Adherex is Developing STS Trial for Otoprotection in Pediatric Cancer Patients; Data is Expected in the Third Quarter

Adherex Note

LifeSci Investment Abstract

Adherex (TSX: AHX.TO, OTCQB: ADHXF) is a clinical-stage biotechnology company developing Sodium Thiosulfate (STS), a chemoprotectant against hearing loss associated with platinum-based chemotherapy. STS is being investigated in two pediatric Phase III studies to evaluate the reduction of ototoxicity and impact on survival.

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Key Points of Discussion

Sodium Thiosulfate may Prevent Chemotherapy-Induced Deafness. Adherex partners, the Children's Oncology Group (COG) and the International Childhood Liver Tumor Strategy Group (SIOPEL) are each conducting a Phase III trial comparing cisplatin versus the combination of cisplatin plus STS in children with cancer. The primary endpoint is hearing loss and the main secondary endpoint is event free survival. The fully-enrolled, COG-sponsored trial was designed to enroll 135 pediatric patients worldwide in five different disease indications. Enrollment for the COG-sponsored trial is complete and data are expected late in the third quarter or early in the fourth quarter of 2013. The SIOPEL sponsored trial will enroll 102 pediatric patients with liver cancer worldwide, of which 76 patients were enrolled as of August 9, 2013.

Data from Phase III Trial in Collaboration with COG Expected in Q3 or Q4 2013. The first Phase III trial for STS is being conducted by COG, at their expense, and completed enrollment of 135 patients in the first half of 2012. The trial is a Phase III, open-label, randomized study with pediatric patients randomized in a 1:1 ratio to receive cisplatin alone or in combination with STS. Patients must

Ticker	ADHXF
Price	$0.23
Market Cap (M)	$6
EV (M)	$5
Shares Outstanding (M)	25.2
Avg. Daily Vol.	8,509
52-week Range:	$0.11-$1.13
Cash (M)	$1.0
Net Cash/Share	$0.04
Debt (M)	$0.0
Annualized Cash Burn (M)	$1.0
Years of Cash Left	1.0
Short Interest (M)	N/A

FY Dec		2011A	2012A	2013A
EPS:	Q1	$0.19A	$0.11A	($0.16)A
	Q2	($0.01)A	($0.02)A	$0.26A
	Q3	($0.17)A	($0.03)A	NA
	Q4	$0.14A	($0.26)A	NA
	FY	$0.19A	($0.20)A	NA

be under 18 years of age and have newly diagnosed germ cell tumor, hepatoblastoma, medulloblastoma, neuroblastoma, osteosarcoma, or other malignancies. STS is delivered as an IV infusion over 15 minutes, six hours post-cisplatin. The primary objective is to compare the proportion of subjects who develop hearing loss in each arm. Secondary objectives are measurement of change in hearing thresholds and the incidences of hematological and rental toxicities that might also be ameliorated by STS.[1] Trial data is expected in the third quarter of 2013 and the Company intends to file an NDA based on this single trial if the results are positive.

Sodium Thiosulfate Addresses an Important Unmet Medical Need and Large Market. The target market for STS is an area of severe unmet medical need, specifically young patients receiving platinum chemotherapy. Of 10,400 new cases of childhood cancer, an estimated 2,000 patients will receive this treatment in the United States. Many of these patients will experience hearing loss related to their chemotherapy, and there is currently no treatment available to inhibit hearing loss. STS has received Orphan Drug designation in the United States for the prevention of ototoxicity induced by platinum cancer chemotherapy in pediatric patients and will therefore receive 7.5 years of marketing exclusivity upon approval. We see a market opportunity for STS in Europe given that the SIOPEL sponsored trial is an international trial based in the United Kingdom.

Hearing loss attributed to platinum-based chemotherapy treatments is very common, and one study found that 61% of children experienced hearing loss after treatment.[2] The incidence and severity depends on several factors including the type of cancer, type of platinum-based chemotherapy, and age of the patient. There is a high unmet need for these patients, as no preventative treatments are currently FDA approved, and we are unaware of any late-stage programs other than STS. Around 2,000 children receive platinum-based chemotherapy each year in the United States, plus a similar number in Europe. Another 30,000 adults are at risk of platinum-induced hearing loss each year. The cost associated with pediatric patients that have substantial hearing loss prior to language development can be large due to hearing aid and cochlear implant costs, as well as specialized schooling for the deaf in the extreme cases. We expect strong market adoption for STS if it is approved due to the ability to reduce costs and improve the long term quality of life for patients.

Sodium Thiosulfate is eligible for Rare Pediatric Disease Voucher. In 2012 the FDA Safety and Innovation Act was signed into law, including the "Rare Pediatric Disease Priority Review Voucher Incentive Program." This clause extends the priority review voucher program, originally designed for developers of treatments for neglected diseases, to rare pediatric diseases, and STS is eligible. Under priority review, drug developers can have the length of time for drug review shortened to 6 months from the standard review of 10-12 months. The voucher program for pediatric diseases includes several changes from the neglected-disease voucher program. For example, the developer can ask the FDA in advance for an indication of whether the disease

[1] http://www.clinicaltrials.gov/ct2/show/NCT00716976

[2] Gilmer Knight, K.R. et al., 2005. Ototoxicity in Children Receiving Platinum Chemotherapy: Underestimating a Commonly Occurring Toxicity That May Influence Academic and Social Development. *Journal of Clinical Oncology*, 23(34), pp8588-8596.

qualifies as a rare, pediatric disease and the voucher can be transferred an unlimited number of times compared to only a single transfer for the neglected-disease voucher. Moreover, the developer using a pediatric voucher user needs to give the FDA only 90 days notification days prior to its use, compared to 1 year for the neglected-disease voucher. The pediatric voucher winner risks having the voucher revoked if the treatment is not marketed within a year. Finally, the pediatric voucher holder must report to the FDA about use of the pediatric treatment within five years of approval.

