE is listed as one of the three (3) “Urgent” threats by the CDC. As a point of reference, methicillin-resistant *Staphylococcus aureus* (MRSA), which is one of the most targeted bacterial species by biotechnology and pharmaceutical companies in drug development, is categorized one step lower as a “Serious” threat on the same scale. We believe from our analysis that the global market opportunity for new antibiotics with potency against a broad spectrum of MDR Gram-negative pathogens should be greater than that for drugs targeting MRSA Gram-positive pathogens. The rationale has not only to do with the pace at which CRE has grown, but also the lack of new agents

in development to treat MDR Gram-negative infections which are associated with a high mortality rate. It is important to understand that the reason why fewer drugs are being developed in this area despite the lucrative market potential has nothing to do with lack of interest and more to do with the complexity associated with developing drugs in this area to treat MDR infections.

Exhibit 4: Drugs In Development For CRE

Drug	Company	Stage	Coverage		CRE	Indications
			KPC	MBL		
Plazomicin	Achaogen	PIII	+	+	+	CRE in BSI & HAP/VAP
Carbavance	The Medicines Company	PIII	+	–	+	cUTI & others
Eravacycline	Tetraphase	PIII	+	+	–	cUTI & cIAI
ceftazidime / avibactam	Actavis	NDA	+	–	–	cUTI, cIAI & HAP/VAP
ceftolozane / tazobactam	Cubist	NDA	–	–	–	cUTI, cIAI & HAP/VAP

Source: SunTrust Robinson Humphrey and SEC documents

Treatment Options Today Are Less Than Optimal Further Supporting A Need For Options

Colistin (polymyxin E), and tigecycline (Tygacil, Pfizer, FDA approved in June 2005) are the current treatment options used by physicians for CRE infections based on their *in vitro* activity. Both antibiotics are far from being optimal therapeutic solutions for CRE:

- Colistin is associated with severe nephrotoxicity
- Tigecycline has a boxed warning relating to increased mortality in treated patients

Potency is the key consideration when choosing an antibiotic and data that continues to be published on the problem of CRE and ways to treat it demonstrate that the use of colistin and tigecycline do nothing to abate the mortality rate.

Exhibit 5: Current “Treatments” For CRE

Drug	All-Cause Mortality ¹	Limitations
Colistin	46%	Nephrotoxic, target attainment difficult, increasing resistance
Tigecycline	47%	Bacteriostatic, increased risk of death in meta-analysis
Fosfomycin	N/A	Limited clinical data, low barrier to resistance
Aminoglycoside	38%	Often not active due to co-expression of aminoglycoside resistance

¹ *Klebsiella pneumoniae* bloodstream infections

Source: SunTrust Robinson Humphrey

For CRE Infection, Colistin Since 1949, Is A Poor First-Line Choice Of Limited Options

Colistin (polymyxin E) is a bactericidal antibiotic that disrupts the outer membrane of Gram-negative bacteria. Colistin has several side effects associated with its use which can be quite severe such as nephrotoxicity and neurotoxicity. Due to the poor side-effect profile, colistin's usage was limited as soon as it was approved.

Colistin is one of a very short list of drug options used against MDR CRE strains. While still rare, the rates of colistin resistance continue to increase each year. At UCLA Medical Center routine colistin susceptibility testing for all *Enterobacteriaceae* was introduced in June 2013. Since there are no FDA approved susceptibility testing protocols in place a routine and stepwise approach must be employed by locations individually.

Colistin is administered as colistimethate sodium, a prodrug that is subsequently hydrolyzed to colistin. The serum half-life of the prodrug is approximately two hours whereas the active drug has a much longer half-life and undergoes reabsorption in the renal tubular cells. Due to this complicated PK profile, and limited PK studies performed in humans, it is difficult to conduct dosing optimization, particularly in critically ill patients with renal failure or other alterations in either drug distribution or metabolism.

Tigecycline or Tygacil With A High Risk Of Mortality Doesn't Fit The Bill

Tigecycline (Tygacil, Pfizer – FDA approved in June 2005) has a similar structure as the tetracyclines and functions as a bacteriostatic antibiotic by binding to the ribosomal subunit of bacteria to inhibit their protein synthesis. It has a broad spectrum covering both Gram-positive and Gram-negative infections.

Tigecycline was specifically developed to address the increasing rates of antibiotic resistance. It received initial FDA approval for cSSSI and cIAI, followed by CABP several years later. Tigecycline has a large shortcoming however, in that it does not have activity against *Pseudomonas* spp. or *Proteus* spp.

The peak serum concentration of tigecycline with standard IV dosing is between 0.6mg/mL and 0.9mg/mL, which is lower than the susceptibility breakpoint of 1mg/mL proposed by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for the treatment of *Enterobacteriaceae*. Dosing at higher concentrations is also an issue as high drug levels are then able to reach other tissue which can increase toxicity.

When pooled looking at data from both on-label and off-label indications an increased overall mortality with tigecycline treatment is observed. In September 2013, the FDA approved a new Boxed Warning to be added to the drug's label. It is advised that tigecycline should only be used when there are no other options available.

Combination Therapies Are The Highly Recommend Course of Treatment

While there is no hard clinical evidence to support the hypothesis that combination therapy is superior to monotherapy. Clinical judgment to-date recommends combination therapy given the high rates of resistance and issues in attaining high plasma concentrations of drug.

Plazomicin: A Next-Generation Aminoglycoside With Greater Potency & Promise

Aminoglycosides are a class of antibiotics that are highly potent and quite familiar to the prescribing community. The class is composed of broad-spectrum bactericidal compounds comprised of amino-modified sugar moieties. The most commonly used antibiotics in this class include streptomycin, kanamycin, tobramycin, and amikacin. The aminoglycoside mechanism of action works by penetrating the bacterial outer membrane through self-promoted uptake. Aminoglycosides inhibit protein synthesis by binding to the 16S rRNA of the 30S ribosomal subunit. Aminoglycosides are often used in the treatment of serious Gram-negative bacterial for infections such as *Escherichia coli*, *Enterobacter*, *Pseudomonas aeruginosa* and *Salmonella* species, as well as Gram-positive pathogens such as *Staphylococcus* and some *Streptococci* and *Mycobacteria*. Aminoglycosides are predominantly administered in IV or IM formulations.

Plazomicin was developed by chemically modifying an existing aminoglycoside, sisomicin, a natural product isolated from bacteria, to shield the regions of the molecule that are targeted by the enzymes responsible for aminoglycoside resistance. Consequently, plazomicin retains activity against MDR organisms even in cases where commercially available aminoglycosides such as gentamicin and amikacin are ineffective.

There is little if any clinical evidence to support the claim that plazomicin will be effective in humans against CRE. That being said a positive aspect of antibiotic preclinical studies is that the results typically carry over into humans. While this is not always the case, in most cases activity against pathogens in humans can be correlated to preclinical studies.

The *in vitro* and preclinical studies that Achaogen has completed to date demonstrate the strong activity of plazomicin against CRE strains. Additionally, pharmacokinetic and pharmacodynamic analysis and results from animal infection models further underscore the hypothesis that plazomicin has a high likelihood of being efficacious in humans infected with CRE.

