FENNEC PHARMA

August 2021 | Corporate Presentation

www.fennecpharma.com

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 U.S. Food and Drug Administration (FDA), the status and timing of ongoing research, corporate partnering activities and other factors affecting the financial condition or operations of Fennec Pharmaceuticals, Inc. (Fennec).

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, including the risk that unforeseen factors may result in delays in or failure to obtain FDA approval of PEDMARK™, the risks and uncertainties relating to the Company's reliance on third party manufacturing, the risks that the Company's NDA resubmission does not adequately address the concerns identified in the CRL previously provided by the FDA, the risk that the NDA resubmission to the FDA will not be satisfactory, that regulatory and guideline developments may change, scientific data and/or manufacturing capabilities may not be sufficient to meet regulatory standards or receipt of required regulatory clearances or approvals, clinical results may not be replicated in actual patient settings, unforeseen global instability, including political instability, or instability from an outbreak of pandemic or contagious disease, such as the novel coronavirus (COVID-19), or surrounding the duration and severity of an outbreak, protection offered by the Company's patents and patent applications may be challenged, invalidated or circumvented by its competitors, the available market for the Company's products will not be as large as expected, the Company's products will not be able to penetrate one or more targeted markets, revenues will not be sufficient to fund further development and clinical studies

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.

Fennec Pharmaceuticals, Inc. | A Snapshot

Focused on the development of PEDMARK™ for the prevention of cisplatin-induced ototoxicity in children (1 month to ≤ 18 years) with localized, non-metastatic solid tumors*

- **TWO successfully completed and published, randomized controlled studies** in pediatric patients
- **FAST TRACK and BREAKTHROUGH Therapy Designations** granted by FDA
- **MAA to EMA submission** completed in February 2020
- **FDA assigned PDUFA target action date of November 27, 2021.** FDA had previously issued CRL August 2020 - no clinical or safety issues identified.
- **Potential for 7.5 YEARS U.S. market exclusivity** with Pediatric Orphan Drug Designation
- **Potential for 10 YEARS E.U. market exclusivity** with Pediatric-use Marketing Authorization (PUMA), if granted
- **Patent Protection in U.S. until 2038** method of use for children <5 years of age
- **Patent Protection in U.S. until 2039** for the unique anhydrous form of the active ingredient, as well as related methods of synthesis

**PEDMARK is an investigational drug and has not yet been approved by the U.S. Food and Drug Administration (FDA) or any regulatory authority*
NDA – New Drug Application
MAA – Marketing Authorization Application
PDUFA – Prescription Drug User Fee Act

FENNEC | Management Team

A dedicated management team with more than a decade of commitment to the development of PEDMARK and nearly two decades of demonstrated experience and commercialization success within the oncology space

Rosty Raykov
CEO & Director

Robert Andrade
Chief Financial Officer

Shubh Goel
Chief Commercial Officer

Mark Gowland
Controller

Amy Winnen
VP, Market Access & Commercial Supply

FENNEC | Board of Directors

Dr. Khalid Islam | Chairman

Dr. Islam has over 30 years of experience in drug discovery and development of anti-infectives, hematology/oncology and CNS therapies. Dr. Islam currently serves as the Managing Director of Life Sciences Management GmbH, since 2014. Previously, Dr. Islam served as Chairman and CEO of Gentium S.p.A., a Nasdaq-listed pharmaceutical company, from 2009 until 2014 (sold to Jazz Pharmaceuticals plc for $1 billion). He has also served as President and CEO of Arpida AG and held various positions at Sanofi-Aventis. Dr. Islam also currently serves as the Chairman of the Board of Directors for Minoryx Therapeutics and Gain Therapeutics and as a Member of the Board of Directors for Immunomedics, Inc. (IMMU).

Dr. Marco Brughera | Director

Dr. Brughera is Group Chief Executive Officer at Leadiant Biosciences S.p.A. Dr. Brughera has extensive experience in drug development, portfolio optimization, business development and general management, particularly in the oncology and rare disease areas. Dr. Brughera successfully out-licensed Defibrotide to Jazz Pharma and Oncaspar to Baxalta, Incorporated for over $1 billion. He is also an active board member for some life-science companies.

Jodi A. Cook, PhD | Director

Dr. Cook is the former head of gene therapy strategy at PTC Therapeutics, Inc. Previously, she was a founding member and Chief Operating Officer of Agilis Biotherapeutics, Inc., a gene therapy company focused on rare disease from 2013 until its acquisition by PTC Therapeutics, Inc. in 2018. She as held executive positions in a number of successful hearing industry biotech companies including Vice President of clinical research and professional relations at InSound Medical, Inc.

Adrian Haigh | Director

Mr. Haigh currently holds the position of SVP and General Manager Europe, ME and AP for PTC Therapeutics, Inc. and has had previous positions as Senior Vice President, Commercial Operations and Chief Operating Officer of Gentium GmbH, playing a pivotal role in the sale of Gentium to Jazz Pharma for $1 billion. Prior to joining Gentium, Mr. Haigh served as Regional Vice President, Commercial Operations at Biogen Idec.

Chris Rallis | Director

Mr. Rallis has served as a director of Fennec since August 2011. Mr. Rallis has been an executive-in-residence at Pappas Capital, 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 (“COO”) and director of Triangle Pharmaceuticals, Inc., which was acquired by Gilead Sciences, Inc. 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 Tenax Therapeutics, Inc., a biopharmaceutical company located in Morrisville, North Carolina. Mr. Rallis received his A.B. degree in economics from Harvard College and a J.D. from Duke University.

FENNEC | Capital Structure and Share Information

Stock Listings Current	FENC – Nasdaq | FRX – TSX, Canada
Shares Outstanding	26.0 Million
Cash and Cash Equivalents[1]	USD $27.2 Million
2020 Cash Burn[2]	USD $15.5 Million
Debt	$5 Million

INSTITUTIONAL OWNERSHIP[3]

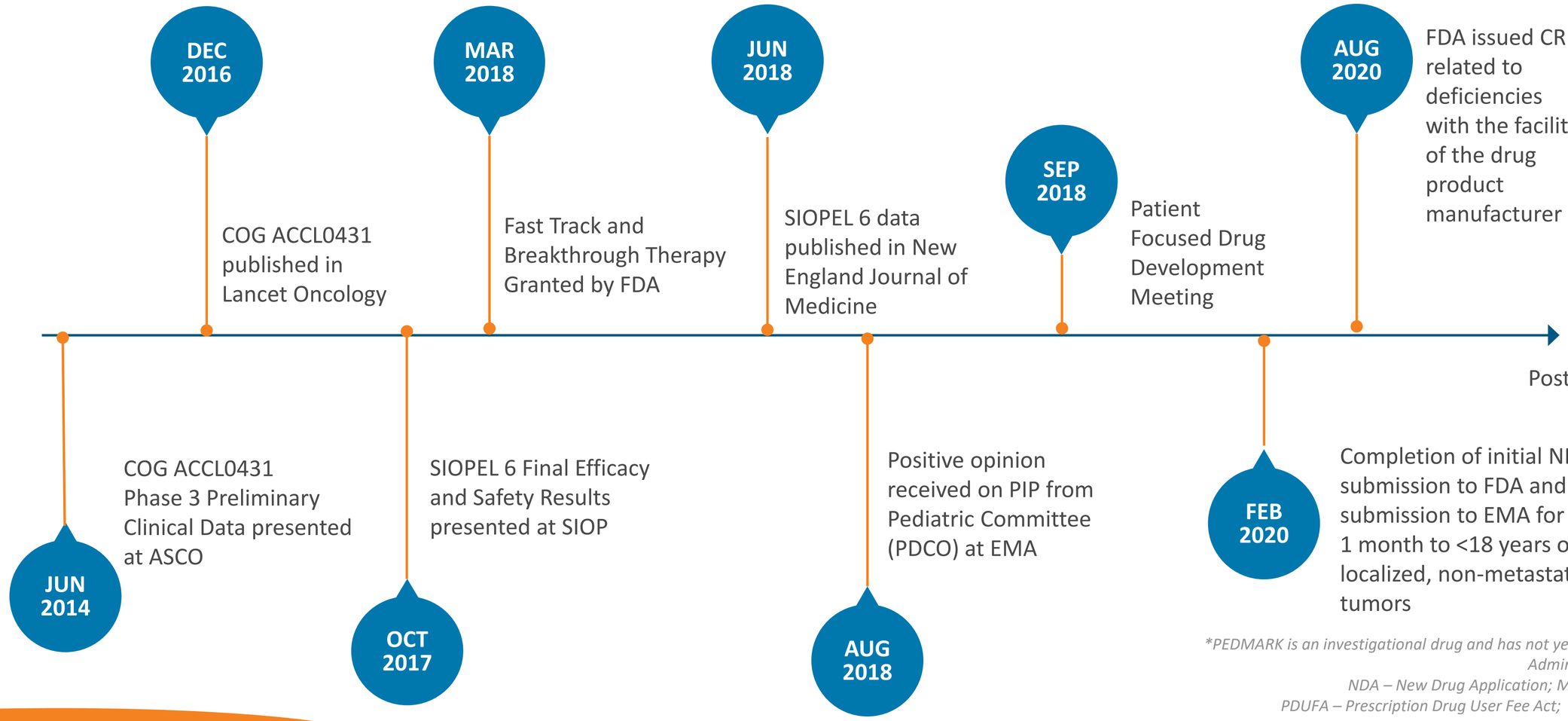
Southpoint Capital	16%
Essetifin	16%
Sonic Fund	9%
Avoro Capital Advisors	6%
683 Capital	4%
Eventide Funds	4%

