CREDIT SUISSE

Achaogen, Inc. (AKAO)

Rating	**OUTPERFORM* [V]**
Price (04 Apr 14, US$)	14.15
Target price (US$)	22.00[1]
52-week price range	18.95 - 14.15
Market cap. (US$ m)	237.45
Enterprise value (US$ m)	165.89

**Stock ratings are relative to the coverage universe in each analyst's or each team's respective sector.*
[1]Target price is for 12 months.
[V] = Stock considered volatile (see Disclosure Appendix).

Research Analysts

Jason Kantor, PhD
415 249 7942
jason.kantor@credit-suisse.com
Jeremiah Shepard, PhD
415 249 7933
jeremiah.shepard@credit-suisse.com
Ravi Mehrotra PhD
212 325 3487
ravi.mehrotra@credit-suisse.com
Lee Kalowski
212 325 9683
lee.kalowski@credit-suisse.com
Koon Ching PhD
212 325 6286
koon.ching@credit-suisse.com
Anuj Shah
212 325 6931
anuj.shah@credit-suisse.com

SMALL & MID CAP RESEARCH

Focus on Killer Bacteria; Aiming for Superiority in Phase III

We are initiating coverage of Achaogen with an Outperform rating and a $22 target price. Our positive thesis is based on the significant unmet medical need in resistant bacteria, the robust Phase III program for plazomicin, and the improving regulatory environment and investor sentiment toward new antibiotics.

- **Phase III Asset Targets Superiority:** AKAO has designed its Phase III trial for plazomicin to show superiority in survival compared with the current standard of care. We believe the trial will be clinically successful, provide lasting competitive advantage, and support premium pricing.
- **Improving Regulatory Environment:** The 2012 GAIN Act provided ten years of exclusivity to new antibiotics and marked a favorable turning point in the FDA's dealings with antibiotic companies. The recently proposed DISARM Act could provide additional benefits in better reimbursement. Driven by these regulatory changes, investor sentiment is also improving.
- **Catalysts:** In 2014, we see progress in Phase II and Phase III studies of plazomicin in CRE. In 2015, catalysts include first interim analysis of Phase III (H2:15), data from the Phase II CRE study (Q4:15), and the initiation of a clinical program for a second antibiotic (2015).
- **Valuation:** Our $22 target price is based on a 65% probability of success for plazomicin, approximately $473M in peak sales, and an ex-U.S. partner. Our estimates could prove conservative on price, penetration, market size, and the economics of the ex-U.S. deal. Our valuation includes a very small nominal value for the preclinical assets.

Financial and valuation metrics

Year	12/13A	12/14E	12/15E	12/16E
EPS (CS adj.) (US$)	-1.36	-1.00	-0.91	-0.95
Prev. EPS (US$)	—	—	—	—
P/E (x)	-10.4	-14.1	-15.5	-14.9
P/E rel. (%)	-60.9	-89.0	-108.8	-115.9
Revenue (US$ m)	18.5	15.0	15.0	15.0
EBITDA (US$ m)	-11.5	-15.6	-16.6	-22.5
OCFPS (US$)	-1.43	-0.26	-0.67	-0.75
P/OCF (x)	—	-54.1	-21.3	-18.9
EV/EBITDA (current)	-20.5	-15.1	-14.2	-10.4
Net debt (US$ m)	-3	-72	-59	-134
ROIC (%)	-241.36	1,691.22	1,413.52	1,574.96

Number of shares (m)	16.78	IC (current, US$ m)	4.96
BV/share (Next Qtr., US$)	7.0	EV/IC (x)	27.1
Net debt (Next Qtr., US$ m)	-72.3	Dividend (current, US$)	—
Net debt/tot cap (Next Qtr., %)	-92.2	Dividend yield (%)	—

Source: Company data, Credit Suisse estimates

Portfolio Manager Summary

Pure-play antibiotic company with a proprietary Phase III asset

AKAO was founded in 2004, and its primary focus is the development of Gram-negative antibiotics. This class of bacteria includes some of CDC's greatest public health threats. AKAO's lead drug, plazomicin, is being specifically developed for one of the most concerning bacteria called CRE (carbopenam-resistant enterobacteriaceae). Other drugs in the pipeline target drug-resistant pseudomonas infections, another high priority pathogen.

- Over the next 12 months, we expect AKAO to make substantial progress in enrolling the Phase III study and advance a new drug candidate for clinical development.
- A first and second interim analysis of the Phase III trial is expected in H2:15 and H2:16, respectively. Data from a smaller open-label trial of plazomicin will likely read out in late 2015, and could provide some visibility into the likely outcome of the Phase III.
- Our expectation is that the Phase III trial will run to completion in H1:17, with FDA approval in 2018. Over that same period, we expect AKAO will likely advance two programs into the clinic and should have substantial proof-of-efficacy data from one or more pipeline programs.

Exhibit 1: AKAO Pipeline

Drug	Indication	Stage	Partner
Plazomicin	Carbapenam-resistant enterobacteriaceae	Phase III	Proprietary
LpxC inhibitor	Pseudomonas	Preclinical (IND 2015)	Proprietary
Antibacterial Ab	Pseudomonas	Preclinical (IND 2015)	Proprietary

Source: Company data, Credit Suisse estimates.

Exhibit 2: AKAO News Flow

Timing	Expected News Flow	Program
2014	Initiate "Supportive" Phase 2	Plazomicin
2014	Select development candidate	Antipseudomonal
H2:15	Initiate safety trial	Plazomicin
H2:15	First interim - Phase 3	Plazomicin
Q4:15	"Supportive" Phase 2 top-line data release	Plazomicin
2015	File IND	Antipseudomonal
2015	File IND	LpxC inhibitor
H2:16	Second interim - Phase 3	Plazomicin
H1:17	Top-line data for Phase 3	Plazomicin
YE:17	File NDA with FDA	Plazomicin

Source: Company data, Credit Suisse estimates.

Investment Positives

- **Plazomicin Is Being Developed to Treat an Urgent Threat:** The CDC identifies CRE as one of the most urgent infectious disease threats and plazomicin is active against these resistant bacteria. The FDA recognizes the need for new agents targeting drug-resistant organisms, and this could help facilitate a faster review of plazomicin.
- **Robust Phase III Study Could Solidify Plazomicin as Leading Agent:** Plazomicin is the only antibiotic being tested for superiority using an overall survival endpoint, and a successful outcome from this study could lead to the drug becoming the preferred agent for CRE and provide the company with significant pricing power.

- **Favorable Regulatory Environment:** Increased concern regarding antibiotic resistant bacteria and the passage of the GAIN Act in 2012, set the stage for a more permissive and cooperative FDA. The GAIN Act gives ten years of exclusivity to new antibiotics and provides regulatory paths to approval that were not previously available. The FDA has indicated a willingness to approve new antibiotics for specific bacteria on smaller trials, and this could directly benefit AKAO.
- **Phase III Largely Funded by BARDA:** The Biomedical Advanced Research and Development Authority (BARDA) has a contract with AKAO to provide funding for the ongoing Phase III trial. BARDA has committed up to $60.4M for the Phase III clinical trial, which is in addition to the $43.4M already received for this program. The BARDA funding provides meaningful leverage to the capital raised from investors for the Phase III trial. AKAO plans to combine approximately $35-$40M from the equity raise with the BARDA funding to complete the Phase III study.
- **Focus on Gram-Negative Drug Development:** In recent years, companies have been more focused on developing Gram-positive antibiotics, and we believe AKAO's focus on Gram-negative antibiotics places it in the area of highest unmet medical need. We expect that AKAO could take one or two new Gram-negative drug candidates into the clinic in 2015. Both candidates are novel and address the problem of drug-resistant pseudomonas infections.
- **Phase II Results in Urinary Tract Infections:** The Phase II data demonstrated plazomicin's efficacy in a standard model of Gram-negative infections using the same target dose as the Phase III study. It also established a safety profile that is consistent with other drugs in its class.

Investment Risks

- **Superiority Trial Is Riskier than Most:** Antibiotics are usually developed using “non-inferiority” studies, in which a new drug needs to be no worse than existing therapies. Superiority is a more difficult endpoint, and it is possible that plazomicin demonstrates efficacy in the CRE setting, yet fails to demonstrate statistically significant improvements in overall survival.
- **Difficult Trial to Conduct:** CRE is still a relatively rare infection and the patients being targeted are extremely ill. Enrollment could be challenging, and predicting enrollment rate and mortality in the control arm is difficult. Even with the projected enrollment, the timeline to final data is not until H1:17.
- **Competition:** Several Gram-negative drugs are in development that could potentially treat CRE, including drugs from The Medicines Company and Forest/AstraZeneca. The Medicines Company has publicly stated that it intends to pursue a faster strategy for potential approval and carbavance could reach the market before or at the same time as plazomicin.
- **Activity and Safety in Pneumonia and Blood Stream Infections Unknown:** The relative efficacy and safety of plazomicin in CRE pneumonia and blood stream infections is not known. The previous clinical trials were conducted in patients with complicated urinary tract infections.
- **Pricing:** Most companies developing drugs for resistant bacteria hope to price their drugs at a significant premium to currently used antibiotics. Another alternative approach is to base pricing on the value captured by using the therapeutic (i.e., improvement in survival, hospital avoidance, etc.). However, value-based pricing is not established in this market place, and real clinical benefits will need to be shown to support higher prices.

- **Safety:** Plazomicin belongs to the class of antibiotics called aminoglycosides, which are known to cause kidney toxicity and ototoxicity (hearing loss). AKAO is using dose adjustments to enhance safety and efficacy, but toxicity remains a clinical, regulatory, and competitive risk.
- **CRE Is an Emerging Threat:** Currently, the outbreak of CRE is concentrated in certain hotspots. Resistance has spread over time and will likely continue to grow, but forecasting the exact future market size is difficult.

Valuation—$22 Target Price

Our $22 target price implies a $395M market cap using current shares outstanding and an enterprise value of $312M using current pro-forma financial values. Our valuation is supported by a probability-weighted DCF of the plazomicin franchise ($355M or $20/share) and a nominal value to its preclinical assets ($40M, $2/share). (See Exhibit 3.) We use a 65% probability of success for plazomicin and a 12.5% discount rate.

We also look at two comparator company metrics to reality check our valuation.

