



**FENNEC PHARMA**

**Corporate  
Presentation**

October 2016

# Safe Harbor Statement

During the course of this presentation we will make statements that constitute forward-looking statements. These statements may include operating expense projections, the initiation, timing and results of pending or future clinical trials, the actions or potential action of the FDA, the status and timing of ongoing research, corporate partnering activities and other factors affecting Fennec Pharma's financial condition or operations. Such forward looking statements are not guarantees of future performance and involve risk, uncertainties and other factors that may cause actual results, performance or achievements to vary materially from those expressed or implied in such statements. These and other risk factors are listed from time to time in reports filed with the SEDAR and the Securities and Exchange Commission, including but not limited to, reports on Forms 10-Q and 10-K. Fennec does not intend to update any forward looking information to reflect actual results or changes in the factors affecting forward-looking information.

# Company Overview

- US based biopharmaceutical company focused on the development of Sodium Thiosulfate (STS) for the prevention of platinum-induced ototoxicity in children with cancer
  - Granted FDA Orphan Drug Designation – 7.5 years market exclusivity
  - Potential for European Market Exclusivity for Pediatric Use – 10 years upon approval
- STS has completed enrollment of two Phase 3 trials
  - COG Study ACCL0431: 131 patients with heterogeneous tumors
    - Achieved primary efficacy endpoint – ASCO 2014
  - SIOPEL 6: 109 patients with standard risk hepatoblastoma
    - Reported no evidence of tumor protection and encouraging interim audiometry results – ASCO 2016
- Completed \$5.0 million financing by Sigma Tau in May 2016 - Provides necessary funds through 2017
- STS has the potential to fill a significant unmet medical need with no approved treatments on market or in development

# Platinum-based Chemotherapy

## Cisplatin

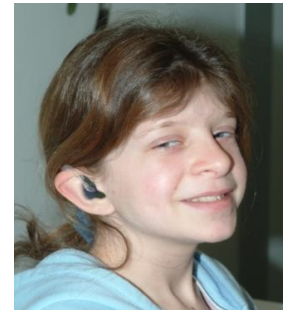
- Cisplatin, a.k.a. “penicillin of cancer” first introduced in the 1970s and subsequently demonstrated high efficacy in the treatment of variety of pediatric tumors
- Despite the approval of new chemotherapy treatments, targeted agents and immunotherapy drugs, cisplatin still finds wide use, as stand-alone or as a valuable part of a combination chemotherapy regimen
- Cisplatin can cause irreversible high frequency hearing loss, or ototoxicity in children
- Ototoxicity is permanent and irreversible
- As high survival rates for childhood cancers have been achieved, there is a growing need for pediatric practitioners to offer health care surveillance for the long-term effects of chemotherapy, including cisplatin-induced ototoxicity, in primary care settings

# Platinum Hearing Loss is Frequent, Severe and Irreversible

**Each year in US and EU ~7000 children receive platinum based chemotherapy for localized tumors, where overall survival is greater than 80%**

**At least 60% develop profound irreversible ototoxicity\***

- Ototoxicity is a dose-limiting side effect
- Effect can be seen after as little as the second or third dose
- Loss of high frequency hearing sensitivity (consonants /f/th/p/k/h/t)
- Background noise compounds disability in critical settings
- Infants and young children at critical stage of development, lack speech language development and literacy
- Older children & adolescents lack social-emotional development and educational achievement



