FONDATION SANFILIPPO SUISSE

4TH INTERNATIONAL CONFERENCE ON SANFILIPPO SYNDROME AND RELATED DISEASES

13 & 14 NOVEMBER 2025, GENEVA

Summary

01

Welcome

WE ARE HONORED TO WELCOME YOU TO THE 4TH WORLD CONFERENCE ON SANFILIPPO SYNDROME, TAKING PLACE ON 13–14 NOVEMBER 2025 AT THE INTERCITYHOTEL GENEVA.

This year, 50 participants from 9 countries — researchers, clinicians, biotech partners, families, caregivers, and associations — are gathered in one place, united by a shared commitment to better understand Sanfilippo syndrome and to build a different future for those living with it.

Over the next two days, discussions will focus on :

- Emerging therapeutic approaches — genetherapy, enzyme replacement, drug repurposing, artificial intelligence, biomarkers, and innovative clinical trials.
- International collaboration and knowledge-sharing, through roundtables and dedicated networking sessions.

Alongside the scientific program, a dedicated program for children and young adults with Sanfilippo or related conditions is offered, supervised by qualified educators. This enables parents to participate fully in the sessions while their children enjoy meaningful, safe, and engaging activities that promote well-being and social interaction.

This conference exists because progress in rare diseases requires both science and people — discoveries in the lab, and families who continue to carry hope.

We warmly thank all those who made this gathering possible — our speakers, our partners and sponsors, and each of you who have traveled to be here.

Together, we advance research, strengthen alliances, and move forward — for every child and every family living with Sanfilippo syndrome.

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Conference schedule & scientific programme

DAY 1 – THURSDAY, NOVEMBER 13, 2025

09:15

Introduction and Welcome
Alexandra Spaethe, Director Fondation Sanfilippo Suisse (CH)
Prof. Stylios Antonarakis, Geneva Medical School (CH)

Gene Therapy and ERT

09:30 – 10:00

OTL-201 – A Clinical Study of the Investigational Haematopoietic Stem Cell Gene Therapy in MPSIIIA.
Prof. Brian Bigger, University of Edinburgh (UK)

10:00 – 10:30

Combination of HSPC transplantation and cathepsin B inhibitors for treatment of Sanfilippo disease.
Prof. Alexey Pshezhetsky, CHU Sainte-Justine (CAN)

10:30 – 11:00 BREAK

11:00 – 11:30

Preclinical validation of an intravenous AAV gene therapy for mucopolysaccharidosis IIIB.
Prof. Jérôme Ausseil, CHU Toulouse (FR)

11:30 – 12:00

JR-441 – An intravenous enzyme replacement therapy to deliver the sulfamidase enzyme to the brain to treat Sanfilippo type A.
Dr. Nicole Muschol, UKE Hamburg (DE)

12:00 – 12:30

MPS IIIC Gene Replacement Therapy with scAAV9/HGSNAT Vector, JLK-247.
Jill Wood, Phoenix Nest Inc (USA) on behalf of Dr. Xin Chen

12:30 LUNCH

DAY 1

Gene Therapy and ERT *continued*

14:00 – 14:30

Investigational Therapies for Sanfilippo syndrome and Related MPS Disorders: Denali Therapeutics' Enzyme Transport Vehicle (ETV) Platform and Clinical Updates.
Dr. Michael Ostland, Denali Therapeutics (USA)

14:30 – 15:00

Long-term intracerebroventricular treatment with Tralesinidase Alfa (AX 250) for Sanfilippo type B.
Dr. Nicole Muschol, UKE Hamburg (DE)

15:00 – 15:30 BREAK

Sanfilippo Symptoms and Natural History

15:30 – 16:00

The role of the inflammasome and systemic inflammation in neurologic progression of Sanfilippo disease.
Prof. Brian Bigger, University of Edinburgh (UK)

16:00 – 16:30

Leveraging Remote Video Capture in MPS IIIC and IIID Natural History Studies: Introducing C-RARE for Real-World Evidence to Support Clinical Trial Treatment Efficacy.
Jill Wood, Phoenix Nest Inc (USA)