1. Murine Neutropenic Thigh Model: A commonly used to evaluate the efficacy of antibiotics in the treatment of bacterial infections.
 - a. Plazomicin demonstrated much stronger bactericidal activity than both colistin and tigecycline against multiple CRE isolates. Neutropenic mice were challenged with CRE pathogens that were injected into the thighs, and the mice were then treated with plazomicin, colistin, or tigecycline. Plazomicin was dosed to generate plasma PK profiles similar to what QD dosing of plazomicin would generate in humans.
2. Bacterial Bioburden Measurements: Compared to colistin and tigecycline, plazomicin achieved a bactericidal effect at a much lower dose.
 - a. The human equivalent dose (~4.3mg/kg/day) of the highest plazomicin dose required to achieve a one log reduction in colony forming units (CFUs, estimates of viable bacterial numbers) against any CRE strains tested in the study was much lower than the proposed human dose of 15mg/kg/day. In contrast, both colistin and tigecycline demonstrated minimal efficacy, failing to achieve a one log reduction in CFUs at a dose that is equivalent to the typical clinical dose.
3. Primate Pneumonic Tularemia Model.
 - a. At a dose approximately two thirds of the human equivalent dose and even when the treatment was delayed, plazomicin treatment led to 100% survival whereas all vehicle-treated animals died within 10 days post infection.

Where Did Plazomicin Come From?

In January 2006, Achaogen entered into a license agreement with Isis Pharmaceuticals for certain aminoglycoside compounds and related know-how for clinical development and commercialization. The agreement requires Achaogen to pay Isis \$4.0 million upon dosing the first patient in the Phase III trial of plazomicin, and up to \$9.75 million for the second aminoglycoside product developed under this agreement. The total payment to Isis upon the achievement of specified development and regulatory milestones relating to plazomicin is up to \$19.5 million, of which \$7 million has been paid in total since the \$4 million Phase III initiation milestone has been paid.

Translating Preclinical Data Into Clinical Practice

Minimum Inhibitory Concentration (MIC) + Pharmacokinetic Parameters

MIC: Does not provide any information with regard to the time required to eradicate an infection or the concentration of drug required to eradicate the infection.

Pharmacokinetic Parameters: Do not explain antibacterial potency.

However, combining an antibiotic’s PK parameters and microbiologic activity provides the following three PK/PD parameters commonly used to predict antibiotic efficacy:

- 1) Cmax / MIC
- 2) AUC / MIC
- 3) T>MIC

This allows antibiotics to be grouped into one of two categories:

- Concentration-dependent (rate of bacterial eradication correlates with antibiotic concentration)
- Time-dependent (rate of bacterial eradication is determined by the duration of antibiotic exposure)

Plazomicin belongs to the aminoglycoside class of antibiotics. Members of this class are principally concentration dependent killers, meaning that the concentration of drug is more of a factor in eradicating the bacterial strain than the amount of time the bacteria is exposed to the drug.

Exhibit 6: Concentration Dependent vs. Time Dependent Killers

Activity Type	Examples	PK / PD Parameter
Concentration-Dependent Killing	Aminoglycosides Fluoroquinolones Glycopeptides / Lipopeptides	24-Hour AUC / MIC Cmax / MIC
Time-Dependent Killing	β-Lactams Macrolides Oxazolidinones Tetracyclines	T > MIC

Source: SunTrust Robinson Humphrey

Plazomicin’s preclinical studies in murine models suggest that a AUC:MIC ratio of ≥95 in bloodstream infections and a ratio of ≥25 in lung infections would predict strong antibiotic treatment efficacy.

Regulatory Agencies Roll Out The Red Carpet For Plazomicin’s Development

Achaogen filed for and received a Special Protocol Assessment (SPA) for its ongoing pivotal Phase III clinical trial for plazomicin in patients with infections caused by CRE. The company is currently enrolling patients in a Phase III comparator trial. If successful, this trial alone will be sufficient to

support an NDA filing in both the U.S. and EU. U.S. Agencies to-date have granted many contracts and designations to Achaogen for the development of plazomicin.

- ✓ BARDA: Contracts totaling \$103.8 million
- ✓ Fast-Track Designation: Six-month priority review and rolling submissions
- ✓ Applying for Qualified Infectious Disease Product (QIDP): Additional exclusivity of 5 years
- ✓ FDA & EMA confirmation that a single Phase III is only requirement for an NDA & MAA

Plazomicin Begins Phase III In A Trial Designed For Superiority

In 1Q14, Achaogen initiated the Phase III clinical trial of plazomicin for the treatment of bloodstream infection and nosocomial pneumonia caused by MDR *Enterobacteriaceae* including carbapenem-resistant *Enterobacteriaceae* (CRE). The study is powered to demonstrate the superiority of plazomicin over active comparator colistin in reducing 28-day all-cause mortality. This is the FIRST pivotal clinical trial in the antibiotic space to have a superiority design. We believe an established survival benefit will allow Achaogen to command premium pricing for plazomicin.

Patient Enrollment Will Take Time, But Could Accelerate

Achaogen management has stated that enrollment completion for the Phase III clinical trial is expected in 2016 with a top-line data read out in 1H17. Our estimates assume an NDA and MAA submission by year-end 2017 and U.S. approval in mid-2018 based on a six-month Priority Review. Preparations for commercialization will likely begin before the Phase III clinical trial is complete. Consequently, Achaogen should be on a time-line to launch plazomicin in the U.S. by year-end 2018. In Europe, we conservatively estimate a one-year lag before a commercial launch occurs, which by our estimates would have an EU launch occurring in 2019.

We believe it will take the full two years to fully enroll patients. Although the prevalence of CRE infections has increased five-fold in the last several years, the absolute patient number is still low, also patients are geographically dispersed which also makes enrollment a bit more challenging. Of importance, Achaogen has established specific inclusion-exclusion criteria which include only patients that are most likely to demonstrate clinical benefit from receiving plazomicin treatment.

The ongoing Phase III is being conducted at 25 sites worldwide with eight of the sites being in the U.S. The trial is a randomized, open-label study designed to demonstrate the superiority of plazomicin as compared to colistin, when combined with a second antibiotic, for the treatment of bloodstream infections or hospital-acquired pneumonia caused by CRE. The study will enroll approximately 360 patients with presumed or confirmed CRE infections or whose infections are caused by pathogens either presumed or confirmed to have an MIC of $\geq 4\text{mg/mL}$ for meropenem.

Patients are equally randomized to receive seven to 14 days of repeated IV infusions of either plazomicin or colistin, each in combination with a second adjunct antibiotic therapy, which can be either meropenem or tigecycline based on the investigator's choice. Patients randomized into the colistin cohort will receive a loading dose, followed by subsequent dose at every eight or 12 hours.

Achaogen is basing the Phase III dose of plazomicin on the most recent PK/PD studies of the drug. The plazomicin dose will be adjusted based on each individual patient's condition and will be capped

at 15mg/kg per administration. Patients who require higher doses will receive multiple administrations per day at lower doses.

Exhibit 7: Phase III Trial Design

Trial	Primary Endpoint(s)	Enrollment	On Plazomicin
Phase III	Superiority to colistin in all-cause mortality at day 28	360	180
Supportive Efficacy	Safety and efficacy of plazomicin	50	50
Safety	Safety	70	70
			300

Source: SunTrust Robinson Humphrey and SEC documents

The trial is powered at 70% to demonstrate an absolute reduction of 12% (from 35% to 23%) in 28-day all-cause mortality, which is the primary endpoint and is consistent with what the current FDA guidelines recommend as the efficacy endpoint for HAP/VAP indications. Secondary endpoints include time to death through 28 days, all-cause mortality at 14 days, clinical response rates at the end of treatment (14 days), at test of cure (21 days), at the end of study (28 days), safety, and PK parameters. There are two interim analyses built into the design of the Phase III clinical trial:

- First interim is expected in 2H15 upon completion of one third patient enrollment
- Second interim is expected in 2H16 after two thirds of targeted patients have been enrolled

There is an efficacy and futility evaluation at both interim analyses.