SIOPEL-Sponsored Phase III Trial Enrolling. The second Phase III trial for STS is a multi-center, open-label, randomized study expected to enroll 100 children with liver cancer, and is being funded by SIOPEL. Patients will be randomized to cisplatin only or cisplatin and STS. Similarly to the COG-sponsored trial, STS will be administered via intravenous infusion over 15 minutes, six hours post-cisplatin. The study will monitor the level of hearing loss as well as safety and tolerability. The Independent Data Monitoring Committee recommended the continuation of the study following two safety analyses. An interim efficacy analysis is planned and there is a possibility that the trial could end early if patients demonstrate reduced hearing loss in the STS arm. The study has enrolled 76 patients as of August 9, 2013.

Current Adherex Market Capitalization Does Not Reflect the Potential for STS. Adherex has the potential to enter the platinum-induced hearing loss market as the sole preventative treatment, allowing patients to achieve high efficacy from chemotherapy but with a reduced risk of hearing loss. Using a conservative estimate of $30 million in yearly sales, and the fact that an NDA could be filed in 2014, we believe that the sales potential for STS is not represented in the current stock price of Adherex. At the current stock price, Adherex has a market cap of $8 million. Phase II data with STS are strong, and if Phase III data are also positive leading to FDA approval, sales could quickly exceed the current market cap.

Financial Discussion

2012 Review. For fiscal year 2012, ended December 31, 2012, Adherex reported net loss from operations of $3.6 million (excluding $1.6 million non-cash loss on derivatives), compared to a net loss of $3.4 million (excluding $8.2 million non-cash gain on derivatives) for fiscal year 2011. Operating expenses for the 2012 were $3.3 million, compared to $3.2 million in 2011. The Company ended the year with $2.3 million in cash and equivalents compared to $5.3 million in 2011. The decreased cash balance is due to clinical trials and corporate expenses in the period offset by $2.5 million in proceeds received by the Company from its March 2011 rights offering.

Second Quarter Financial Results. For the second quarter of fiscal year 2013, ended June 30, 2013, Adherex reported net loss from operations of $0.9 million (excluding $7.5 million non-cash gain on derivatives), compared to a net loss of $1.2 million (excluding $0.6 million non-cash gain on derivatives) during the same period in fiscal year 2012. The Company reported research and development costs of $0.5 million in the second quarter of 2013, a decrease of $0.4 million from the

second quarter of 2012. General and administrative costs were $373,000 in the second quarter of 2013 and slightly down from $390,000 in the second quarter of 2012.

Cash Position and Financial Outlook. Cash burn for the first 6 months of 2013 was $1.3 million. Adherex does not anticipate the need for additional financing before the Company announces final data from the Children's Oncology Group (COG) sponsored Phase III late in the third quarter or early in the fourth quarter of 2013. Adherex ended the second quarter with $1.0 million in cash and equivalents.

Expected Upcoming Milestone

- 3Q 2013–Efficacy and safety data from the Children's Oncology Group (COG) sponsored Phase III trial comparing the level of hearing loss associated with cisplatin alone versus the combination of cisplatin plus Sodium Thiosulfate (STS).

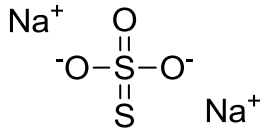
Company Description

Adherex Technologies (TSX: AHX.TO, OTCQB: ADHXF), Inc. is a clinical-stage biopharmaceutical company focused on developing drugs to treat cancer. The Company's lead drug candidate, Sodium Thiosulfate (STS), a chemoprotectant against hearing loss often caused by platinum-based anti-cancer agents. Adherex partnered the STS program with the International Childhood Liver Tumor Strategy Group (SIOPEL) and the Children's Oncology Group (COG). The SIOPEL sponsored Phase III trial is expected to enroll 102 pediatric patients with liver cancer worldwide, of which 76 patients were enrolled as of August 9, 2013. The COG sponsored Phase III trial (ACCL0431) was designed to enroll 135 pediatric patients worldwide in five different cancers. The trial completed enrollment in 2012, and data is expected to be available late in the third quarter or early in the fourth quarter of 2013.

Sodium Thiosulfate (STS): A Chemoprotectant Against Hearing Loss

Adherex is developing sodium thiosulfate (STS, **Figure 1**) as an otoprotectant against hearing loss caused by platinum-based chemotherapy in childhood cancer. By background, Adherex acquired an exclusive license to STS as a chemoprotectant from the Oregon Health Science University (OHSU) through the acquisition of Oxiquant in November 2002. The STS program is partnered with two groups, the Children's Oncology Group (COG) announced in March 2008, and the International Childhood Liver Tumor Strategy Group (SIOPEL), which was announced in 2007. Under the terms of agreements, both partners will conduct and fund the clinical trials and Adherex will provide drug, drug distribution for the studies.

Figure 1: Chemical Structures of STS



Sodium Thiosulfate

Source: LifeSci Advisors

The COG-sponsored Phase III trial completed enrollment during 2Q12, enrolling 135 pediatric patients worldwide in five different disease indications. The SIOPEL-sponsored Phase III trial is designed to enroll 102 children with liver cancer worldwide, of which 76 patients were enrolled as of August 9, 2013.

Ototoxicity in Children Resulting from Platinum Chemotherapy

Pathogenesis of Platinum-Induced Otoxicity. Platinum-based chemotherapy plays a key role in the treatment of various pediatric cancers, however partial or complete hearing loss is potential adverse event. Ototoxicity from platinum-based chemotherapy may result from deposition of protein-bound platinum in the inner ear. Platinum-drugs can destroy the outer sensory hair cells in cochlea, the auditory portion of the inner. These sensory hair cells are responsible for converting the mechanical vibrations (or sound) that enters the ear canal into electrical signals, which are carried to the brain by the auditory nerve. However when sensory hair cells are damaged, sound waves still move through the inner ear fluid but transduction no longer occurs and the sound does not reach the brain. This type of hearing loss is referred to as sensory-neural hearing loss. Additionally, unlike rapidly dividing tumor cells, cochlear hair cells do not grow back and therefore loss of these cells results in permanent hearing loss. Platinum agents initially impair hearing in the high frequencies and progresses to lower frequencies with increasing cumulative dose.