16:30 – 17:30

Combining Therapeutic Approaches for Sanfilippo treatment (Participants based on attendees present)
Scientific Round Table Discussion

19:00 COCKTAIL
19:30 GALA DINNER
Dress Code: Business Attire

DAY 2 – FRIDAY, NOVEMBER 14, 2025

Novel Therapies and Approaches

08:30 – 09:00

Harnessing the power of deep learning to repurpose drugs for the treatment of the Sanfilippo syndrome.
Dr. Anna Fournier, Swiss Data Science Center with the Fondation Sanfilippo Suisse (CH)

09:00 – 09:30

Targeting protein amyloids and brain autophagy-lysosomal pathway in Sanfilippo syndrome and other neuronopathic MPSs.
Prof. Alessandro Fraldi, University of Naples "Federico" II & CEINGE (IT)

09:30 – 10:00

VRO073 – A novel molecule for the potential treatment of GM1, GM2 gangliosidosis and Gaucher Disease type 3.
Dr. Vincent Mutel, Dorphan SA (CH)

10:00 – 10:30 BREAK

Screening, Biomarkers and Animal Models

10:30 – 11:00

Biomarkers, diagnostic testing and drug development for Sanfilippo syndrome and other MPS diseases.
Prof. Peter Bauer, Centogene (DE)

11:00 – 11:30

Assessment of a central nervous system demyelination in Sanfilippo disease by diffusion tensor imaging: a non-invasive method to evaluate disease progression and therapeutic response.
Prof. Alexey Pshezhetsky, CHU Sainte-Justine (CAN)

11:30 – 12:00

The effect of treatment with a heparanase-inhibiting polysaccharide on the MPS III A mouse model.
Prof. Stéphane Sizonenko, University of Geneva & HUG (CH)

12:00 – 12:45

Family Voices Panel

12:45

Closing Remarks and Conference Wrap-up
Frédéric Morel, Founder & President, Fondation Sanfilippo Suisse

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13:00 CLOSING LUNCH

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Prof. Jérôme Ausseil

He is Full Professor in Medical Biochemistry at the Medical School of Toulouse University and he is the Head of the clinical biochemistry department at Toulouse University Hospital. He is an expert in the pathophysiology of mucopolysaccharidosis type III disease and his group is working on the design and the development of new biotherapies (in particularly gene therapy) and their implementation at the preclinical and clinical steps.

Preclinical validation of an intravenous AAV gene therapy for mucopolysaccharidosis IIIB.

Prof. Jérôme Ausseil[1,2], N. Ballout[1,2], M. Rouahi[1,2], E.G. Banchi[3], R. Alonso[3], F. Roux[4], M-A Colle[5], K. Deiva[6], F. Piguet[3].

[1]Infinity, INSERM UMR1291, CNRS UMR5051, University of Toulouse III, Toulouse, France; [2]Laboratory of Biochemistry and Molecular Biology, Toulouse University Hospital, Toulouse, France; [3]TIDU GENOV Paris Brain Inst, Paris, France; [4]ONIRIS Vet Sch Nantes, Nantes, France; [5]Ecole Natl Vet Agroalimentaire & Alimentat Nante, PAnTher INRAE, UMR 703, Oniris, Nantes, France; [6]Service de Neuropédiatrie, APHP, Paris, France

MPS IIIB is an autosomal recessive lysosomal storage disorder caused by NAGLU enzymatic deficiency. A previous study demonstrated promising results in four MPS IIIB patients following intracerebral AAV5 gene therapy, with best results being obtained in the youngest patient. Building on this, an improved approach using the next-generation AAV serotype AAVMacPNS1 – capable of efficient blood–brain barrier crossing after intravenous delivery notably in large animals – showed broad CNS transduction and supraphysiological NAGLU expression in mice and non-human primates, with excellent tolerability in the tissues.

Evaluation in the dog model at symptomatic stage of the disease is ongoing with 3 animals with also 7T imaging data. *In vivo* monitoring demonstrates significant MRI improvement with regression of all brain abnormalities, prevention of cerebral loss, neurobehavioral improvement and reduction of GAG accumulation. Efficacy and safety studies will be presented in both MPS IIIB mouse and dog models of the pathology.