[1]As of June 30, 2021

[2]Cash and Cash Equivalents as of December 31, 2019 less Cash and Cash Equivalents as of December 31, 2020

[3]As of most recent Schedule 13G or Schedule 13F filing by respective fund

PEDMARK™ | Development Timeline



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NDA – New Drug Application; MAA – Marketing Authorization Application;

PDUFA – Prescription Drug User Fee Act; ASCO - American Society Clinical Oncology;

SIOP - Society of Pediatric Oncology

Pediatric Oncology Incidence is Consistent in U.S. and EU

Annual incidence of pediatric solid tumor cases eligible for Platinum-based therapy in both U.S. and EU markets*

~30% 1,462 Metastatic
~70% 3,554 Localized, non-metastatic

~30% 1,710 Metastatic
~70% 4,215 Localized, non-metastatic

**Sources: https://accis.iarc.fr/index.php Accessed May 2021;*
Ward et al. CA Cancer J Clin. 2014;64:83-103.
Localized vs metastatic breakdown based on Qualitative Market Research Study Completed Feb, 2018

Cisplatin is the Standard of Care for Pediatric Solid Tumors

Cisplatin | Penicillin of Chemotherapy

- Interferes with DNA replication killing fast proliferating cells
- Administered as intravenous infusion in normal saline
  - For treatment of solid and hematological malignancies
  - Relatively short half-life
- First licensed in 1979
  - Introduced in pediatric patients in 1980s
  - It is on the WHO's List of Essential Medicines
  - High cure rates achieved in pediatric patients, in contrast to adults

Common Childhood Cancers Treated with Cisplatin

- Brain and CNS cancers
- Neuroblastoma
- Hepatoblastoma
- Osteosarcoma
- Germ cell tumors
- Retinoblastoma

Treatment plan depends on the individual cancer diagnosis, stage of disease and patient age

Platinum cancer drugs. Available at cisplatin.org Accessed October 24, 2019
Robertson J, et al. Bull World Health Organ. 2016 Oct 1; 94(10): 735–742.
Ward et al. CA Cancer J Clin. 2014;64:83-103.

One of the unfortunate complications with cisplatin therapy is **ototoxicity**

Cisplatin Results in High-Frequency Hearing Loss in Children

Common Clinical Presentation of Hearing Loss

- High frequency (≥4 kHz) sensorineural hearing loss[1,2]
  - Bilateral (both ears)
  - Progressive
  - Irreversible
  - Can progress to include lower frequencies (<4 kHz)[3]
- Can be accompanied by tinnitus[3]
- Prolonged retention of platinum may cause hearing loss progression after completion of therapy[4]
- Hearing aids may be necessary in up to 40%; and cochlear implants in an additional percentage of children affected[3]

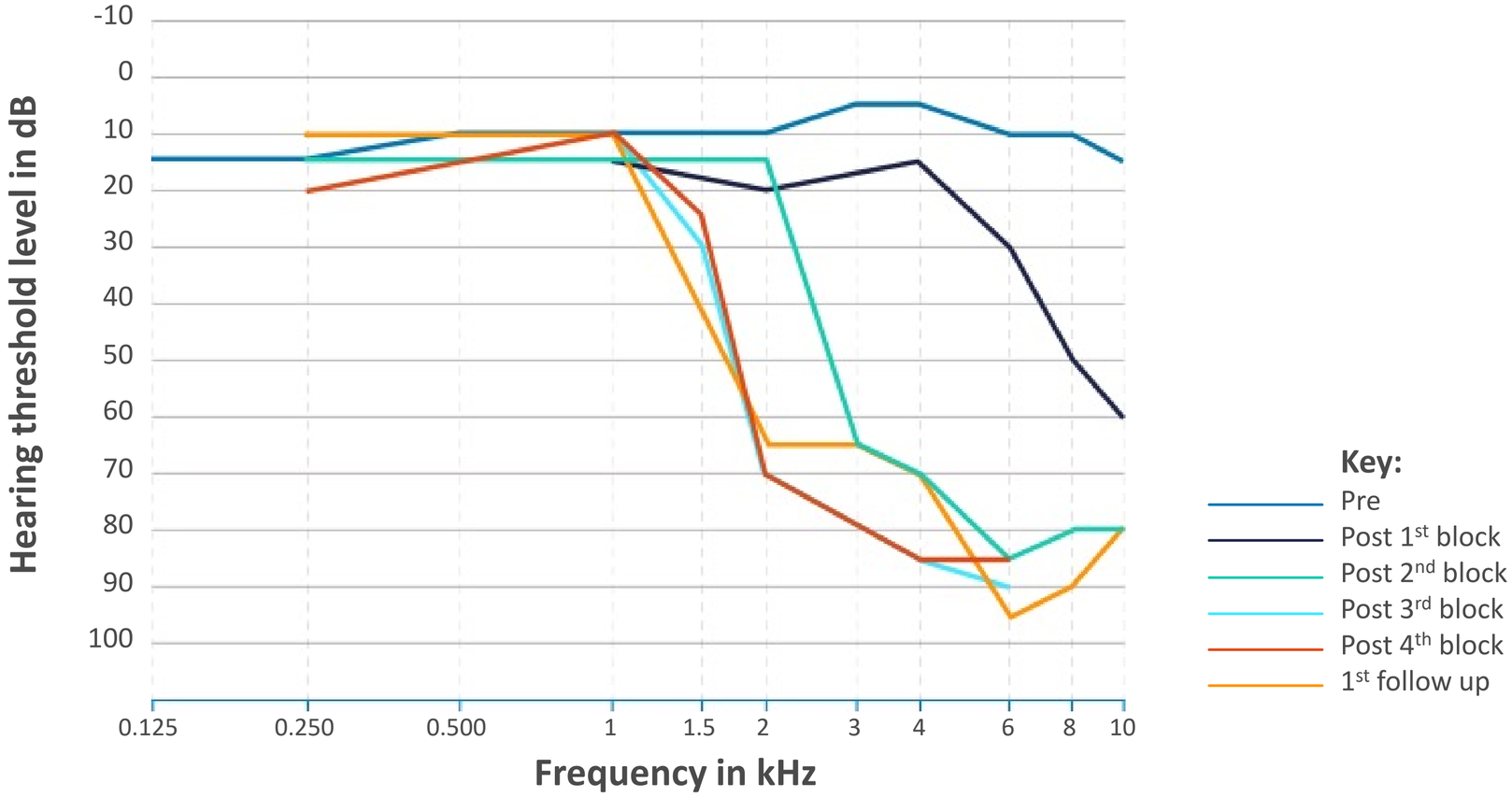
Risk Factors for Ototoxicity[1,2]

- Younger age (<5 years of age)
- Cranial irradiation
- Total dose and duration of platinum agent
- Exposure to other ototoxic medications
- Pre-existing renal insufficiency
- Pre-exposure to therapies that impair hearing ability
- Genetic factors

Hearing loss that is serious enough for hearing aid use has been independently associated with declines in cognition and educational performance[5]

1. Waissbluth S et al. Int J Pediatr Otorhinolaryngol. 2018;111:174-179. 2. Paken J et al. J Toxicol. 2016;2016:1809394.
3. Langer T et al. Trends in Pharmacological Sciences. 2013;34:458-469.
4. Sprauten M. J. Clin Oncol. 2012;30:300-307. 5. Schreiber et al., Neuro Oncol, 2014;16(8):1129-36.