Sodium Thiosulfate Mechanism of Action. STS is a thiol-reducing agent used industrially in photographic processing and clinically it is FDA approved as an antidote against cyanide poisoning and is used to treat nitroprusside overdose. Although the mechanism of STS otoprotection is not fully known, it may involve free radical scavenging and/or covalent binding to inactivate the platinum compound. Due to concerns regarding reduced platinum antitumor activity when given with STS, the time of administration of chemotherapy and STS may be staggered.

Staging of Hearing Loss. Numerous ototoxicity criteria or grading systems to classify hearing loss in children exist. The two main types of ototoxicity assessment criteria include those that: (1) rely on change of hearing from baseline, and (2) are specifically written for children and measure absolute hearing levels. The most widely used system is the American Speech-Language-Hearing Association

(ASHA).[3] Two other grading systems also used today are the Common Terminology Criteria for Adverse Events (CTCAE) and Brock's grading scale. **Figure 2** provides further detail of the three scales.[4]

Figure 2: Definition of the Ototoxicity Criteria and Grades

ASHA Ototoxicity Criteria	NCI CTCAE Ototoxicity Grades	Brock's Hearing Loss Grades
(A) 20 dB or greater decrease in pure tone threshold at one test frequency	Grade 1: threshold shift or loss of 15-25 dB relative to baseline, averaged at two or more contiguous frequencies in at least one ear	Grade 0: hearing thresholds less than 40 dB HL at all frequencies
(B) 10 dB or greater decrease at two adjacent test frequencies		
(C) Loss of response at 3 consecutive test frequencies where responses were previously obtained		
	Grade 2: threshold shift or loss of 25-90 dB, averaged at two contiguous test frequencies in at least one ear	Grade 1: thresholds 40 dB or greater at 8,000 Hz
	Grade 3: hearing loss sufficient to indicate therapeutic intervention, including hearing aids (eg, 20 dB bilateral HL in the speech frequencies; 30 dB unilateral HL; and requiring additional speech-language related services)	Grade 2: thresholds 40 dB or greater at 4,000-8,000 Hz
	Grade 4: indication for cochlear implant and requiring additional speech-language related services	Grade 3: thresholds 40 dB or greater at 2,000-8,000 Hz
		Grade 4: thresholds at 40 dB or greater at 1,000-8,000 Hz

Source: Gilmer, K. et al., 2005.

- The American Speech-Language Hearing Association Ototoxicity Criteria were developed as a sensitive index of measurable change in hearing due to ototoxic therapy. Hearing thresholds during treatment are monitored and compared with the patient's baseline evaluation. However, obtaining baseline level in young children can sometimes be difficult and may be inaccurate. A major limitation of ASHA is the lack of a grading scale to show the severity of acquired hearing loss.

[3] Grewal, S. et al., 2010. Auditory late effects of childhood cancer therapy: a report from the children's oncology group. *Pediatrics*125, pp938-950.
[4]Gilmer, K. et al., 2005. Ototoxicity in children receiving platinum chemotherapy: underestimating a commonly occurring toxicity that may influence academic and social development. *Journal of Clinical Oncology,* 23(34), pp8588-8596.

- The Brock criteria were specifically designed to measure platinum-induced hearing loss in children in the clinical trial setting. Hearing loss grades 0 to 4 are assigned based on the standard pure-tone audiologic frequencies at which hearing thresholds equal or exceed 40 dB hearing loss. A baseline assessment is not required. A key limitation of the Brock criteria is that they do not distinguish between normal hearing and mild hearing loss. Additionally, the Brock grades do not apply to extended high frequencies (>8,000 Hz) or account for hearing loss at 3,000 and 6,000 Hz.

- The National Cancer Institute Cancer Therapy Evaluation Program's CTCAE system also requires a baseline evaluation.

Incidence and Prevalence of Platinum-Induced Hearing Loss in Children

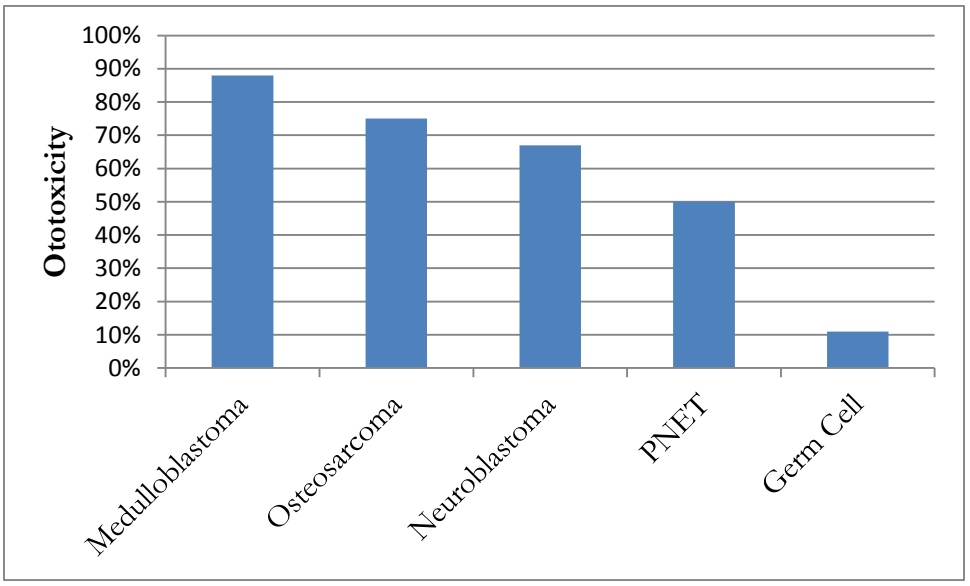
Treatment for most cases of pediatric cancer typically involves chemotherapy, surgery and/or radiation while less common treatments include transplants and immunotherapy. Chemotherapy regimens for cancers such as neuroblastoma, hepatoblastoma, retinoblastoma, germ cell tumors, osteosarcoma, medulloblastoma and other brain tumors routinely include cisplatin and/or carboplatin.[5] According to the American Cancer Society Facts and Figures 2012, there were approximately 12,060 new cases of childhood cancer (age 0–14 years) in the US last year.