- The current mean and median enterprise values for Phase III antibiotic companies are $289M and $208M (AKAO, DRTX, TTPH, CEMP, INSM). (See Exhibit 4.)
- Take-out comps also support a strong valuation, including TSRX at $707M in cash (+$111M in CVRs), OPTR at $535M (+$266M in CVRs), and privately held Rempex at $140M (+$334M in CVRs). (See Exhibit 4.)

The biggest levers in our valuations are the following.

(1) **Probability of Success:** We assign a 65% probability of success to plazomicin. We believe existing clinical data and preclinical activity against CRE are sufficient to predict success in CRE pneumonia and blood stream infection. The primary risk is in the powering assumptions underlying the Phase III design.

(2) **Pricing of Plazomicin:** We model a net price of $1,300/day. We believe this could be a conservative estimate, given the (1) high mortality rate of CRE infections, (2) significant value that can be captured by curing a patient of CRE, and (3) proposed legislation that could support a higher price point of antibiotics developed for treating drug-resistant infections.

(3) **Timing of U.S. and EU approvals:** We assume a U.S. launch for plazomicin in 2018 following the final data analysis in 2017. However, if the efficacy is compelling in one of the two planned interim looks, AKAO may be able file for approval ahead of our expectations. Additionally, AKAO will conduct a "supportive" Phase II study in CRE, and if the results are positive and the FDA is open to an earlier filing based on the small data set, AKAO may be able to obtain accelerated approval for the product.

(4) **Introduction of New Pipeline Program(s):** AKAO is expected to start clinical trials with at least one new Gram-negative pipeline candidate in 2015. We do not include this in our valuation. Introducing one or two new drugs into the clinic could add significant value to the stock, especially if initial proof-of-efficacy data are disclosed prior to the completion of the plazomicin Phase III trial.

(5) We Assume an EU Partnership: We assume that AKAO enters into an EU partnership that includes a $25M upfront payment and a $30M EU approval milestone. If AKAO can negotiate a larger deal, this could help extend the cash runway for the company and positively affect our valuation.

Exhibit 3: Probability-Adjusted Valuation

	Value	$/share
DCF value of plazomicin	355	$20
Pipeline	40	$2
Total	395	$22

Source: Company data, Credit Suisse estimates.

Exhibit 4: Public Comps and Recent Takeouts

Comp analysis

Company	Ticker	Price	Market cap	Enterprise value	Stage
Cempra, Inc.	CEMP	$10.85	$360	$278	Phase III
Insmed Inc.	INSM	$17.39	$683	$588	Phase III
Achaogen, Inc.	AKAO	$15.13	$250	$167	Phase III
Durata Therapeutics	DRTX	$12.89	$343	$208	NDA filed
Tetraphase Pharma.	TTPH	$11.43	$295	$203	Phase III
Mean				$289	
Median				$208	

Recent takeouts

Company	Ticker	Acquirer	Date	Price
Trius Therapeutics	TSRX	CBST	July 30, 2013	$707M in cash + $111 in CVRs
Optimer Pharma.	OPTR	CBST	July 30, 2013	$535M in cash + $266 in CVRs
Rempex Pharma.	Private	MDCO	Dec. 4, 2013	$140M upfront + $334M in milestones

Source: Company data, Credit Suisse estimates.

Exhibit 5: AKAO Earnings Model

	2013A	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenues												
Plazomicin US sales										63.5	105.0	154.4
Plazomicin EU royalties (20%)										3.1	7.3	18.0
Contract revenue	18.5	3.8	3.8	3.8	3.8	15.0	15.0	15.0	40.0	45.0	11.3	
Total revenues	18.5	3.8	3.8	3.8	3.8	15.0	15.0	15.0	40.0	111.6	123.6	172.4
Expenses												
COGS										7.6	13.0	20.0
R&D	23.5	8.2	4.5	4.7	5.0	22.4	22.6	24.8	27.3	39.5	35.0	46.1
G&A	7.0	2.1	2.1	2.2	2.2	8.5	9.3	11.1	17.0	50.0	55.0	57.8
Total operating expenses	30.5	10.3	6.6	6.9	7.2	30.9	31.9	37.9	57.0	97.1	103.0	123.8
Operating income (loss)	(12.0)	(6.5)	(2.8)	(3.1)	(3.4)	(15.9)	(16.9)	(22.9)	(17.0)	14.5	20.6	48.6
Total Other Income (Expense)	(1.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.4)	0.3	0.4	0.4	0.5	0.5	0.5
Pre Tax Income	(13.1)	(6.7)	(2.9)	(3.2)	(3.5)	(16.3)	(16.6)	(22.5)	(16.6)	15.0	21.1	49.1
Income tax expense (benefit)												
Net Income	(13.1)	(6.7)	(2.9)	(3.2)	(3.5)	(16.3)	(16.6)	(22.5)	(16.6)	15.0	21.1	49.1
EPS - diluted (proforma)		($0.60)	($0.16)	($0.18)	($0.19)	($1.00)	($0.91)	($0.95)	($0.69)	$0.56	$0.79	$1.83
Shares outstanding - diluted (proforma)		11.13	17.82	17.91	18.00	16.22	18.23	23.63	24.11	26.64	26.77	26.90

Source: Company data, Credit Suisse estimates.

Key Modeling Assumptions for Plazomicin

We model first plazomicin sales in 2018 and peak share in 2021. Our model projects $274M (unadjusted) in U.S. sales at a peak penetration of approximately 25%; ex-U.S. sales in that year are estimated at $213M (unadjusted). Sales continue to grow through price and market growth through 2024. Our model is based on projections of the CRE market globally and assumes that patients are treated both for confirmed CRE and empirically for suspected CRE (shorter course).

Market assumptions could prove conservative both on price and penetration

Assumptions

Market size could also become larger if CRE spread continues at a rapid pace

- **Pricing:** We estimate that plazomicin is priced at $1,300 per day (increases 5% per year thereafter), suggesting a $9,000 to $18,000 price for 7-14 days of therapy. Recent legislation introduced in the House of Representatives (DISARM Act) could support higher pricing for antibiotics approved for serious infections like CRE.
- **Empirical Treatment:** We believe patients suspected of having CRE will be treated empirically with plazomicin before confirmation of the pathogen. We estimate that approximately three patients will be treated empirically for each patient treated with a confirmed infection. We model an average of 2.5 days of empiric therapy, while those with confirmed CRE will receive an average of 10 days of therapy.
- **Market Size:** We use a starting patient population of 18,000 with confirmed CRE in the U.S. in 2013 (growing at 12% initially, before leveling off at 5%). We assume plazomicin reaches a peak penetration of 25% in 2021 in the U.S. and reaches peak U.S. sales of $285M in 2024. We assume that AKAO markets the drug in the U.S. by itself and partners in EU. We assume a 20% royalty rate on EU sales.

BARDA Funding for Phase III Program

Total government funding for plazomicin from the Biomedical Advanced Research and Development Authority (BARDA) is $103.8M. AKAO has already received $43.4M to support earlier development and manufacturing, and BARDA is committed to up to $60.4M for the Phase III clinical trial.

BARDA has committed $103.8M for plazomicin development

The BARDA contract also has an option to support the proposed safety study, but the funding potentially provided by this option has not been determined. Importantly, there are no commercial obligations for the funding received from BARDA (i.e., no royalties or future financial rights).

We view the BARDA funds as a significant source of non-dilutive funding that provides leverage to its current cash resources. While there is inherent risk with government contracts, including the potential for a unilateral change in terms by the Government, we expect that AKAO is likely to receive the full benefit of the committed funds from BARDA.

Pricing—A Potential Benefit of the Phase III Design

We believe that AKAO will have significant pricing power if it demonstrates an overall survival benefit over the current standard of care, colistin. The value proposition for an antibiotic that has a survival benefit in blood stream and pneumonia infections caused by CRE is significant. Relative to cancer therapeutics that extend the life of a patient by a short period (i.e., months), an antibiotic may allow a patient to fully recover from their infection and lead a normal life not possible without the therapeutic. The company intends to conduct pharmaeconomic analyses during the Phase III study (i.e., reduction in days on ventilation, days in ICU, etc.) that will help support the value proposition of the therapy to payors.

Exhibit 6: Plazomicin Sales Model

	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Confirmed CRE	45,600	50,136	37,632	42,148	47,206	52,870	55,514	58,289	61,204	64,264	67,477	70,851
US	18,000	20,160	22,579	25,289	28,323	31,722	33,308	34,974	36,722	38,558	40,486	42,511
EU5	12,000	13,440	15,053	16,859	18,882	21,148	22,206	23,316	24,482	25,706	26,991	28,340
Rest of EU	15,600	16,536	17,528	18,580	19,695	20,876	21,920	30,311	31,826	33,417	35,088	36,843
Suspected CRE	136,800	100,800	112,896	126,444	141,617	158,611	166,541	174,868	183,612	192,792	202,432	212,554
US	54,000	60,480	67,738	75,866	84,970	95,166	99,925	104,921	110,167	115,675	121,459	127,532
EU5	36,000	40,320	45,158	50,577	56,647	63,444	66,617	69,947	73,445	77,117	80,973	85,021
Rest of EU	46,800	49,608	52,584	55,740	59,084	62,629	65,760	90,932	95,478	100,252	105,265	110,528
						Early in 2018						
US Build	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Confirmed CRE												
Penetration						10%	15%	20%	25%	25%	25%	25%
Patients treated						3,172	4,996	6,995	9,181	9,640	10,122	10,628
Treatment course (days)						10	10	10	10	10	10	10
Days of treatment						31,722	49,962	69,947	91,806	96,396	101,216	106,277
Cost per day (gross)						1,300	1,365	1,433	1,505	1,580	1,659	1,742
Cost per day (net)						1,144	1,201	1,261	1,324	1,391	1,460	1,533
Sales (M)						$36.3	$60.0	$88.2	$121.6	$134.0	$147.8	$162.9
Suspected CRE												
Penetration						10%	15%	20%	25%	25%	25%	25%
Patients treated						9,517	14,989	20,984	27,542	28,919	30,365	31,883
Treatment course (days)						2.5	2.5	2.5	2.5	2.5	2.5	2.5
Days of treatment						23,791.61	37,472	52,461	68,854	72,297	75,912	79,708
Cost per day (net)						1,144	1,201	1,261	1,324	1,391	1,460	1,533
Sales (M)						$27.2	$45.0	$66.2	$91.2	$100.5	$110.8	$122.2
Total US sales						**$63.5**	**$105.0**	**$154.4**	**$212.8**	**$234.6**	**$258.6**	**$285.1**