Ototoxicity Can Occur Early in Treatment - As Early As Cycles 1-2[1]



Audiogram indicates how loud a sound must be to hear it at a given frequency

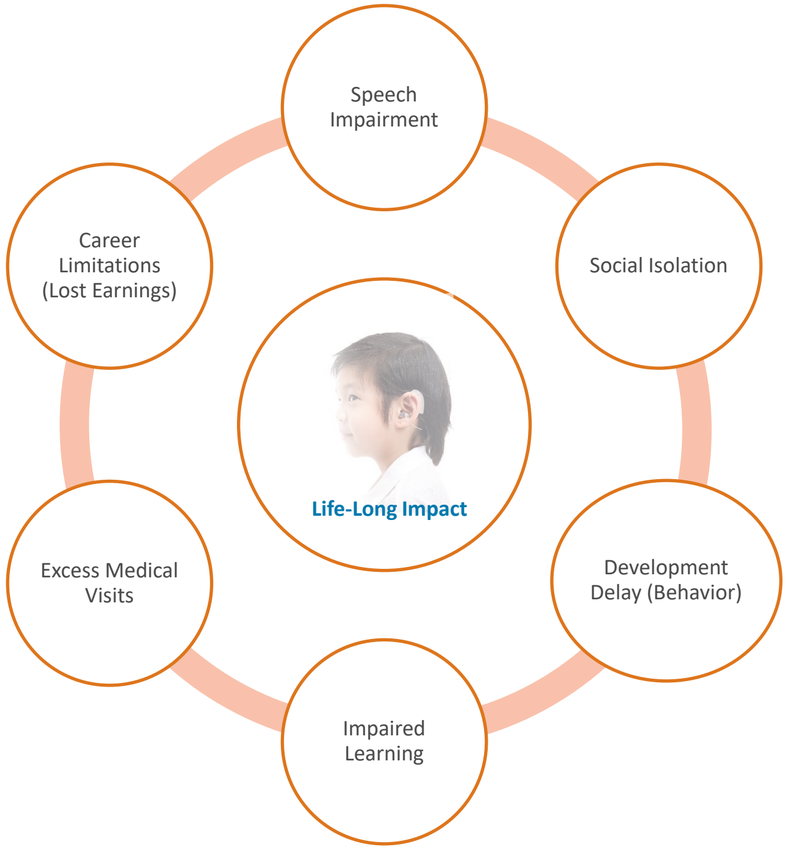
- Ototoxicity is a cisplatin dose-limiting toxicity[1] meaning that efficacy of chemotherapy could be compromised due to ototoxicity management
- Effects can be seen as soon as the second or third dose of cisplatin
- Survivors are at risk of hearing deterioration years after completion of therapy[2]

1. Langer T et al. *Trends in Pharmacological Sciences*. 2013;34:458-469
2. Bertolini P et al, J Pediatric Hem Onc 2004;26:649-655.

Clinical Manifestations

Effects on growth and development

- Certain consonants (f/th/p/k/h/t) are inaudible, compromising speech recognition and comprehension in young children[1]
- High frequency hearing loss affects recognition of plurals such as /s/ in ‘ducks’ and /z/ in ‘girls’, resulting in delayed language development[3]
- Speech perception in background noise is hindered, resulting in poorer school performance (e.g. literacy)[1,4,5]
- Impaired perception of music and ambient noises, resulting in a poorer quality of life[1]
- Delayed neurocognitive and psychosocial development[1]



Hearing loss is associated with a lower IQ, phonetic decoding and reading comprehension[6]

1. Langer T et al. Trends in Pharmacological Sciences. 2013;34:458-469. 2.Bertolini P et al, J Pediatric Hem Onc 2004;26:649-655.
3. Brock PR et al. J Clin Oncol 2010;30:2408-2417. 4. Gurney JG et al. Pediatrics. 2007;e1229-e1236. 5. Crandell CC. Ear & Hearing. 1993; 14:210-217
6. Hennegan, K, Silber A, Dehipawala S, Chithran K, Lockhart D. Poster PIH67. ISPOR Annual Meeting 2020

The Impact of Ototoxicity is Profound

- The overall 5-year survival rate for children with localized, non-metastatic disease is close to 80%, making the permanent and progressive impact of ototoxicity an important consideration[1], yet audiological follow up, today, is inconsistent
- Current interventions occur after hearing loss has occurred and do not restore normal hearing[4]

- **Nearly 1 in 5 children (18%)** considered at-risk for hearing loss **do not** have hearing tests during follow-up[2]

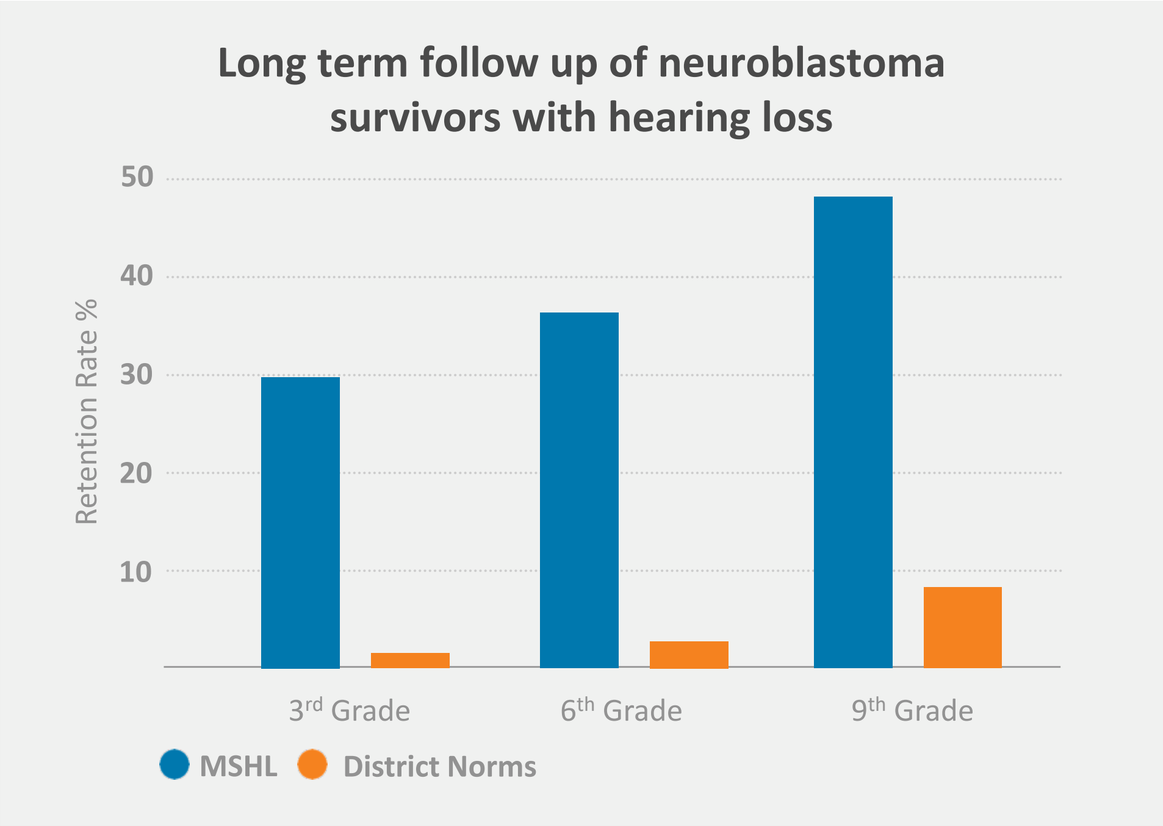
- **More than half (57%)** children **do not have** full audiological monitoring before, during, and after treatment[2]