The Phase III design that Achaogen has implemented is based on a meta-analysis that Achaogen conducted, based on both published and unpublished observational data, on the mortality in patients with bloodstream infections caused by carbapenemase-producing *Enterobacteriaceae*.

The meta-analysis included a total of 309 patients:

- 224 patients had isolates with a carbapenem MIC of $\geq 4\mu\text{g/mL}$ and received any type of combination therapy
- 85 patients had isolates with a carbapenem MIC of $< 4\mu\text{g/mL}$ and received combination therapy that included a carbapenem
 - Note that the production of carbapenemase does not necessarily lead to carbapenem resistance

The meta-analysis revealed that the mortality rate in patients with carbapenem-resistant pathogens (MIC $\geq 4\text{mg/mL}$) was 35% with currently available therapy whereas the mortality rate was only 14% when the pathogens were fully or partially susceptible to carbapenems and a carbapenem was included in therapy. This is equal to an absolute reduction in mortality of 21% when effective antibiotics are used for treatment.

Exhibit 8: Meta-Analysis Leading To Phase III Design

Type 2 Carbapenem MIC	Patients	Mortality
Carbapenem MIC >4mg/mL	224	35%
Carbapenem MIC <4mg/mL	85	14%

Source: SunTrust Robinson Humphrey and Achaogen Reports

Plazomicin-treated patients in Achaogen’s Phase III study, by having the same CRE pathogens with an MIC ≥ 4µg/mL, are slightly different from those who demonstrated a 14% mortality rate in the meta-analysis. We still believe it is possible to draw an analogy since plazomicin has demonstrated strong potency in CRE pathogens with an MIC well below 4µg/mL.

Based on the strong data from the *in vitro* and preclinical studies that Achaogen has completed, we believe that the 23% target mortality that Achaogen has set for the plazomicin-treated patients in the Phase III clinical trial is quite conservative. The powering of the pivotal Phase III clinical trial at 70% is lower than that of a typical Phase III study. We do not believe this is an issue for the following two reasons:

- 1) The design of the pivotal study to demonstrate an absolute reduction of 12% in mortality is conservative as compared to the 21% reduction observed in the meta-analysis.
- 2) A higher powering would require more patients to be enrolled and will further prolong the duration of the study. Achaogen has an SPA for this trial design.

The Phase III Indications Being Pursued By Achaogen Which Are Caused By CRE

Nosocomial Pneumonia (NP)

Nosocomial pneumonia, frequently referred to as hospital acquired pneumonia (HAP) is pneumonia that is contracted by a patient after being admitted to a hospital for 48 to 72 hours.

Gram-negative bacterial infections are responsible for 64% of all HAP and ventilator associated pneumonia (VAP) episodes.

- *Pseudomonas aeruginosa* infections account up for 21% of cases
- *S. aureus* is responsible for 20% of the Gram-negative VAP cases in the intensive care unit
- *Klebsiella pneumoniae* accounts for 18.1% of all infection cases

Bloodstream infections (BSI) Also Known As Bacteremia

BSI is a serious infection caused by bacteria that enter the bloodstream. According to the National Institute of General Medicine Science every year severe sepsis affects over one million people in the U.S. It’s been estimated that between 28% and 50% of people with sepsis die which is far more than the number of U.S. deaths from prostate cancer, breast cancer and AIDS combined.

BSI usually occurs as a severe complication of infections such as pneumonia or meningitis, or when bacteria enter the blood during surgical procedures, or through catheters that are placed in patients’ arteries or veins. Bacteria in the blood can cause sepsis, which is a systemic inflammatory response that is associated with a high mortality rate. According to data from Johns Hopkins Hospital, an

estimated 80,000 patients with central-line catheters develop BSIs in the U.S. each year and result in 31,000 deaths. The annual cost of treating BSIs is approximately \$3 billion.

Therapeutic Drug Management A Must Given The Severity Of Disease

A plazomicin-specific assay is being employed in the the Phase III trial to quantitatively measure plasma concentrations of plazomicin so that dose adjustment is possible to optimize drug exposure in each patient. The assay was developed by Achaogen in collaboration with ARK Diagnostics; a private company based in Fremont, CA, and has been approved by the FDA for use in the Phase III clinical trial.

The purpose of using therapeutic drug management in the Phase III is to ensure that every patient's serum exposure to plazomicin is within an acceptable range of the target mean steady-state area under the curve (AUC). The technology used in the assay is similar to what is being used for other aminoglycosides and Achaogen plans to conduct the clinical performance evaluation, which is required for the FDA to approve the assay, in parallel with the Phase III clinical trial.

We believe that Achaogen could potentially develop the assay into a product to be bundled with plazomicin and that it will enhance the uptake of plazomicin by the physician community.

Enrollment Criteria For Phase III Trial Designed To Optimized Outcome

The APACHE II (Acute Physiology and Chronic Health Evaluation II) score will be employed to screen for patients who have the highest possibility of demonstrating a clinical benefit with plazomicin treatment. The APACHE II score is a classification system based on disease severity that can be used to project ICU mortality based on a number of laboratory values and patient signs and taking into account both the patient's acute and chronic disease. The measurement is conducted within 24 hours after patient admission to the ICU and an integer score from 0 to 71 is generated based on the measurements. A higher score suggests a higher disease severity and a higher risk of death.

In the ongoing Phase III study, Achaogen is enrolling patients with APACHE II scores of between 15 and 30 (both inclusive). This range will help Achaogen exclude patients who either are not likely to die even without effective antibacterial treatment (APACHE II score <15) or likely to die even with effective antibacterial treatment (APACHE II score >30). Thus, the target patient population is enriched for those whose mortality will most likely be impacted through administration of an effective antibiotic and as a result, the possibility of plazomicin demonstrating a clinical benefit is maximized.

After patients have been screened using the APACHE Scoring system, they then undergo a screening period where the patient's pathogen will be tested for carbapenem resistance. Either presumptive identification of CRE with a rapid testing method from an appropriate culture specimen, or definitive identification with susceptibility testing conducted at a local laboratory, will qualify the patient to be enrolled into the study. Isolates from all patients will eventually be confirmed for carbapenem resistance through central laboratory testing and the primary analysis population will be the patients with isolates that are confirmed by central lab to have MICs $\geq 4\text{mg/mL}$. Patients who have received greater than 72 hours of empirical antibiotic therapy or who have CRE isolates with reduced susceptibility to colistin will be excluded from the study, among other exclusion criteria.

Additional Studies To Run In Parallel With The Phase III To Boost Safety Database

Additional Study #1

Achaogen plans to initiate a single-arm, open-label, supportive efficacy study in patients with serious CRE infections by year-end 2014 and to report top-line data in 4Q15. The company has not disclosed the specific design of the study except that approximately 50 patients with serious CRE infections will be enrolled. We believe Achaogen will likely target a slightly different patient population from those who would qualify for the pivotal Phase III study to avoid generating a negative impact on patient enrollment in the pivotal study.

Additional Study #2

Achaogen will initiate a non-randomized safety study after the first interim analysis in 2H15 to expand the safety database that will be required for global regulatory approval (300 patients). The patients to be enrolled into the safety study will include those who are not eligible for the pivotal Phase III study so we do not expect the safety study to have any impact on the pivotal study enrollment.

What Has Plazomicin Demonstrated Historically In The Clinic?