EU5 Build	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Confirmed CRE												
Penetration						3%	8%	14%	21%	21%	21%	21%
Patients treated						719	1,699	3,170.95	5,202	5,462	5,736	6,022
Treatment course (days)						10	10	10	10	10	10	10
Days of treatment						7,190	16,987	31,709	52,023	54,625	57,356	60,224
Cost per day (net)						975	975	975	975	975	975	975
Sales (M)						$7.0	$16.6	$30.9	$50.7	$53.3	$55.9	$58.7
Suspected CRE												
Penetration						3%	8%	14%	21%	21%	21%	21%
Patients treated						2,157	5,096	9,513	15,607	16,387	17,207	18,067
Treatment course (days)						2.5	2.5	2.5	2.5	2.5	2.5	2.5
Days of treatment						5,393	12,740	23,782	39,018	40,968	43,017	45,168
Cost per day (net)						975	975	975	975	975	975	975
Sales (M)						$5.3	$12.4	$23.2	$38.0	$39.9	$41.9	$44.0
Total EU sales						**$12.3**	**$29.0**	**$54.1**	**$88.8**	**$93.2**	**$97.9**	**$102.8**

Rest of EU	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Confirmed CRE												
Penetration						2.7%	6%	11%	17%	17%	17%	17%
Patients treated						568	1,342	3,298	5,410	5,681	5,965	6,263
Treatment course (days)						10	10	10	10	10	10	10
Days of treatment						5,678	13,415	32,978	54,104	56,809	59,650	62,632
Cost per day (net)						780	780	780	780	780	780	780
Sales (M)						$4.4	$10.5	$25.7	$42.2	$44.3	$46.5	$48.9
Suspected CRE												
Penetration						3%	6%	11%	17%	17%	17%	17%
Patients treated						1,704	4,025	9,893	16,231	17,043	17,895	18,790
Treatment course (days)						2.5	2.5	2.5	2.5	2.5	2.5	2.5
Days of treatment						4,259	10,061	24,733	40,578	42,607	44,737	46,974
Cost per day (net)						780	780	780	780	780	780	780
Sales (M)						$3.3	$7.8	$19.3	$31.7	$33.2	$34.9	$36.6
Total rest of EU sales						**$7.8**	**$18.3**	**$45.0**	**$73.9**	**$77.5**	**$81.4**	**$85.5**

Sales summary	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Sales by region												
US						$63.5	$105.0	$154.4	$212.8	$234.6	$258.6	$285.1
EU5						$12.3	$29.0	$54.1	$88.8	$93.2	$97.9	$102.8
Rest of EU						$7.8	$18.3	$45.0	$73.9	$77.5	$81.4	$85.5
Total						$83.5	$152.3	$253.5	$375.4	$405.3	$437.9	$473.4
Sales by setting												
Confirmed CRE						$47.7	$87.0	$144.9	$214.5	$231.6	$250.2	$270.5
Suspected CRE						$35.8	$65.3	$108.6	$160.9	$173.7	$187.7	$202.9
Total						**$83.5**	**$152.3**	**$253.5**	**$375.4**	**$405.3**	**$437.9**	**$473.4**

Source: Company data, Credit Suisse estimates.

Plazomicin Pivotal Trial Plans

Plazomicin is a member of the aminoglycoside class of antibiotics designed to overcome aminoglycoside resistance mechanisms (i.e., enzyme mediated degradation). The compound was discovered by modifying the chemical structure of an existing aminoglycoside, sisomicin, to shield regions of the molecule targeted by aminoglycoside degrading enzymes.

Plazomicin was discovered and developed at AKAO, specifically to overcome drug resistance

Plazomicin is active against many MDR pathogens for which other antibiotics including available aminoglycosides have limited activity. The drug is being developed in Phase III for the treatment of MDR enterobacteriaceae infections including CRE, particularly pneumonia and blood stream infections. Previously, the Phase II trial demonstrated non-inferiority to a comparator in treating complicated urinary tract infections arising from non-CRE bacteria.

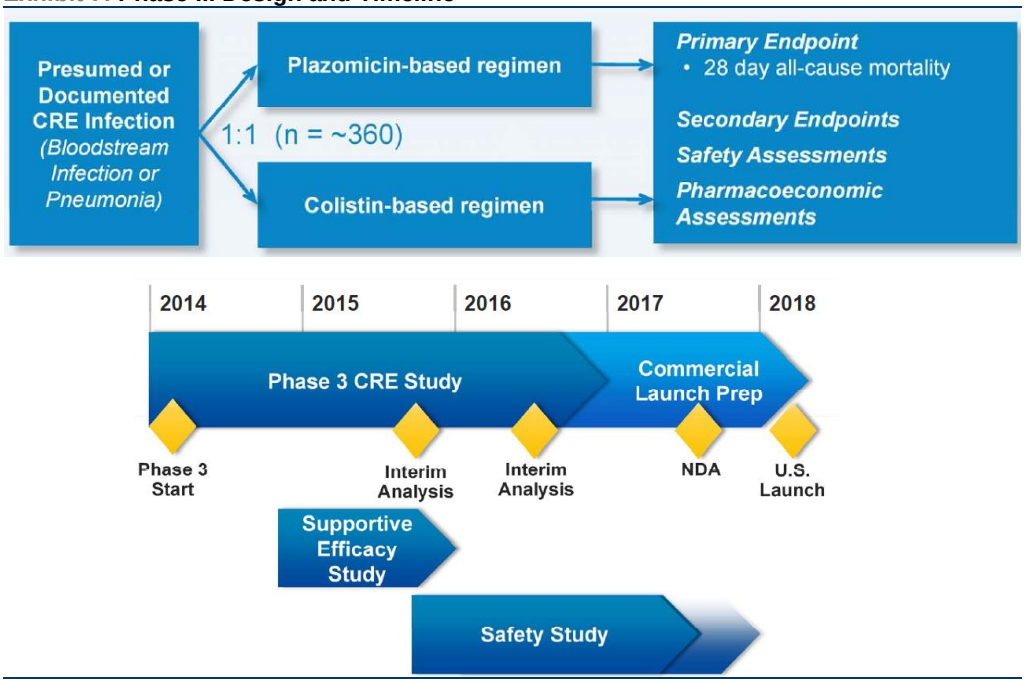
Phase III Overview

AKAO has initiated a Phase III study that will serve as a single pivotal study for full approval of plazomicin. This study is unique in that it will have a primary endpoint based on overall survival, which is different from a typical antibiotic study based on a non-inferiority endpoint.

Only antibiotic targeting a survival benefit over standard of care

The study will randomize approximately 360 patients with presumed or documented bloodstream or pneumonia CRE infections, to either a plazomicin-based regimen or a colistin-based regimen. (See Exhibit 7.) Physicians will have the discretion to add an additional antibiotic (meropenem of tigycycline) to either regimen after randomization. The choice of meropenam or tigycycline is left to investigators and is not part of the stratification.

Exhibit 7: Phase III Design and Timeline



Source: Company data, Credit Suisse estimates.

Stratification

Key risk factors should be balanced

Patients will be stratified based on three criteria that would be expected to affect the primary endpoint of 28-day mortality.

- **Type of Infection:** blood stream infection versus pneumonia
- **Time from Empiric Therapy to Definitive Therapy:** 0-36 hours versus 36-72 hours. All patients in the study need to be randomized within 72 hours of initial treatment.
- **APACHE II Score:** 15-20 versus 20-30. The inclusion criteria is 15-30 on this 0-71 point scale. APACHE II is the Acute Physiology and Chronic Health Evaluation II scoring system. An APACHE II score of 15-30 would be expected to have an approximate 35% mortality rate when treated with an effective antibiotic

Clinical Assumptions in Phase III

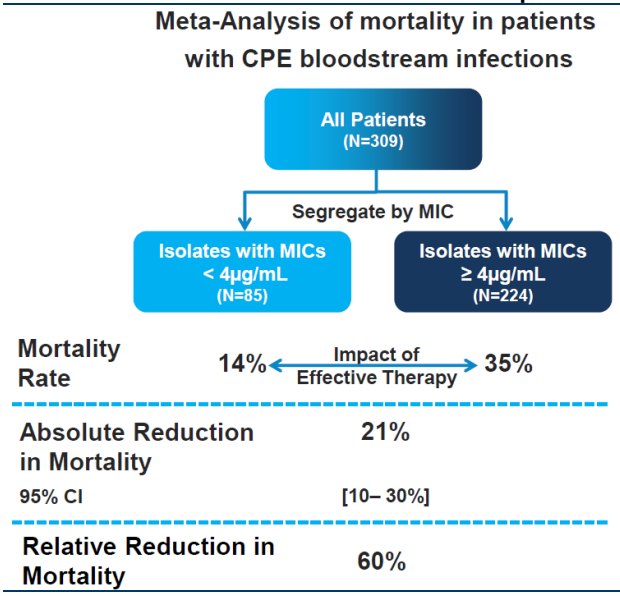
Looking for a 35% relative reduction in 28-day mortality

The Phase III trial aims to demonstrate a 35% relative reduction in mortality assuming a 35% 28-day mortality rate in the control arm. This translates into an absolute difference of approximately 12% (23% versus 35%).

AKAO bases its assumption on a meta-analysis of 309 patients treated for cabapenamase-producing enterobacteriaceae. In that study, patient outcome was analyzed based on baseline susceptibility/resistance to the antibiotic used. Patients deemed susceptible had a 14% mortality rate and patients deemed resistant had a 35% mortality rate. This is an overall 21% absolute difference and a 60% relative difference.

AKAO assumes that a CRE population treated with a partially effective colistin regimen should have mortality in line with the "resistant" arm of the meta-analysis (i.e., 35%). Patients treated with an effective regimen containing plazomicin should have mortality in-line with the "susceptible" arm of the meta-analysis (i.e., 14%). The trial was powered for a less significant benefit of 12% absolute and 35% relative.

Exhibit 8: Clinical Basis for Statistical Assumptions



Source: Company data, Credit Suisse estimates.

Regulatory Interactions and Expectations

The Phase III study is being conducted under an SPA from the FDA. Both the FDA and the EMA have confirmed that the single Phase III study will be sufficient for approval if positive.

Final data are anticipated in H1:17 based on enrollment projections, and there are two prespecified interim analyses projected, one in H2:15 and another in H2:16. The study can be stopped early for efficacy or futility. However, the company has not released the threshold for stopping early for efficacy for either interim look.