CENTOGENE
GUIDING PRECISION MEDICINE

Prof. Peter Bauer, M.D.

He is a Member of the Executive Board of CENTOGENE GmbH, where he has led large-scale screening projects and implemented diagnostic Whole Genome Sequencing, making CENTOGENE the first European provider in rare disease diagnostics. Since 2017, as Chief Scientific Officer, he has focused on integrating bioinformatics across genomics, transcriptomics, and peptidomics for rare diseases and somatic cancer.

Diagnostic testing and drug development for Sanfilippo syndrome and other MPS diseases.

Steffen Fischer, Peter Bauer. Centogene GmbH, Rostock, Germany

Centogene's platform diagnoses MPS patients via genetic testing and enzyme activity screening from dried blood spots (DBS). The integrated multiomic "CentoMetabolic" and whole exome / genome sequencing are applied in routine diagnostic requests. In cases with uncertain, often novel genetic variants, enzyme activity testing provides functional evidence and supports reclassification of variants of uncertain significance into (likely) pathogenic and (likely) benign.

In addition, clinical development and patient monitoring require more quantitative markers that reflect disease severity and ideally also respond to treatment. Centogene developed a DBS-based panel to quantify gangliosides – elevated in serum of MPS II patients most prominent in the severe neuronopathic subtype –, including the lyso-form of GM1 and GM2. This assay may be used as an add-on to the current diagnostic pipeline and potentially as low-effort assay in treatment efficacy studies.

Another complementary test, sequencing RNA from DBS, identifies splice variants missed by conventional DNA sequencing. This illustrates the potential of multiomic approaches to bridge existing biomarker gaps in clinical development.

THE UNIVERSITY of EDINBURGH

Prof. Brian Bigger

He is Chair of Advanced Therapeutics at the University of Edinburgh, and Honorary Professor at the University of Manchester, UK. The Bigger lab develops lentiviral ex vivo, iPSC neural stem cell and AAV gene therapies for childhood dementias, such as Sanfilippo disease, with two clinical trials underway in Manchester, and was the first to show the role of the inflammasome in neurodegeneration in lysosomal diseases.

Sustained biochemical correction and improved neurological outcomes at 36-months post hematopoietic Stem Cell Gene Therapy for Sanfilippo Disease.

Brian Bigger[1,2], Jane Kinsella, Jane Potter, Karen Buckland, Stuart Ellison, Helena Lee, Heather Church, Rachel Searle, Yuko Ishikawa-Learmonth, Rebecca Holley, Claire Booth, Adrian Thrasher, Stewart Rust, Simon Jones, and Rob Wynn[2]

[1]University of Edinburgh, Edinburgh, UK; [2]University of Manchester, Manchester, UK

HSC-GT is an autologous ex vivo lentiviral gene therapy delivering functional N-sulphoglucosamine sulphohydrolase (SGSH) in children with the severe form of MPS IIIA.

In this phase I/II clinical trial, five patients under 2 years of age underwent myeloablative conditioning and received autologous hematopoietic stem and progenitor cells (HSPCs) transduced ex vivo with a lentiviral vector expressing SGSH under the CD11b myeloid promoter.

All patients have a 36-months follow-up post-treatment. All patients engrafted within 52 days of transplant, with a total of 6 SAEs reported in 3 out of 5 patients.

HSC-GT treatment of MPS IIIA patients resulted in rapid and sustained engraftment, with supraphysiological SGSH activity, HS reduction, and improved neurological outcomes in patients.

The role of the inflammasome and systemic inflammation in neurologic progression of Sanfilippo disease.

Brian Bigger, Helen Parker, Oriana Mandolfo, Rachel Searle University of Edinburgh, Edinburgh, UK; University of Manchester, Manchester, UK

Mucopolysaccharidosis IIIA patients develop behavioral disturbances and cognitive decline, a possible consequence of neuroinflammation and abnormal substrate accumulation.