The incidence of hearing loss in children depends upon the dose and duration of chemotherapy. Platinum-induced hearing loss is more prevalent in younger children. This is likely due to the developing nature of the auditory system in younger children (<4 years), making this group more vulnerable to damage. It may also be due to a different platinum pharmacokinetic profile in younger children that could result in slower clearance and increased exposure to the drug. Cochlear toxicity from cisplatin is more prevalent than with carboplatin, and is a dose-limiting side effect for cisplatin. Statistics regarding prevalence of platinum-induced hearing loss vary, with reported incidence of cisplatin ototoxicity in children ranging from 26% to more than 90%.[6]

Figure 3 describes a study that shows ototoxicity ranging from 11% to 88% in various cancers. The trial assessed audiological data from 67 cancer patients aged 8 months to 23 years who received platinum-based chemotherapy. Specifically, the medulloblastoma group had the highest rate of ototoxicity (n=15/17 or 88%), and the Germ cell group had the lowest (n=1/9; 11%). According to the study, 22% of patients required dose reductions due to ototoxicity.

[5]Gurney, J. et al., 2012. New international society of pediatric oncology Boston ototoxicity grading scale for pediatric oncology: still room for improvement. *Journal of Clinical Oncology*, 30, pp1-4.
[6]Knight, K. et al., 2005. Ototoxicity in Children Receiving Platinum Chemotherapy: Underestimating a Commonly Occurring Toxicity That May Influence Academic and Social Development. *Journal of Clinical Oncology,* 23, pp8588-8596.

Figure 3: Ototoxicity Rate in Children (n=67) Treated with Cisplatin and/or Carboplatin



Source: Knight, K. et al., 2005.

Treatment for Pediatric Platinum-Induced Otoxicity. There are no approved treatments to prevent hearing loss in chemotherapy. Hearing is typically monitored at various stages of chemotherapy, particularly in younger children. The primary treatment for ototoxicity related to chemotherapy is withdrawal of the offending drugs if symptoms arise.

Disease Market Information

Sodium Thiosulfate Market Estimates

We do not believe that the market potential for STS is taken properly into consideration when investors value Adherex. Given that platinum based drugs remains a mainstay in cancer treatment and with no current treatment approved to prevent platinum-induced hearing loss, we believe a viable market opportunity exists for STS. For illustration purposes, **Figure 4** provides a scenario analysis of penetration versus annual cost of STS therapy based on 2,000 eligible patients in the US per year. Of note, we also see a market opportunity in Europe given that the SIOPEL trial is based in the UK and involves many countries.

Additionally, in 2012 the FDA Safety and Innovation Act was signed into law, which included the "Rare Pediatric Disease Priority Review Voucher Incentive Program". This clause extends the priority review voucher program, originally designed for developers of treatments for neglected diseases, to rare pediatric diseases, and STS would be eligible. Under priority review, drug developers can have the length of time for drug review shortened to 6 months. The voucher program for pediatric diseases includes several changes from the neglected-disease voucher program. For

example, the developer can ask the FDA in advance for an indication of whether the disease qualifies as a rare, pediatric disease and the voucher can be transferred an unlimited number of times compared to only a single transfer for the neglected-disease voucher. Moreover, the developer using a pediatric voucher user needs to give the FDA only 90 days notification days prior to its use, compared to 1 year for the neglected-disease voucher. The pediatric voucher winner risks having the voucher revoked if the treatment is not marketed within a year. Finally, the pediatric voucher holder must report to the FDA about use of the pediatric treatment within five years of approval.

Figure 4: Scenario Analysis of US Peak Annual Sales ($, MM)

Penetration	Patients	Annual Cost of STS Treatment					
	2,000	$15,000	$20,000	$25,000	$30,000	$40,000	$50,000
	20%	6	8	10	12	16	20
	30%	9	12	15	18	24	30
	40%	12	16	20	24	32	40
	50%	15	20	25	30	40	50
	60%	18	24	30	36	48	60
	70%	21	28	35	42	56	70
	80%	24	32	40	48	64	80

Source: LifeSci Advisors

Competitive Landscape for Prevention of Platinum-Induced Hearing Loss

Hearing Aids/Cochlear Implants. Hearing aids have been recommended for 30% to 40% of survivors of childhood cancers who experience hearing loss.[7] Cochlear implants are small electronic devices with an estimated cost of more than $75,000 that are surgically placed in the inner ear to assist with certain types of deafness. While cochlear implant and hearing aids may provide some benefit, there is no treatment for hearing restoration. Further, hearing loss in younger children can result in communication difficulties and impaired speech and language development. What is most important for patients like these is that they have a treatment to protect their hearing before it is lost.

We do not know of any late stage drugs in development aside from STS; however **Figure 5** includes additional emerging otoprotection candidates still early in development.[8]

[7] Grewal, S. et. al., 2010. Auditory late effects of childhood cancer therapy: a report from the children's oncology group. *Pediatrics*125, pp938-950.

[8]Brock, P.R. et al., 2012. Platinum-Induced Ototoxicity in Children: A Consensus Review on Mechanisms, Predisposition, and Protection, Including a New International Society of Pediatric Oncology Boston Ototoxicity Scale. *Journal of Clinical Oncology*, 30(19), pp2408-2417.