The FDA has asked for a safety database of 300 patients treated at the recommended dose of 15mg/kg for 7-14 days. The prior studies tested doses up to 20mg/kg for 5 days, so AKAO needs to augment its safety database with patients dosed at the 15mg/kg for 7-14 days. These will include a 50-patient descriptive study in patients with serious CRE infections and a 70-patient safety study (both described in more detail in later sections).

Thorough Diligence Behind Phase III Preparation

One of the primary investor concerns is the potential difficulty of conducting a randomized Phase III trial in seriously ill CRE patients. AKAO's preparations in advance of the trial are critical in lowering this risk and giving us confidence in the conduct of the trial.

AKAO has assessed the practicality of the Phase III study with in-depth analyses of many of the study parameters. It has completed the following steps to strengthen the probability of success for the study:

- **Target Enrollment:** AKAO assessed each clinical site to determine the number of CRE patients currently treated and if the planned study sites would be able to enroll the target number of patients collectively within the proposed timeline of the study.
- **Overall Survival Endpoint:** The assumption of a 35% relative benefit in 28-day mortality is based on a meta-analysis that aimed to determine the benefit of an effective treatment in the setting of drug-resistant bloodstream infections. In that analysis, there was a 60% relative benefit, making AKAO's assumptions conservative. (See Exhibit 8.) The APACHE II entry criteria is also designed to ensure patients are sick enough to expect a 35% mortality rate in the control arm.
- **Identification of "Presumed" CRE Infections:** AKAO confirmed that each site has the necessary laboratory equipment to perform the required diagnostic tests to determine the presence of one or more carbapenemase enzymes, a likely indication of a CRE infection. This assay should aid enrollment and ensure a higher level of confirmed CRE cases.
- **Confirmation of CRE Infections:** Each site needs to conduct microbiological tests to confirm the CRE infection within a two- to three-day window. All sites have adequate microbiology on-site. AKAO defines CRE as an enterobacteriaceae isolate with a MIC ≥ 4 µg/mL for a type 2 carbapenem (Imipenem, doripenem, and meropenem).
- **Study Design Has an SPA from FDA:** AKAO received an SPA from the FDA regarding the Phase III design, which removes some of the regulatory risk associated with trial design, comparator arm, endpoints, etc. Both the FDA and EMA have indicated that the proposed Phase III study will be sufficient to support approval.

Dosing to Be Monitored with *In Vitro* Assay

AKAO has developed an *in vitro* assay that will help monitor the blood levels of plazomicin through a process known as therapeutic drug monitoring. The assay will measure plazomicin following the dosing to ensure that the blood levels do not get too low or get too high during the treatment period in the Phase III study.

The goal of therapeutic drug monitoring is to ensure that therapeutic levels of the drug are reached and maintained, while minimizing the safety risk. Therapeutic drug monitoring is frequently used for aminoglycosides and the FDA has cleared this assay for use in the Phase III study. While this process adds complexity to the study, we view it as a risk reduction in the final analysis. The clinical performance evaluation necessary for approval will be completed in parallel to the Phase III study.

Additional Trials—Supportive and Safety Studies

Phase II "Supportive" Study

Supportive trial could provide first data in CRE by year-end 2015

AKAO plans initiate a 50-patient supportive trial in CRE patients. AKAO plans to start this study by YE:14, and top-line data from this study could be available by Q4:15.

The specific design is not yet described, but it will be an open label study and enroll patients with serious CRE infections requiring 7-14 days of therapy. Infections may include blood stream infections and pneumonia (like the Phase III) but will likely have wider entry criteria, which could include cUTI or patients resistant to colistin.

The goal of the study will be to gain additional experience with the drug in the target population. If very successful, AKAO may be able to approach U.S. and EU regulators about a faster path to market, although this would be data dependent and there is no specific guidance from regulators or the company with respect to a fast-to-market strategy.

This trial could have two key benefits for investors:

- It will provide data in CRE patients ahead of the Phase III results. This could give investors greater confidence in the Phase III trial design and ultimate outcome.
- This data set, in combination with its prior clinical data, could potentially be sufficient to support a filing for approval in CRE if FDA is compelled by the results and the unmet medical need (this is not in our assumptions).

Phase II "Safety" Study

FDA has asked for a safety database of 300 patients treated at 15mg/kg for 7-14 days. To reach that target number, AKAO plans to conduct a non-randomized safety study of an additional 70 patients. This trial will run in parallel to the Phase III trial. The primary goal will be to expand the safety database. If AKAO decides to pursue a fast-to-market strategy, this trial could be expanded or accelerated to gain greater safety experience, but there is no guidance from the company with respect to a fast-to-market strategy.

Prior Clinical and Preclinical Results Predict Success

Preclinical and PK/PD data are highly predictive of efficacy for antibiotics

The development program in CRE is based on proven Phase II efficacy and safety in Gram-negative infections, PK/PD analysis, and *in vitro* findings of efficacy against CRE isolates. If therapeutic drug levels can be safely achieved, preclinical efficacy data becomes highly predictive of clinical success in antibiotic development generally, and we believe the same is true for plazomicin.

In Vitro Activity Against CRE Isolates at Doses Easily Achieved

Anti-CRE drug levels can be easily attained

AKAO examined the activity of plazomicin relative to other antibiotics in CRE clinical isolates. Plazomicin has better efficacy than all other antibiotics examined (see Exhibit 9), and this activity was within the range achievable with a single daily dosing of plazomicin. Additionally, one of the Phase I studies demonstrated that plazomicin penetrated the lungs in healthy subjects, which is critical for success in pneumonia.

Safety Demonstrated at Target Doses

Safety at the target dose has been established

The safety profile of plazomicin has been consistent with other members of the aminoglycoside class of antibiotics. Importantly, the Phase I and Phase II studies suggest that plazomicin can be administered safely at therapeutic doses predicted to have efficacy against CRE.

Plazomicin has been administered to 239 healthy volunteers or patients with infections at doses from 1 to 20 mg/kg. The primary toxicities were renal (kidney) and ototoxicity (hearing), which are both class effects of aminoglycosides.

In the Phase II trial, patients were dosed at 15mg/kg for five days. The ongoing Phase III trial uses this same dose but for a longer 7-14 treatment regimen, which adds some safety risk.

Exhibit 9: Superior Potency Against CRE

Microbiological Potency of Plazomicin and Available Therapies vs. Clinical Isolates of CRE

Compound	Class	N	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)
Plazomicin	**Aminoglycoside**	**807**	**0.5**	**2**
Gentamicin	Aminoglycoside	807	4	128
Amikacin	Aminoglycoside	806	32	64
Ciprofloxacin	Fluoroquinolone	767	8	8
Ceftazidime	Cephalosporin	510	64	>128
Piperacillin/tazobactam	Penicillin/Beta-lactamase inhibitor	731	>128	>128
Tigecycline	Glycycline	723	1	2
Colistin/polymyxin B	Polymyxin	692	1	4

Susceptible
Non-Susceptible

N=number of strains within the overall set of 807 strains tested vs. the given antibiotic.
CLSI 2012 susceptibility criteria were used except for tigecycline and colistin, for which EUCAST 2013 criteria were used because CLSI criteria were not available. Isolates selected had an MIC≥2 µg/mL for any type 2 carbapenem, a value defined as non-susceptible for this class according to CLSI..
Data includes clinical isolates from three studies: 1) J Chemother. 2012 Aug;24(4):191-4, 2) J Antimicrob Chemother. 2011 Jan;66(1):48-53, 3) J Antimicrob Chemother. 2010 Oct;65(10):2123-7

Source: Company data, Credit Suisse estimates.

Phase II Study in cUTI—Clear Efficacy Demonstrated

Phase II demonstrated efficacy against Gram-negative bacteria

The Phase II study in patients with complicated urinary tract infections (cUTI) demonstrated that plazomicin had similar clinical activity to levofloxacin against Gram-negative bacteria. This study was a randomized, double-blind study examining two doses or plazomicin (10 mg/kg and 15 mg/kg) versus a single dose of levofloxacin (750 mg). The primary endpoint was microbiological eradication for the mITT patient population at day 12. The goal was non-inferiority.

Plazomicin dosed at the 10 mg/kg and 15 mg/kg demonstrated a 50.0% and 60.8% eradication, respectively, versus 58.6% for levofloxacin in the mITT group.

Exhibit 10: Positive Phase II in cUTI

By-Patient Microbiological Response	Plazomicin 10 mg/kg	Plazomicin 15 mg/kg	Levofloxacin 750 mg
Microbiologically Evaluable (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%)
Modified Intent-to-Treat (MITT)			
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: Company data, Credit Suisse estimates.

Safety Consistent with Aminoglycosides

Kidney and ear toxicity is consistent with aminoglycoside class

There were reports of mild nephrotoxicity and ototoxicity in the Phase II study. There was one case of mild azotemia (increased urea nitrogen in the blood) that was considered drug related and mild acute renal insufficiency that was not considered drug related. Importantly, the average serum creatinine values were consistent over the five-day dosing period, suggesting there was no global change in the kidney function for the patients in the study. There were two reports of ototoxicity, one case of unilateral permanent ringing noise (tinnitus) and mild transient vertigo, and both cases were deemed related to the drug. Both of these adverse events are frequently observed with aminoglycosides.

Exhibit 11: Phase I and II Clinical Trials of Plazomicin

Trial	Objectives	Design	Plazomicin Doses	# of Subjects
Phase 1 PK, Safety and Tolerability				
490-001	Safety and PK after single and multiple doses in healthy subjects	Double-blind, randomized, placebo-controlled, parallel-group, dose-escalation study	1, 4, 7, 11, 15 mg/kg IV for 3−10 days	39
490-003	Safety, PK and lung penetration in healthy subjects	Double-blind, randomized, placebo-controlled	Cohort 1: 15 mg/kg IV for 5 days Cohort 2A/2B: 10.7/15 mg/kg IV, single dose	40
490-004	Safety and PK in subjects with renal impairment	Open label	7.5 mg/kg IV, single dose	24
490-006	Thorough QT or TQT in healthy subjects	Randomized, double-blind, placebo and positive-controlled crossover	15 mg/kg IV, single dose 20 mg/kg IV, single dose	Part 1=8 Part 2=56
Phase 2 Efficacy and Safety				
490-002	Safety, efficacy, and PK in patients with cUTI	Double-blind, randomized, comparator-controlled, multicenter	10 mg/kg IV for 5 days 15 mg/kg IV for 5 days	145

Source: Company data, Credit Suisse estimates.