**Devastating and life long impact on Quality of Life**

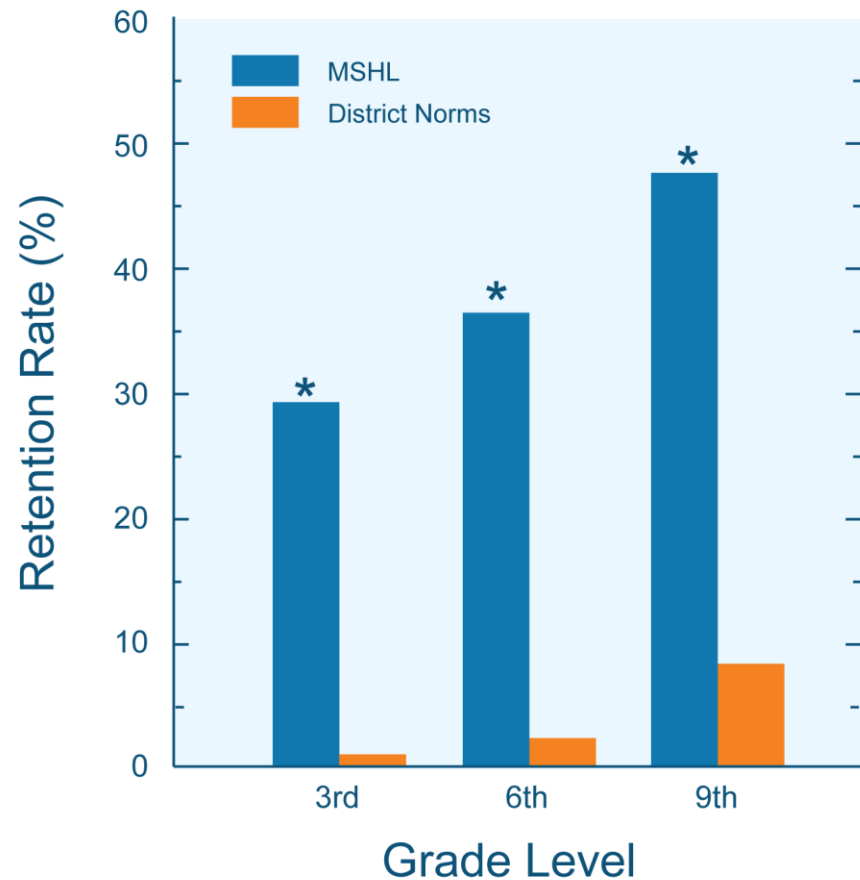
# Devastating Impact on Quality of Life

## Even minimal hearing loss (MSHL) is damaging

- High risk for being held back a grade (37% versus 3%)

## Neuroblastoma survivors with hearing loss

- Twice the rate of parent reported problems with reading, math, attention and need for special education
- Poorer child-reported quality of life and school functioning

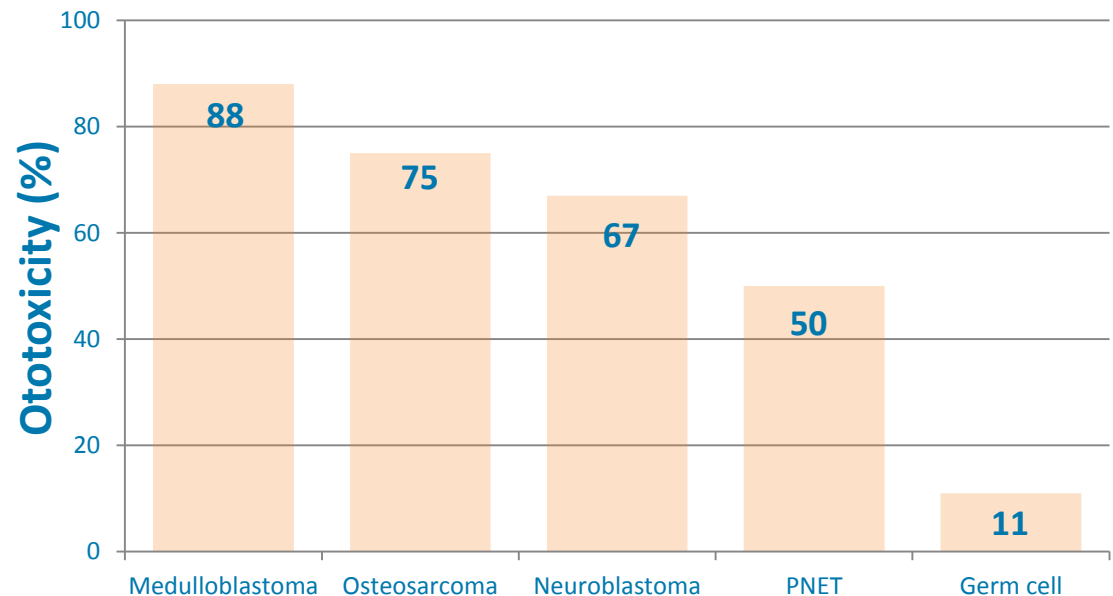


\*Bess et al., Ear and Hearing, 1998, 19:339-54

\*Gurney et al., Pediatrics, 2007 120(5):229-36

# Ototoxicity in Children Treated with Cisplatin and/or Carboplatin\*

- 61% bilateral hearing loss (ASHA criteria) at the end of treatment
- 41% required hearing aids that only partially restore hearing
- 22% of patients had dose reductions due to ototoxicity
- N=67 age 8 m -20 years



\*Gilmer-Knight et al., Journal of Clinical Oncology, 2005, 23:8588-96

# Sodium thiosulfate (STS)

## Indication

- Approved in US and some EU countries for the treatment of cyanide poisoning

## Mechanism of Action\*

- STS is a competitive inhibitor of cisplatin: STS reacts irreversibly with cisplatin to form  $\text{Pt}(\text{S}_2\text{O}_3)$  which is not cytotoxic and is readily excretable
- Inactivation of protein-bound platinum complexes causing ototoxicity in the inner ear
- Anticancer activity of cisplatin occurs during the first two hours after administration when the free (unbound) cisplatin distributes into the cancer cells

## Drug Delivery

- STS is administered 6 hours post cisplatin infusion in a bolus dose iv over 15 min

## Toxicology

- STS is generally recognized as safe (GRAS in US)