Figure 5: Emerging Otoprotectants for Use with Platinum-Based Chemotherapy

Agent	Route	Mechanism	Comment
STS	IV	Thiol-reducing agent	In rats, STS protects against ototoxicity[14] without reducing antitumor efficacy.[101] Currently in phase III trials. Possible approaches include delayed administration,[14,87,100] two-compartment models,[4,5,104] and cochlear application.[85,96]
Amifostine	IV	Metabolized to WR-1065, a thiol-reducing agent	Most trials show no otoprotection; dose intensity may be critical; routine use of amifostine to prevent platinum-associated neurotoxicity or ototoxicity is not currently supported by the American Society of Clinical Oncology 2008 Clinical Practice Guideline.[105]
NAC	IV	Thiol-reducing agent	High dose (1,000 mg/kg) IV or intra-arterial NAC protects against cisplatin ototoxicity in the rat when given either 30 minutes prior to or 4 hours after chemotherapy and also blocks kidney toxicity and weight loss.[14,78] Delayed IV NAC does not block chemotherapy antitumor efficacy.[101]
D-methionine	PO, IV, or delivery to the round window	Glutathione modulator, free-radical scavenger	Animal studies have confirmed D-methionine protection from carboplatin- and cisplatin-induced ototoxicity.[99] Effective delivered PO,[99] systemically, or to the round window.[96] Animal studies have not shown significant antitumor interference.[106] One small-scale clinical trial showed complete otoprotection.[107] Larger-scale clinical trials will be needed.
Ebselen	PO	Glutathione peroxidase promoter	In animal studies, ebselen, a selenium-containing compound, has reduced cisplatin-induced outer hair cell loss with and without allopurinol co-administration[89] and does not appear to comprise cisplatin's antitumor efficacy.[108] To date, ebselen has not been tested in clinical trials, but trials are in the planning stages.
Ringer's solution or dexamethasone	Intratympanic injection	Agent dependent (anti-inflammatory)	Compartmental therapy via tympanostomy tubes.[92,95]

Abbreviations: IV, intravenous; NAC, N-acetylcysteine; PO, orally; STS, sodium thiosulfate.

Source: Brock, P.R. et al., 2012.

Sodium Thiosulfate Clinical Data Discussion

Investigators at OHSU conducted Phase I and Phase II studies showing that STS reduces the hearing loss associated with platinum-based chemotherapy. In one study at OHSU, the need for hearing aids to correct high frequency hearing loss was reduced from about 50% to less than 5%. Below we highlight results from an OHSU trial assessing STS as an otoprotectant against carboplatin-induced hearing loss in patients with malignant tumors.

Sodium Thiosulfate Phase II Trial in Platinum-Induced Ototoxicity.

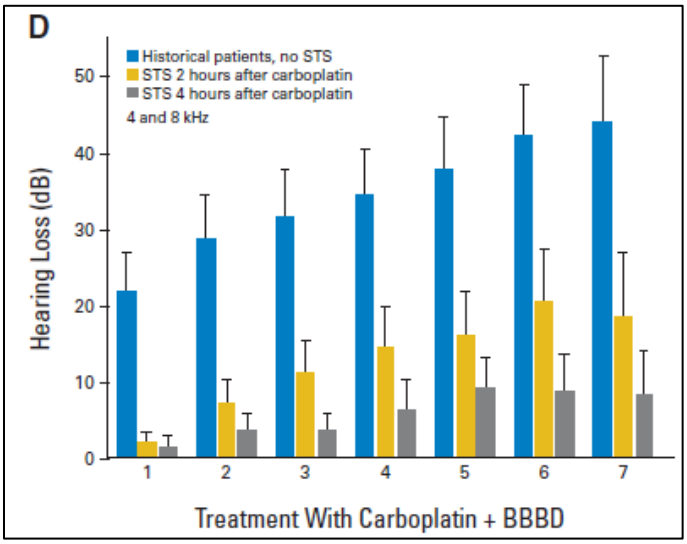
Doolittle and colleagues conducted a Phase II trial to determine if delayed administration of STS, given after blood-brain barrier (BBB) closure, protected against carboplatin ototoxicity.[9] Patients received carboplatin treatment with osmotic opening of the BBB monthly on 2 consecutive days for up to 1 year. Audiological assessment was conducted at baseline and within 24 hour before each monthly treatment. STS was administered intravenously as one (20 g/m^2) or two (20 g/m^2 and 16 g/m^2) 15-minute doses, depending on baseline hearing status. Group STS2 (n=24) received the first STS dose 2 hours (or 2 and 6 hours) after carboplatin (STS2) and group STS4 (n=17) received STS 4 hour (or 4 and 8 hours) after carboplatin. Patients that received STS were compared to a historical population as a control. The historical population (n=19) underwent carboplatin treatment in conjunction with opening of the blood brain barrier (BBB), and an audiological assessment was conducted at baseline and monthly following treatment. A total of 53% of these patients suffered

[9] Doolittle, N.D. et al., 2001. Delayed Sodium Thiosulfate as an Otoprotectant Against Carboplatin-induced Hearing Loss in Patients with Malignant Brain Tumors. *Clinical Cancer Research*, 7, pp493-500.

ototoxicity after just a single carboplatin treatment, which is in line with expectations. The median ages were 30 years, 44, and 44 for STS2, STS4 and HCG, respectively.

Phase II Trial Results. Results of the trial showed that there was a significant difference between STS administered at 4 hours after chemotherapy and the historical control group, with respect to time to ototoxicity and maintenance of hearing sensitivity at 8000 Hz ($p = 0.0010$) and 4000 Hz ($p = 0.0075$). Further, there was a trend toward differences between STS administered at 2 hours and at 4 hours in delaying ototoxicity and in maintaining hearing sensitivity; however the sample size was not large enough to demonstrate statistical significance. **Figure 6** highlights the average change in thresholds from baseline against carboplatin treatment at 4000Hz for groups STS2, STS4 and HCG. As the graph makes clear, hearing loss is a much smaller problem for the experimental treatment groups when compared to the historical control group, patients who did not receive STS.

