



**FENNEC PHARMA**

**Corporate  
Presentation**

May 2017

# 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.

# 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

# Company Overview

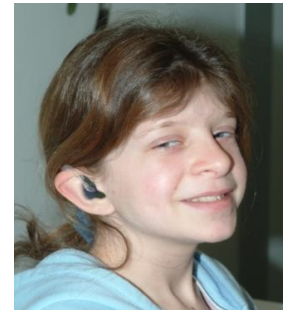
- US based biopharmaceutical company focused on the development of Sodium Thiosulfate (STS) for the prevention of platinum-induced ototoxicity in children with cancer
  - Granted FDA Orphan Drug Designation – 7.5 years market exclusivity
  - Potential for European Market Exclusivity for Pediatric Use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

# Platinum Hearing Loss is Frequent, Severe and Irreversible

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

At least 60% of children 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

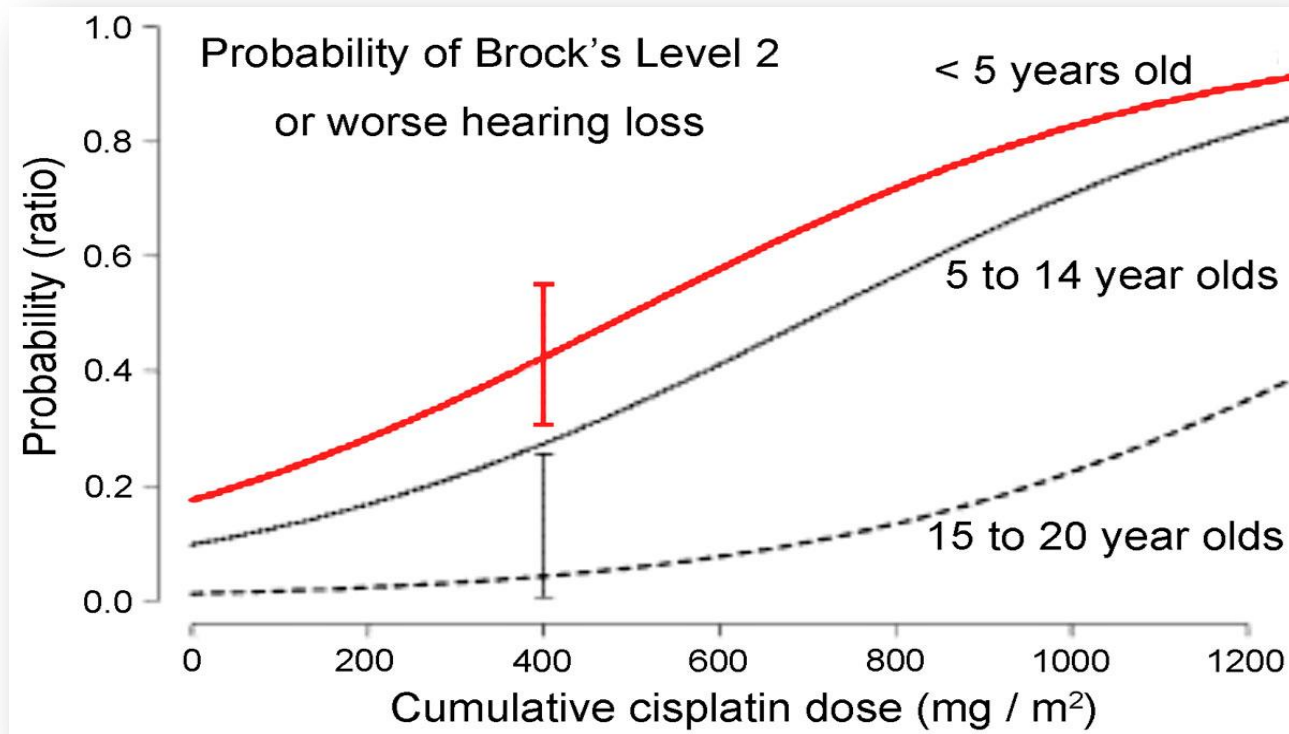


**Devastating and life long impact on Quality of Life**

\* Fennec internal estimates

\*\* Neuwelt and Brock. J Clin Oncol 2010;28:1630-1632

# Cisplatin Ototoxicity Risk Factors



**Children < 5 years old: 21 times the risk for hearing loss compared to adolescents**

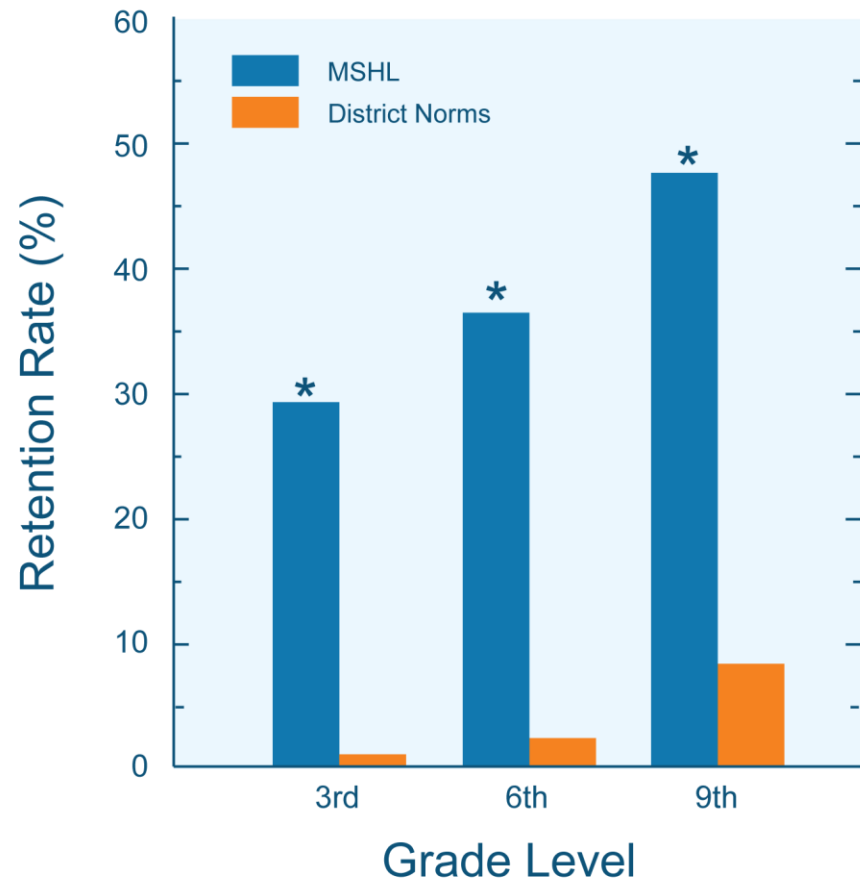
# Devastating Impact on Quality of Life

## 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

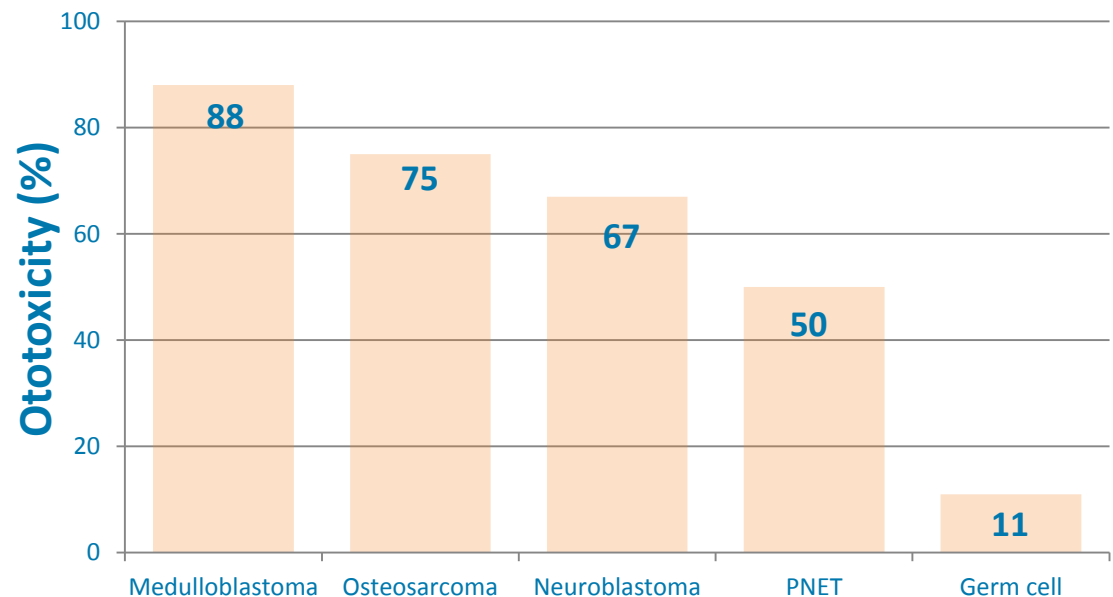


\*Bess et al., Ear and Hearing, 1998, 19:339-54

\*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\*