\* Howell and Taetle 1980; Neuwelt, Brummett et al. 1996

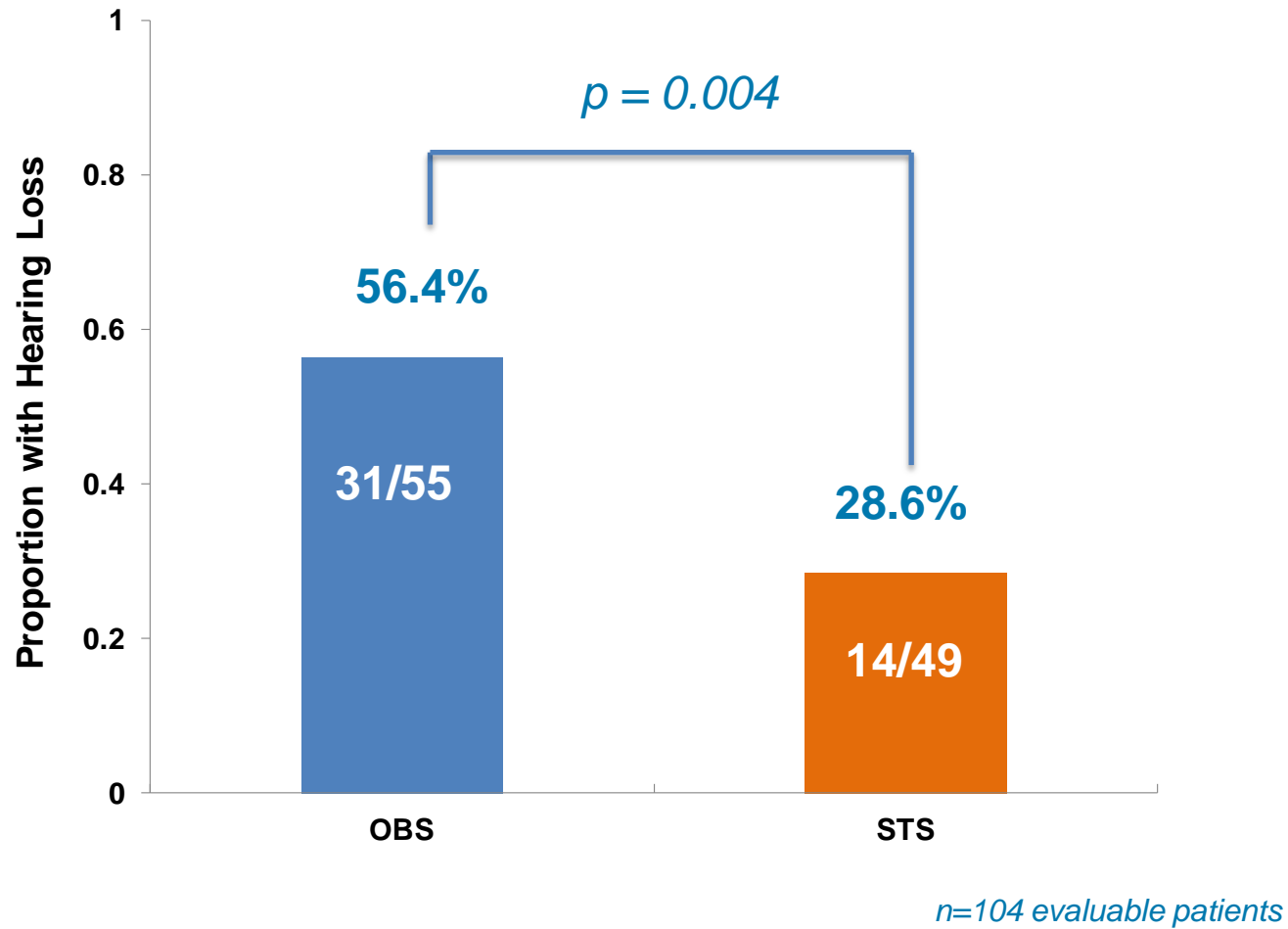


# COG ACCL0431 (ASCO 2014)

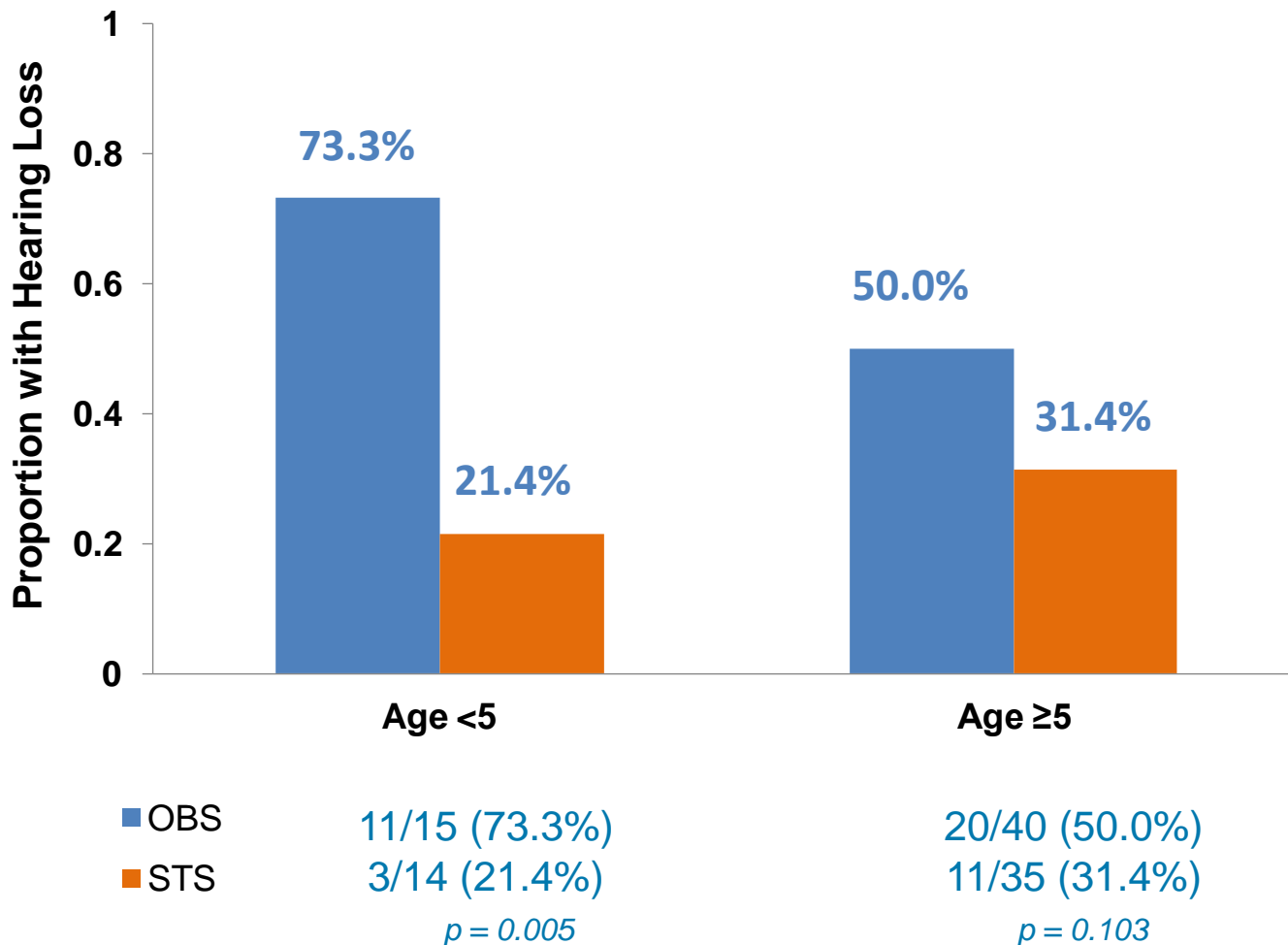
## Objectives, Population, Dosing

- Randomized study of STS for prevention of cisplatin-induced hearing loss in children - newly diagnosed children with, germ cell tumor, osteosarcoma, neuroblastoma, medulloblastoma, hepatoblastoma, and others
- 131 randomized patients with local and metastatic disease
- Study Chair: David Freyer, DO, MS
- Objective – powered to detect 50% relative reduction in hearing loss
- Study completed in 1Q 2012 with data presented at ASCO 2014
- Patients ranged from 1-18 years with any malignancy treated with cisplatin at a planned cumulative dose of  $\geq 200\text{mg/m}^2$
- Dosing Schedule:
  - Disease specific chemotherapy regimen containing cisplatin followed by STS  $16\text{g/m}^2$  IV infusion 6 hours post cisplatin dose
  - Disease specific chemotherapy regimen containing cisplatin without STS