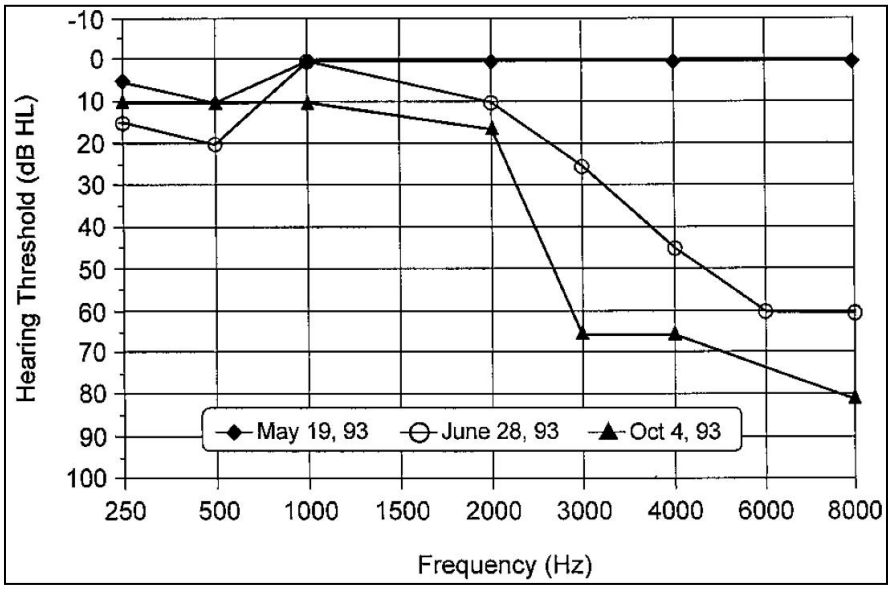
Figure 6: Comparison of Hearing Loss with and without STS in Carboplatin Treatment



Source: Brock, P.R. et al., 2012.

The audiogram from one of the historical control patients is shown in **Figure 7.** The baseline hearing threshold for that patient is indicated by the solid black line. Data are also plotted for one month and five months following carboplatin. There is a substantial loss in hearing threshold just one month after carboplatin treatment and additional losses at five months.

Figure 7. Audiogram of Control Patient at Baseline and Following Carboplatin Treatment

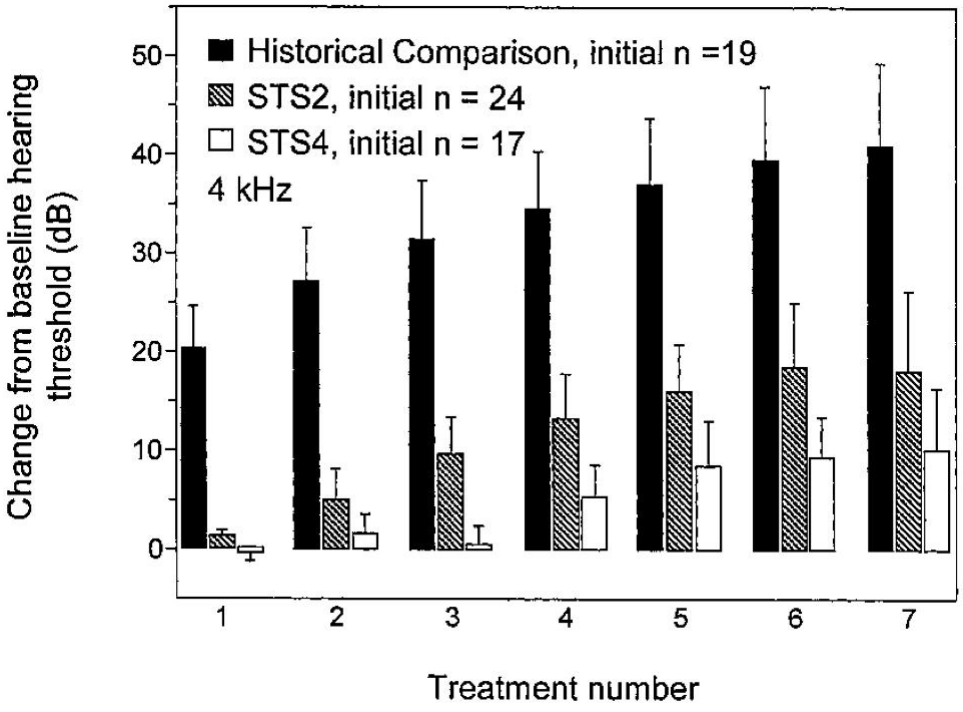


Source: Doolittle, N.D. et al., 2001.[Error! Bookmark not defined.]

STS Treatment Significantly Reduces Ototoxicity. As mentioned above, there was a statistically significant difference with respect to ototoxicity and maintenance of hearing sensitivity at 8000 Hz ($p=0.0010$) and 4000 Hz ($p=0.0075$) between the historical control group and the group that received STS 4 hours after chemotherapy. Furthermore, there was a trend toward differences between STS administered at 2 hours and at 4 hours in delaying ototoxicity and in maintaining hearing sensitivity.

Figure 8 highlights the average change in thresholds from baseline at 4000 Hz for the two STS treatment groups and the historical population. The change in thresholds is plotted for the three groups after 1 to 7 treatments of carboplatin. Hearing loss is progressively worse over the course of many carboplatin treatments and intervention with STS reduces the loss. These positive Phase II data spurred the launch of the two Phase III clinical trials that are currently underway.

Figure 8. Comparison of Hearing Loss with and without STS in Carboplatin Treatment



Source: Doolittle, N.D. et al., 2001.[Error! Bookmark not defined.]

Sodium Thiosulfate Phase III Trials in Platinum-Induced Ototoxicity

The STS program is partnered with two groups, COG and SIOPEL, who are conducting two Phase III trials. Patients will receive cisplatin alone or cisplatin plus STS. The primary endpoint is hearing loss, which will be evaluated by the ASHA and Brock grading systems. The SIOPEL-sponsored Phase III trial (n=100 pediatric patients with liver cancer) has enrolled 76 patients as of August 9, 2013. The fully enrolled COG trial (n=135 pediatric patients with various cancers) completed enrollment during the second quarter of 2012 and data is expected in 2013.