- **More than half (55%)** of children with hearing loss **have not been** documented to require hearing aids[3]

60% [and up to 90%] of children develop irreversible ototoxicity resulting in a devastating and life-long impact[1]

1. *Freyer et al, www.thelancet.com/oncology Vol 18 January 2017*
2. *Clemens E, van den Heuvel-Eibrink MM, Mulder RL, et al.; Lancet Oncol. 2019;20(1):e29-e41.*
3. *Hennegan, K, Silber A, Dehipawala S, Chithran K,Lockhart D. Poster PIH67. ISPOR Annual Meeting 2020*
4. *Landier W.; Cancer. June 2016; Vol. 122,No.11: 1647-1658*
5. *Langer T, Zehnhoff-Dinnesen A; Trends in Pharmacological Sciences. August 2013, Vol. 34, No. 8: 458-469*

Ototoxicity Can Have a Devastating Impact



- High risk for being **held back a grade** (37% vs. 3%)[1]
- Twice the rate of parents reported **learning problems** with reading, math, attention and need for special education[2]
- **Poorer child-reported** school functioning

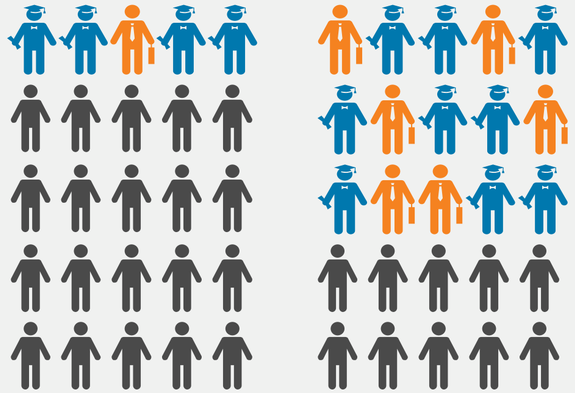
Even minimal hearing loss is damaging, resulting in compromised learning and language development[1]

1. Bess et al., Ear and Hearing, 1998, 19:339-54
2. Gurney et al., Pediatrics, 2007 120 (5):229-36
Minimum sensorineural hearing loss (MSHL)

Treatment-Induced Hearing Loss and Adult Social Outcomes in Survivors of Childhood Non-CNS Solid Tumors | Results From the St. Jude Lifetime Cohort Study[1]

Among 226 survivors of non-CNS tumors*:

- 39% had severe hearing loss; 20% of these patients had hearing aids or cochlear implants
- 39% were not living independently
- 45% had never married
- 34% had not graduated high school or were unemployed



Twice the amount of patients with serious hearing loss did not graduate from high school; were unemployed or were not living independently vs those without hearing loss

Survivors with serious hearing loss were twice as likely to report perceived negative impact on social functioning

* The most common cancer diagnoses included osteosarcoma (19.9%), germ cell tumor (15.0%), neuroblastoma (16.8%), rhabdomyosarcoma (13.7%), and nasopharyngeal carcinoma (9.3%).

1. Brinkman TM et al. *Cancer* 2015;121:4053-61.

Until Now, Intervention for Ototoxicity Was Not Preventative

Intervention occurs after hearing loss has been detected

Hearing Aids[1]

- Do not block out background noise
- Unable to separate speech and noise in loud environments
- Don’t allow distant sounds to be heard
- Generally replaced every 3-5 years[2]

Personal Frequency Modulation
(FM Classroom Amplification)

- Patients with hearing loss as a result of cisplatin therapy are more likely to need hearing loss amplification technology
  e.g. extended bandwidth hearing aids[1]
- There is no data suggesting improvement in speech recognition with this technology[3]

Cochlear Implants[1]

- A surgically implanted neuro-prosthetic device to provide a modified sense of sound for moderate to profound sensorineural hearing loss
- Could be unilateral or bilateral
- Lifelong commitment

Speech Rehabilitation[3]

- Speech reading and counseling on compensatory communication strategies are needed
- Counseling should include family members including parents and siblings

*1.*Landier W. *Cancer.* 2016;122:1647-1658.
2. https://www.starkey.com/blog/2014/02/5-common-questions-about-hearing-aids accessed Feb 18th 2020
3 Paken et al, Journal of Toxicology 2016, 1809394 | Image: https://pubs.asha.org/

PEDMARK™

Unique Formulation of Sodium Thiosulphate (STS)

Development*

- We believe PEDMARK* is the only agent that is specifically in development for the prevention of ototoxicity from cisplatin in pediatric patients
- PEDMARK is a small molecule, unique formulation of STS

Drug Delivery

PEDMARK STS is administrated 6 hours post completion of cisplatin infusion in a bolus dose i.v. over 15 minutes

Toxicology

STS is generally recognized as safe (GRAS) in U.S. with respect to active ingredient STS, but not established in current proposed use*

Intended 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[1]
- Cisplatin is readily cleared from most organs but is longer term retained in the cochlea[2]
- Cisplatin-induced ototoxicity is caused by irreversible damage to hair cells in the cochlea[3]
- Cochlea is very sensitive to oxidative stress, which has been shown to be involved in ototoxicity[4]
- STS inhibits oxidative stress[5]
- Administering STS 6 hours after completion of cisplatin infusion ensures that levels of unbound cisplatin are minimal[5]

**www.accessdata.fda.gov/scrips/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=184.1807*

1. PLATINOL. Cisplatin FDA.gov.pdf; Accessed February 17, 2020. 2. Breglio AM et al. Nature Communications. 2017;8:1654-1663 3. Landier W. Cancer. 2016;122:1647-1658. 4. Langer T et al. Trends in Pharmacological Sciences. 2013;34:458-469 5. Data on file, Fennec Pharmaceuticals 2020.

**PEDMARK is an investigational drug. Safety and efficacy data have not been established by any agency and it has not yet been approved by the U.S. Food and Drug Administration (FDA) or any regulatory authority*

PEDMARK™ | Development and Regulatory Status

Two Randomized Studies Complete:

Proof of Concept Study | COG ACCL0431

- 131 patients with heterogeneous solid tumors
- Achieved primary efficacy endpoint - ASCO 2014
- Final results : Lancet Oncology - December 2016