# Hearing Loss By Randomized Arm

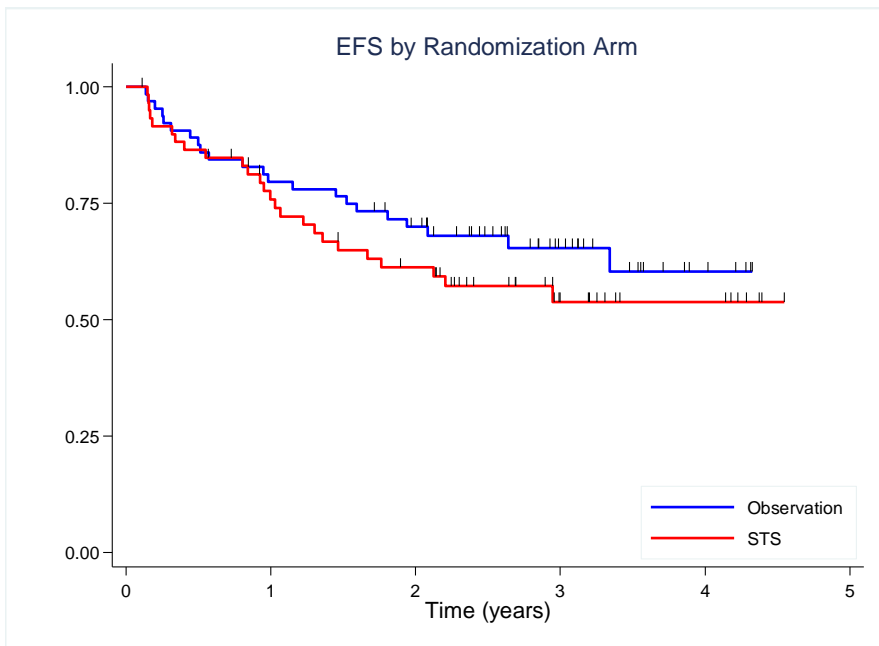


# Hearing Loss By Randomized Arm and Age

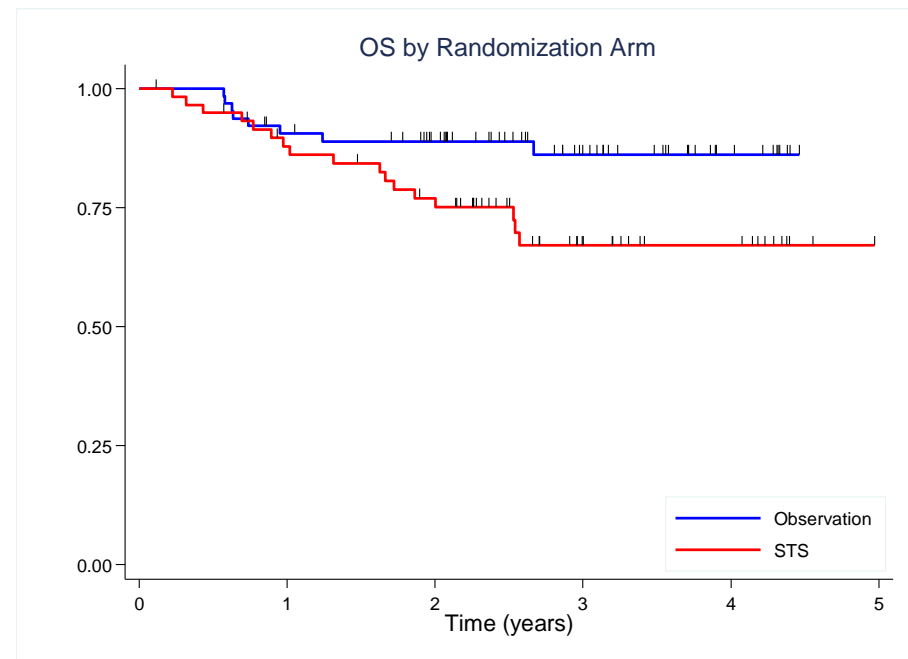


# EFS/OS by Randomization Arm

All Patients, n=126 at median f/u of 2.9 yrs



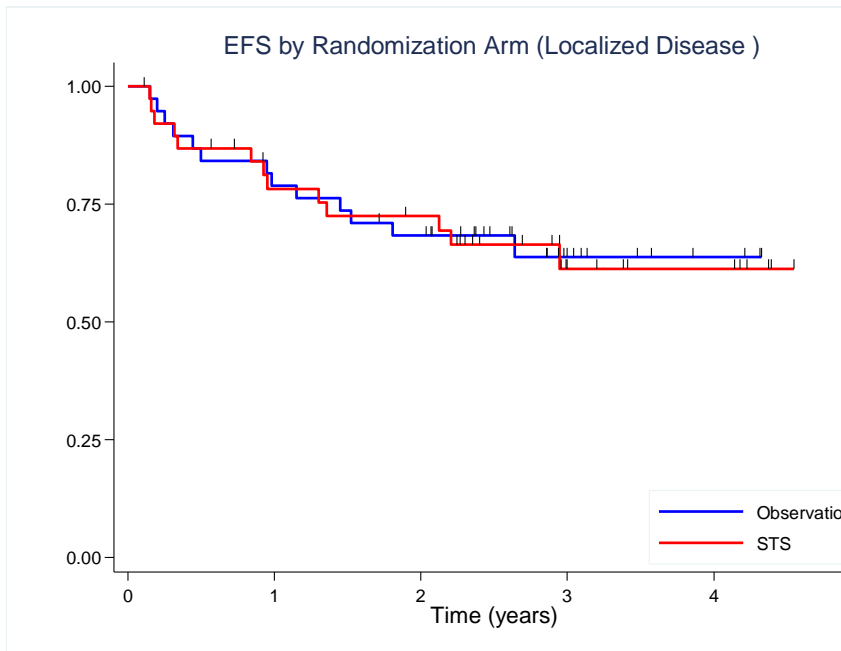
Log Rank  $p = 0.31$



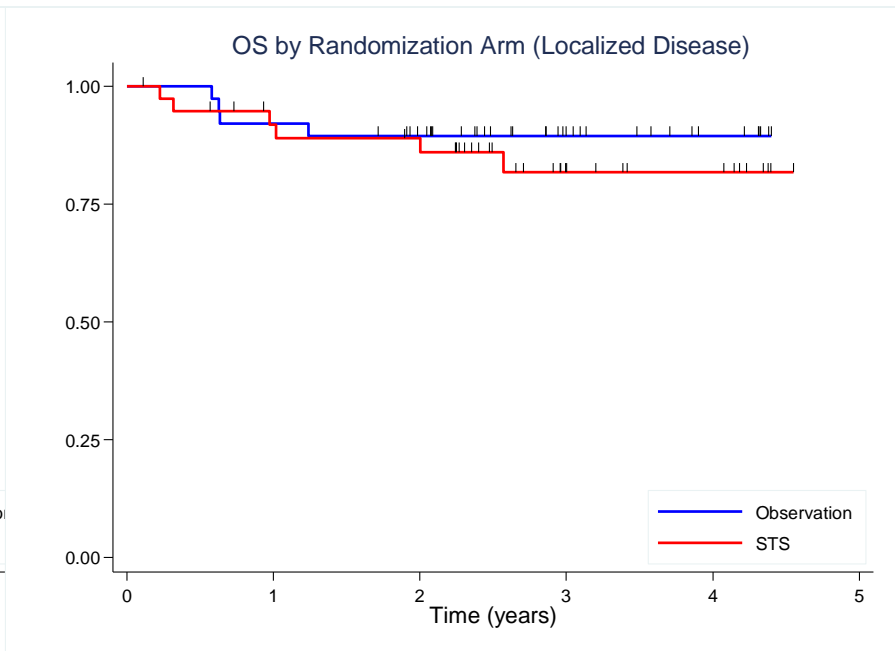
Log Rank  $p = 0.03$

# EFS/OS by Randomization Arm

Localized Disease Only, n=78



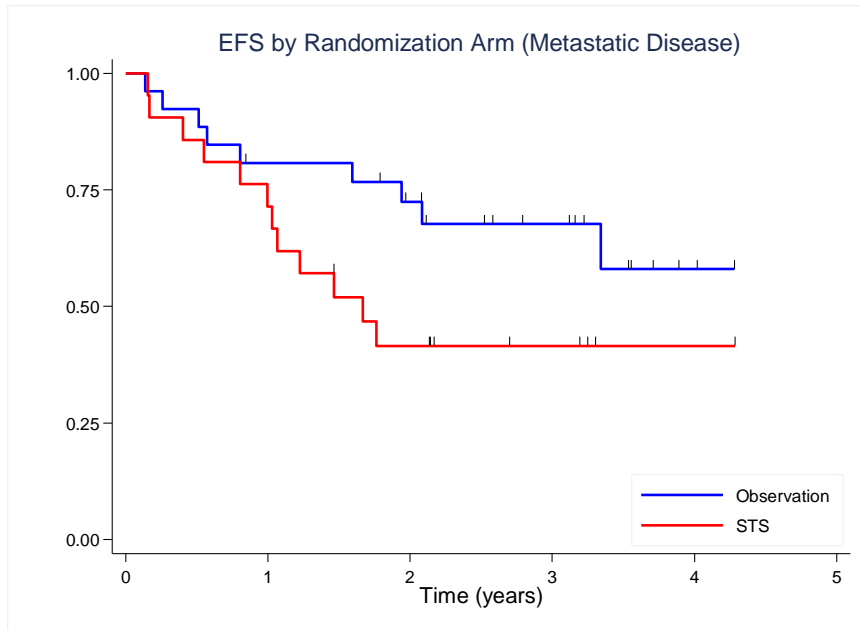
Log Rank  $p = 0.94$



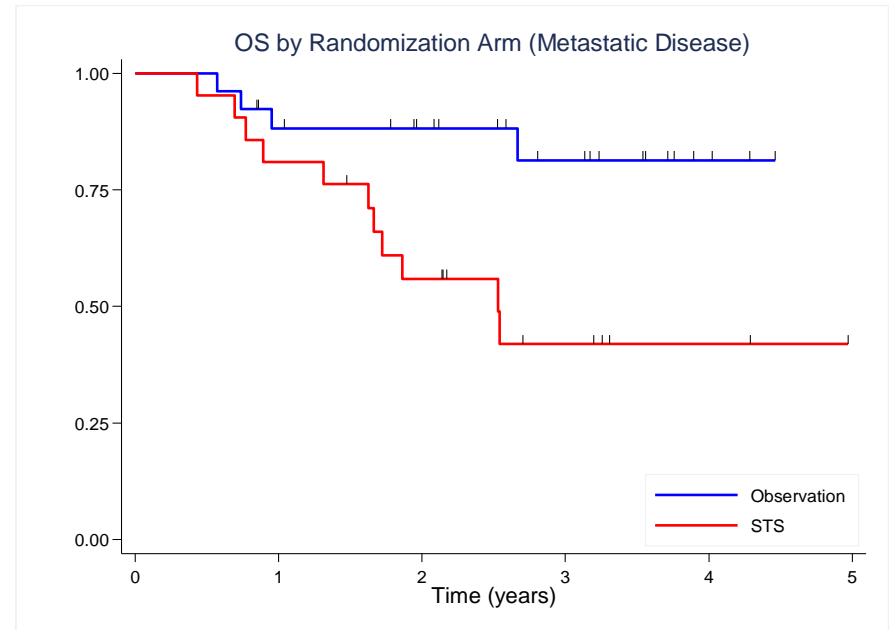
Log Rank  $p = 0.48$

# EFS/OS by Randomization Arm

Disseminated Disease Only, n=47



Log Rank  $p = 0.085$



Log Rank  $p = 0.011$

# EFS, OS and Hearing Loss by Tumor Type

Tumor Type	Projected COG 3-year EFS	STS 2.9 yrs EFS	OBS 2.9 yrs EFS	STS 2.9 yrs OS	OBS 2.9 yrs OS	Hearing Loss STS	Hearing Loss OBS
Germ Cell	75%	14/16 (87.5%)	13/16 (81.3%)	15/16 (93.8%)	16/16 (100%)	0	3/15 (20%)
Hepatoblastoma	60%	2/2	4/5	2/2	5/5	1/2	4/5
Medulloblastoma*	55%	7/12 (58.3%)	9/14 (64.3%)	8/12 (66.7%)	12/14 (85.7%)	3/9 (33.3%)	10/10 (100%)
Neuroblastoma	45%	8/14 (57.1%)	6/12 (50.0%)	11/14 (78.6%)	9/12 (75.0%)	4/10 (40%)	6/9 (66.7%)
Osteosarcoma	70%	5/15 (33.3%)	7/15 (46.7%)	9/15 (60.0%)	11/15 (73.3%)	5/12 (41.7%)	7/15 (46.7%)
Others**		0/3	1/2	0/3	2/2	1/2	1/1