Plazomicin was well-tolerated at doses of up to 15mg/kg for the duration that is required for the treatment of typical bacterial infections in all Phase I PK studies that have been conducted to-date. It was determined from these studies that dose adjustment is required for patients with impaired kidney function since the majority of plazomicin is metabolized through the kidney. A thorough QT study was completed and no cardiovascular risks were observed from the use of plazomicin.

Exhibit 9: Plazomicin Phase I Studies

Study	Endpoint(s)	Trial Design	Plazomicin Doses	Enrollment	Results
001	Safety and PK after single and multiple doses in healthy subjects	Randomized, double-blind, placebo-controlled, parallel-group, dose escalation study	1, 4, 7, 11, 15mg/kg IV for 3-10 days	39	Plazomicin was well tolerated at doses of up to 15mg/kg for 3 days
003	Safety, plasma PK and lung penetration in healthy subjects	Randomized, double-blind, placebo-controlled	Cohort 1: 15mg/kg IV for 5 days Cohort 2A/2B: 10.7/15mg/kg IV, single dose	40	Plazomicin was well tolerated at doses of up to 15mg/kg for 5 days and penetrated into the lung
004	Safety and PK in healthy and impaired kidney function subjects	Open-label	7.5mg/kg IV, single dose	24	Plazomicin's dose needs to be adjusted in patients with moderately or severely impaired kidney function
006	Thorough QT/QTc trial in healthy subjects	Randomized, double-blind, placebo and positive-controlled, crossover	15mg/kg IV, single dose 20mg/kg IV, single dose	64 (8 in part 1, 56 in part 2)	Plazomicin demonstrated no clinically relevant potential to increase risk for cardiac arrhythmias at single doses of up to 20mg/kg

Source: Achaogen Filings

Phase II Was Successful But For A Different Indication - cUTI

The Phase II study was a multi-national, randomized, double-blind study in cUTI and acute pyelonephritis. The trial evaluated the safety and efficacy of plazomicin at 10mg/kg or 15mg/kg as compared to an active comparator, levofloxacin (750mg), in a total of 145 patients.

Patients were randomized to receive IV plazomicin at 10mg/kg or 15mg/kg, or levofloxacin for five consecutive days. The primary endpoint of the trial was microbiological eradication rates in the modified intent to treat (mITT) population and microbiologically evaluable (ME) population at the test of cure visit (day 12). The secondary endpoint was clinical cure based on the investigator's assessment throughout the study up to day 12.

Patients were equally randomized to 10mg/kg plazomicin, 15mg/kg plazomicin, or 750mg levofloxacin during the first phase of the trial. During the second phase of the trial, the 10mg/kg treatment arm was eliminated and patients were randomized 2:1 to 15mg/kg plazomicin or levofloxacin 750mg due to patients from the two plazomicin cohorts demonstrating highly overlapping responses.

In May 2012, Achaogen announced positive results from the study. Both doses of plazomicin met the primary endpoint by demonstrating non-inferiority to levofloxacin. In microbiologically evaluable subjects, plazomicin 10mg/kg and 15mg/kg resulted in 85.7% and 88.6% eradication, respectively while levofloxacin (750mg) resulted in 81.0% eradication.

Exhibit 10: Plazomicin Phase II vs. Levofloxacin In cUTI

Microbiological Response		Plazomicin		Levofloxacin
		10mg/kg	15mg/kg	750mg
ME	N	7	35	21
	Eradication, n (%)	6 (85.7%)	31 (88.6%)	17 (81.0%)
	95% CI	(42.1% - 99.6%)	(73.3% - 96.8%)	(58.1% - 94.6%)
	Difference (95% CI)*		-7.6% (-31.3%, 16.0%)	
ITT	N	12	51	29
	Eradication, n (%)	6 (50.0%)	31 (60.8%)	17 (58.6%)
	95% CI	(21.1% - 78.9%)	(46.1% - 74.2%)	(38.9% - 76.5%)
	Difference (95% CI)*		-2.2% (-27.2%, 22.9%)	

Source: SunTrust Robinson Humphrey and Achaogen documents

No serious adverse events (SAEs) attributed to plazomicin were reported. Most adverse events (AEs) were mild or moderate in severity with headache, diarrhea, dizziness, nausea and vomiting being the most frequently reported AEs and occurring in a comparable proportion of the patients from the three cohorts of the study.

A low incidence of aminoglycoside-related toxicities was observed in plazomicin-treated patients. There were two AEs, mild unilateral permanent tinnitus and mild transient vertigo, and both were considered to be related to treatment by the investigators. However, formal audiometry or vestibular testing did not reveal any clinically relevant changes in plazomicin-treated patients. There were also two AEs associated with renal dysfunction. One mild azotemia (elevation of blood urea nitrogen) was considered to be related to plazomicin treatment but one mild renal insufficiency was considered to be unrelated. Although one case of Grade 2 serum creatinine lab abnormality was recorded, the mean serum creatinine values remained stable over the five-day treatment period.

Achaogen Switches Focus For Plazomicin From cUTI to CRE

In September 2013, Achaogen received a Special Protocol Assessment (SPA) from the FDA for the Phase III trial of plazomicin for the treatment of bloodstream infections and nosocomial pneumonia caused by CRE.

Achaogen has successfully differentiated itself from other antibiotic developers by focusing on infections with a severe unmet medical need and this will help the company avoid competition once plazomicin becomes commercially available by focusing specifically on CRE isolates.

Achaogen was able to adopt a superiority design for the pivotal Phase III clinical trial since none of the currently available treatments for CRE infections are optimal and all are associated with high mortality. We believe Achaogen will be able to implement a premium pricing for plazomicin if plazomicin demonstrates a solid survival benefit.

In summary, we believe Achaogen's decision to pursue clinical development for CRE infections is well justified with the market potential for this indication being significant and well supported by strong *in vitro* and preclinical data.

Competitive Landscape – Competition Is Limited

Achaogen's ongoing Phase III clinical trial is designed specifically for CRE pathogens. We believe Achaogen's approach – by selecting CRE infections instead of other common Gram-negative infections such as complicated urinary-tract infections (cUTI) and complicated intra-abdominal infections (cIAI) as the lead indication – should help the company effectively avoid competition.

The Medicines Company is the ONLY other company that is conducting a late stage clinical trial for CRE infections. The details of the program, as well as other programs targeting Gram-negative pathogens, can be found in our Cubist initiation report. We believe Achaogen is at an advantageous position compared to The Medicines Company since the latter's Phase III study is a descriptive study (comparing study drug to best available treatments) in fewer patients (150 patients vs. 360 patients in Achaogen's Phase III clinical trial).

Intellectual Property

Achaogen holds global rights to plazomicin. The U.S. Composition of Matter patent that covers this drug candidate (U.S. Patent No.8,383,596; "Antibacterial aminoglycoside analogs) provides strong protection through **June 2031**, including 923 days of patent term adjustment. Upon regulatory approval, and depending on the date of such approval, plazomicin will further be entitled to up to five years of patent term extension based on the Hatch-Waxman Act. Additionally there is one pending U.S. patent application and 14 corresponding foreign patents and patent applications, in addition to the above issued U.S. patent.

Achaogen Maintains A Strong Balance Sheet For The Development Of Plazomicin

Cash and cash equivalents were \$74.5 million at the end of 2Q14. In March 2014, Achaogen completed an initial public offering and raised a total of \$82.8 million in gross proceeds. Achaogen expects to use approximately \$35 million to \$40 million of net proceeds from the offering, in combination with the expected funding of approximately \$60 million from the BARDA contract, to support plazomicin's ongoing registration programs.