Anecdotal reports indicated a more severe cognitive decline in MPS IIIA patients, following recovery from infection, which suggests inflammation as a potential driver of neuropathology progression.

To test whether infection exacerbates disease, an acute in vivo study was conducted in which wild-type and MPS IIIA mice were challenged with the viral mimetic poly(I:C).

The study demonstrates that abnormal heparan sulphate and other secondary storage components drive interleukin-1β secretion, which in turn drives neuroinflammation and cognitive decline in mucopolysaccharidosis IIIA. This process can also be exacerbated by infection, but in turn limited by targeted intervention of IL1RA.

This has resulted in several subsequent clinical trials in patients with Sanfilippo disease using the off label IL1RA drug product anakinra, and meeting with some success.

SDSC

Dr. Anna Fournier

She is a Principal Data Scientist at the Swiss Data Science Center. Anna led a deep learning-based drug repurposing project, funded by Fondation Sanfilippo Suisse. They integrated biomedical datasets that served as a foundation for the novel predictions of Sanfilippo syndrome drug candidates. The list of the candidates and user-friendly interface was delivered to the Foundation for further analysis.

Harnessing the power of deep learning to repurpose drugs for the treatment of the Sanfilippo syndrome.

Sanfilippo syndrome is a rare and devastating genetic disorder with no approved treatment. To address this urgent unmet need, this research presents a novel strategy focused on drug repurposing—identifying new therapeutic uses for existing FDA-approved molecules.

It introduces a computational framework that leverages Graph Neural Networks (GNNs) to analyze complex biological data.

By modeling the intricate relationships between drugs, proteins, and diseases as a graph, our GNN-based model can effectively learn feature representations and predict novel drug-target interactions. This method allows to identify existing drugs that could be repurposed for Sanfilippo syndrome, offering a promising, cost-effective, and accelerated path toward finding a cure.

Prof. Alessandro Fraldi

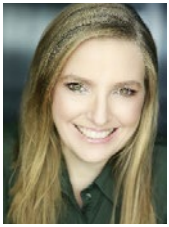
He is Associate Professor of Histology, at Department of Clinical Medicine, University of Naples "Federico II" and Principal Investigator at CEINGE-*Advanced Biotecnology Franco Salvatore*. He has a long-standing interest in neuronopathic mucopolysaccharidoses, particularly in Sanfilippo syndrome. His research is focused both on the study of mechanisms underlying neurodegeneration and on the development of therapeutic strategies.

Targeting protein amyloids and brain autophagy-lysosomal pathway in Sanfilippo syndrome and other neuronopathic MPSs.

Brain deposition of multiple amyloid proteins is a key contributor to neurodegenerative processes in neuronopathic MPSs. CLR01 is the lead compound of "molecular tweezers", a class of molecules that act as potent and safe broad-spectrum inhibitors of the aberrant amyloid protein self-assembly. The study demonstrated that inhibiting amyloid deposition provides prolonged relief and considerable delay of disease onset and progression, thus protecting against neurodegeneration in a mouse model of MPS-IIIA.

Additionally, using brain samples and neuronal cultures from MPS-IIIA mice, the study demonstrated mechanistic data supporting the concept that amyloid aggregation affects autophagy-lysosomal pathway, thus triggering a vicious cycle, which boost neurodegenerative cascades.

Results show that targeting amyloids may represent an innovative therapeutic avenue for Sanfilippo and other MPS and uncover mechanistic insights linking amyloid aggregation to ALP-mediated brain homeostasis and neuroinflammation in these diseases.



Dr. Nicole Maria Muschol, PD

She is a Paediatrician and Metabolic Specialist at the University Medical Center Hamburg-Eppendorf (UKE) in Germany. She is Head of the lysosomal disease unit and spokeswoman of the International Center for Lysosomal Disorders. She is the healthcare provider representative for UKE within the Metab-ERN and is actively involved in many national and international clinical trials for lysosomal storage disorders (phase I-IV).

JR-441 - an intravenous enzyme replacement therapy to deliver heparan-N-sulfatase enzyme to the brain to treat Sanfilippo A syndrome.

