

## **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 pediatric patients
  - 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 2 Phase 3 trials
  - COG Study ACCL0431 achieved primary efficacy endpoint of greater than 50% improvement in hearing 2014 ASCO
  - SIOPEL 6 presented no adverse outcome related to STS on end of treatment antitumor efficacy after final safety interim review – 2015 ASCO
- STS has the potential to fill a significant unmet medical need with no approved treatment on market or in development



## **Capital Structure and Share Information**

Stock Listings	FRX – TSX, Canada FENCF – USA
<b>Current Share Price</b>	USD\$2.30
<b>Shares Outstanding (millions)</b>	10.9
Market Cap. (millions)	USD\$25.3
Warrants (millions)	1.3 with USD \$1.50 exercise price (Nov. 22, 2018) 0.1 with USD \$1.50 exercise price (Mar. 29, 2016) 0.4 with USD \$3.60 exercise price (Dec. 3, 2016) 0.8 with CAD\$4.32 exercise price (Mar. 29, 2016)
Insider Ownership	Approx. 10% fully diluted
Cash@ March 31, 2015	USD\$2.5 million with no debt (includes \$0.5 million proceeds from exercise of warrants in April 2015)
2015 Cash Burn	USD\$1.8 million
Institutional Ownership	Southpoint Capital – 36%; Manchester Mgmt – 16%; 683 Capital – 8%

## **Board of Directors and Management**

### **Adrian Haigh** – Director

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

#### **Dr. Khalid Islam** – Director

 Chairman and CEO 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.

### Steve Skolsky – Director

Currently Global Head of Site
 Management at Quintiles. Previously
 President and CEO of Sequoia
 Pharmaceuticals and CEO of Trimeris.

Rosty Raykov – Chairman and CEO

Robert Andrade – Corp. Development

**Anne McKay –** Regulatory Affairs

Franck Rousseau, MD – Development Advisor

**Lei Fang –** Biostatistics

Krysia Lynes – CFO

**Lex Smith –** Pharmaceutical Development

**Roy Swaringen –** Chemical Development



# Platinum Hearing Loss is Frequent, Severe and Irreversible

# Globally, >7,000 children receive platinum based chemotherapy for localized cancers

USA: 2,000 EU: 3,000 RoW: 2,000

#### 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







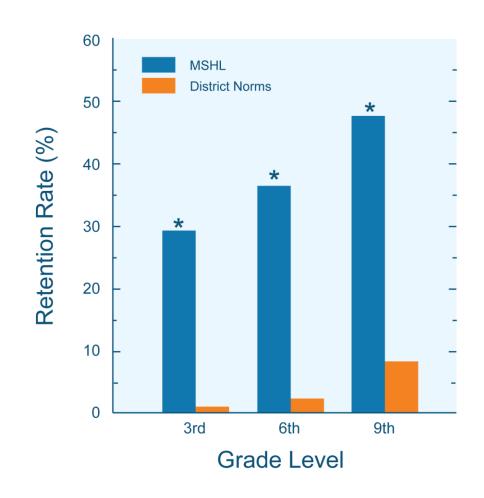
## **Devastating Impact on Quality of Life**

# **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





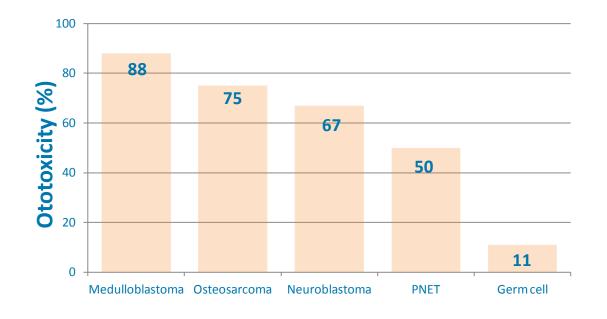
<sup>\*</sup>Bess et al., Ear and Hearing, 1998, 19:339-54 \*Gurney et al., Pediatrics, 2007 120(5):229-36

# 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





## **STS Market Opportunity**

### **Pediatric Market Opportunity**

- Approximately 2,000 children receive platinum-based chemotherapy for localized disease in the US each year
- Approximately 5,000 children receive platinum-based chemotherapy for localized disease in RoW each year