Improved Regulatory Environment for Antibiotics

Over the past few years the regulatory environment for new antibiotics has significantly improved and we believe that this trend is going to continue. The impact on AKAO and other companies in the space includes:

1) Longer exclusivity period for approved drugs
2) More cooperation with FDA to design appropriate trials
3) Faster drug approvals
4) Potential fast-to-market strategies for high unmet medical needs
5) Potential improvements in the reimbursement landscape

GAIN Act Provides New Incentives for Antibiotic Development

Congress passed the GAIN Act in 2012 to promote the development of new antibiotics. The Act set up the qualified infectious disease product (QIDP) designation that is granted to antibiotics in specific indications. AKAO plans to submit the QIDP application for plazomicin, and we believe FDA will grant the designation (as it has for almost all new antibiotics).

The QIDP provides antibiotic drug developers with two key incentives.

- **Extra Five Years of Market Exclusivity in Addition to the Five Years Already Provided under Hatch-Waxman:** We believe this is the most significant portion of the legislation and it is unique to antibiotic development. A Paragraph IV challenge can be made one year prior to the end of data exclusivity, which is in year four for most drugs and now year nine for drugs with the QIDP designation (potentially six months longer with a pediatric extension).
- **FDA Priority Review Potentially Shortens Review Period to Six Months:** The six-month review clock potentially means that drugs could reach the market quicker.

The QIDP designation also makes the drugs eligible for fast track status but AKAO already received fast track status for plazomicin in 2012. This might help facilitate additional discussions ahead of potential receipt of QIDP status.

GAIN Act Could Provide Faster Route to Approval for Drug-Resistant Organisms

The GAIN Act also calls for the FDA to develop new guidelines for the development of antibiotics to treat multidrug-resistant infections. These clinical/regulatory pathways will be developed for each indication and could provide drug developers with faster paths to market in more limited indications with high unmet medical need. These new pathways are likely to be tested first for some of the emerging Gram (-) antibiotics that target highly resistant pathogens, such as plazomicin and/or carbavance.

Under these guidelines, it may be possible for AKAO to pursue a faster to-market strategy in CRE, potentially based on the Phase II "Supportive" study in CRE. AKAO has not outlined any potential fast-to-market strategy, as it would be dependent on particularly good results.

Reimbursement Could Turn More Favorable

A new Bill was recently introduced into the House of Representatives called the DISARM Act, which aims to improve the reimbursement environment for new antibiotics that treat significant disease threats, such as drug-resistant bacteria.

This Bill aims to replace the current DRG reimbursement model, which penalizes hospitals for using expensive drugs with an ASP plus a CMS-determined percentage. This could remove the "penalty" for using more expensive drugs and provide a framework for companies to charge higher prices, more in-line with the high unmet need and smaller target patient populations.

The specific pathogens targeted in this legislation would include those listed in the recent CDC report, and include many of the drug-resistant, Gram-negative bacteria including pseudomonas and CRE and *C. difficile*. We believe that AKAO is one of the few antibiotic companies that would stand to benefit most from the proposed legislation, as its only clinical stage product is being developed for an agent on the CDC list.

The Gram-Negative Threat and Current Landscape

The Centers for Disease Control and Prevention (CDC) published its 2013 Threat Report, which highlighted the top antibiotic resistant threats in the United States. This list provides investors with a general roadmap for FDA's likely prioritization of new antibiotics in development.

There are two observations that are key for AKAO:

- Of the 14 urgent and serious threats, 5 are Gram-negative bacteria, the stated focus and area of expertise at AKAO.
- CRE is among the top three, listed as urgent threats; plazomicin is the only drug solely targeting this organism in its pivotal development program.

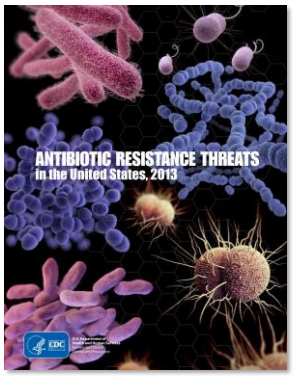
Exhibit 12: Top Antibiotic Resistance Threats in 2013

Urgent Threats

- *Clostridium difficile*
- ✗ Carbapenem resistant Enterobacteriaceae (CRE)
- ✗ Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- ✗ Multi-drug resistant *Acinetobacter*
- Drug-resistant *Campylocaber*
- Fluconazole-resistant *Candida* (a fungus)
- ✗ Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant *Enterococcus* (VRE)
- ✗ Multi-drug resistant *Pseudomonas aeruginosa*
- Drug-resistant *Salmonella* Typhi (and non-typhodal)
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant tuberculosis
- Drug-resistant *Shigella*



✗ = Gram-negative

Source: Antibiotic Resistance Threats in the United States, 2013, CDC.

Current Treatments

The landscape of Gram-negative antibiotics includes broad-spectrum drugs (target both Gram-negative and Gram-positive). The typical drug approval path has been to run trials in both intra-abdominal and urinary tract infections (cIAI and cUTI). These infections are typically caused by Gram-negative bacteria. The largest market and greatest unmet need for Gram-negative antibiotics is pneumonia, which can be either hospital acquired (HAP) or community acquired (CAP). Approved drugs for serious Gram-negative infections span the range of antibiotic drug classes. (See Exhibit 13.)

The biggest problem in the field of Gram-negative infections is the emergence of resistance to the most powerful available drugs, such as carbapenam. This is further complicated by the presence of multiple resistance mechanisms yielding so called multidrug-resistant (MDR) bacteria, the so-called killer bugs.

Exhibit 13: Marketed Gram-Negative Therapeutics

Antibiotic name	Company	ROA	Dosing	Class of molecule	Approved Indications			
					NP	IAI	UTI	cSSSI
Zosyn (piperacillin/tazobactam)	Pfizer / GENERIC	IV	3-4X / day	Amplicillin / β-lactamase inhibitor	✓	✓	✗	✓
Doriba (doripenem)	janssen	IV	3X / day	Carbapenem	✗	✓	✓	✗
Primaxin (imipenem / cilastatin)	MERCK / GENERIC	IV, IM	3-4X / day	Carbapenem	✓	✓	✓	✓
Merrem IV (Meropenem)	AstraZeneca / GENERIC	IV	3X / day	Carbapenem	✗	✓	✗	✓
Fortaz (ceftazidime)	gsk GlaxoSmithKline / GENERIC	IV	3X / day	3rd Generation cephalosporin	✓	✓	✓	✓
Maxipim (cefepime)	Bristol-Myers Squibb / GENERIC	IV	2X / day	4th Generation cephalosporin	✓	✓	✓	✓
Cipro (ciprofloxacin)	Bayer / GENERIC	Oral and IV	2-3X / day	Quinolone	✓	✗	✓	✓
Levaqui (levofloxacin)	janssen / GENERIC	Oral and IV	1X / day	Quinolone	✓	✗	✓	✓

NP nosocomial (hospital-acquired) pneumonia, IAI intraabdominal infection, UTI urinary tract infection, cSSSI complicated skin and skin structure infections; ROA route of administration, IV intravenous, IM intramuscular.
Source: Company data, Credit Suisse estimates.

Strategies to Overcome Resistance

The current treatment strategies advancing for drug-resistant Gram-negative infections include:

- New cephalosporin combined with an existing betalactamase inhibitor (Cubist)
- Existing cephalosporin combined with a new betalactamase inhibitor (Forest)
- Existing carbapenam with a new betalactamase inhibitor (The Medicines Company)
- New aminoglycoside (Achaogen)
- New tetracycline (Tetraphase)

Each of these approaches is very likely to work. However, each drug and drug combination will likely have slightly different antibiotic coverage and safety profile. (See Exhibit 14.)

Exhibit 14: Therapeutics in Late-Stage Development

							Indications Sought & Clinical Stage			
Antibiotic name	Company	Status	CRE trials	Dosing	Bactericidal	Class of molecule	Pneum.	IAI	UTI	Other
CXA-201 (ceftolozane/tazobactam)	CUBIST PHARMACEUTICALS	NDA filing H1:14	No	3X / day	Yes	Cephalosporin / β-lactamase inhibitor	Phase III ready	Phase III complete	Phase III complete	--
Ceftazidime/Avibactam	Forest Laboratories, Inc. / AstraZeneca	Phase III	No	3X / day	Yes	Cephalosporin / β-lactamase inhibitor	Phase III	Phase III	Phase III	--
Eravacycline	TETRAPHASE PHARMACEUTICALS	Phase III	No	Testing 1-2X / day	No	Tetracycline	--	Phase III	Phase III	--
Plazomicin	ACHAOGEN	Phase III	Yes	1X / day	Yes	Aminoglycoside	--	--	Phase II	CRE Phase III
Teflaro (ceftaroline) & Avibactam	Forest Laboratories, Inc.	Phase II	No	Testing 2-3X / day	Yes	Cephalosporin / β-lactamase inhibitor	--	--	Phase II	Phase I
KB001	KALOBIOS / SANOFI	Phase II	No	NA	No	PcrV antibody	Phase II	--	--	CF - Phase II
Carbavance	THE MEDICINES COMPANY	Phase I	Yes	NA	Yes	Carbapenem / β-lactamase inhibitor	--	--	Phase III ready	CRE Phase II

Source: Company data, Credit Suisse estimates.

The Emergence of a New Killer Bug and the Landscape for CRE Drugs

Carbapenem-resistant bacteria were first identified more than 20 years ago. During the 1980s and 1990s, increased prevalence of ESBL K. pneumonia and E. coli contributed to increased use of carbapenems (imipenem, meropenem, etc.), which are typically one of the last lines of defense against Gram-negative infections. Eventually, resistance to carbapenems increased.

Carbapenem-resistant bacteria are commonly resistant to other types of antibiotics used to treat Gram-negative infections, including cephalosporins, beta-lactam / beta-lactamase inhibitor combinations, fluoroquinolones, and aminoglycosides. Common carbapenem-resistant Gram-negative pathogens include enterobacteriaceae, acinetobacter baumannii, and pseudomonas aeruginosa.

Currently, available therapies for the treatment of multidrug-resistant infections include tigecycline (Tygacil - marketed by Pfizer), generic aminoglycosides such as gentamicin, amikacin, and tobramycin, and generic polymixins, such as colistin and polymixin B. Even with these treatments, bloodstream infections due to carbapenemase-producing K pneumonia typically have mortality rates approaching 50%.