JR-441 is an investigational drug designed to address the underlying enzyme deficiency in Sanfilippo syndrome type A in order to mitigate central nervous system (CNS) pathology through CNS penetration via transferrin receptor-mediated transcytosis.

This ongoing, open-label, multicenter Phase I/II study evaluates the safety, tolerability, pharmacokinetics, and preliminary efficacy of JR-441 in pediatric patients with confirmed MPS IIIA. Participants receive weekly intravenous infusions of JR-441 with comprehensive assessments including biomarkers, neurocognitive function, adaptive behavior, and neuroimaging endpoints. Safety is evaluated through adverse event monitoring, laboratory parameters, and immunogenicity testing.

The study set-up and status of the clinical trial will be presented.

Long-term intracerebroventricular treatment with Tralesinidase Alfa (TA) for Sanfilippo syndrome type B.

Tralesinidase alfa (TA) is a recombinant fusion protein comprising human α-N-acetylglucosaminidase (NAGLU) linked to an insulin-like growth factor II (IGF-II) peptide to facilitate receptor-mediated cellular uptake.

Administered via intracerebroventricular (ICV) infusion, TA enzyme replacement therapy (ERT) is designed to bypass the blood–brain barrier and deliver enzyme directly to the Central Nervous System. In a Phase I/II, open-label clinical trial, 22 pediatric patients aged 1 to <11 years received weekly ICV infusions of 300 mg TA-ERT over 48 weeks.

Treatment resulted in rapid and sustained reductions in cerebrospinal fluid (CSF) heparan sulfate (HS) and non-reducing end (HS-NRE) levels. Neuroimaging showed stabilization of cortical grey matter and cognitive assessments using Bayley-III also showed stabilization in treated patients relative to natural history cohorts.

ICV administration of TA-ERT led to normalization of HS-NRE biomarkers and long-term stabilization of brain structure and cognition. These findings support the therapeutic potential of ICV-administered TA-ERT for patients with Sanfilippo syndrome type B.

A Phase III clinical trial is expected to start in 2026.

DORPHAN

Dr. Vincent Mutel

He is Expert in CNS pharmacology and drug development, and Executive Chairman of Dorphan SA, a company involved in the development of molecules for the treatment of GM1-gangliosidosis and Morquio B. He is also CEO of GAOMA Therapeutics, a company developing novel small molecules anti neuroinflammatory drugs for the treatment of neurodegenerative diseases like Alzheimer or Parkinsons disease.

VRO073, a novel molecule for the potential treatment of GM1, GM2 gangliosidosis and Gaucher Disease type 3.

Aloxistatin is a cysteine protease inhibitor shown to rescue the activity of certain mutated β-galactosidase in fibroblasts of patients suffering from GM1-gangliosidosis and Morquio disease type B (MPS IV) *in vitro*. Using aloxistatin as a scaffold, Dorphan developed and patented a new molecule named VRO073, much more active than aloxistatin *in vitro*.

VRO073 significantly restored the activity of deficient beta-galactosidase and increased the activity of deficient β-Hexosaminidase A in fibroblasts isolated from patients suffering from GM1-gangliosidosis and GM2-gangliosidosis, respectively, treated for 6 days *in vitro*.

Finally, VRO073 was able to significantly increase the deficient glucocerebrosidase activity in cell culture of fibroblasts from two individual suffering from Type 3 Gaucher disease (neurological form) and showed a trend of activity in one culture of fibroblasts from Type 2 Gaucher disease patient. It seems that this new molecule has a pleiotropic effect, is able to rescue deficient enzyme activities in at least three independent lysosomal storage diseases, and could play a significant role in their treatment in humans.

Dr. Michael Ostland

He is Head of Development Europe for Denali Therapeutics. He has worked in the biotech industry for 26 years. In 2022, he joined Denali Therapeutics to open an office in Zürich, focused on clinical development for Denali's MPS portfolio. Michael served as project leader for Denali's tividenofusp alfa, currently under FDA review for the treatment of MPSII. He currently leads the DNL126 project in Sanfilippo syndrome type A.