Pivotal Study | SIOPEL 6

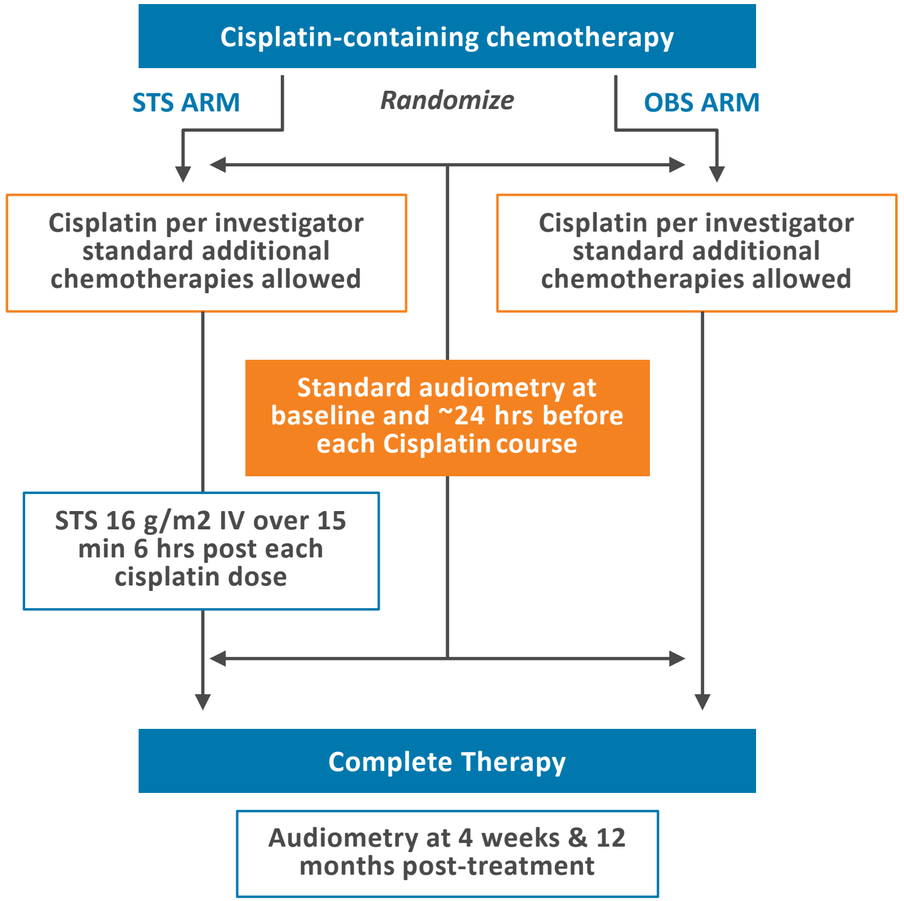
- 109 patients with standard risk hepatoblastoma (SR-HB)
- Achieved primary efficacy endpoint - SIOP 2017 Showed no evidence of tumor protection
- Final results : New England Journal of Medicine - June 2018

Regulatory Milestones Achieved:

- Granted Fast Track and Breakthrough Therapy Designation by FDA
- Positive opinion on PIP received by PDCO at EMA
- Completed NDA to FDA and MAA to EMA | PEDMARK (U.S.) is proposed to be indicated for the prevention of ototoxicity induced by cisplatin chemotherapy in patients 1 month to < 18 years of age with localized, non-metastatic, solid tumors
- EMA Validation Received for MAA
- Pre-Approval identified deficiencies with the facility of the drug product manufacturer resulting in CRL. No clinical or safety issues identified
- FDA acceptance received for NDA resubmission, with an assigned PDUFA target action date of November 27, 2021

PEDMARK has the potential to be the first and only therapy indicated in this area of significant high unmet medical need

Proof of Concept Study | COG ACCL0431



Primary Endpoint

- Evaluate efficacy of STS for prevention of hearing loss in children receiving cisplatin chemotherapy
- Measured by hearing status at 4 weeks post-therapy defined by American Speech-Language-Hearing Association (ASHA) criteria of >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 Event Free Survival (EFS) and Overall Survival (OS) *(no formal comparison)*

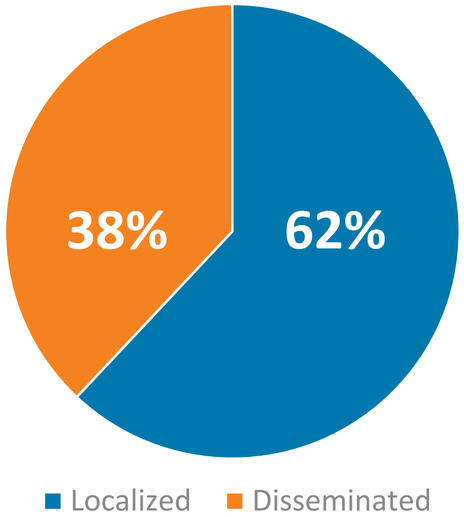
Stratification Factors for Randomization

Risk for hearing loss only: Age, duration of cisplatin infusion and receipt of cranial irradiation

Freyer et al, www.thelancet.com/oncology Vol 18 January 2017

COG ACCLO431 | Study Patient Characteristics

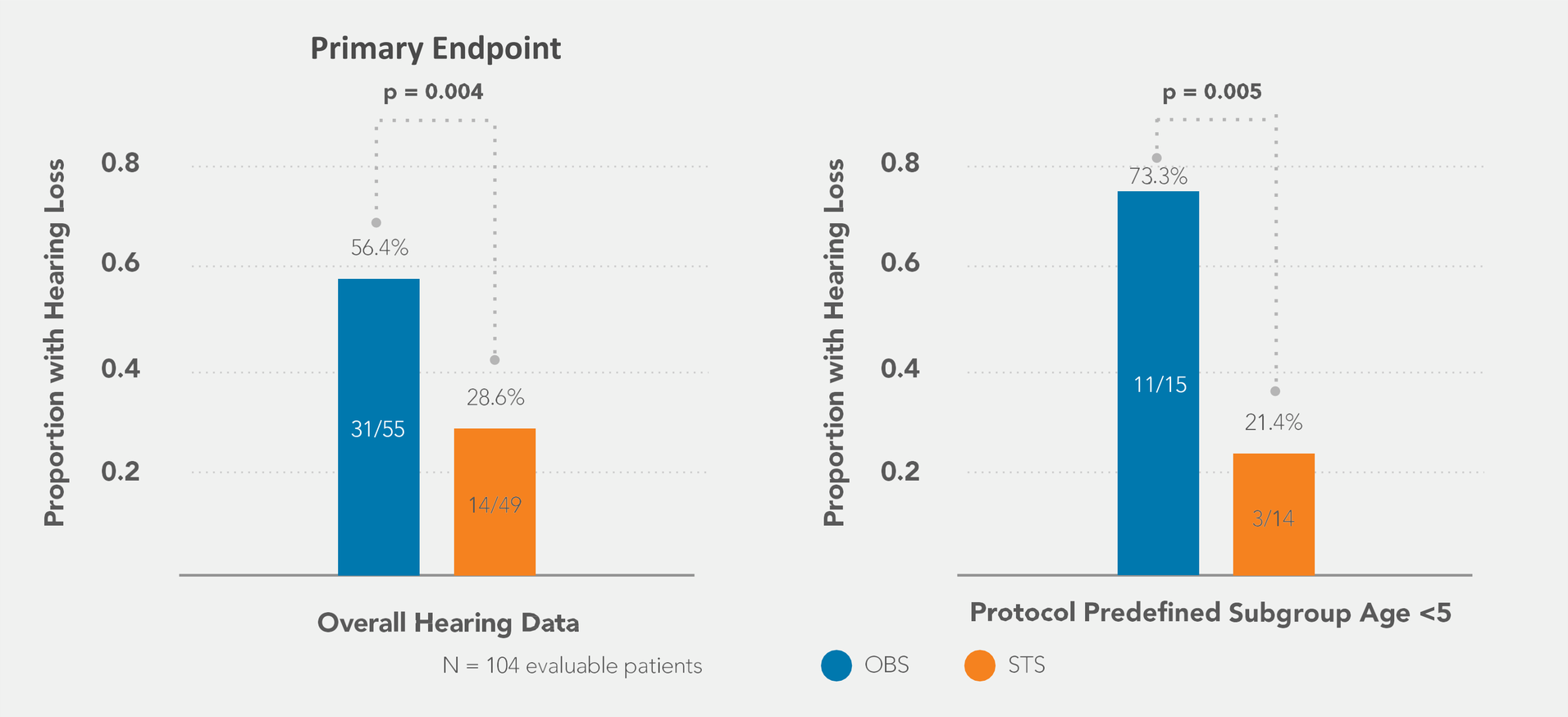
Patients with Localized or Disseminated Diagnoses



		n CONTROL %		n STS %	
	Number Eligible	64		61	
Age (years)	<5	22	34	22	36
	5 – 9	13	20	7	11
	10 – 14	14	22	16	26
	15 – 18	15	23	16	26
Diagnosis	Germ Cell Tumor	16	25	16	26
	Hepatoblastoma	5	8	2	3
	Medulloblastoma/PNET	14	22	12	20
	Neuroblastoma	12	19	14	23
	Osteosarcoma	15	23	14	23
	Other	2	3	3	5
Extent of disease	Localized	38	59	39	64
	Disseminated	26	41	21	34
	Unknown	0	0	1	1.6