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

## 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 (Freyer 2016)

## Specific aims

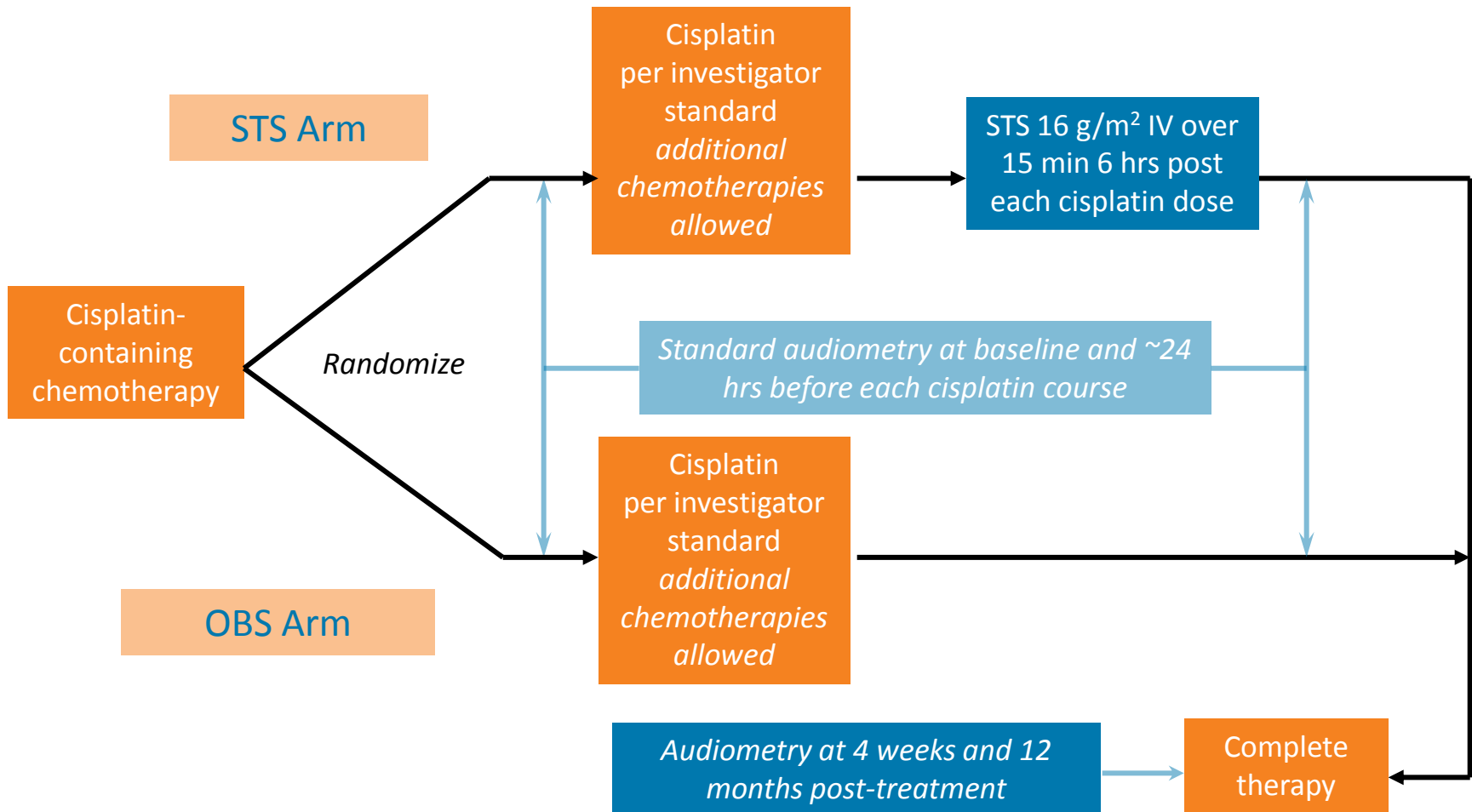
### Primary

- Evaluate efficacy of STS for prevention of hearing loss in children receiving cisplatin chemotherapy (hypothesis: 50% relative reduction in hearing loss). Measured by hearing status at 4 weeks post-therapy defined by American Speech-Language-Hearing Association (ASHA) criteria:
  - > 20 dB loss at 1 frequency or > 10 dB at 2 consecutive frequencies

### Secondary

- Compare change in mean hearing thresholds
- Compare incidence of other Grade 3/4 toxicities (renal and hematological)
- Monitor EFS and OS in two randomized groups