Investigational Therapies for Sanfilippo syndrome and Related MPS Disorders: Denali Therapeutics' Enzyme Transport Vehicle (ETV) Platform and Clinical Updates.

Denali Therapeutics is committed to developing therapies that address both the neurological and systemic manifestations of lysosomal storage disorders by leveraging its proprietary Enzyme Transport Vehicle (ETV) technology.

Tividenofusp alfa (DNL310) and DNL126 are investigational fusion proteins designed to deliver therapeutic enzymes to both the brain and body. DNL310, currently under FDA Priority Review for the treatment of Hunter syndrome, consists of idursulfase fused to the ETV technology to enhance enzyme delivery across the blood–brain barrier.

DNL126, being studied in Sanfilippo syndrome type A, fuses two N-sulfoglucosamine sulfohydrolase enzymes to the same platform, with the goal of addressing disease pathology in both central nervous system and peripheral tissues.

By combining innovative science with meaningful engagement, Denali Therapeutics aims to advance treatments that have the potential to improve outcomes for individuals living with Sanfilippo syndrome and related MPS disorders.

Prof. Alexey Pshezhetsky

He is Scientific Director of medical genetics diagnostic laboratory of CHU Ste-Justine, Director of Elisa Linton Laboratory of lysosomal biology at CHU Ste-Justine Research Center and Adjunct Professor at the Department of Anatomy and Cell Biology, McGill University. His current research interests include molecular basis of lysosomal and other inherited metabolic disorders, glycobiology, proteomics and functional genomics of the cell.

Combination of HSPC transplantation and cathepsin B inhibitors for treatment of Sanfilippo disease.

Shuxian Fan, Xuefang Pan, Charlotte Betus, Longguo Zhang, Jean-Sebastien Joyal and Alexey V. Pshezhetsky

CHU Ste-Justine Research Centre, University of Montreal, Canada

Neuronal dysfunction and neurodegeneration in the CNS of Sanfilippo (MPS III) patients and mouse models are associated with accumulation of neurotoxic misfolded protein aggregates including those of β-amyloid, and coincides with overexpression of cathepsin B (CTSB), a lysosomal cysteine endopeptidase involved in amyloidogenic processing of amyloid precursor protein.

This study tested whether combining the brain-permeable irreversible CTSB inhibitor E64 (Aloxistatin) with hematopoietic stem cell (HSPC) transplantation – a therapy reducing neuroimmune response, can prevent the development of neuropathology in MPS IIIC mice.

Mice receiving wild-type HSPC transplantation and chronic E64 treatment show complete rescue of behavioral and memory deficits and prolonged survival. These results show preclinical efficacy of the combination therapy and suggest that CTSB may become a novel pharmacological target for MPS III. Importantly, E64 and its analogues show oral bioavailability and have been approved for clinical trials which may simplify their translation.

Assessment of a central nervous system demyelination in Sanfilippo disease by diffusion tensor imaging: a non-invasive method to evaluate disease progression and therapeutic response.

Erjun Zhang[1],Travis Moore[1], Patricia Dubot[1], Jill Wood[2], Gregory A. Lodygensky[1] and Alexey V. Pshezhetsky[1]

[1]CHU Ste-Justine Research Centre, University of Montreal, Canada; [2]Phoenix Nest Inc., Brooklyn NY, USA.

Progressive severe demyelination is a hallmark of CNS pathology in both human MPS IIIC patients and the mouse models of the disease.

This study tested whether Diffusion Tensor Imaging (DTI) may be used as a non-invasive method to reveal biomarkers of demyelination and brain injury predictive of disease progression and response to a therapy.

DTI biomarkers were assessed in the brains of WT, MPS IIIC (*Hgsnat*P304L) and MPS IIIA (Sgshmps3a) mice either untreated or treated with an anti-inflammatory and neuroprotective peptide, AVP6, to study drug effects on the grey and white matter injury.

DTI findings were validated by the immunofluorescence analysis of the levels of Myelin Basic Protein (MBP) in coronal sections of the same mouse brains after completion of DTI.