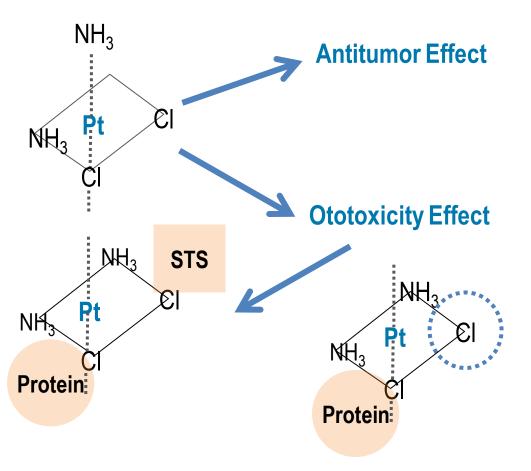
### **Competitive Position**

- · No alternative treatments available or in development
- Hearing aids and cochlear implants do not prevent hearing loss and cost \$2000 \$6000 each (replaced every 5 years)
- Cochlear implants cost up to \$75,000 each

### Market research confirms high unmet medical need



## Target and Proposed STS Mechanism



- Requires both Cl unbound to crosslink DNA
- Binding to plasma proteins occurs within first hour which inactivates one binding site
- Free cDDP (unbound) short t1/2
  :1.5 hr
- Requires one Cl unbound to affect cochlear hair cells
- Binding to plasma proteins occurs within first hour which inactivates one binding site
- STS will bind second site preventing ototoxicity



# COG ACCL0431: Randomized Phase 3 Study of STS for Prevention of Cisplatin-induced Hearing Loss

- Newly diagnosed children with hepatoblastoma, germ cell tumor, osteosarcoma, neuroblastoma, medulloblastoma, and others
- Local and metastatic disease
- Study Chair: David Freyer, DO, MS
- 131 randomized patients fully enrolled
- 126 eligible patients
- Study completed in 1Q 2012 with data presented at ASCO 2014



## COG ACCL0431: Specific Aims

## **Primary Endpoint**

- 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) criteria1:
  - > 20 dB loss at 1 frequency or > 10 dB at 2 consecutive frequencies