\*One death on STS arm Supratent Primitive Neuro Tumor. \*\*Per protocol amendment to include other tumors. Three deaths on STS arm other tumors: 2 pts with ATRTs and 1 pt with Carcinoma, NOS. No deaths in OBS arm other tumors: 1 pt with choroid plexus carcinoma and 1 pt with anaplastic astrocytoma.

# COG ACCL0431: Conclusions

- STS protects against cisplatin-induced hearing loss in children
- Conclusions on the risk of tumour protection by STS in children treated with cisplatin confounded due to:
  - Heterogeneity of the population
    - Various diseases and tumor stages
  - Imbalances between prognostic groups
  - Protocol amendment to include other tumors
  - Longer term follow up required to assess EFS and OS in some cancers
  - Missing information: doses of cisplatin, concomitant treatments, timing of administration of STS after the last cisplatin dose



# SIOPEL 6 (ASCO 2016)

## Objectives, Population, and Endpoints

### Objectives

- To assess the efficacy of STS to reduce the hearing impairment caused by Cisplatin in SR-HB
- To carefully monitor any potential impact of STS on response (protocol pre-specified IDMC tumour response review at 20, 40, 60, 80 and 100 patients) to Cisplatin and overall survival

### Study population

- Children 1 month–18 years old with histologically confirmed newly diagnosed SR-HB, PRETEXT I, II or III, serum AFP > 100 µg/L
- First patient in the study enrolled in 2007, last patient in Dec 2014

### Primary endpoint

- Centrally reviewed absolute hearing threshold, at the age of  $\geq 3.5$  yrs, by pure tone audiometry, graded by Brock criteria
- 80% power to detect 60% vs. 35% hearing loss

**Secondary endpoints:** response, resection, EFS, OS and long term renal function

# SIOPEL 6 (ASCO 2016)

## Preliminary Chemotherapy Efficacy

Tumor Response		CIS N=52	CIS+STS N=53
Status at end of treatment	Complete Remission	44 (84.6%)	48 (90.5%)
	Partial Response	4 (7.6%)	5 (9.4%)
	Progressive Disease	2 (4.5%)	0
	Died	1 (1.9%)	0
	Not Evaluable	1 (1.9%)	0
Status at last follow up (February 2016)	Complete Remission	48 (92.3%)	50 (94.3%)
	Partial Remission	0	1 (1.9%)
	Recurrent Disease	0	1 (1.9%)
	Death	4 (7.6%)	1 (1.9%)

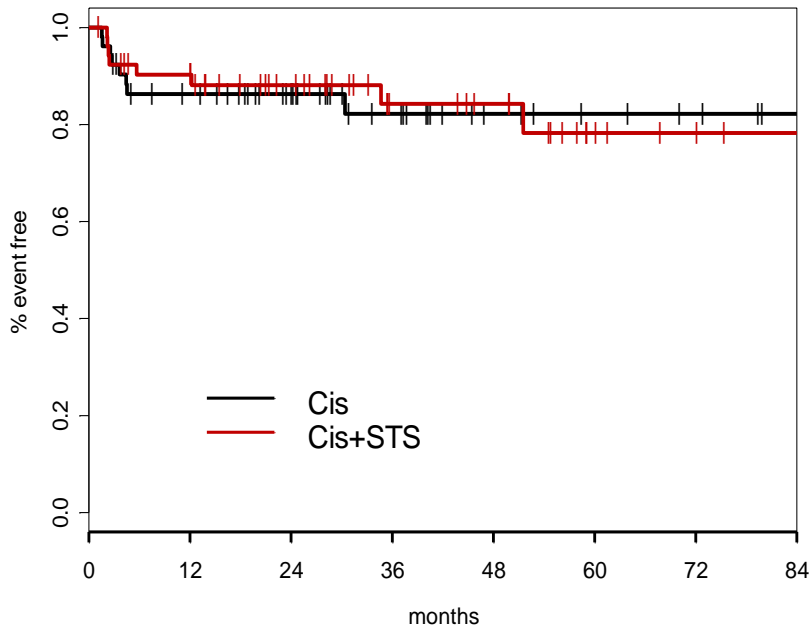
**18 patients received between 1 and 6 courses of doxorubicin (CIS:9; CIS+STS:9)**