Freyer et al, www.thelancet.com/oncology Vol 18 January 2017

COG ACCLO431 | Primary Outcome (Hearing Loss)



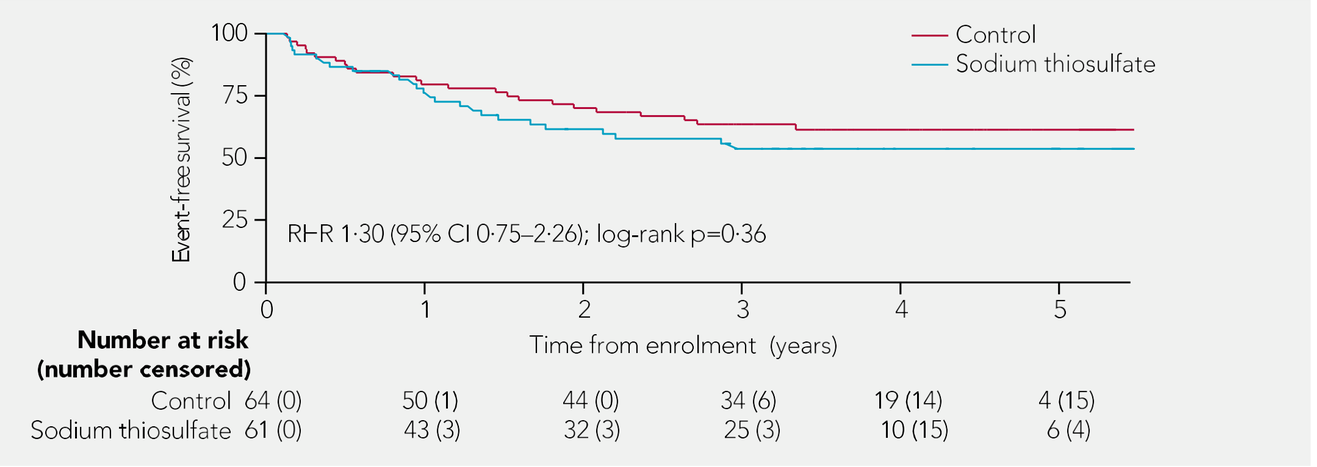
48% Reduction in Risk of Hearing Loss

70% Reduction in Risk of Hearing Loss

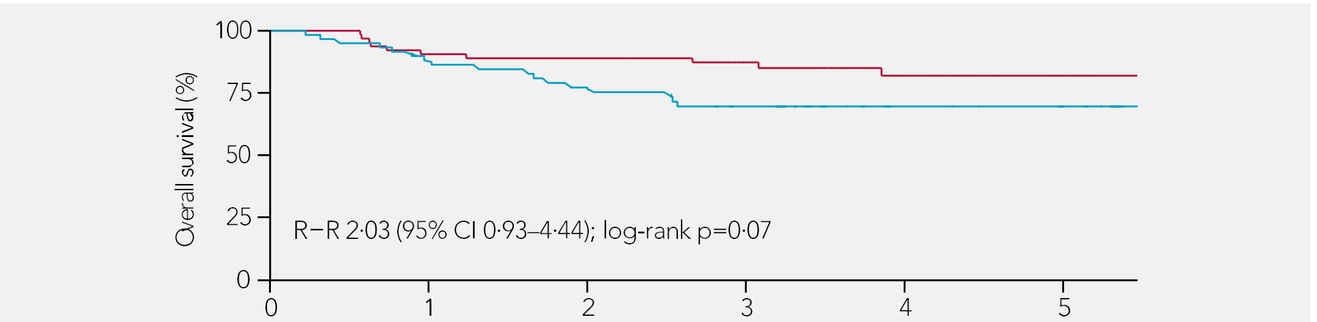
Freyer et al, www.thelancet.com/oncology Vol 18 January 2017

COG ACCLO431 | EFS and OS in ITT (All Patients)

Per Protocol | Monitor Event Free Survival (EFS) and Overall Survival (OS) (no formal comparison)



Number at risk (number censored)						
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)

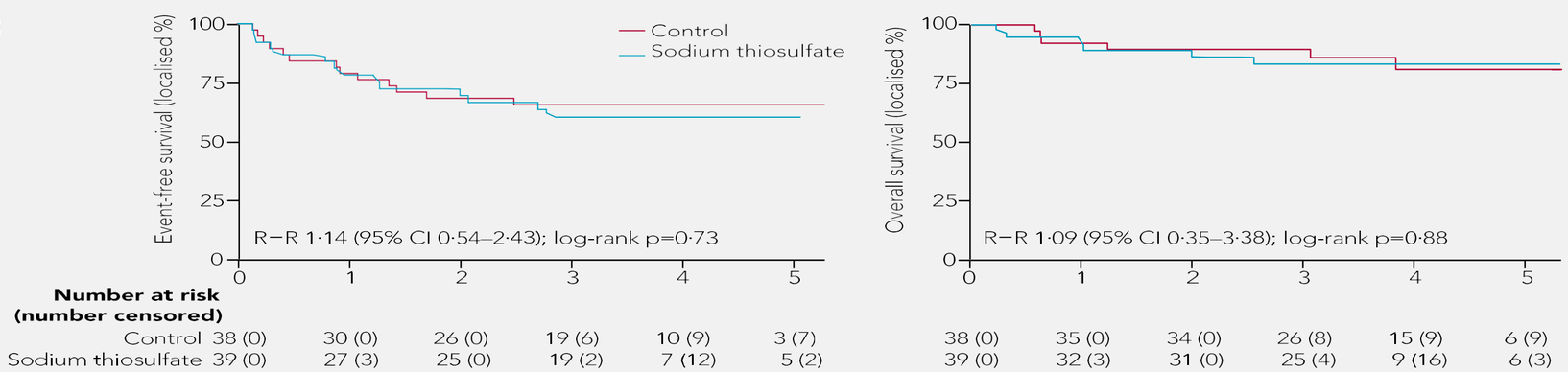


Number at risk (number censored)						
Control	64 (0)	56 (2)	54 (1)	44 (9)	26 (16)	8 (18)
Sodium thiosulfate	61 (0)	50 (3)	41 (3)	32 (5)	13 (19)	8 (5)

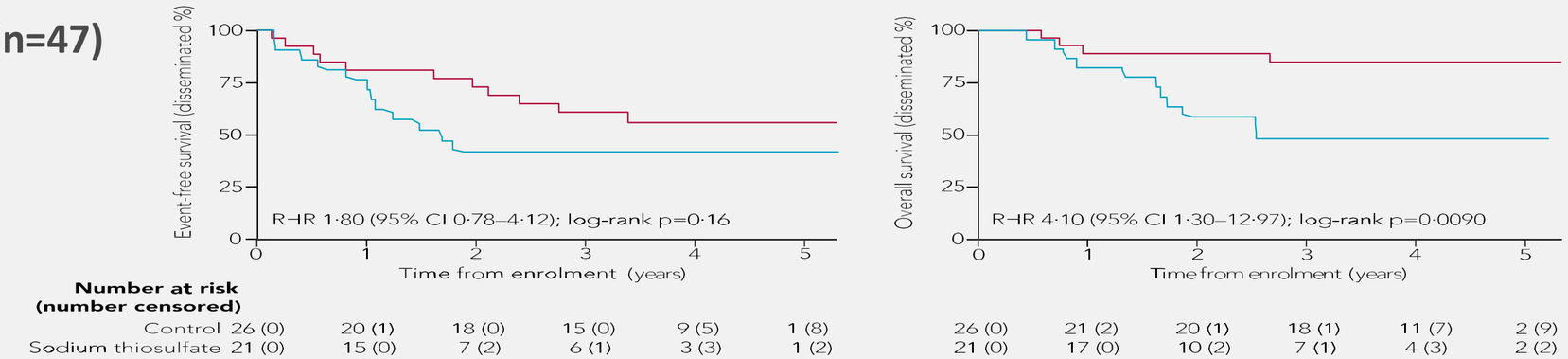
Freyer et al, www.thelancet.com/oncology Vol 18 January 2017