COG-Sponsored Phase III Trial Description

Study ACCL0431 was initiated in June 2008 by the Children's Oncology Group (COG) primarily at sites in the US and Canada. The study enrolled approximately 135 patients, most of whom have diagnoses of one of five childhood cancers typically treated with intensive cisplatin therapy, including newly diagnosed hepatoblastoma, germ cell tumor, osteosarcoma, neuroblastoma, and medulloblastoma. Other cancer patients whose treatment regimen includes cisplatin are also eligible, for example those with nasopharyngeal carcinoma, but few such patients are expected to have enrolled. After completion of study, patients will be followed periodically for 10 years.

Patients are stratified according to prior cranial radiation status, age (≥5 years or <5 years) and duration of cisplatin infusion (≥ 2 hours or <2 hours). Patients are randomized to 1 of 2 arms:

- Arm 1 (STS): Patients receive intravenous STS over 15 minutes beginning 6 hours after the completion of each cisplatin infusion. Treatment with STS continues until the completion of cisplatin therapy.
- Arm 2 (control): Patients do not receive STS. Patients undergo audiological assessment at baseline, prior to each course of cisplatin, and then at 4 weeks and 1 year after the last course of cisplatin or other cancer treatment. Some patients may undergo saliva collection for DNA studies.

Two interim analyses to protect patient safety were part of the study protocol. The first was to assess and compare early tumor response to chemotherapy between the two study regimens (STS vs. Control). In this semi-quantitative analysis involving the first 45 study subjects for whom tumor response data were available, the best response for each patient as reported by the institution was used to estimate whether there were any striking differences in treatment failures among the STS-treated patients. The second was to perform a futility analysis on the efficacy of STS for otoprotection using hearing outcomes data for approximately 75 patients. The results of these analyses were submitted for review by the COG Data Safety Monitoring Committee in April 2011 and no changes were recommended to the protocol.

SIOPEL-Sponsored Phase III Trial Description.

The Phase III SIOPEL 6 trial is being conducted by The International Childhood Liver Tumour Strategy Group, SIOPEL, a group of medical specialists founded in 1987 under the umbrella of the International Society of Paediatric Oncology (SIOP). The study was initiated in October 2007 and is expected to enroll 102 evaluable patients in up to 33 participating countries. As of August 9 2013, 76 children were enrolled. The trial is being conducted in standard risk hepatoblastoma where the effectiveness of the platinum treatment is very high, and the trial is being carefully monitored to identify an excess treatment failure rate.

Trial treatment consists of the following phases:

- Pre-operative randomized 1:1 chemotherapy (4 courses of cisplatin, with or without STS, every second week).
- Surgical removal of all remaining tumor lesions. If surgery has to be delayed, 1 or 2 cycles of the post-operative chemotherapy may be given pre-operatively.
- Post-operative chemotherapy (2 courses of cisplatin, with or without STS, every second week).
- Patients with progressive disease after 2 or more courses of cisplatin, with or without STS, will discontinue trial treatment

Investigators in SIOPEL 6 had a desire to study the influence of STS on cisplatin pharmacokinetics, but this is not possible because STS is administered 6 hours after cisplatin, long after levels of plasma cisplatin can be measured. As a surrogate for the presence of cisplatin, cisplatin-DNA adducts are measured at various times in peripheral blood cells to determine the extent of cisplatin anti-tumor activity as a secondary endpoint for the trial.

In case of concerns of an adverse effect of STS on the short-term efficacy of the cisplatin chemotherapy, the trial may be stopped early as well. Interim efficacy results on response to chemotherapy will be evaluated after every 20 patients. The first two reviews on the first 40 patients have been conducted by the Independent Data Monitoring Committee (IDMC) and concluded that current cancer efficacy results do not raise any concerns of impairment of the efficacy of cisplatin related to the addition of STS.

Intellectual Property & Licensing

Sodium Thiosulfate (STS)

Adherex licensed one US and 9 foreign patents from Oregon Health and Science University for STS, with an additional 5 patents pending. The STS methods of use patents expire in Europe in 2021 and are currently pending in the US. In 2004, the FDA granted Orphan Drug designation to STS, providing seven and a half years of market exclusivity upon regulatory approval.

Management and Board of Directors

Rosty Raykov
Chairman and Chief Executive Officer

Mr. Raykov has served as a director of Adherex and Chief Executive Officer since July 2009. Mr. Raykov is a General Partner at DCML, a private investment partnership. Prior to DCML, Mr. Raykov was a co-founder and portfolio manager for Alchem Investment Partners, an event driven hedge fund. Mr. Raykov also worked as a portfolio manager for Purchase Associates, an event driven hedge fund owned by John Levin & Co. He began his career as a financial analyst in the natural resources group at Bear Stearns. Mr. Raykov also serves on the board of Wesdome Gold Mines, a gold producer in Canada and Amarillo Gold, a gold explorer in Brazil. Mr. Raykov graduated from University of North Carolina at Chapel Hill, where he earned a Bachelor of Science degree in business administration.

Chris Rallis
Director

Mr. Rallis has served as a director of Adherex since August 2011. Mr. Rallis has been an executive-in-residence at Pappas Ventures, a life science venture capital firm since January 2008. Previously, Mr. Rallis was the President and Chief Executive Officer of ImmunoBiosciences, Inc. ("IBI"), a vaccine technology company formerly located in Raleigh, North Carolina from April 2006 through June 2007. Prior to joining IBI, Mr. Rallis served as an executive in residence (part time) for Pappas Ventures, and as a consultant for Duke University and Panacos Pharmaceuticals, Inc. Mr. Rallis is the former President and Chief Operating Officer and director of Triangle Pharmaceuticals, Inc., which was acquired by Gilead Sciences in January 2003 for approximately $465 million. Prior to assuming the role of President and COO in March 2000, he was Executive Vice President, Business Development and General Counsel. While at Triangle, Mr. Rallis participated in 11 equity financings generating gross proceeds of approximately $500 million. He was also primarily responsible for all business development activities which included a worldwide alliance with Abbott Laboratories and the in-licensing of ten compounds. Before joining Triangle in 1995, Mr. Rallis served in various business development and legal management roles with Burroughs Wellcome Co. over a 13-year period, including Vice President of Strategic Planning and Business Development. Mr. Rallis also serves on the board of Aeolus Pharmaceuticals, a biopharmaceutical company located in Mission Viejo, California. Mr. Rallis received his A.B. degree in economics from Harvard College and a J.D. from Duke University.