The BARDA contract contains an unexercised option for additional funding to provide further support for plazomicin's registrational studies. We believe Achaogen's current balance sheet will be sufficient to fund the clinical development of plazomicin through top-line data readout from the pivotal Phase III clinical trial.

Plazomicin Pricing And The Benefits Of Targeting Severe Indications Alone

It Is All About The Pharmacoeconomics

Bacteremia and pneumonia, the two indications targeted by Achaogen in the Phase III clinical trial for plazomicin, constitute the majority of the hospital-associated infections affecting a total of 1.7 million patients at a rate of one in every 20 hospitalizations per year. The infections impose substantial economic costs of up to \$9.8 billion annually. In cases involving invasive surgery, the mean length of stay is approximately 11 days costing \$32,900 for sepsis, and 14 days at a cost of \$46,400 for pneumonia. Most CRE infected patients are in acute healthcare settings such as ICUs, the cost of treatment is expected to be greater.

We believe a premium pricing for plazomicin should be justified if the drug candidate receives FDA approval based on successful Phase III superiority data on mortality benefit.

A reasonable comparator to plazomicin from a pricing standpoint would be daptomycin from Cubist Pharmaceuticals which is currently approved for the treatment of complicated skin and skin structure infections (cSSSI) and *Staphylococcus aureus* bloodstream infections (bacteremia), including those with right-sided infective endocarditis.

Daptomycin is also administered intravenously and the average length of treatment is approximately 14 days (7 to 24 days). The current wholesale acquisition cost (WAC) is \$354.72 per 500mg in reconstituted solution. In 2013, Cubist recorded U.S. daptomycin net revenue of \$908 million. Daptomycin, as well as all other currently available antibiotics, received FDA approval based on non-inferiority as the primary efficacy endpoint.

We estimate a cost per treatment cycle of \$15,000 in our revenue buildup model and believe the number is well justified if the pivotal Phase III study meets the primary endpoint of a statistically significant reduction in mortality. The patient outcome data from the study, if convincing, should present a strong case to both hospital formulary committees and payers. Pharmacoeconomic analyses also suggests that even with premium pricing, plazomicin should lead to a net cost savings for hospitals since any extra days that patients spend on mechanical ventilation and/or in ICUs are associated with significant expense.

Moreover, the small absolute prevalence of CRE infections in the U.S., estimated in our model to be approximately 80,000 per year, would in fact qualify as an Orphan disease. This point, we believe, would limit the impact that premium pricing would have on any one individual insurance payer. As a result, we would not expect to see pricing push back from payers.

Our revenue model suggests a market opportunity of approximately \$415 million for plazomicin in the U.S. In Europe where companies typically face more pricing pressure and a less favorable reimbursement environment, we conservatively estimate that plazomicin will be priced at a 70% discount to U.S. pricing and also achieve a lower market penetration.

The ex-U.S. CRE prevalence is higher than the U.S. prevalence and Achaogen expects the ongoing pivotal Phase III study to enroll the majority of its patients from ex-U.S. sites, predominantly Latin American and Eastern Europe. However, due to the lack of reliable information regarding patient

numbers, physician treating behavior, and Achaogen's pricing power, we conservatively base our valuation mainly on the U.S. market and treat the ex-U.S. market as additional upside potential.

Plazomicin is being developed for hospital-based indications so a hospital-targeted specialty sales force will be required for commercialization. Moreover, CRE infections are concentrated typically within large metropolitan areas in states such as New York, Pennsylvania, New Jersey, Texas and California. This epidemiologic pattern should further help Achaogen in commercializing plazomicin independently with a small sales force to maximize market penetration. Our model assumptions have Achaogen hiring approximately 30 sales representatives by year-end 2018 for the U.S. launch of plazomicin. In Europe, we estimate that Achaogen will enter into a partnership and receive back-end tiered royalties on plazomicin sales.

Another Undervalued Antibiotic Story

We ascertain the value of Achaogen shares by employing four different methodologies. First, we utilize a discounted earnings model whereby the first year of meaningful EPS is discounted back to 12 months from the present. We apply a P/E multiple that is in line with the mean multiple of the profitable biotech companies and employ a discount rate that takes into account clinical, regulatory and commercialization risk. Our model assumes profitability in 2019, with a fully diluted estimated EPS of \$1.38. However, we base our valuation on the estimated EPS of \$3.43 in 2020 since that will be the first year Achaogen will book full-year worldwide sales and royalty revenue. We then apply a 25x multiple that is in line with the forecasted industry average in 2015. Based on the risk associated with an investment in Achaogen, we discount back 30% and arrive at what we believe to be a fair 12-month target price of \$21.61.

Exhibit 11: Discounted Earnings Model

			Discount Rate							
			55.0%	50.0%	45.0%	40.0%	35.0%	30.0%	25.0%	20.0%
Diluted	\$3.43									
PE	25									
Discount Years	5.25	15x	\$5.15	\$6.12	\$7.31	\$8.79	\$10.64	\$12.97	\$15.93	\$19.74
Discount Rate	30.0%	20x	6.87	8.16	9.74	11.72	14.18	17.29	21.24	26.32
Valuation	\$21.61	25x	8.58	10.19	12.18	14.65	17.73	21.61	26.55	32.90
		30x	10.30	12.23	14.62	17.57	21.27	25.93	31.86	39.48
		35x	12.02	14.27	17.05	20.50	24.82	30.25	37.17	46.06
		40x	13.73	16.31	19.49	23.43	28.36	34.58	42.48	52.64
		45x	15.45	18.35	21.93	26.36	31.91	38.90	47.79	59.22
		50x	17.17	20.39	24.36	29.29	35.45	43.22	53.10	65.80
		55x	18.88	22.43	26.80	32.22	39.00	47.54	58.41	72.37

Source: SunTrust Robinson Humphrey

We then use a discounted cash flow (DCF) model to discount the estimated future cash flow booked by Achaogen to arrive at the calculated present value of the company's shares. From our revenue buildup model, we estimate the final year cash flow of \$238 million to the company in 2025. We apply an industry standard discount rate of 12% but apply a conservative perpetual growth rate of -5% given the potential competition in out years.

Exhibit 12: Discounted Cash Flow Model

Final year FCF	238
Perpetual Growth Rate	-5.0%
Terminal Value	1,328
Discount Factor	0.28
Present Value of Terminal Value	375
Present Value of Cash Flows	396
Enterprise Value	771
Add: Net cash	75
Market Value	846
Fully Diluted Shares Outstanding	18.6
Value per Fully Diluted Share	\$45.47
<i>Possibility of success</i>	50%
Risk aAdjusted Value per Fully Diluted Share	\$22.74

Source: SunTrust Robinson Humphrey

We further determine the value of Achaogen shares by using a clinical net present value (NPV) model based on the peak U.S. sales revenue in the year 2025, the out-year of our revenue buildup model. We estimate a peak market penetration of 25% for plazomicin and our projected 2025 revenue is approximately \$415.1million in the U.S. and \$278.9 million from rest of world. In both our DCF and clinical NPV models, we assign a success probability of 50% based on the safety and clinical efficacy of plazomicin as well as the current clinical development stage. We employ 100% for the overall economics from the U.S. market, based on the projection that Achaogen will commercialize plazomicin independently in the U.S., and a 15% royalty rate from ex-U.S. territories. Taking into account the number of current shares outstanding, we obtain a total clinical NPV of \$22.78.