Overall, results demonstrate an important role for white matter injury in the pathophysiology of MPS III.

This study also defines specific parameters and brain regions for DTI analysis and suggests that it may become a crucial non-invasive method to evaluate disease progression and therapeutic response.

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FACULTÉ DE MÉDECINE

Prof. Stéphane Sizonenko, MD-PhD

As a Developmental Paediatrician and Neonatologist, he has been interested in developmental brain injury that leads to functional deficits in children. Using a mice model of Sanfilippo disease, he has characterized brain neuropathology including in vivo metabolic and structural changes using magnetic resonance and effects of treatment with marine sulphated polysaccharides to alleviate brain damage.

Low-molecular-weight sulfated marine polysaccharides: Promising molecules to prevent neurodegeneration in mucopolysaccharidosis IIIA.

A5_3 is a low-molecular-weight highly sulfated compound derived from marine diabolican with heparanase inhibiting properties. A5_3 was tested in a MPSIIIA cell line model, resulting in limited degradation of intracellular HS.

Next, the effects of intraperitoneal injections of A5_3 were observed in MPS IIIA mice from 4 to 12 weeks of age. 1H-Magnetic Resonance Spectroscopy indicated deficits in energetic metabolism, tissue integrity, and neurotransmission at both 4 and 12 weeks in MPS IIIA mice, with partial protective effects of A5_3.

Ex-vivo Diffusion Tensor Imaging showed white matter microstructural damage in MPS IIIA, with noticeable protective effects of A5_3. Protein and gene expression assessments displayed both pro-inflammatory and pro-apoptotic profiles in MPS IIIA mice, with benefits of A5_3 counteracting neuroinflammation.

Overall, derivative A5_3 was well tolerated and was shown to be efficient in preventing brain metabolism failure and inflammation, resulting in preserved brain microstructure in the context of MPS IIIA.

Jill Wood

She founded Jonah's Just Begun-Foundation to Cure Sanfilippo in 2010. Later, she established Phoenix Nest, a for-profit biotech company advancing pre-clinical research, enzyme replacement therapies, gene therapies, and natural history studies for Sanfilippo syndromes types C and D. As co-author of six peer-reviewed papers and a frequent subject of media coverage, Jill Wood continues to champion research and advocacy for rare diseases.

Leveraging Remote Video Capture in MPS IIIC and IIID Natural History Studies: Introducing C-RARE for Real-World Evidence to Support Clinical Trial Treatment Efficacy.

Jill Wood[1], Bernice Kuca[2], Paul Williams PsyD[2], Srikanth Singamsetty PhD[1]

[1]Phoenix Nest Inc, Brooklyn, NY, USA; [2]Freelance Consultant, USA.

Two observational studies conducted at Columbia University, examining MPS IIID with six participants over two years (ALL-127) and at CHU de Lyon, France, tracking MPS IIIC with eight participants (JLK-447) explored innovative ways to measure changes in disease progression meaningful to patients and caregivers.

Novel patient-focused clinical outcome assessments were crafted using feedback from caregivers, FDA guidance, and prior research. A prototype Optical Coherence Tomography (OCT) machine designed for use with uncooperative patients successfully captured retinal images, providing valuable biomarkers previously unattainable. The C-RARE initiative launched three new patient-reported outcome questionnaires specifically addressing endpoints important to patients and families.

In addition, a video task protocol encompassing nine daily living activities was well-received, with families showing strong compliance and engagement.

The introduction of innovative imaging and tailored questionnaires has enabled more meaningful data collection, capturing aspects of disease progression that matter most to patients and caregivers.

UT Southwestern Medical Center

Dr. Xin Chen

He is an Assistant Professor in the Department of Pediatrics at UT Southwestern Medical Center. His research focuses on developing AAV gene therapies for neurological disorders, such as aspartylglucosaminuria, with preclinical results in rodents supporting clinical evaluation for these diseases. Dr. Chen is advancing gene therapy approaches for other neurological disorders, incl. MPSIIIC, with the goal of facilitating translation to human patients.