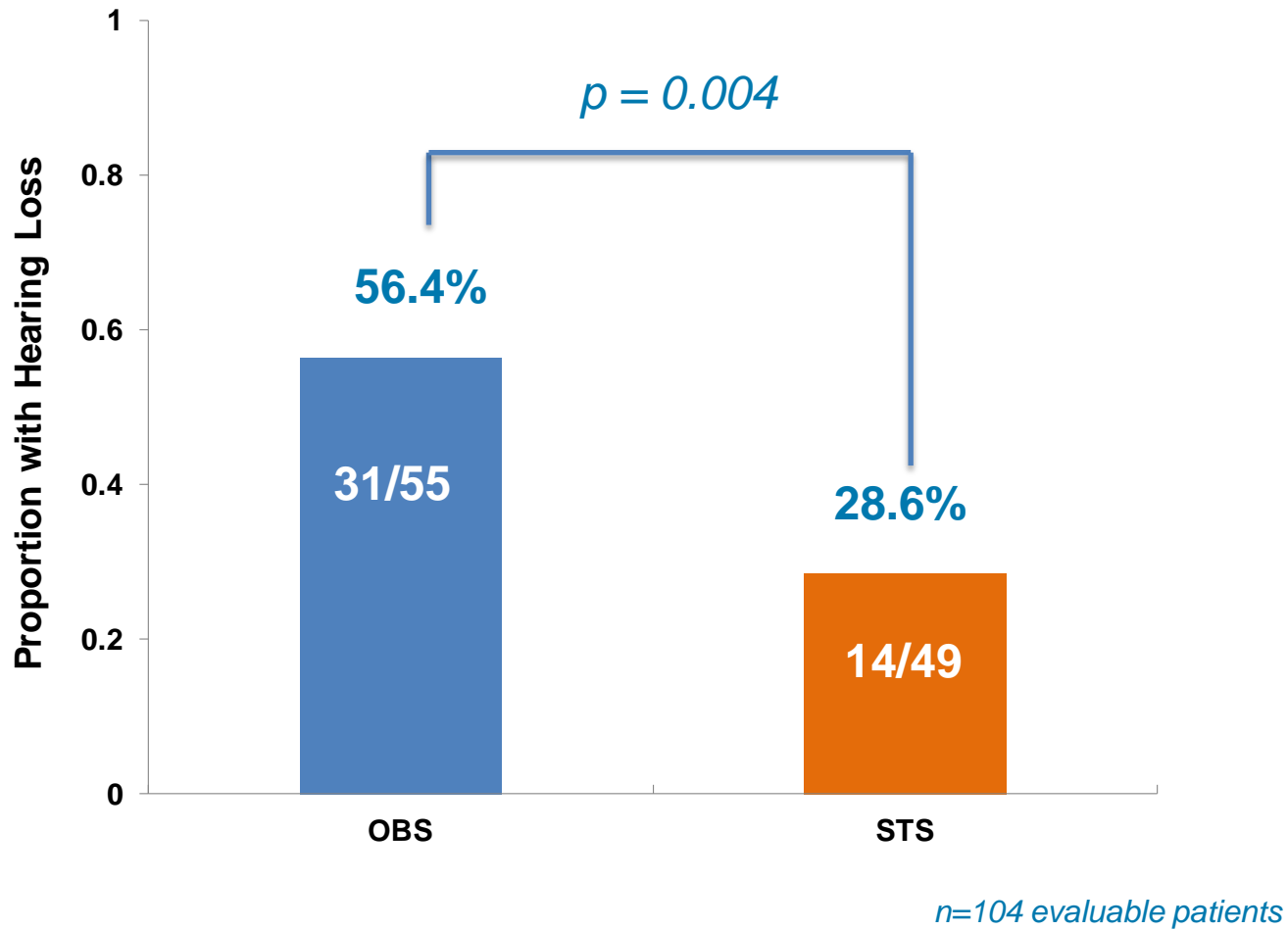
# COG ACCL0431 (Freyer 2016) Study Design