# SIOPEL 6 (ASCO 2016)

## EFS/OS by Randomization Arm

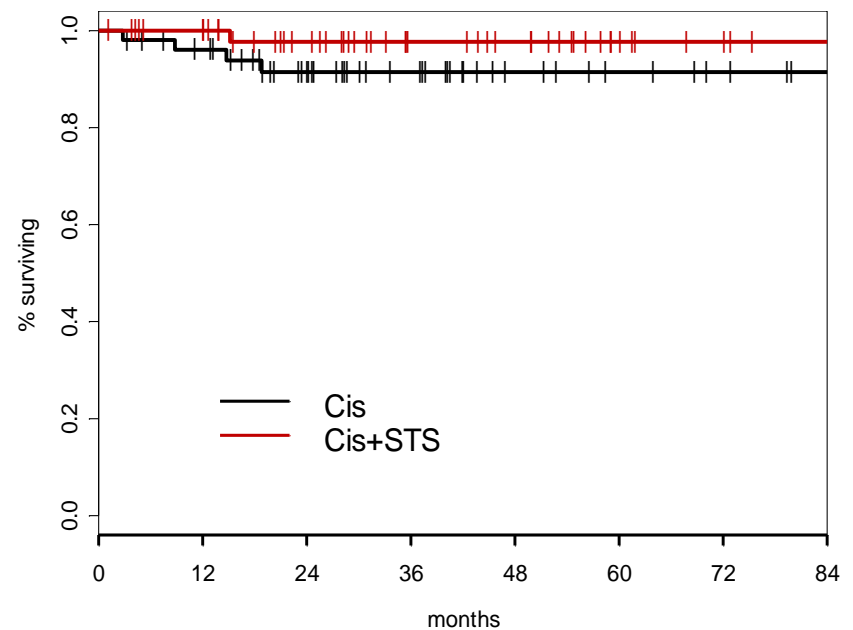
Median Follow-Up 34 Months

EFS



2yr-EFS per protocol Cis 86.3%, CIS+STS 89.0%

OS



2yr-OS Cis 91.4%, Cis+STS 97.7%

# SIOPEL 6 (ASCO 2016)

## Preliminary Conclusions

- Study is fully enrolled with 109 patients
- It is safe to deliver Sodium Thiosulphate for otoprotection in Standard Risk Hepatoblastoma treated according to the SIOPEL 6 regimen
- There is no evidence of tumor protection
- The interim results of the first 68 patients centrally reviewed for pure tone audiometry were encouraging
- Results for the audiology primary end point will be available in 2017

# STS: Development Strategy

EVENT	TIMING
FDA Type C Clinical Development Meeting ✓	Mar 2011
Presented to Pediatric ODAC ✓ ODAC recognized challenge of demonstrating STS does not reduce efficacy of cisplatin and agreed adult study would not be appropriate	Nov 2011
COG ACCL0431 Phase 3 Clinical Data ✓	Jun 2014
SIOPEL 6 Phase 3 Final Interim Safety Analysis (N=100)✓	Feb 2015
SIOPEL 6 34 Months Safety and End of Treatment Anti Tumor Efficacy Results ✓	Jun 2016
FDA & EMA Regulatory Development Meetings	2016-2017
SIOPEL 6 Final Efficacy and Safety Results	2017
NDA/MAA Submissions	TBD

# Capital Structure and Share Information

Stock Listings	FRX – TSX, Canada FENCF – OTCQB, USA
Current Share Price	USD \$2.03
Shares Outstanding (millions)	13.6
Market Cap. (millions)	USD \$27.6
Warrants (millions)	1.3 with USD \$1.50 exercise price (Nov. 22, 2018) 0.4 with USD \$3.60 exercise price (Dec. 3, 2016)
Insider Ownership	Approx. 10% fully diluted
Cash@ June 30, 2016	USD\$5.1 million with no debt
2015 Cash Burn	USD \$1.5 million
Institutional Ownership	Southpoint Capital – 36%; Sigma Tau –19.4%, Manchester Mgmt – 16%; 683 Capital – 8%

# Board of Directors and Management

## **Dr. Khalid Islam** – Chairman

- Chairman and CEO at Gentium S.p.A. - sold to Jazz Pharma for \$1 billion.

## **Dr. Marco Brughera**– Director

- Currently CEO and Global Head of Sigma Tau Rare Disease. Successfully out licensed Defibrotide US rights to Jazz Pharmaceuticals to Baxalta for \$1 billion.

## **Adrian Haigh** – Director

- Currently SVP and General Manager PTC Therapeutics. Previously COO at Gentium S.p.A. - sold to Jazz Pharma for \$1 billion.

## **Chris Rallis** – Director

- Previously President & COO of Triangle Pharmaceuticals - sold to Gilead for \$500 million.

## **Rosty Raykov** – CEO and Board Member

## **Robert Andrade** – CFO

## **Anne McKay** – Regulatory Affairs

## **Lei Fang** – Biostatistics

## **Mark Gowland** – Controller

## **Lex Smith** – Pharmaceutical Development

# STS Investment Highlights

- Completed \$5.0 million financing by Sigma Tau in May 2016
- US Orphan Drug Designation (7.5 years market exclusivity)
- Potential for European Market Exclusivity for Pediatric Use (10 years)
- Completed enrollment of two Phase 3 trials
- COG Phase 3 trial achieved primary endpoint for hearing
- SIOPEL 6 Phase 3 trial reported no evidence of tumor protection and encouraging hearing results on protocol pre-specified interim analysis
- Significant unmet medical need with no approved treatment on market or in development
- Fennec has exclusive regulatory rights to data from both studies
- Well positioned to submit MAA/NDA after hearing data from SIOPEL 6 is available in 2017