COG ACCLO431 | Post Hoc Analysis of EFS and OS*

Localized Disease (n=77)



Disseminated Disease (n=47)



Freyer et al, www.thelancet.com/oncology Vol 18 January 2017

**Determined post hoc (i.e., retrospectively during the preliminary data analysis after completion of accrual).*

Pivotal Study | SIOPEL 6

Objectives

- Assess the efficacy of STS to reduce the hearing impairment caused by cisplatin in SR-HB
- Monitor any potential impact of STS on response (protocol pre-specified Independent Data Monitoring Committee (IDMC) tumor 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 ≥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

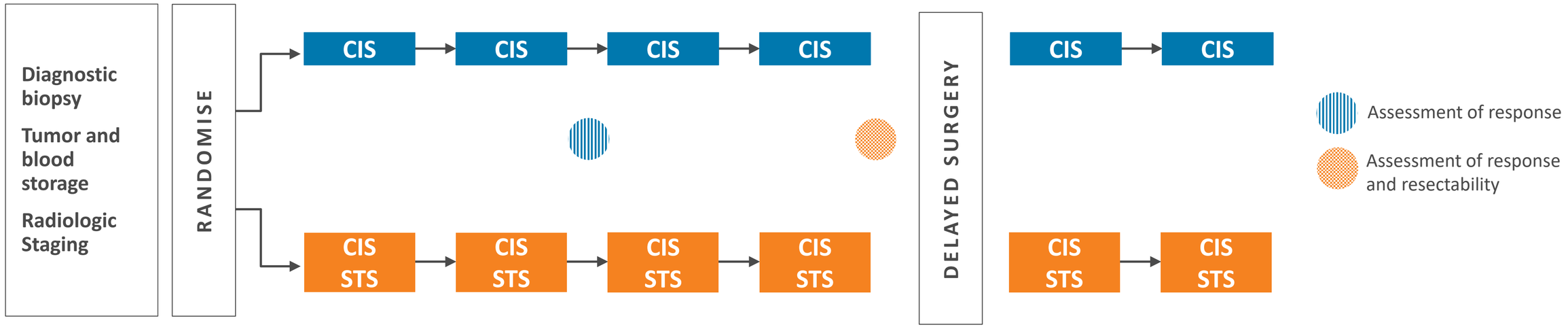
Stratification Factors for Randomization

Risk stratified based treatment and disease stage: Country, age and PRETEXT* classification

Brock et al, N Engl J Med 2018;378:2376-85.

**Pre-treatment tumor extension classification (a primary method of risk stratification for hepatoblastoma)*

SIOPEL 6 | Study Design



CIS **Cisplatin alone:** IV infusion over 6 hrs (80 mg/m2 for children > 10kg, 2.7 mg/ kg for infants and children 5-10kg or 1.8 mg/kg for infants < 5kg)

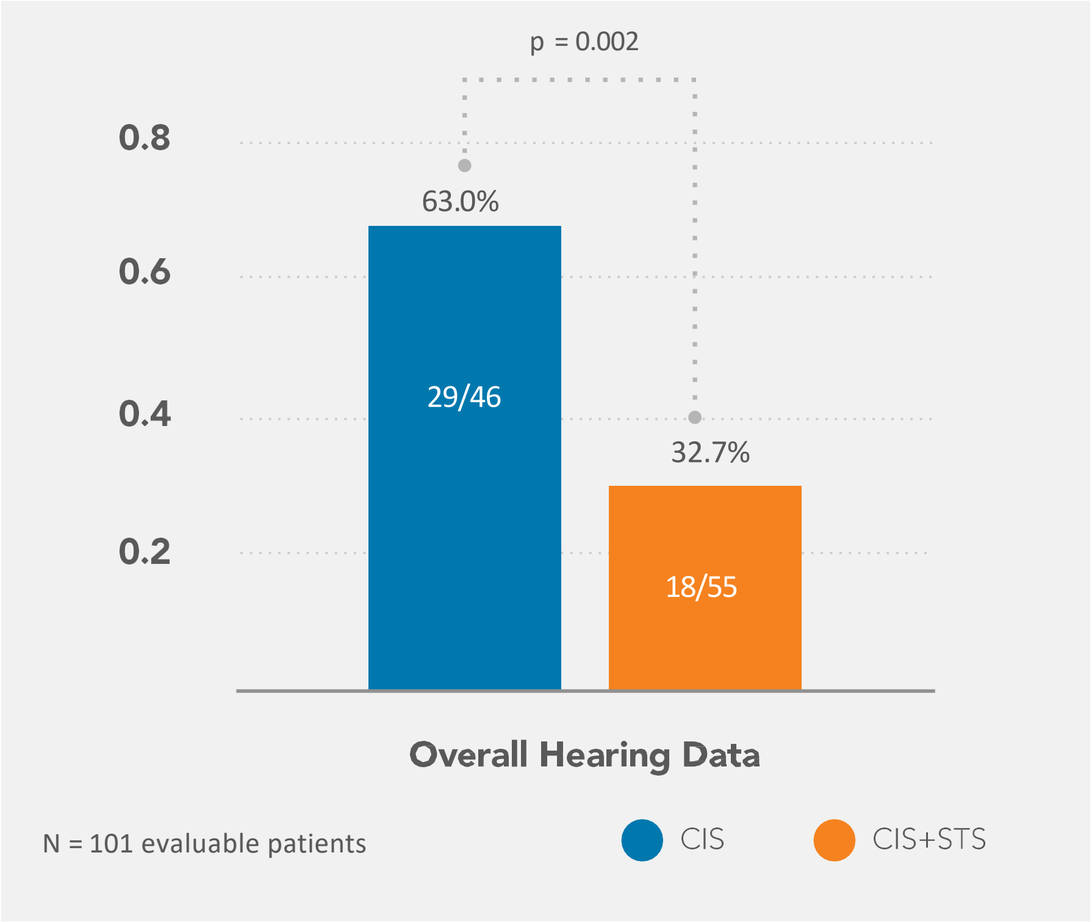
- or -

CIS STS **Cisplatin (same dose) and STS:** administered IV exactly 6 hours after stop of cisplatin over 15 minutes at 20 g/m2 for children > 10kg, 15 g/m² for infants and children of 5-10 kg or 10 g/m2 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
- Tumor response assessed preoperatively, after 2 and 4 cycles, with serum AFP and liver imaging

Brock et al, N Engl J Med 2018;378:2376-85.