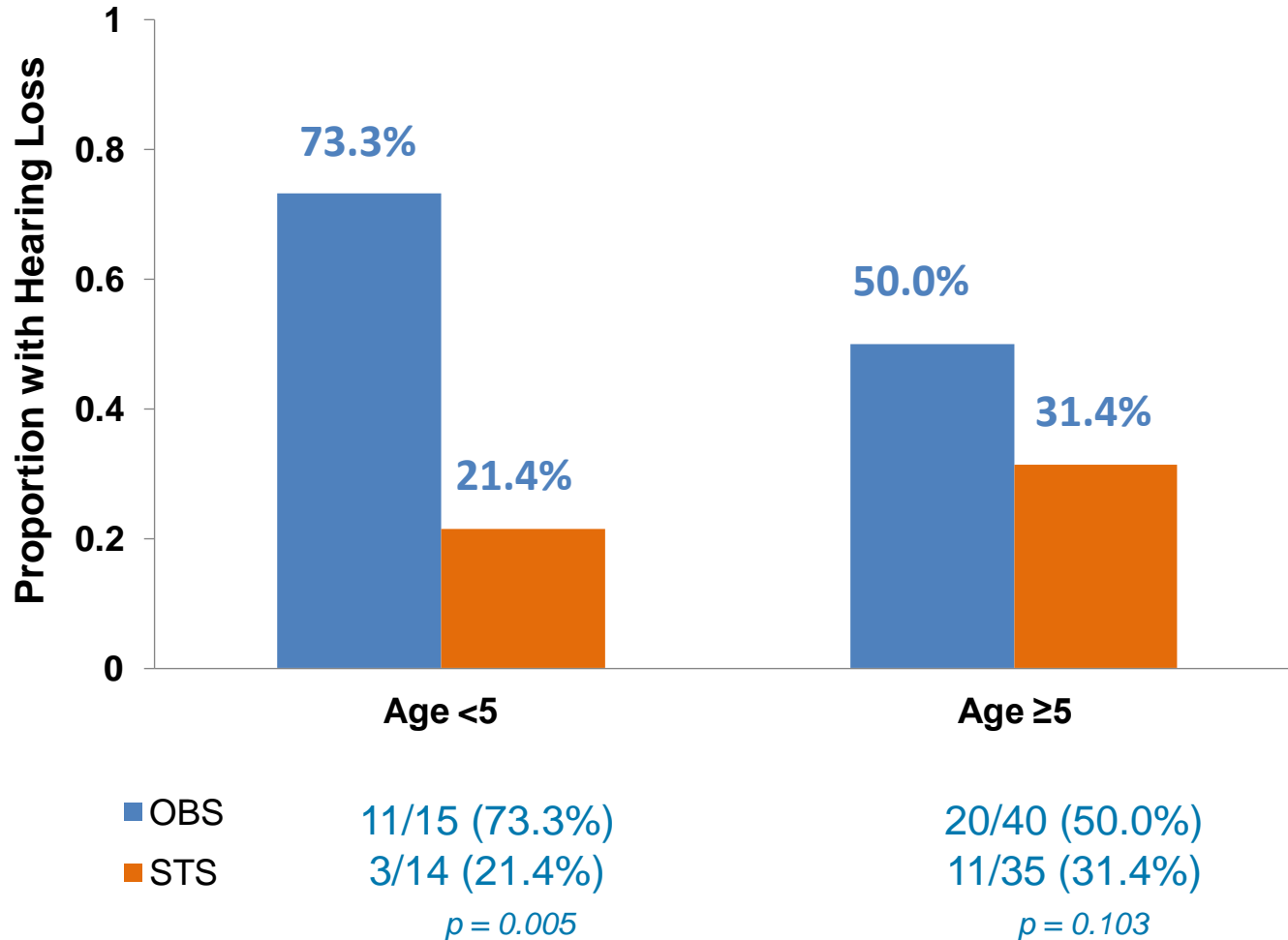
# Participant Characteristics

Characteristic	Treatment			
	Control		STS	
	n	%	n	%
Number eligible	64	-	61	-
Age (years)				
<5	22	34.4	22	36.1
5-9	13	20.3	7	11.5
10-14	14	21.9	16	26.2
15-18	15	23.4	16	26.2
Diagnosis				
Germ cell tumor	16	25.0	16	26.2
Hepatoblastoma	5	7.8	2	3.2
Medulloblastoma/PNET	14	21.9	12	19.7
Neuroblastoma	12	18.8	14	23.0
Osteosarcoma	15	23.4	14	23.0
Other	2	3.1	3	4.9
Extent of disease				
Localized	38	59.4	39	63.9
Disseminated	26	40.6	21	34.4
Unknown	0	0	1	1.6

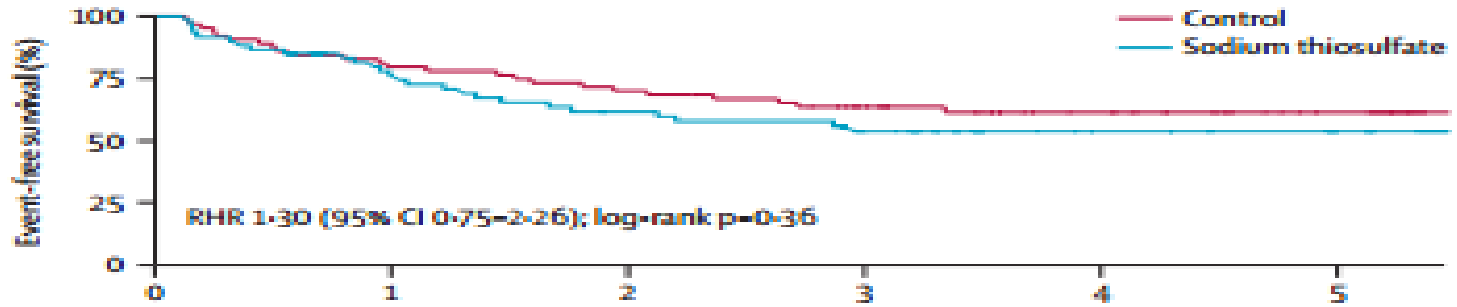
# Hearing Loss By Randomized Arm



# Hearing Loss By Randomized Arm and Age

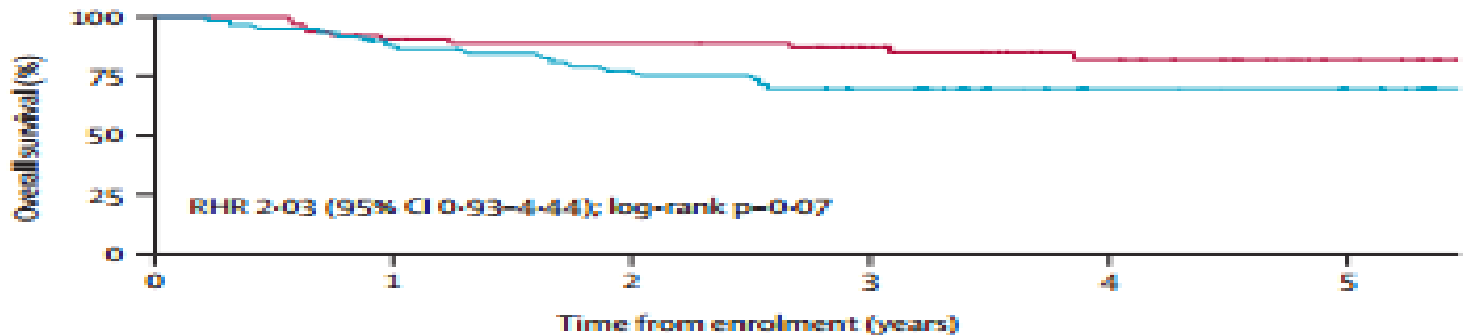


# EFS/OS for All Participants



Number at risk  
(number censored)