Exhibit 13: Net Present Value Model

Drug name	Indication	Status	Launch	Success	Peak Sales (\$MM)	Economics	Profitability	NPV (U.S.\$)
Plazomicin U.S.	CRE	Phase III	2018	50%	415	100%	85%	20.37
Plazomicin ex-U.S.	CRE	Phase III	2019	50%	279	15%	100%	2.42
Total								22.78

Source: SunTrust Robinson Humphrey

Finally, we created a comparable company analysis, which is composed of companies working within the same or similar therapeutic area as Achaogen or that are at the same stage of clinical development, namely late-stage clinical trials focused on a defined therapeutic area. We then compare the mean technology value of the comparable universe (\$776.4MM) to that of Achaogen (\$113.6MM). The comparison demonstrates that shares of Achaogen are currently trading at a discount of 85% to the mean technology value of the comparable universe.

Exhibit 14: Comparable Company Analysis

Company	Ticker	Enterprise Value (\$MM)	Price: 10-31-14	Shares Out (MM)	Market Cap (\$MM)	Cash (\$MM)	Debt (\$MM)
Achillion Pharmaceuticals	ACHN	1,017.5	\$11.8	97.8	1,149.0	131.5	0.0
Chimerix	CMRX	933.0	\$31.0	36.5	1,132.2	200.6	1.5
Novavax	NVAX	1,183.3	\$5.6	238.4	1,335.1	152.7	0.9
Inovio Pharmaceuticals	INO	577.3	\$11.4	60.4	686.1	108.9	0.0
SAGE Therapeutics	SAGE	956.7	\$39.1	25.7	1,005.9	49.1	0.0
Otonomy	OTIC	469.0	\$26.4	20.3	535.9	68.2	1.3
Tetraphase	TTPH	643.7	\$23.9	30.0	716.2	75.4	2.9
Cempra	CEMP	430.9	\$13.6	35.8	487.4	74.2	17.7
Mean		776.4					
Achaogen	AKAO	113.6	10.62	17.71	188.1	74.496	0.0

Source: SunTrust Robinson Humphrey

AKAO Company History, Management And Compensation

Company History

Achaogen was incorporated in Delaware in 2002 and commenced operations in 2004. It initiated a Phase I trial of plazomicin (formerly ACHN-490) for the treatment of MDR Gram-negative bacterial Infections in 2009. Achaogen was awarded a contract worth up to \$64 Million by BARDA for the development of plazomicin in 2010. One year later, in 2011, Achaogen appointed Chief Medical Officer Kenneth Hillan to Chief Executive Officer. On January 29, 2014, Achaogen filed a Registration Statement with the SEC for a proposed Initial Public Offering (IPO). The company financed aggregate gross proceeds of \$82.8M through the IPO in March 12, 2014.

Management

Kenneth J. Hillan, M.B., Ch.B., President and Chief Executive Officer

Dr. Hillan joined Achaogen in April 2011 as Chief Medical Officer and was appointed Chief Executive Officer and a member of its board of directors in October 2011. Prior to joining Achaogen, Dr. Hillan served at Genentech from August 1994 to April 2011. He served in a number of key leadership positions in research and development, including Senior Vice President Clinical Development, Inflammation, Vice President Immunology, Tissue Growth and Repair (ITGR), Vice President Development Sciences and Vice President Research Operations and Pathology. Previously, Dr. Hillan served as Senior Vice President and head of Clinical Development and Product Development Strategy in Asia-Pacific for Roche in Shanghai, China. Dr. Hillan has an M.B. Ch.B. (Bachelor of Medicine and Surgery) degree from the Faculty of Medicine at the University of Glasgow, U.K. Dr. Hillan is a Fellow of the Royal College of Surgeons (FRCS), and a Fellow of the Royal College of Pathologists (FRCPath). Dr. Hillan has authored a number of scientific publications and has more than 50 issued patents.

Becki Filice, Senior Vice President, Development Operations and Portfolio Management

Ms. Filice has served as Achaogen's Senior Vice President, Development Operations and Portfolio Management since November 2012. She is responsible for development sciences, clinical operations, biometrics, CMC, project management and human resources. Previously Ms. Filice served as Achaogen's Vice President, Development Operations and Portfolio Management from May 2011 to October 2012. Prior to joining Achaogen, Ms. Filice worked at Genentech for 15 years

with positions of Senior Director, Project Excellence in Global Development, and Senior Director, Project Portfolio Management in Product Development. She also served as Project Team Leader for both the Avastin® and Nutropin AQ® products. Earlier in her career, Ms. Filice held management positions in clinical research with Ligand Pharmaceuticals Inc. and Syntex, Inc. She started her career as a clinical microbiologist at El Camino Hospital in Mountain View, California. Ms. Filice has a B.A. in Microbiology from University of California, Davis, and an MBA from Santa Clara University, California. She also holds a Project Management Certification from the Pharmaceutical Education and Research Institute and has served as a faculty member of the American Course on Drug Development and Regulatory Sciences (ACDRS).

Executive Compensation

Achaogen's Named Executive Officers (NEO) include Kenneth J. Hillan, M.B., Ch.B., President and Chief Executive Officer; Becki Filice, Senior Vice President, Development Operations and Portfolio Management; and Dennis Hom, Vice President, Finance and Corporate Development. A summary of compensations is listed in the exhibit below.

Exhibit 15: Summary Of AKAO Management Compensation

Name	Principal Position	Year	Salary (\$)	Bonus (\$)	Stock awards (\$)	Option awards ⁽¹⁾ (\$)	Non-equity incentive plan compensation ⁽²⁾ (\$)	All other compensation ⁽³⁾ (\$)	Total (\$)
Kenneth J. Hillan	President and Chief Executive Officer	2013	367,200	—	—	—	—	7,650	374,850
		2012	360,000	—	—	965,541	126,000	—	1,451,541
Becki Filice ⁽⁴⁾	Senior Vice President, Development Operations and Portfolio Management	2013	285,600	—	—	—	—	7,650	293,250
		2012	271,667	—	—	227,617	70,000	7,500	576,784
Dennis Hom	Vice President, Finance and Corporate Development	2013	248,106	—	—	403,440	—	7,443	658,989

(1) For the option awards column, amounts shown represent the grant date fair value of stock awards and options granted during 2012 or 2013, as applicable, as calculated in accordance with ASC Topic 718.

(2) The amounts reported in the Non-Equity Incentive Plan Compensation column represent the annual cash performance-based bonuses earned by the NEOs pursuant to the achievement of certain Company and individual performance objectives. The amounts listed for 2012 were paid to the named executive officers in early 2013. For Ms. Filice, the amount represents the payment of her performance bonus with a pro rata adjustment to reflect her promotion to Senior Vice President in November 2012. Annual cash performance-based bonuses for the NEOs for 2013 have not yet been determined.

(3) The amounts reported in the All Other Compensation column constitute the Company's matching contribution under its 401(k) plan.

(4) Ms. Filice was promoted to Senior Vice President in November 2012.

Annual cash performance-based bonuses for the NEOs for 2013 have not yet been released.

Source: Achaogen Filings

We believe that Achaogen's compensation rules are aligned with shareholder interest.