Steven Skolsky
Director

Mr. Skolsky has served as a director since August 2011. With a distinguished career spanning 30 years in the life sciences, Mr. Skolsky is a recognized industry leader who has held numerous international general management and executive leadership roles in the pharmaceutical and biotech sectors with a principal emphasis on commercialization, product strategy, and new product development. He was recently appointed to the position of Global Head of Clinical and Data Operations at Quintiles Transnational after serving as Principal of EXPIS Partners, a strategic life science consultancy. Mr. Skolsky also currently serves on the Board of Basilea Pharmaceutica, a Swiss based biopharmaceutical company where he previously served as Vice Chairman of the Board. Mr. Skolsky is the former President and Chief Executive Officer of Sequoia Pharmaceuticals, a privately held company specializing in novel antiviral therapeutics. Prior to his appointment at Sequoia, he held the position of Chief Executive Officer at Trimeris, Inc., a publicly held company that discovered and commercialized Fuzeon®, a first- in-class HIV therapeutic in collaboration with partner F. Hoffmann-La Roche. Previously, Mr. Skolsky served over 20 years at GlaxoSmithKline in a range of senior leadership roles, including Senior Vice President of Global Product Strategy and Clinical Development, Managing Director of GSK's operations in Australia and New Zealand and

Head of Glaxo Wellcome's Division of HIV/Oncology. Mr. Skolsky received his Bachelor's Degree in Biology from the University of North Carolina at Chapel Hill.

Risk to Investment

We view Adherex as being a high-risk, high-reward investment. As with any development-stage biopharmaceutical company, the primary risk associated with investing in Adherex shares relates to development and commercial activities. While the development for AHX's lead drug STS is supported by clinical data, unexpected safety problems, a lack of efficacy, and other problems may arise to impede development. Adherex may face regulatory problems with the FDA. It is also possible that if STS is approved for marketing, sales could be lower than expected. Beyond STS, AHX lacks a mid-stage pipeline. At some point in the future, lack of further development candidates could exert pressure on the Company to increase spending to in-license and develop new drug candidates. With any development stage biotechnology company it is possible that stock holders could be diluted by fundraising activities. A delay in, or disappointing data from the ongoing Phase III clinical trials for STS trial could pose a risk to future funding opportunities.

DISCLOSURES

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Adherex Technologies, Inc
9/6/2013

Number in Thousands	FY09A	FY10A	FY11A	1Q12A	2Q12A	3Q12A	4Q12A	FY12A	1Q13A	2Q13A
REVENUES										
Total Revenues	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**
SG&A	1,214.0	3,896.0	1,944.0	320.0	390.0	273.0	562.0	1,545.0	359.0	554.0
R&D	2,113.0	708.0	1,494.0	296.0	860.0	357.0	561.0	2,074.0	178.0	373.0
Other income (loss)	(111.0)		-					-		
Total Operating Expense	**$ 3,216.0**	**$ 4,604.0**	**$ 3,438.0**	**$ 616.0**	**$ 1,250.0**	**$ 630.0**	**$ 1,123.0**	**$ 3,619.0**	**$ 537.0**	**$ 927.0**
Operating Income	**$ (3,216.0)**	**$ (4,604.0)**	**$ (3,438.0)**	**$ (616.0)**	**$ (1,250.0)**	**$ (630.0)**	**$ (1,123.0)**	**$ (3,619.0)**	**$ (537.0)**	**$ (927.0)**
Interest income and other	204.0	32.0	52.0	8.0	3.0	(134.0)	(5,388.0)		(3,571.0)	7,534.0
Unrealized gain (loss)	-	(3,251.0)	8,072.0	3,323.0	645.0			3,968.0		
Total Other Income (expense)	**$ 204.0**	**$ (3,219.0)**	**$ 8,124.0**	**$ 3,331.0**	**$ 648.0**	**$ (134.0)**	**$ (5,388.0)**	**$ 3,968.0**	**$ (3,571.0)**	**$ 7,534.0**
Net Income (loss) Before Taxes	**$ (3,012.0)**	**$ (7,823.0)**	**$ 4,686.0**	**$ 2,715.0**	**$ (602.0)**	**$ (764.0)**	**$ (6,511.0)**	**$ 349.0**	**$ (4,108.0)**	**$ 6,607.0**
Net Income	**$ (3,012.0)**	**$ (7,823.0)**	**$ 4,686.0**	**$ 2,715.0**	**$ (602.0)**	**$ (764.0)**	**$ (6,511.0)**	**$ 349.0**	**$ (4,108.0)**	**$ 6,607.0**
EPS - Basic	**$ (0.42)**	**$ (0.49)**	**$ 0.20**	**$ 0.11**	**$ (0.02)**	**$ (0.03)**	**$ (0.26)**	**$ 0.01**	**$ (0.16)**	**$ 0.26**
EPS - Diluted	**$ (0.42)**	**$ (0.49)**	**$ 0.19**	**$ 0.11**	**$ (0.02)**	**$ (0.03)**	**$ (0.26)**	**$ 0.01**	**$ (0.16)**	**$ 0.26**
Shares Out - Basic	7,124	16,015	23,983	25,158	25,158	25,158	25,156	23,983	25,158	25,158
Shares Out - Diluted	7,124	16,015	24,050	25,158	25,158	25,158	25,156	24,050	25,158	25,158