MPS IIIC Gene Replacement Therapy with scAAV9/HGSNAT Vector, JLK-247.

Xin Chen[1], Thomas Dong[1*], Merve Emecen Sanli1, Anjala Jiji[1], Jina Oh[1], Xuefang Pan[2], Alexey V Pshezhetsky[2], Srikanth Singamsetty[3], Jill Wood[3], and Steven J. Gray[1]*

*[1]UT Southwestern Medical Center, Dallas, TX, USA; [2]University of Montreal, Montreal, Quebec, Canada; [3]Phoenix Nest Inc, Brooklyn, NY, USA; *Co-first authors*

scAAV9/HGSNAT (JLK-247) is a gene replacement therapy evaluated for MPS IIIC in a mouse model.

The vector was administered intrathecally to *Hgsnat* P304L mutant mice at postnatal days 7–10 (early dosing) or 150 days (delayed dosing). Efficacy was assessed by behavioral tests, enzymatic activity assays, and histopathological analyses. Safety was monitored through serum toxicity panels, organ weights, and survival analysis.

Early dosing resulted in robust and sustained *Hgsnat* mRNA expression, partial enzymatic restoration in key organs, significant rescue of urinary retention phenotype compared with delayed treatment and improved survival. Impaired novel object recognition was rescued regardless of dosing age, and no adverse effects on body weight or serum toxicology were observed. These findings support JLK-247 as a promising gene therapy candidate for MPS IIIC.

GLP toxicology studies will be conducted to further assess the safety profile of JLK-247 in rats and support the advancement of this experimental therapy toward clinical application.

04

Sponsors & Partners

WE WOULD LIKE TO EXTEND OUR WARMEST THANKS TO OUR PARTNERS WHO ARE PROVIDING FINANCIAL SUPPORT FOR THIS EVENT AND MAKING IT POSSIBLE.

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05

Logistics

THE EVENT IS TAKING PLACE AT THE INTERCITYHOTEL GENEVA, CONVENIENTLY LOCATED NEAR GENEVA AIRPORT AND THE TRAIN STATION.

IntercityHotel Geneva
Route de Meyrin 127
1219 Châtelaine, Switzerland

HOW TO GET THERE?

Public transport

- Tram 14 or 18, Avanchets-Etang STOP
- Bus 28, Etang Casa-Bamba STOP

Free airport shuttle service every 20 minutes

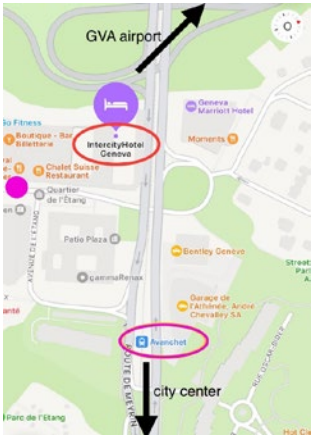
- Departure from Airport to the Hotel, every 20 minutes: From 4:40am to 9:00am, then from 10:00am to 06:40pm, and from 07:40pm to 11:40pm.
- Departure from Hotel, level RI, to Airport, every 20 minutes:
  From 4:30am to 08:50am, then from 09:50am to 06:30pm, and from 07:30pm to 11:30pm.

PARKING

A parking lot is available directly underneath the Intercity Hotel.

Red: IntercityHotel Geneva

Pink: Bus and tram stops



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Key Contacts & Practical Details

If you would like more information about the conference, our activities, or the research projects we support, please do not hesitate to contact us:

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External Scientific Consultants:
Dr. Andrea Dardis & Dr. Alexander Alanine

Organizing Committee

Dr. Ron Hogg, Scientific Consultant, in charge of the programme and speakers

Frédéric Morel, Founding President, Fondation Sanfilippo Suisse

Corinne Féry-von Arx, Board Member, Fondation Sanfilippo Suisse

Dr. Danielle Bertola Reymond, Board Member, Fondation Sanfilippo Suisse

Anaïs di Nardo di Maio, Board Member & Family Representative, Fondation Sanfilippo Suisse

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