Other drugs in development (besides plazomicin) that have the potential to treat serious infections caused by CRE include:

- **Ceftazidime / avibactam** is being developed by Forest Laboratories and AstraZeneca for pneumonia and cUTI and cIAI. The combination includes an existing cephalosporin (ceftazidime) with a novel β-lactamase inhibitor (avibactam). Ceftazidime/avibactam has strong activity in KPC (kleb and E. Coli), particularly ESBL enterobacteriaceae.
- **Carbavance** is being developed by The Medicines Company for cUTI and MDR Gram-negative infections, including CRE. The drug combines an existing carbapenam (not yet named) with a novel beta-lactamase inhibitor designed to block a wide range of carbapenamases.

- **Eravacycline** is a novel fluorocycline antibiotic, similar to tigecycline, with broad activity against all Gram-negative organisms. It is active against MDR Gram-negative and Gram-positive bacteria, A. baumannii, and ESBL and CRE enterobacteriaceae species.

A Pipeline Targeting Pseudomonas

AKAO's pipeline includes two drugs in preclinical development specifically targeting drug-resistant *Pseudomonas aeruginosa*. This bacteria is a common cause of pneumonia and is listed as a serious threat by CDC.

AKAO expects to advance one or both of its anti-pseudomonas candidates into the clinic in 2015.

- **Anti-pseudomonas Therapeutic Antibody:** The target of this antibody has not been disclosed, but it is a functionally important cell surface antigen, and the antibody has direct antibiotic activity. With a potential half-life of two weeks, this drug could potentially be dosed infrequently or be used in a prophylactic setting. As an antibody, it is unlikely to have significant toxicity and would likely be readily combinable with other antibiotic drug classes.
- **LpxC Inhibitor:** This evolutionarily conserved enzyme is required for synthesis of the outer membrane of Gram-negative organisms. AKAO had taken a candidate known as ACHN-975 forward into the clinic, but there were safety issues for this drug (which were likely drug related and not target related). AKAO is working to identify another LpxC inhibitor for future clinical studies.

There are several novel drugs in development that target drug-resistant pseudomonas. These include CBST's Ceftolozane/tazobactam and KaloBios' KB001.

- **Ceftolozane/tazobactam** is a novel cephalosporin combined with a beta-lactamase inhibitor. Ceftolozane/tazobactam has shown positive results in its Phase III program for both cUTI and cIAI. Phase III studies are planned in HABP and VABP. The drug's main target is pseudomonas aeruginosa, including MDR strains, and many ESBL-producing enterobacteriaceae. However, this drug combination is likely not a good candidate for CRE infections.
- **KB001** has demonstrated promising activity against pseudomonas lung infections and is currently in Phase II development. KB001 is an antibody that is specific for pseudomonas. It is intended to be an adjunct to antibiotic therapy by blocking a key protein on the surface of pseudomonas, which is responsible for its virulence.

Management

Kenneth J. Hillan, M.B., Ch.B.—Director 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 the board of directors in October 2011. Prior to joining Achaogen, from August 1994 to April 2011, Dr. Hillan was at Genentech, Inc. and was responsible for numerous successful drug approvals and led the medical and scientific strategies for its Immunology, Tissue Growth and Repair drug portfolio. 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. Dr. Hillan also previously 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).

Derek A. Bertocci—Chief Financial Officer

Mr. Bertocci joined Achaogen as Senior Vice President and Chief Financial Officer in February 2014. Previously Mr. Bertocci was Senior Vice President and Chief Financial Officer of Accuray Incorporated from January 2009 to September 2013. Prior to Accuray, he was Chief Financial Officer of BioForm Medical, Inc. from October 2006 through December 2008, and Chief Financial Officer of Laserscope from June 2005 to July 2006. Before that, Mr. Bertocci served in various roles at VISX Incorporated, including as Chief Financial Officer from March 2004 to May 2005 and Vice President and Controller from 1998 to March 2004. Mr. Bertocci has a B.A. from Stanford University and an M.B.A. from the University of Southern California.

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

Ms. Filice has been the Senior Vice President, Development Operations and Portfolio Management since November 2012. She also served as the Vice President, Development Operations and Portfolio Management from May 2011 to October 2012. Before joining Achaogen, Ms. Filice worked at Genentech for 15 years, and held positions of Senior Director, Project Excellence in Global Development, Senior Director, Project Portfolio Management in Product Development, other roles in Clinical Data Management and Clinical Operations. She also served as Project Team Leader for both the Avastin and Nutropin AQ. Ms. Filice also worked in clinical research at Ligand Pharmaceuticals Inc. and at Syntex, Inc. Ms. Filice has a B.A. in Microbiology from University of California, Davis, and an MBA from Santa Clara University, California.

Christine Murray—Vice President, Regulatory Affairs

Ms. Murray has served as Vice President, Regulatory Affairs at Achaogen since October 2012. Ms. Murray also held the position of Senior Director, Regulatory Affairs and Quality Assurance. Previously she was Senior Director, Regulatory Affairs at Alexza Pharmaceuticals, Inc., Director and then Senior Director in the Global Regulatory Affairs department of Gilead Sciences, Inc. Before Gilead, Ms. Murray was a regulatory affairs consultant in the U.K. Ms. Murray also worked at Smithkline Beecham Pharmaceuticals, in the Western General Hospital in Edinburgh, and in Yorkhill Hospital in Glasgow. Ms. Murray has a B.S. in Biochemistry from the University of Liverpool in the U.K. and a M.S. degree in Clinical Biochemistry from the University of Newcastle-upon-Tyne in the U.K.

Financial Statements

Exhibit 15: AKAO Financial Statements

Achaogen (AKAO)

Jason Kantor, Ph.D. (415) 249-7942
Jeremiah Shepard Ph.D. (415) 249-7933

Income statement

	2013A	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenues												
Plazomicin US sales										63.5	105.0	154.4
Plazomicin EU royalties (20%)										3.1	7.3	18.0
Contract revenue	18.5	3.8	3.8	3.8	3.8	15.0	15.0	15.0	40.0	45.0	11.3	
Total revenues	18.5	3.8	3.8	3.8	3.8	15.0	15.0	15.0	40.0	111.6	123.6	172.4
Expenses												
COGS										7.6	13.0	20.0
R&D	23.5	8.2	4.5	4.7	5.0	22.4	22.6	24.8	27.3	39.5	35.0	46.1
G&A	7.0	2.1	2.1	2.2	2.2	8.5	9.3	11.1	17.0	50.0	55.0	57.8
Total operating expenses	30.5	10.3	6.6	6.9	7.2	30.9	31.9	37.9	57.0	97.1	103.0	123.8
Operating income (loss)	(12.0)	(6.5)	(2.8)	(3.1)	(3.4)	(15.9)	(16.9)	(22.9)	(17.0)	14.5	20.6	48.6
Total Other Income (Expense)	(1.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.4)	0.3	0.4	0.4	0.5	0.5	0.5
Pre Tax Income	(13.1)	(6.7)	(2.9)	(3.2)	(3.5)	(16.3)	(16.6)	(22.5)	(16.6)	15.0	21.1	49.1
Income tax expense (benefit)												
Net Income	(13.1)	(6.7)	(2.9)	(3.2)	(3.5)	(16.3)	(16.6)	(22.5)	(16.6)	15.0	21.1	49.1
EPS - diluted (proforma)		($0.60)	($0.16)	($0.18)	($0.19)	($1.00)	($0.91)	($0.95)	($0.69)	$0.56	$0.79	$1.83
Shares outstanding - diluted (proforma)		11.13	17.82	17.91	18.00	16.22	18.23	23.63	24.11	26.64	26.77	26.90

Balance sheet

	2013A	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total Current Assets	19.8	91.1	87.1	84.5	81.8	81.8	69.1	143.9	131.5	151.9	176.2	230.5
TOTAL ASSETS	20.8	92.1	88.1	85.6	82.9	82.9	70.4	145.4	133.2	153.8	178.4	232.9
Total Current Liabilities	11.0	13.3	11.7	11.8	11.9	11.9	12.4	12.8	13.3	14.8	14.2	15.7
Total Liabilities	13.1	13.7	12.1	12.2	12.3	12.3	12.7	13.2	13.6	15.2	14.6	16.0
Total Equity	7.7	78.5	76.0	73.4	70.6	70.6	57.7	132.2	119.6	138.6	163.8	216.9
TOTAL LIABILITIES & EQUITY	20.8	92.1	88.1	85.6	82.9	82.9	70.4	145.4	133.2	153.8	178.4	232.9

Cash Flow

	2013A	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Net Cash Provided by Operating Activities	(13.9)	(3.9)	(3.9)	6.2	(2.6)	(4.2)	(12.1)	(17.7)	(11.8)	20.9	24.9	54.9
Net Cash provided by investing activities	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.6)	(0.6)	(0.6)	(0.6)	(0.6)	(0.6)	(0.6)
Net Cash Provided by Financing Activities	17.6	75.3				75.3		93.0				
Net Cash Increase (Decrease)	3.7	71.3	(4.1)	6.0	(2.7)	70.5	(12.7)	74.8	(12.3)	20.3	24.3	54.3
Beginning Cash	7.1	10.7	82.0	78.0	84.0	10.7	81.2	68.6	143.3	131.0	151.4	175.7
Ending Cash	10.7	82.0	78.0	84.0	81.2	81.2	68.6	143.3	131.0	151.4	175.7	230.0

Source: Company data, Credit Suisse estimates

Companies Mentioned *(Price as of 04-Apr-2014)*

Achaogen (AKAO.OQ, $14.15, OUTPERFORM[V], TP $22.0)
AstraZeneca (AZN.L, 3923.0p)
Bayer (BAYGn.DE, €99.0)
Bristol Myers Squibb Co. (BMY.N, $49.89)
Cempra (CEMP.OQ, $11.21)
Cubist Pharmaceuticals (CBST.OQ, $70.35)
Durata Therapeutics (DRTX.OQ, $12.85)
Forest Laboratories Inc. (FRX.N, $90.56)
GlaxoSmithKline plc (GSK.L, 1577.0p)
Insmed (INSM.OQ, $18.39)
Johnson & Johnson (JNJ.N, $98.42)
KaloBios (KBIO.OQ, $2.41)
Merck & Co., Inc. (MRK.N, $56.12)
Pfizer (PFE.N, $32.16)
Sanofi (SASY.PA, €75.85)
Tetraphase (TTPH.OQ, $11.13)
The Medicines Company (MDCO.OQ, $25.38)

Disclosure Appendix

Important Global Disclosures

I, Jason Kantor, PhD, certify that (1) the views expressed in this report accurately reflect my personal views about all of the subject companies and securities and (2) no part of my compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed in this report.