For 2013, Dr. Hillan, Ms. Filice, and Mr. Hom each had an annual bonus target of 35%, 30%, and 25%, respectively, of base salary awarded based on the achievement of certain milestones established by the board of directors. To determine the performance bonus amounts for the NEOs for 2012 and 2013, the board of directors set certain corporate performance goals, using a mixture of research, clinical, regulatory, government funding, workplace satisfaction and other financing targets. These performance goals were not expected to be attained based on average or below average performance. After determining performance targets, each performance target was given a different weight for determining the overall bonus amount based on the importance to the success of the company for each performance target. For fiscal year 2013, the target achievement percentage is based on:

- Plazomicin clinical, regulatory, partnering, and government funding targets - 40%
- ACHN-975 clinical and government funding targets - 20%
- Additional research targets - 15%
- Financing target - 15%
- Workplace satisfaction targets - 10%
- The financing target can also increase bonus amounts by an additional 15%.

For 2012, the performance goal and actual achievement percentage is listed below:

Exhibit 16: AKAO Executive Performance Goal And Achievement Rate

Performance Goal	Target Achievement Percentage	Actual 2012 Achievement Percentage
Plazomicin Clinical, Regulatory and Government Funding Targets	35.0%	35.0%
ACHN-975 Clinical and Government Funding Targets	25.0%	10.0%
Research, Clinical, Regulatory and Government Funding Targets for Subsequently Terminated Aminoglycoside Program	15.0%	5.0%
Additional Research Targets	15.0%	15.0%
Workplace Satisfaction Targets	10.0%	10.0%
Financing Targets	+/-20%	10%
Total	100%(+/-20%)	85.0%

Source: Achaogen Filings

Following its review and determinations of the target achievement for 2012, the board of directors awarded cash bonuses to the NEOs of 100% of their target bonus opportunities.

Exhibit 17: Achaogen, Inc. Revenue Buildup Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Plazomicin for Carbapenem-Resistant Enterobacteriaceae (CRE)								
U.S.								
Annual number of hospitalizations (MM)	36.0	36.4	36.7	37.1	37.5	37.8	38.2	38.6
% of hospitalized patients who are infected with pneumonia	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
Number of patients infected with nosocomial pneumonia (NP) (MM)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
% of hospitalized patients who are infected with bloodstream infections	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%
Number of patients infected with bloodstream infections (BSI) (MM)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Total number of patients with NP and nosocomial BSI (MM)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
% of carbapenem-resistant clones in nosocomial bacterial infections	4.0%	4.0%	4.1%	4.1%	4.2%	4.2%	4.2%	4.3%
Annual number of carbapenem resistant NP and nosocomial BSI cases	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Annual number of CRE cases (MM)	0.08	0.08	0.08	0.09	0.09	0.09	0.09	0.09
% of patients treated with plazomicin	2.0%	8.0%	14.0%	18.0%	20.0%	22.0%	24.0%	25.0%
Number of patients treated with plazomicin (MM)	0.002	0.007	0.012	0.015	0.017	0.020	0.022	0.023
Cost per treatment cycle	\$9,000	\$15,000	\$15,450	\$15,914	\$16,391	\$16,883	\$17,389	\$17,911
U.S. Total Plazomicin Revenue (\$MM)	\$14.5	\$98.7	\$181.5	\$245.2	\$286.3	\$330.8	\$379.2	\$415.1
ROW								
Annual number of CRE cases (MM)	0.10	0.10	0.10	0.10	0.10	0.11	0.11	0.11
% of patients treated with plazomicin	5.0%	9.0%	12.0%	14.0%	16.0%	18.0%	18.0%	20.0%
Number of patients treated with plazomicin (MM)	0.005	0.009	0.012	0.015	0.017	0.020	0.020	0.022
Cost per treatment cycle	\$10,500	\$10,815	\$11,139	\$11,474	\$11,818	\$12,172	\$12,538	\$12,911
ROW Total Plazomicin Revenue (\$MM)	51.8	98.0	137.3	168.3	202.1	238.9	278.9	318.9
ROW Royalty Revenue Booked by Achaogen (\$MM) (15% - 25%)	\$7.8	\$17.6	\$24.7	\$30.3	\$40.4	\$47.8	\$55.8	\$63.8
WW Total Sales and Royalty Revenue Booked by Achaogen (\$MM)	\$14.5	\$106.5	\$199.1	\$269.9	\$316.6	\$371.3	\$427.0	\$470.8

Source: SunTrust Robinson Humphrey

Exhibit 18: Achaogen, Inc. Quarterly P&L Model (\$MM)

	2012A	Q1-Q3:13A	Q4:13A	2013A	Q1:14A	Q2:14A	Q3:14E	Q4:14E	2014E	Q1:15E	Q2:15E	Q3:15E	Q4:15E	2015E
Plazomicin Sales Revenue	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
Plazomicin Royalty Revenue	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
Contract Revenue	▼ 17.9	12.3	6.2	18.5	6.0	5.2	6.6	7.2	25.0	6.5	6.8	7.2	7.5	28.0
Total Revenues	17.9	\$12.3	\$6.2	\$18.5	\$6.0	\$5.2	\$6.6	\$7.2	\$25.0	\$6.5	\$6.8	\$7.2	\$7.5	\$28.0
COGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Research and Development	▼ 26.6	16.7	6.8	23.5	6.6	6.2	7.4	7.8	28.0	▼ 7.6	7.8	8.0	8.1	31.5
General and Administrative	7.3	5.4	1.6	7.0	2.6	2.3	2.5	2.7	10.2	2.5	2.6	2.7	2.7	10.5
Sales	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Operating Expenses	33.9	22.1	8.4	30.5	9.2	8.5	9.9	10.5	38.2	10.1	10.4	10.7	10.8	42.0
Income (Loss) from Operations	(\$16.0)	(\$9.8)	(\$2.2)	(\$12.0)	(\$3.2)	(\$3.3)	(\$3.3)	(\$3.3)	(\$13.2)	(\$3.6)	(\$3.6)	(\$3.5)	(\$3.3)	(\$14.0)
Interest Expense and Other, net	▼ (2.4)	(1.1)	(0.2)	(1.3)	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)
Interest Income and Other, net	0.1	0.3	(0.1)	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	(\$18.4)	(\$10.6)	(\$2.5)	(\$13.1)	(\$3.5)	(\$3.6)	(\$3.5)	(\$3.5)	(\$14.0)	(\$3.8)	(\$3.8)	(\$3.7)	(\$3.5)	(\$14.8)
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Income Tax	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
Net Income (Loss) Attributable to Common Shareholders	(18.4)	(10.6)	(2.5)	(13.1)	(3.5)	(3.6)	(3.5)	(3.5)	(14.0)	(3.8)	(3.8)	(3.7)	(3.5)	(14.8)
GAAP EPS, Basic and Diluted	(\$4.80)	(\$2.50)	(\$0.58)	(\$3.08)	(\$1.00)	(\$0.20)	(\$0.20)	(\$0.19)	(\$0.99)	(\$0.21)	(\$0.21)	(\$0.20)	(\$0.19)	(\$0.81)
Weighted Average Shares Outstanding - Basic and Diluted	3.8	4.2	4.3	4.3	3.5	▼ 17.7	17.8	17.9	14.2	18.0	18.1	18.2	18.3	18.2

Source: SunTrust Robinson Humphrey

Exhibit 19: Achaogen, Inc. Annual P&L Model (\$MM)