	0	1	2	3	4	5
Control	64 (0)	50 (1)	44 (0)	34 (6)	19 (14)	4 (15)
Sodium thiosulfate	61 (0)	43 (3)	32 (3)	25 (3)	10 (15)	6 (4)

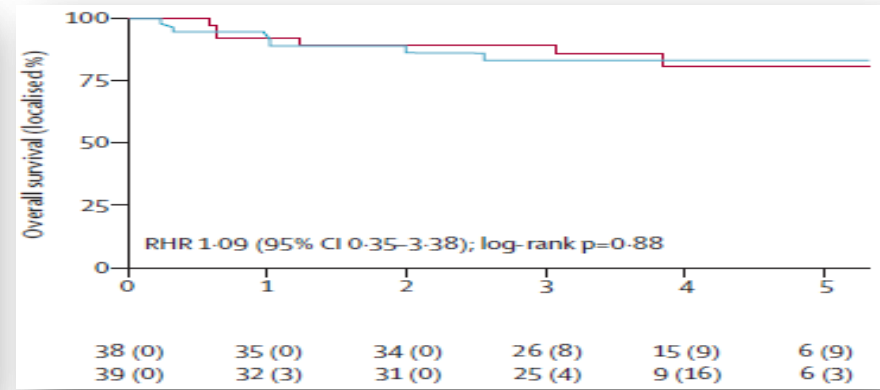
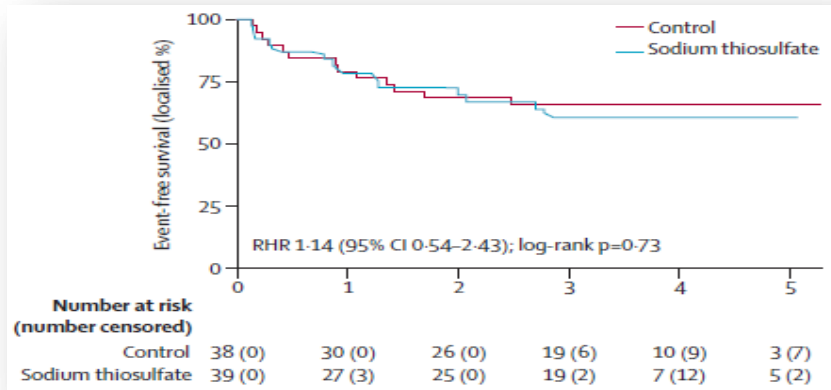


Number at risk  
(number censored)

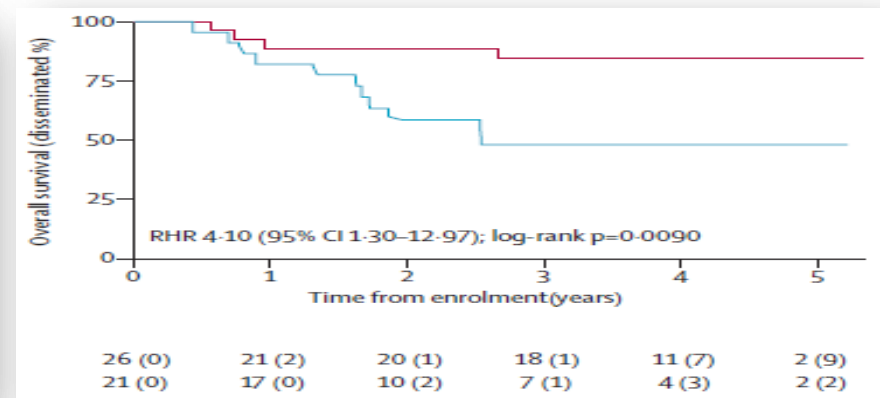
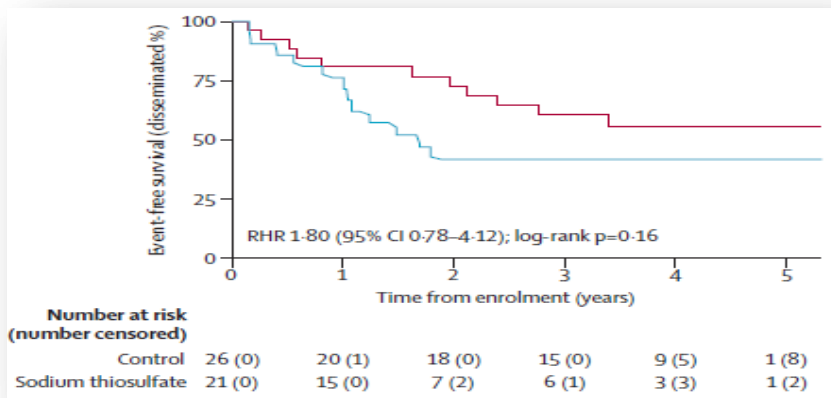
	0	1	2	3	4	5
Control	64 (0)	56 (2)	54 (1)	44 (9)	26 (16)	8 (18)
Sodium thiosulfate	61 (0)	50 (3)	41 (3)	32 (5)	13 (19)	8 (5)