The analyst(s) responsible for preparing this research report received Compensation that is based upon various factors including Credit Suisse's total revenues, a portion of which are generated by Credit Suisse's investment banking activities

As of December 10, 2012 Analysts' stock rating are defined as follows:

Outperform (O) : The stock's total return is expected to outperform the relevant benchmark*over the next 12 months.

Neutral (N) : The stock's total return is expected to be in line with the relevant benchmark* over the next 12 months.

Underperform (U) : The stock's total return is expected to underperform the relevant benchmark* over the next 12 months.

**Relevant benchmark by region: As of 10th December 2012, Japanese ratings are based on a stock's total return relative to the analyst's coverage universe which consists of all companies covered by the analyst within the relevant sector, with Outperforms representing the most attractive, Neutrals the less attractive, and Underperforms the least attractive investment opportunities. As of 2nd October 2012, U.S. and Canadian as well as European ratings are based on a stock's total return relative to the analyst's coverage universe which consists of all companies covered by the analyst within the relevant sector, with Outperforms representing the most attractive, Neutrals the less attractive, and Underperforms the least attractive investment opportunities. For Latin American and non-Japan Asia stocks, ratings are based on a stock's total return relative to the average total return of the relevant country or regional benchmark; Australia, New Zealand are, and prior to 2nd October 2012 U.S. and Canadian ratings were based on (1) a stock's absolute total return potential to its current share price and (2) the relative attractiveness of a stock's total return potential within an analyst's coverage universe. For Australian and New Zealand stocks, 12-month rolling yield is incorporated in the absolute total return calculation and a 15% and a 7.5% threshold replace the 10-15% level in the Outperform and Underperform stock rating definitions, respectively. The 15% and 7.5% thresholds replace the +10-15% and -10-15% levels in the Neutral stock rating definition, respectively. Prior to 10th December 2012, Japanese ratings were based on a stock's total return relative to the average total return of the relevant country or regional benchmark.*

Restricted (R) : In certain circumstances, Credit Suisse policy and/or applicable law and regulations preclude certain types of communications, including an investment recommendation, during the course of Credit Suisse's engagement in an investment banking transaction and in certain other circumstances.

Volatility Indicator [V] : A stock is defined as volatile if the stock price has moved up or down by 20% or more in a month in at least 8 of the past 24 months or the analyst expects significant volatility going forward.

Analysts' sector weightings are distinct from analysts' stock ratings and are based on the analyst's expectations for the fundamentals and/or valuation of the sector* relative to the group's historic fundamentals and/or valuation:

Overweight : The analyst's expectation for the sector's fundamentals and/or valuation is favorable over the next 12 months.

Market Weight : The analyst's expectation for the sector's fundamentals and/or valuation is neutral over the next 12 months.

Underweight : The analyst's expectation for the sector's fundamentals and/or valuation is cautious over the next 12 months.

**An analyst's coverage sector consists of all companies covered by the analyst within the relevant sector. An analyst may cover multiple sectors.*

Credit Suisse's distribution of stock ratings (and banking clients) is:

Global Ratings Distribution

Rating	Versus universe (%)	Of which banking clients (%)
Outperform/Buy*	43%	(53% banking clients)
Neutral/Hold*	40%	(50% banking clients)
Underperform/Sell*	14%	(45% banking clients)
Restricted	2%	

**For purposes of the NYSE and NASD ratings distribution disclosure requirements, our stock ratings of Outperform, Neutral, and Underperform most closely correspond to Buy, Hold, and Sell, respectively; however, the meanings are not the same, as our stock ratings are determined on a relative basis. (Please refer to definitions above.) An investor's decision to buy or sell a security should be based on investment objectives, current holdings, and other individual factors.*

Credit Suisse's policy is to update research reports as it deems appropriate, based on developments with the subject company, the sector or the market that may have a material impact on the research views or opinions stated herein.

Credit Suisse's policy is only to publish investment research that is impartial, independent, clear, fair and not misleading. For more detail please refer to Credit Suisse's Policies for Managing Conflicts of Interest in connection with Investment Research: http://www.csfb.com/research and analytics/disclaimer/managing_conflicts_disclaimer.html

Credit Suisse does not provide any tax advice. Any statement herein regarding any US federal tax is not intended or written to be used, and cannot be used, by any taxpayer for the purposes of avoiding any penalties.

Price Target: (12 months) for Achaogen (AKAO.OQ)

Method: Our $22 target is based on a 65% probability of success for plazomicin, approximately $473M in peak sales, and an ex-US partner. Our estimates could prove conservative on price, penetration, market size, and the economics of the ex-US deal. Our valuation includes a very small nominal value for the preclinical assets

Risk: Risks to our $22 target are (1) unexpected safety signal in the "supportive" Phase 2 or pivotal Phase 3 study, (2) slower than expected spread of CRE in the developed world, and (3) competitive product for CRE reaches the market ahead of or at the same time as plazomicin.

Please refer to the firm's disclosure website at https://rave.credit-suisse.com/disclosures for the definitions of abbreviations typically used in the target price method and risk sections.

See the Companies Mentioned section for full company names

The subject company (AKAO.OQ, PFE.N, BAYGn.DE, GSK.L, FRX.N, JNJ.N, AZN.L, MRK.N, BMY.N, DRTX.OQ) currently is, or was during the 12-month period preceding the date of distribution of this report, a client of Credit Suisse.

Credit Suisse provided investment banking services to the subject company (AKAO.OQ, PFE.N, BAYGn.DE, GSK.L, FRX.N, MRK.N, BMY.N, DRTX.OQ) within the past 12 months.

Credit Suisse provided non-investment banking services to the subject company (PFE.N, BAYGn.DE, GSK.L, FRX.N, AZN.L, MRK.N, BMY.N) within the past 12 months

Credit Suisse has managed or co-managed a public offering of securities for the subject company (AKAO.OQ, PFE.N, BAYGn.DE, FRX.N, MRK.N, BMY.N, DRTX.OQ) within the past 12 months.

Credit Suisse has received investment banking related compensation from the subject company (AKAO.OQ, PFE.N, BAYGn.DE, GSK.L, FRX.N, MRK.N, BMY.N, DRTX.OQ) within the past 12 months

Credit Suisse expects to receive or intends to seek investment banking related compensation from the subject company (AKAO.OQ, PFE.N, BAYGn.DE, GSK.L, FRX.N, JNJ.N, CBST.OQ, MDCO.OQ, AZN.L, MRK.N, BMY.N, DRTX.OQ) within the next 3 months.

Credit Suisse has received compensation for products and services other than investment banking services from the subject company (PFE.N, BAYGn.DE, GSK.L, FRX.N, AZN.L, MRK.N, BMY.N) within the past 12 months

As of the date of this report, Credit Suisse makes a market in the following subject companies (AKAO.OQ, PFE.N, FRX.N, JNJ.N, CBST.OQ, MDCO.OQ, MRK.N, BMY.N, DRTX.OQ).

As of the date of this report, an analyst involved in the preparation of this report has the following material conflict of interest with the subject company (PFE.N). As of the date of this report, an analyst involved in the preparation of this report, Vamil Divan, has following material conflicts of interest with the subject company. The analyst or a member of the analyst's household has a long position in the common stock Pfizer (PFE.N). A member of the analyst's household is an employee of Pfizer (PFE.N).

As of the date of this report, an analyst involved in the preparation of this report has the following material conflict of interest with the subject company (PFE.N). As of the date of this report, an analyst involved in the preparation of this report, Ronak Shah, has the following material conflict of interest with the subject company. The analyst has a long position in the common stock Pfizer (PFE.N).

For other important disclosures concerning companies featured in this report, including price charts, please visit the website at https://rave.credit-suisse.com/disclosures or call +1 (877) 291-2683.

Important Regional Disclosures

Singapore recipients should contact Credit Suisse AG, Singapore Branch for any matters arising from this research report.

The analyst(s) involved in the preparation of this report have not visited the material operations of the subject company (AKAO.OQ, PFE.N, PFE.N, PFE.N, BAYGn.DE, GSK.L, FRX.N, JNJ.N, SASY.PA, CBST.OQ, MDCO.OQ, AZN.L, MRK.N, BMY.N, DRTX.OQ) within the past 12 months

Restrictions on certain Canadian securities are indicated by the following abbreviations: NVS--Non-Voting shares; RVS--Restricted Voting Shares; SVS--Subordinate Voting Shares.

Individuals receiving this report from a Canadian investment dealer that is not affiliated with Credit Suisse should be advised that this report may not contain regulatory disclosures the non-affiliated Canadian investment dealer would be required to make if this were its own report.

For Credit Suisse Securities (Canada), Inc.'s policies and procedures regarding the dissemination of equity research, please visit http://www.csfb.com/legal_terms/canada_research_policy.shtml.

The following disclosed European company/ies have estimates that comply with IFRS: (SASY.PA, AZN.L, BMY.N).

Credit Suisse has acted as lead manager or syndicate member in a public offering of securities for the subject company (AKAO.OQ, PFE.N, BAYGn.DE, GSK.L, FRX.N, MRK.N, BMY.N, DRTX.OQ) within the past 3 years.

As of the date of this report, Credit Suisse acts as a market maker or liquidity provider in the equities securities that are the subject of this report.

Principal is not guaranteed in the case of equities because equity prices are variable.

Commission is the commission rate or the amount agreed with a customer when setting up an account or at any time after that.

For Credit Suisse disclosure information on other companies mentioned in this report, please visit the website at https://rave.credit-suisse.com/disclosures or call +1 (877) 291-2683.