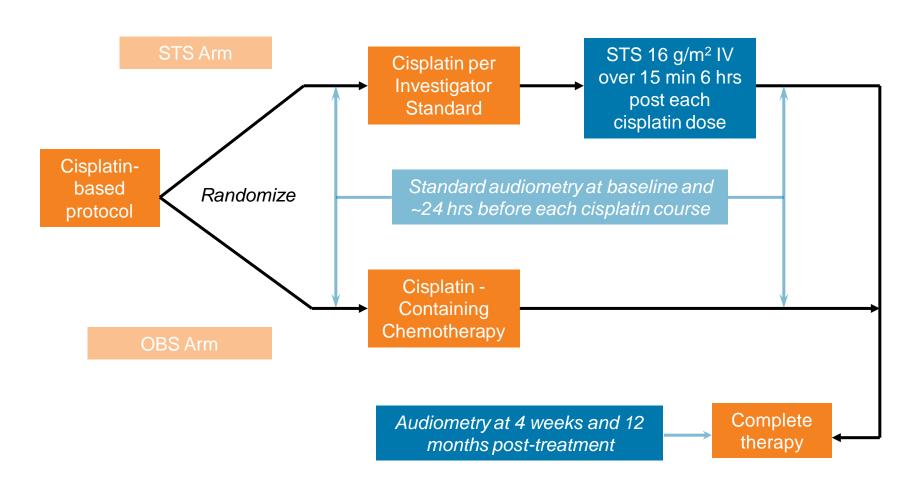
## **Secondary Endpoints**

- 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: Study Design







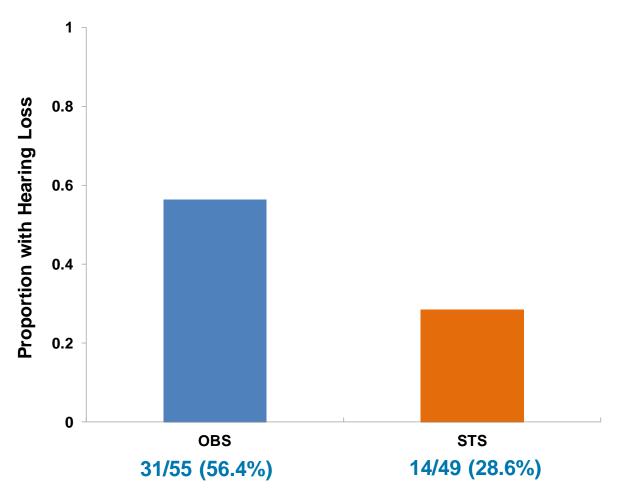
## **Patient Characteristics**

Characteristic	Observation (%)	STS (%)	
Eligible	64	62	
Germ Cell Tumor	16 (25.0)	16 (25.8)	
Osteosarcoma	15 (23.4)	15 (24.2)	
Medulloblastoma	14 (21.9)	12 (19.4)	
Neuroblastoma	12 (18.8)	14 (22.6)	
Hepatoblastoma	5 (7.8)	2 (3.2)	
Other	2 (3.1)	3 (4.8)	
Extent of Disease			
Localized	38 (59.4)	40 (64.5)	
Disseminated	26 (40.6)	21 (33.9)	
Unknown	0	1 (1.6)	
Cum. CDDP dose (mg/m²)	389 (198-1441)	393 (91-605)	
Prior Cranial Irradiation	5	4	





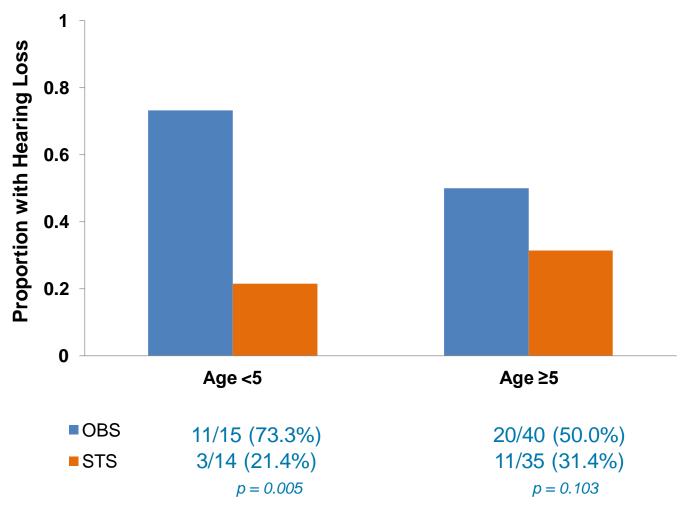
# **Hearing Loss By Randomized Arm**



n=104 evaluable patients / p = 0.004

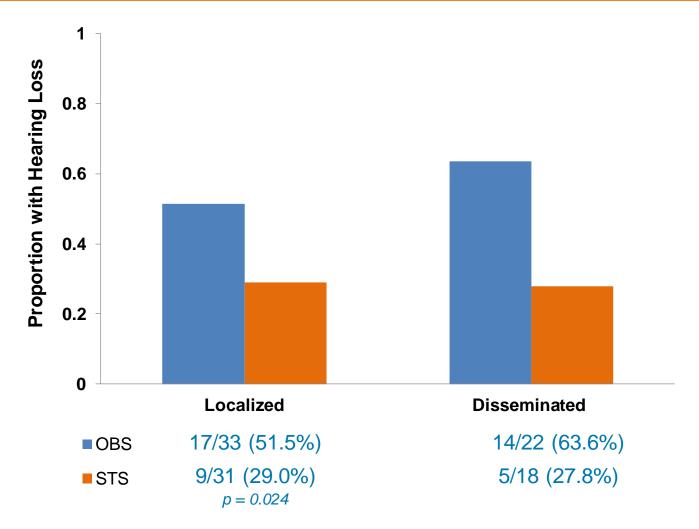


# Hearing Loss By Randomized Arm and Age



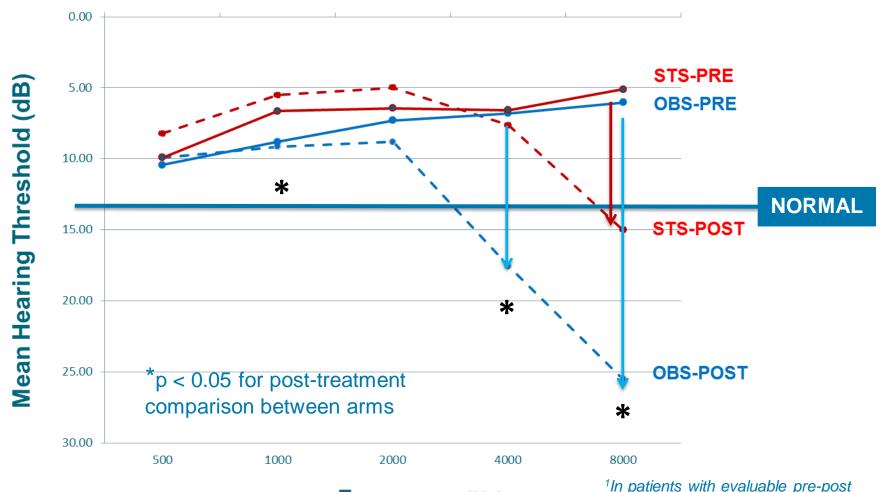


# Hearing Loss By Randomized Arm and Disease





# Change in Mean Hearing Thresholds by Randomized Arm<sup>1</sup>



Frequency (Hz)