# EFS/OS by Extent of Disease\*

## Localized Disease (n=77)



## Disseminated Disease (n=47)



\*Determined post hoc (ie, retrospectively during the preliminary data analysis after completion of accrual)



# Pivotal Study: SIOPEL 6

## 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

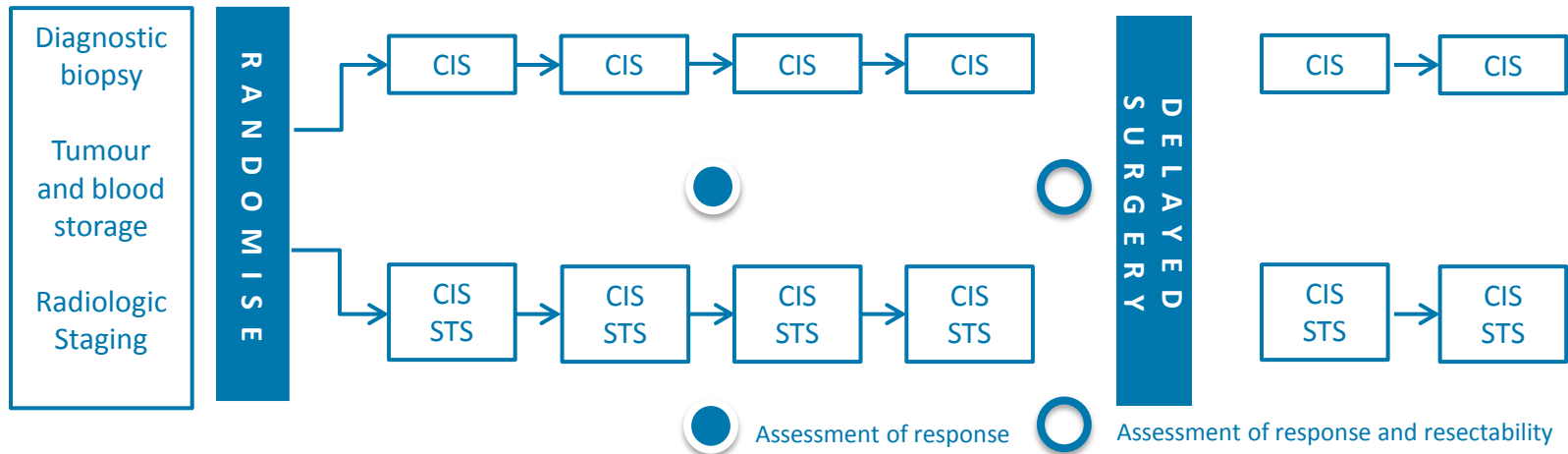
### Primary endpoint

- 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

## Study Methods and Design



- cisplatin alone : IV infusion over 6 hrs (80 mg/m<sup>2</sup> for children > 10kg, 2.7 mg/kg for infants and children 5-10kg or 1.8 mg/kg for infants < 5kg),

OR

- cisplatin (same dose) and STS administered IV exactly 6 hours after stop of cisplatin over 15 minutes at 20 g/m<sup>2</sup> for children > 10kg, 15 g/m<sup>2</sup> for infants and children of 5-10 kg or 10 g/m<sup>2</sup> for infants < 5kg
- Stratification by Country, age (above and below 15 months), PRETEXT (I and II vs III)
- Serum sodium monitored 1 hr, 6 hrs and 18 hrs post STS
- Tumour response assessed preoperatively, after 2 and 4 cycles, with serum AFP and liver imaging
- In case of progressive disease: stop STS and add doxorubicin

# SIOPEL 6

## 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 (October 2016)	Complete Remission	48 (92.3%)	50 (94.3%)
	Partial Remission	0	1 (1.9%)
	Recurrent Disease	0	0
	Death	4 (7.6%)	2 (3.8%)