	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Plazomicin Sales Revenue	0.0	0.0	0.0	0.0	0.0	0.0	14.5	98.7	181.5	245.2	286.3	330.8	379.2	415.1
Plazomicin Royalty Revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.8	17.6	24.7	30.3	40.4	47.8	55.8
Contract Revenue	17.9	18.5	25.0	28.0	23.0	17.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	17.9	18.5	25.0	28.0	23.0	17.5	14.5	106.5	199.1	269.9	316.6	371.3	427.0	470.8
COGS	-	-	-	-	-	-	2.2	13.8	23.6	29.4	31.5	33.1	37.9	41.5
Research and Development	26.6	23.5	28.0	31.5	32.0	30.0	28.0	28.0	28.0	30.0	32.0	35.0	35.0	35.0
General and Administrative	7.3	7.0	10.2	10.5	8.0	8.5	9.5	11.0	12.5	14.0	15.0	16.0	17.0	18.0
Sales	-	-	-	-	-	-	4.5	8.0	8.4	8.8	9.3	9.7	10.2	10.7
Total Operating Expenses	33.9	30.5	38.2	42.0	40.0	38.5	44.2	60.8	72.5	82.2	87.7	93.8	100.1	105.2
Income (Loss) from Operations	(\$16.0)	(\$12.0)	(\$13.2)	(\$14.0)	(\$17.0)	(\$21.0)	(\$29.7)	\$45.7	\$126.7	\$187.7	\$228.8	\$277.5	\$326.9	\$365.6
Interest Expense and Other, net	(2.4)	(1.3)	(0.8)	(0.8)	(0.5)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest Income and Other, net	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	(\$18.4)	(\$13.1)	(\$14.0)	(\$14.8)	(\$17.5)	(\$21.0)	(\$29.7)	\$45.7	\$126.7	\$187.7	\$228.8	\$277.5	\$326.9	\$365.6
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	8%	13%	18%	23%	27%	35%
Income Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.1	24.4	41.2	63.8	88.3	128.0
Net Income (Loss) Attributable to Common Shareholders	(18.4)	(13.1)	(14.0)	(14.8)	(17.5)	(21.0)	(29.7)	45.7	116.5	163.3	187.6	213.6	238.6	237.6
GAAP EPS, Basic and Diluted	(\$4.80)	(\$3.08)	(\$0.99)	(\$0.81)	(\$0.93)	(\$0.82)	(\$1.12)	\$1.38	\$3.43	\$4.66	\$5.21	\$5.77	\$6.28	\$6.09
Weighted Average Shares Outstanding - Basic and Diluted	3.8	4.3	14.2	18.2	18.8	25.5	26.5	33.0	34.0	35.0	36.0	37.0	38.0	39.0

Source: SunTrust Robinson Humphrey

Company Description

Achaogen is a biotechnology company focused on the clinical development of new antibiotic agents to fight the most highly resistant pathogens with limited clinical options. The company is in Phase III development with plazomicin for the treatment of bloodstream infections and hospital-based pneumonia caused by the CRE pathogen. The company's Phase III pivotal trial is the first Phase III pivotal trial in the antibiotic space that has been designed as a superiority study. Achaogen has received significant funding from BARDA for the development of plazomicin, which we believe underlines the government's support and need for this therapeutic.

Investment Thesis

The pathogen-focused approach taken Achaogen in developing plazomicin for the treatment of CRE infections, which cause high mortality due to lack of optimal treatments, has won Achaogen strong support from both the FDA and BARDA. The ongoing pivotal Phase III clinical trial is being conducted with an SPA and plazomicin has been granted Fast Track Designation. Additionally, BARDA has committed a total of \$103.8MM in grant funding for plazomicin development, including \$60MM to fund the pivotal study. Plazomicin has demonstrated strong potency against CRE pathogens and PK/PD modeling in combination with preclinical studies in animal infection models suggest a high likelihood of success in the pivotal study. The study is designed to demonstrate the superiority of plazomicin over currently available therapies. We believe a well established survival benefit will entitle plazomicin to premium pricing and will provide Achaogen with strong revenue potential.

Valuation and Risks

Our 12-month price target of \$22 is determined by taking an average of three different model methodologies. We reach a 12-month price target of \$21.61 with a discounted earnings model, a price target of \$22.73 with a discounted cash flow model, and a price target of \$22.78 with a clinical net present value model. Details of these models are contained within this report.

The risks associated with an investment in Achaogen are the same as they are for all early-stage biotechnology companies. There is clinical risk, which encompasses the failure of the molecule being tested to successful complete clinical trials. There is regulatory risk whereby approval is not given or is delayed by the regulatory agency for a number of reasons. Finally there is the financial risk of not having enough funding to complete clinical development and if approved there is always the commercial risk associated with a launch. Specifically to Achaogen, we believe the prime risk is the inability to complete the Phase III enrollment in a timely manner that will allow for the interim analyses to read out as planned.

Companies Mentioned in This Note

Cubist Pharmaceuticals, Inc. (CBST, \$72.29, Buy)

Cempra, Inc. (CEMP, \$13.60, Buy)

Merck & Co. Inc. (MRK, \$57.94, Buy)

Pfizer Inc. (PFE, \$29.95, Reduce)

The Medicines Company (MDCO, \$25.32, NR)

AstraZeneca (AZN, \$72.94, NR)

Johnson and Johnson (JNJ, \$107.78, NR)

Actavis plc (ACT, \$242.74, NR)

Tetraphase Pharmaceuticals (TTPH, \$23.90, NR)

Isis Pharmaceuticals (ISIS, \$46.06, NR)

Analyst Certification

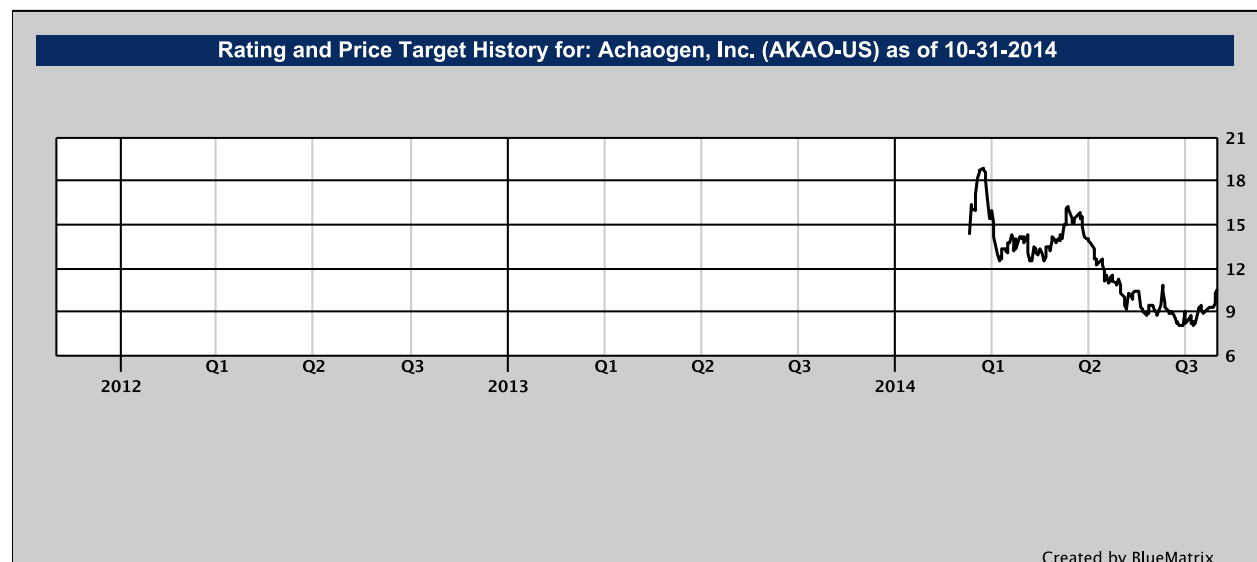
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**Price targets are within a 12-month period, unless otherwise noted

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T = transfer coverage

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