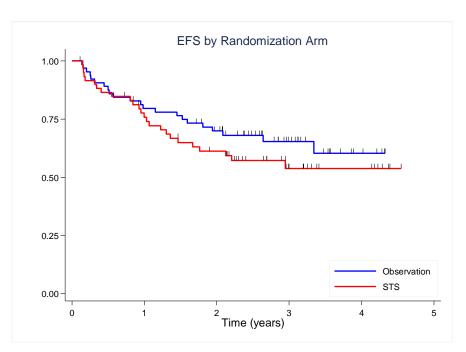
<sup>1</sup>In patients with evaluable pre-post frequency-specific audiometry, n=84-94



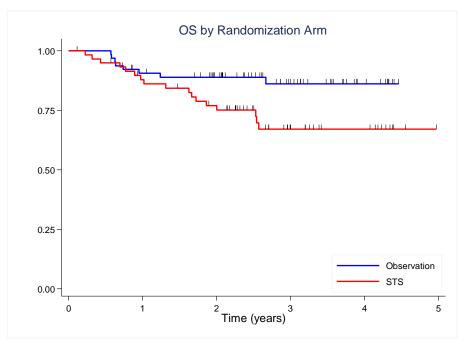


## **EFS/OS** by Randomization Arm

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



Log Rank p = 0.31



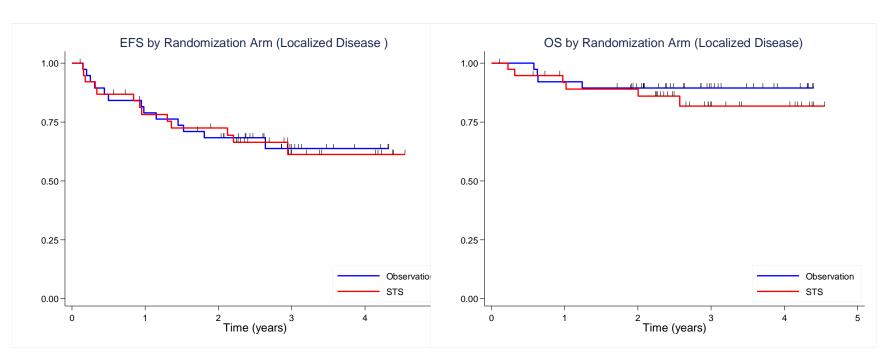
Log Rank p = 0.03





## **EFS/OS** by Randomization Arm

#### Localized Disease Only, n=78



Log Rank p = 0.94

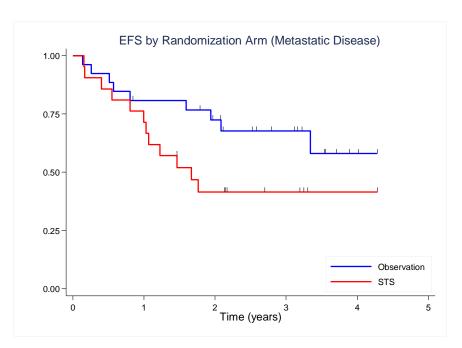
Log Rank p = 0.48

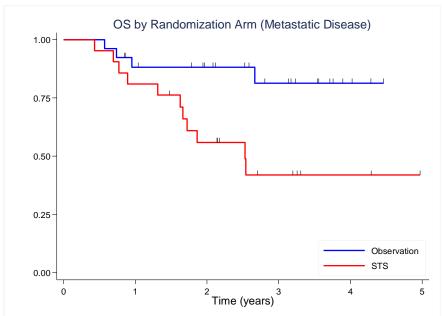




## **EFS/OS** by Randomization Arm

### Disseminated Disease Only, n=47





Log Rank p = 0.085

Log Rank p = 0.011





## **COG ACCL0431: Conclusions**

- STS protects against cisplatin-induced hearing loss in children
- STS appears to be safe in patients with localized disease
- Lower overall survival among children with disseminated cancer at onset of treatment, tumor protection or artifact?\*

<sup>\*</sup> The protocol did not specify a subset analysis of *localized* vs. *metastatic* disease and therefore the post-hoc results are limited to *hypothesis generation*.