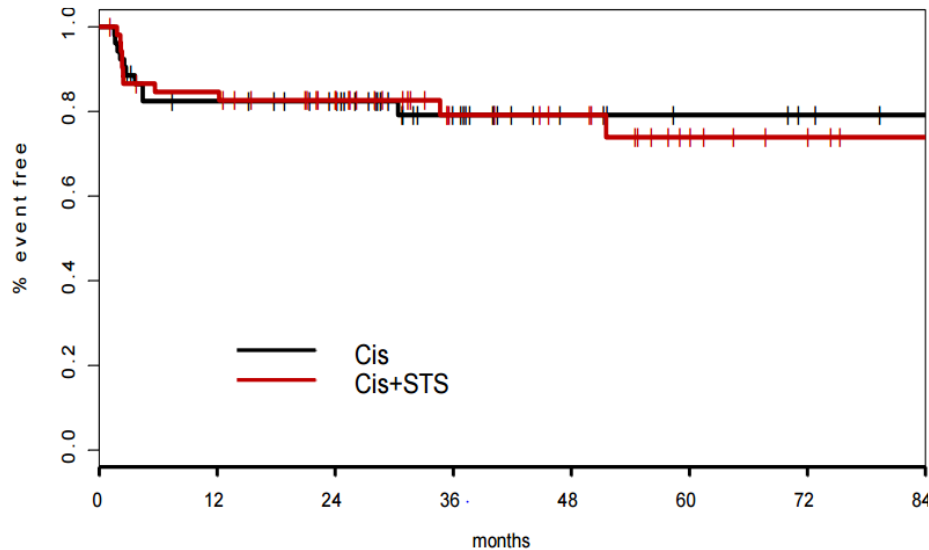
**18 patients received between 1 and 6 courses of doxorubicin (CIS:9; CIS+STS:9)**

# SIOPEL 6

## EFS/OS by Randomized Arm

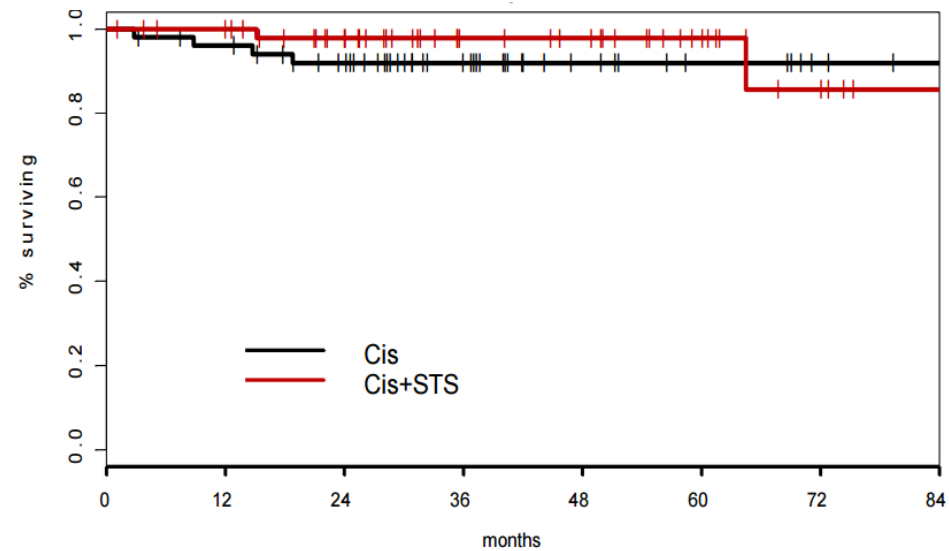
Median Follow-Up 36 Months

EFS



2yr-EFS Cis 82.4%, CIS+STS 82.6%

OS



2yr-OS Cis 91.9%, Cis+STS 97.9%

# CONCLUSION

- STS prevents cisplatin related hearing loss in the heterogeneous COG ACCL0431 population (Freyer 2016)
- Its effect is even more pronounced in the predefined subgroup of children < 5 years (Freyer 2016)

## SR-HB

- **Homogenous Disease, Excellent Prognosis**
- **Very Young Children** / hearing loss is frequent, irreversible with devastating life long impact on quality of life
- **Specific tumour marker able to detect early recurrence**
- **SIOPEL 6:**
  - Pending results on hearing loss (primary endpoint)
  - STS safe to treat SR-HB with six cycles of cisplatin monotherapy with the delayed addition of STS (ASCO/SIOP 2016)

# 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/Oct 2016
FDA & EMA Regulatory Development Meetings	2017
SIOPEL 6 Final Efficacy and Safety Results	Q4 2017
NDA/MAA Submissions	TBD

# Capital Structure and Share Information

Stock Listings	FRX – TSX, Canada FENCF – OTCQB, USA
Current Share Price	USD \$3.50
Shares Outstanding (millions)	13.6
Market Cap. (millions)	USD \$47.6
Warrants (millions)	1.3 with USD \$1.50 exercise price (Nov. 22, 2018)
Insider Ownership	Approx. 10% fully diluted
Cash@ March 31, 2017	USD \$3.2 million with no debt
2016 Cash Burn	USD \$2.0 million
Institutional Ownership	Southpoint Capital – 36%; Essetifin (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 Lediant Bio (Sigma Tau Rare Disease). Successfully out licensed defibrotide US rights to Jazz Pharmaceuticals and sold Oncaspar 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

## **Ryan Aldridge** – Investor Relations