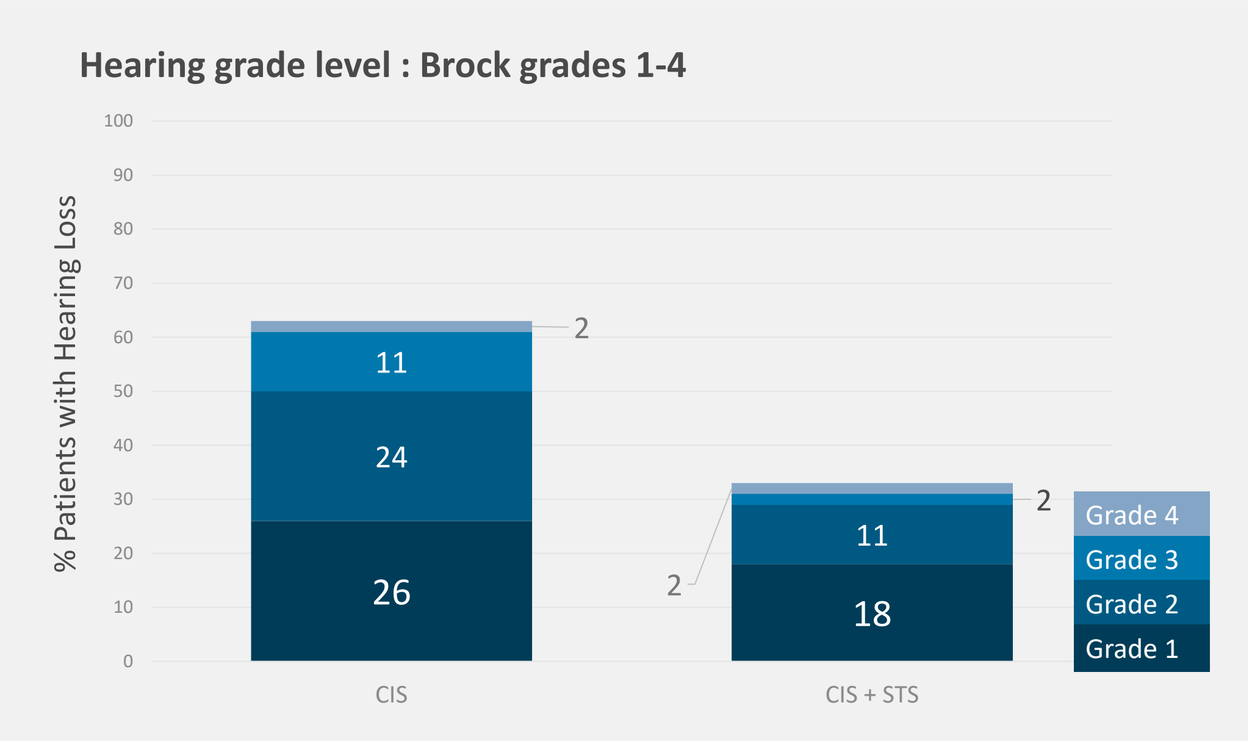
SIOPEL 6 | Primary Outcome (Hearing Loss)



Consistent with COG study, there was a 48% decrease in the risk of hearing loss

Brock et al, N Engl J Med 2018;378:2376-85.

SIOPEL 6 | Hearing Loss Sensitivity by Brock Grade



- The proportion of children with more severe grades of hearing was lower In the CIS+STS group vs the CIS alone group
- Any grade hearing loss Grade 1-4 63% CIS vs 33% STS

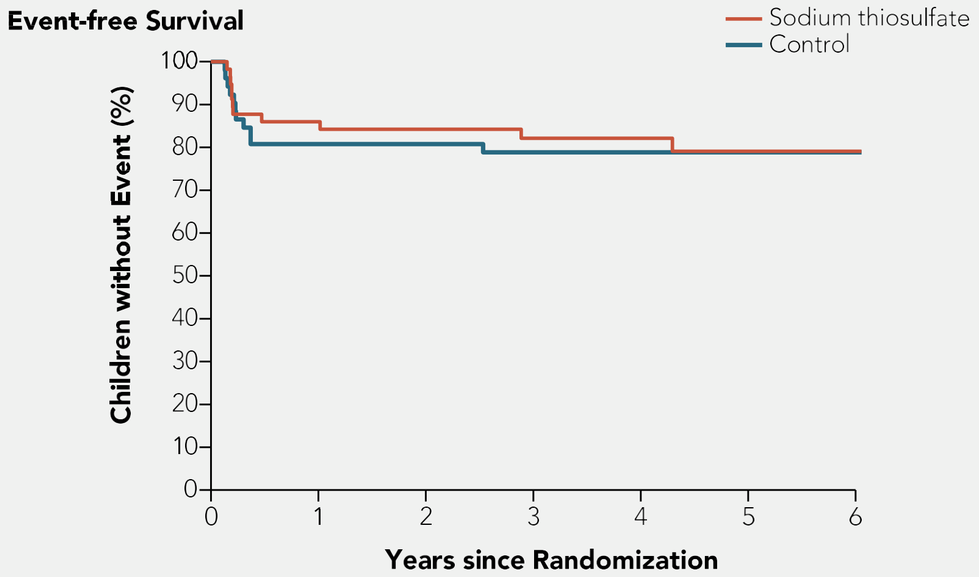
Bilateral Hearing Loss	Grade	Designation
< 40 dB at all frequencies	0	Minimal
>= 40 dB at 8kHz only	1	Mild
>= 40 dB at 4kHz and above	2	Moderate
>= 40 dB at 2kHz and above	3	Marked
>= 40 dB at 1Khz and above	4	Severe

- A Brock grade of 0 indicates hearing at < 40 dB at all frequencies; does not necessarily equate to completely normal hearing
- The grade was determined according to the hearing level in the child's better ear

Brock et al, N Engl J Med 2018;378:2376-85.

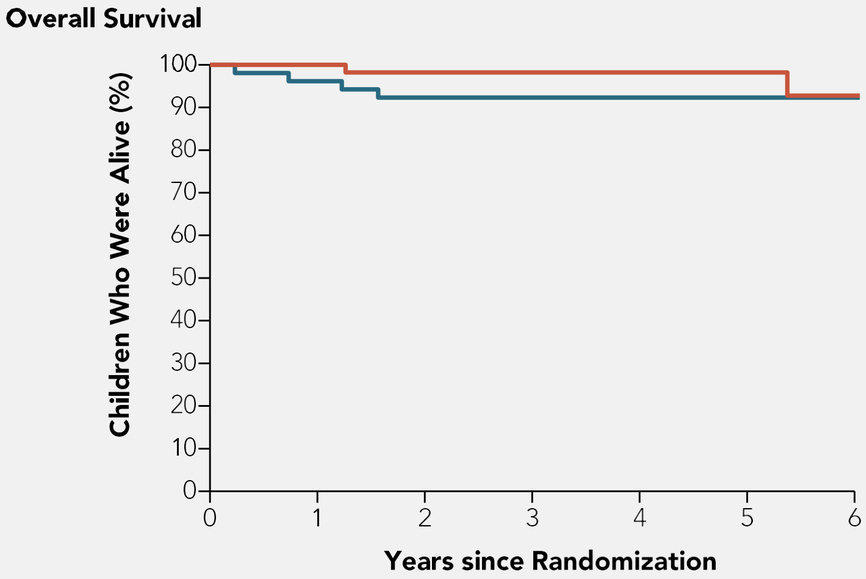
SIOPEL 6 | Secondary Endpoints EFS and OS

Median Follow-Up 52 months 3yr-EFS: CIS 78.8% CIS+STS 82.1%



No. at Risk							
Cisplatin–sodium thiosulfate	57	49	46	37	29	19	9
Cisplatin alone	52	42	42	37	22	13	8

3yr-OS : CIS 92.3% CIS+STS 98.2%



No. at Risk							
Cisplatin–sodium thiosulfate	57	57	54	45	35	24	12
Cisplatin alone	52	50	48	43	28	17	11

Brock et al, N Engl J Med 2018;378:2376-85.

SIOPEL 6 Study | KOL Perspectives

"Taken together, these trials provide definitive evidence that sodium thiosulfate reduces the incidence of cisplatin-induced hearing loss and suggest that sodium thiosulfate is safe to use in patients with standard-risk hepatoblastoma and probably in those with other localized cancers. However, the use of sodium thiosulfate in patients with disseminated disease may affect survival, and caution is warranted in that context."

David R. Freyer, D.O.
Lindsay Frazier, M.D.
Lillian Sung, M.D., Ph.D.

"We agree with Freyer et al. that drawing conclusions for clinical practice from our trial and ACCL04311 would support the use of sodium thiosulfate for protection from cisplatin-induced hearing loss in patients with any localized solid tumor and encourage careful further clinical assessment in patients with metastatic disease. No definitive conclusion or therapeutic direction should be drawn from any post hoc analysis, particularly in ACCL0431, in which children were not randomly assigned according to disease-specific key prognostic factors that are important in determining outcome in metastatic disease."

Penelope R. Brock, M.D., Ph.D.
Rudolf Maibach, Ph.D.
Edward A. Neuwelt, M.D.

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