# SIOPEL 6: Rand. Phase 3 Study - Efficacy of STS in Reducing Ototoxicity in Hepatoblastoma Patients

- Newly diagnosed children with standard risk hepatoblastoma
- Single localized disease with very high historic survival rates
- Cisplatin monotherapy treatment
- Study Chair: Peppy Brock, MD, PhD, FRCPCH, International Chair of SIOPEL 6
- 116 randomized patients recruitment completed December 2014
- 113 Enrolled / 108 Evaluable
- IDMC safety reviews of 20, 40, 60, 80 and 100 patients each time recommended study continue
- Last interim safety analysis of 100 patients accepted for poster at ASCO '15



# **SIOPEL 6: Objectives and Primary Endpoint**

### **Objectives:**

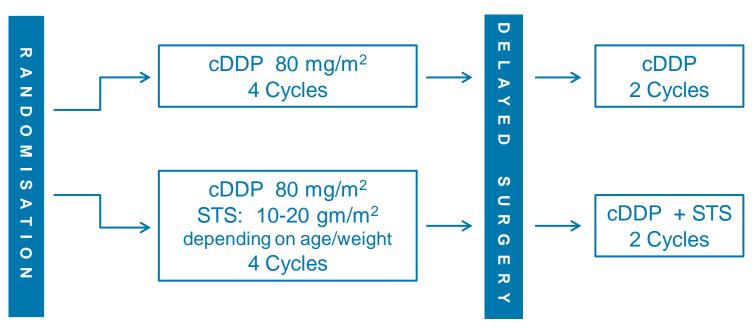
- To assess the efficacy of STS to reduce the hearing impairment caused by Cisplatin (CDDP)
- To carefully monitor any potential impact of STS on response to CDDP and survival

### **Primary endpoint:**

 Centrally reviewed absolute hearing threshold, at the age of ≥3.5 yrs, by pure tone audiometry, graded by Brock criteria



# SIOPEL 6 – Study Design



80% power to detect 60% vs 35% hearing loss

Interim efficacy results on response to chemotherapy evaluated after every 20 patients and reviewed by Independent Data Monitoring Committee

Two interim and one final efficacy analyses planned for early stopping in case of a greater than expected difference between treatment arms in terms of hearing loss



# SIOPEL 6: Interim Safety Results ASCO 2015 ABSTRACT

• Tumour response after 4 pre-operative chemo cycles for first 94 patients

	Cisplatin (n=47)	Cisplatin + STS (n=47)
Partial response	86%	90%
Stable disease	8%	5%
Progressive disease	6%	5%

# SIOPEL 6: Interim Safety Results ASCO 2015 ABSTRACT

The following results are as of January 2015:

	Cisplatin (n=47)	Cisplatin + STS (n=47)
Complete Remission*	92%	98%
Progression	2 pts	1 pt
Deaths	2 pts	0 pt

<sup>\*</sup>Complete remission after resection and post-op chemo.

# SIOPEL 6: Interim Safety Results ASCO ABSTRACT – May 2015

 Preliminary results of end of treatment anti-tumour efficacy evaluated in 94 patients with a median age of 12.8 months do not show any adverse outcome in cisplatin+STS treatment compared with cisplatin alone

### Results on primary hearing endpoint:

- Analysis of the primary endpoint of hearing loss at ≥3.5 yrs of age will be available in 2017
- Two interim analyses are planned per protocol, after 34 and 68 patients have their definitive audiometry results
- If the nominal alpha levels for the test of the primary endpoint will be <0.00069 (34 pts), <0.016 (68 pts), early stopping of the trial will be considered



# **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 Phase 3 Safety and End of Treatment Anti Tumor Efficacy Results ✓	May 2015
SIOPEL 6 Phase 3 Primary Endpoint Interim Efficacy Results (N=68)	H1 2016
FDA & EMA Regulatory Development Meetings	H1 2016
NDA/MAA Submissions	TBD

## **STS Investment Highlights**

- US Orphan Drug Designation (7.5 years market exclusivity)
- Potential for European Market Exclusivity for Pediatric Use (10 years)
- Completed enrollment of 2 Phase 3 trials
- COG Phase 3 trial achieved primary endpoint for hearing
- SIOPEL 6 Phase 3 trial reported no adverse outcomes of STS plus Cisplatin vs. Cisplatin alone
- 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 initiate discussions with US & European regulators once hearing data is available from SIOPEL 6