CREDIT SUISSE

References in this report to Credit Suisse include all of the subsidiaries and affiliates of Credit Suisse operating under its investment banking division. For more information on our structure, please use the following link: https://www.credit-suisse.com/who_we_are/en/This report may contain material that is not directed to, or intended for distribution to or use by, any person or entity who is a citizen or resident of or located in any locality, state, country or other jurisdiction where such distribution, publication, availability or use would be contrary to law or regulation or which would subject Credit Suisse AG or its affiliates ("CS") to any registration or licensing requirement within such jurisdiction. All material presented in this report, unless specifically indicated otherwise, is under copyright to CS. None of the material, nor its content, nor any copy of it, may be altered in any way, transmitted to, copied or distributed to any other party, without the prior express written permission of CS. All trademarks, service marks and logos used in this report are trademarks or service marks or registered trademarks or service marks of CS or its affiliates. The information, tools and material presented in this report are provided to you for information purposes only and are not to be used or considered as an offer or the solicitation of an offer to sell or to buy or subscribe for securities or other financial instruments. CS may not have taken any steps to ensure that the securities referred to in this report are suitable for any particular investor. CS will not treat recipients of this report as its customers by virtue of their receiving this report. The investments and services contained or referred to in this report may not be suitable for you and it is recommended that you consult an independent investment advisor if you are in doubt about such investments or investment services. Nothing in this report constitutes investment, legal, accounting or tax advice, or a representation that any investment or strategy is suitable or appropriate to your individual circumstances, or otherwise constitutes a personal recommendation to you. CS does not advise on the tax consequences of investments and you are advised to contact an independent tax adviser. Please note in particular that the bases and levels of taxation may change. Information and opinions presented in this report have been obtained or derived from sources believed by CS to be reliable, but CS makes no representation as to their accuracy or completeness. CS accepts no liability for loss arising from the use of the material presented in this report, except that this exclusion of liability does not apply to the extent that such liability arises under specific statutes or regulations applicable to CS. This report is not to be relied upon in substitution for the exercise of independent judgment. CS may have issued, and may in the future issue, other communications that are inconsistent with, and reach different conclusions from, the information presented in this report. Those communications reflect the different assumptions, views and analytical methods of the analysts who prepared them and CS is under no obligation to ensure that such other communications are brought to the attention of any recipient of this report. CS may, to the extent permitted by law, participate or invest in financing transactions with the issuer(s) of the securities referred to in this report, perform services for or solicit business from such issuers, and/or have a position or holding, or other material interest, or effect transactions, in such securities or options thereon, or other investments related thereto. In addition, it may make markets in the securities mentioned in the material presented in this report. CS may have, within the last three years, served as manager or co-manager of a public offering of securities for, or currently may make a primary market in issues of, any or all of the entities mentioned in this report or may be providing, or have provided within the previous 12 months, significant advice or investment services in relation to the investment concerned or a related investment. Additional information is, subject to duties of confidentiality, available on request. Some investments referred to in this report will be offered solely by a single entity and in the case of some investments solely by CS, or an associate of CS or CS may be the only market maker in such investments. Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance. Information, opinions and estimates contained in this report reflect a judgment at its original date of publication by CS and are subject to change without notice. The price, value of and income from any of the securities or financial instruments mentioned in this report can fall as well as rise. The value of securities and financial instruments is subject to exchange rate fluctuation that may have a positive or adverse effect on the price or income of such securities or financial instruments. Investors in securities such as ADR's, the values of which are influenced by currency volatility, effectively assume this risk. Structured securities are complex instruments, typically involve a high degree of risk and are intended for sale only to sophisticated investors who are capable of understanding and assuming the risks involved. The market value of any structured security may be affected by changes in economic, financial and political factors (including, but not limited to, spot and forward interest and exchange rates), time to maturity, market conditions and volatility, and the credit quality of any issuer or reference issuer. Any investor interested in purchasing a structured product should conduct their own investigation and analysis of the product and consult with their own professional advisers as to the risks involved in making such a purchase. Some investments discussed in this report may have a high level of volatility. High volatility investments may experience sudden and large falls in their value causing losses when that investment is realised. Those losses may equal your original investment. Indeed, in the case of some investments the potential losses may exceed the amount of initial investment and, in such circumstances, you may be required to pay more money to support those losses. Income yields from investments may fluctuate and, in consequence, initial capital paid to make the investment may be used as part of that income yield. Some investments may not be readily realisable and it may be difficult to sell or realise those investments, similarly it may prove difficult for you to obtain reliable information about the value, or risks, to which such an investment is exposed. This report may provide the addresses of, or contain hyperlinks to, websites. Except to the extent to which the report refers to website material of CS, CS has not reviewed any such site and takes no responsibility for the content contained therein. Such address or hyperlink (including addresses or hyperlinks to CS's own website material) is provided solely for your convenience and information and the content of any such website does not in any way form part of this document. Accessing such website or following such link through this report or CS's website shall be at your own risk. This report is issued and distributed in Europe (except Switzerland) by Credit Suisse Securities (Europe) Limited, One Cabot Square, London E14 4QJ, England, which is authorised by the Prudential Regulation Authority and regulated by the Financial Conduct Authority and the Prudential Regulation Authority. This report is being distributed in Germany by Credit Suisse Securities (Europe) Limited Niederlassung Frankfurt am Main regulated by the Bundesanstalt fuer Finanzdienstleistungsaufsicht ("BaFin"). This report is being distributed in the United States and Canada by Credit Suisse Securities (USA) LLC; in Switzerland by Credit Suisse AG; in Brazil by Banco de Investimentos Credit Suisse (Brasil) S.A or its affiliates; in Mexico by Banco Credit Suisse (México), S.A. (transactions related to the securities mentioned in this report will only be effected in compliance with applicable regulation); in Japan by Credit Suisse Securities (Japan) Limited, Financial Instruments Firm, Director-General of Kanto Local Finance Bureau (*Kinsho*) No. 66, a member of Japan Securities Dealers Association, The Financial Futures Association of Japan, Japan Investment Advisers Association, Type II Financial Instruments Firms Association; elsewhere in Asia/ Pacific by whichever of the following is the appropriately authorised entity in the relevant jurisdiction: Credit Suisse (Hong Kong) Limited, Credit Suisse Equities (Australia) Limited, Credit Suisse Securities (Thailand) Limited, having registered address at 990 Abdulrahim Place, 27 Floor, Unit 2701, Rama IV Road, Silom, Bangrak, Bangkok 10500, Thailand, Tel. +66 2614 6000, Credit Suisse Securities (Malaysia) Sdn Bhd, Credit Suisse AG, Singapore Branch, Credit Suisse Securities (India) Private Limited regulated by the Securities and Exchange Board of India (registration Nos. INB230970637; INF230970637; INB010970631; INF010970631), having registered address at 9th Floor, Ceejay House, Dr.A.B. Road, Worli, Mumbai - 18, India, T- +91-22 6777 3777, Credit Suisse Securities (Europe) Limited, Seoul Branch, Credit Suisse AG, Taipei Securities Branch, PT Credit Suisse Securities Indonesia, Credit Suisse Securities (Philippines) Inc., and elsewhere in the world by the relevant authorised affiliate of the above. Research on Taiwanese securities produced by Credit Suisse AG, Taipei Securities Branch has been prepared by a registered Senior Business Person. Research provided to residents of Malaysia is authorised by the Head of Research for Credit Suisse Securities (Malaysia) Sdn Bhd, to whom they should direct any queries on +603 2723 2020. This report has been prepared and issued for distribution in Singapore to institutional investors, accredited investors and expert investors (each as defined under the Financial Advisers Regulations) only, and is also distributed by Credit Suisse AG, Singapore branch to overseas investors (as defined under the Financial Advisers Regulations). By virtue of your status as an institutional investor, accredited investor, expert investor or overseas investor, Credit Suisse AG, Singapore branch is exempted from complying with certain compliance requirements under the Financial Advisers Act, Chapter 110 of Singapore (the "FAA"), the Financial Advisers Regulations and the relevant Notices and Guidelines issued thereunder, in respect of any financial advisory service which Credit Suisse AG, Singapore branch may provide to you. This research may not conform to Canadian disclosure requirements. In jurisdictions where CS is not already registered or licensed to trade in securities, transactions will only be effected in accordance with applicable securities legislation, which will vary from jurisdiction to jurisdiction and may require that the trade be made in accordance with applicable exemptions from registration or licensing requirements. Non-U.S. customers wishing to effect a transaction should contact a CS entity in their local jurisdiction unless governing law permits otherwise. U.S. customers wishing to effect a transaction should do so only by contacting a representative at Credit Suisse Securities (USA) LLC in the U.S. Please note that this research was originally prepared and issued by CS for distribution to their market professional and institutional investor customers. Recipients who are not market professional or institutional investor customers of CS should seek the advice of their independent financial advisor prior to taking any investment decision based on this report or for any necessary explanation of its contents. This research may relate to investments or services of a person outside of the UK or to other matters which are not authorised by the Prudential Regulation Authority and regulated by the Financial Conduct Authority and the Prudential Regulation Authority or in respect of which the protections of the Prudential Regulation Authority and Financial Conduct Authority for private customers and/or the UK compensation scheme may not be available, and further details as to where this may be the case are available upon request in respect of this report. CS may provide various services to US municipal entities or obligated persons ("municipalities"), including suggesting individual transactions or trades and entering into such transactions. Any services CS provides to municipalities are not viewed as "advice" within the meaning of Section 975 of the Dodd-Frank Wall Street Reform and Consumer Protection Act. CS is providing any such services and related information solely on an arm's length basis and not as an advisor or fiduciary to the municipality. In connection with the provision of the any such services, there is no agreement, direct or indirect, between any municipality (including the officials, management, employees or agents thereof) and CS for CS to provide advice to the municipality. Municipalities should consult with their financial, accounting and legal advisors regarding any such services provided by CS. In addition, CS is not acting for direct or indirect compensation to solicit the municipality on behalf of an unaffiliated broker, dealer, municipal securities dealer, municipal advisor, or investment adviser for the purpose of obtaining or retaining an engagement by the municipality for or in connection with Municipal Financial Products, the issuance of municipal securities, or of an investment adviser to provide investment advisory services to or on behalf of the municipality. If this report is being distributed by a financial institution other than Credit Suisse AG, or its affiliates, that financial institution is solely responsible for distribution. Clients of that institution should contact that institution to effect a transaction in the securities mentioned in this report or require further information. This report does not constitute investment advice by Credit Suisse to the clients of the distributing financial institution, and neither Credit Suisse AG, its affiliates, and their respective officers, directors and employees accept any liability whatsoever for any direct or consequential loss arising from their use of this report or its content. Principal is not guaranteed. Commission is the commission rate or the amount agreed with a customer when setting up an account or at any time after that.

Investment principal on bonds can be eroded depending on sale price or market price. In addition, there are bonds on which investment principal can be eroded due to changes in redemption amounts. Care is required when investing in such instruments.

When you purchase non-listed Japanese fixed income securities (Japanese government bonds, Japanese municipal bonds, Japanese government guaranteed bonds, Japanese corporate bonds) from CS as a seller, you will be requested to pay the purchase price only.