Agenda and speakers Thursday 14 November

Day	Time	Subject	Presenter
Thu	09:00	Welcome incl. introduction of participants	Mette Behnke, DK
Notes: Welcome to the 3rd Nordic conference, 83 participants this year. We are here because we want a greater corporation between the Nordic countries, and this year broadened with professionals from more countries – holistic perspective. Mentioning sponsors. Thanks! Captured on film by Ingun and also tomorrow by Danish TV. Short notes will be taken. Short self-introduction of participants.			
Thu	09:20	A reminder; Why we are here	Trine Paus, NO
Notes: Mixture of sorrow and hope – my daughter died peacefully in her own bed 28 years old. Remind us why we are here today. You all bringing hope to NCL families! Shared her family's story. Mari's story reminds us of the need for further research on this rare disease.			
Thu	09:30	How to ensure Patient, Parent, Public Involvement (PPPI) in NCL research - experience at the Hamburg NCL specialty clinic	Angela Schulz, UKE Hamburg, DE
Notes: This presentation shows your importance as parents. All research should involve the children – with or by patients or parents rather than being about them. This includes language, developing questionaries, joint planning, relevant outcomes and public information. The most important thing is that this will benefit our children, and in addition also benefit the researchers. There are more and more internation examples of including patients in research. 7 centers in Germany focusing on rear diseases funded by the government. Information about the center in Hamburg. Also collaborating internationally. Gave example of how NCL is included. Focus: Improve early diagnoses, optimize standard care, collect precise natural history data, establish evaluation tools and outcome measures. Feedback from parents: Importance of Natural History, collaboration with regulatory agencies, collaboration with medical companies. A large cohort of patients and families coming to Hamburg providing important biomarkers and quality of life assessments. Antibody detection is important. Developed a new method to isolate lysosomes for analyses. Research is not only collecting data, but also giving something back to the families. Phone: +49 (0) 40 7410-20440. Open to international participants. Emphasis on collaboration between investment companies, parents can emphasize this.			
Thu	10:00	Support for families of children with CLN3-disease concerning emotion and behaviour: a Delphi-study	Yvonne Kruithof, Bartimeus, NL
Notes: Shared own experiences with a ncl child and his different emotions connected to changes and development of the disease. Motivates to provide help. Researchers started			

analyzing data from 8 participants connected to emotions and behaviors. The first result is an overview of behavioral and emotional problems. Another result shows changes in behavior. Anxiety was a result with all patients. Third result shows what causes behavioral and emotional problems. Published an article from this research. The second research is the Delphi study including 8 parents and 21 professionals. Three rounds of questions from open questions to more specified questions. Conclusions from the study: Guidelines for supporting emotions and behavior, list with advice, checklist for monitoring the developing and also including and overview checklist. Further the checklist will be implemented and developed. Results will be assessed and further studies done.			
10:25 Coffee Break			
Thu	10:55	Moving forward! - From data to knowledge to advice, to preserve walking for as long as possible	Marieke Schut & Linda van Eck, Bartimeus, NL
Notes: Presentation from psyholigists from NL, National expertise center. Four specialists teams. Children can every year visit the hospital for various tests. Walk tests to try to see changes in walking. Setuptest 6 minute walk for 10 meters. As many meters as possible for 6 minutes also with walking aids. Different was of walking is tested and filmed. Some films was shown. Comparsion has been made between CLN children and children with only visual imparment and you can see a big difference. Stiffer movement, start stop problems, delay for example. How to maintain walking? Important to keep the walking speed, give the child your arm to the child and describe the surroundings. Also music can help. It can also be good to walk on a treadmile, You can also run on the treadmile. When looking on a movie you can see that the speed is much higher for the child. The advice is to keep walking with the child.			
Thu	11:10	Research update from Norway	Ingrid Helland, Oslo University Hospital, NO
Notes: Miglustat, Norway has applied individually, and all children has been granted the medicin off label. A regisrty has to start with startup status and tenh children will be followed closely. Mental health investigation, by questionaries, course of mental health during the life of NCL 3. The paper is in process so no results can be shared yet. Another project is how parents inform children and siblings. Not published yet, but some results were shared. The parents in the study believe that the children should have a basic understanding of the illness, but they also would like more support around these questions. Collaboration between Norway, Sweden and Denmark.			
Thu	11:20	Research update from Sweden	Niklas Darin, Queen Silvias Hospital, SE
Notes: Project, Living with CLN3 in Scandinavia: Background – great psychosocial impact, burden on the family and also the support system is different between the three countries.			

The goal is better health and care provision in Scandinavia and beyond. The main objective is to describe the phenotype spectrum and also the course of the life of the childrens life and the familys life and compare the different countries. You can see differences between the countries, Denmark has one center and Sweden has not, for example. A study specific survey has been made. Long term hopes are a register and study endpoints.			
Thu	11:35	Research update from Denmark	Mette Handrup & John Østergaard, Aarhus University Hospital, DK
Notes: NCL center in Aarhus also adults also other disorders not only NCL. Doctors, nurses and other professions. Gastrointestinal system in CLN3, bowel and bladder dysfunction, in late teens, gradually lose control. With progressive disease the neurons are getting fewer and the transaction time is going slower. A clinical study in underway to investigate the gastrointestinal system. The clinical study is performed by a questionaire in Denmark, Norway and Sweden. Denmark has already started. If the problm is what they believe, can we treat this problem? New HRV study, published, the aim is to look into treatment possibilities. Fear related behavior, they have looked at what is happenig with the heart during these episodes. Some patients have these fearful periods, and you can see an increase when the children get older. Focus is to identify potential treatment, stimulation of the vagal nerve could potentially restore the imbalance. The aim is to start a pilot study.			
12:00 Lunch			
Thu	13:00	Finding new ways to treat CLN3 disease: Latest update	Herman van der Putten, NCL-Stiftung, DE
Notes: Mission of foundation is networking, education and science and getting to the fundamentals of CLN3. Studying the subcellar metabolism has begun to unmask the fundamentals of CLN3 loss. LysoIP was developed to study intra lysosomal metabolism in cln3 diseases. A lot of insight is wrong in the disease. Massive accumulation of the GPD s. Cln3 defficiency is not the only problem. Cln3 deficiency also affects catabolism and recycling of other main lipids. While many of these accumulate the levels of the endo-lysosome specific lipid BMP and multivesicular bodies are reduced. BMP deficiency occurs in many CLNs. Lysosomal damage and repair in CLN3 is still poorly understood parameter in the disease. Microglia guardians of brain helath, crtitical rolie in CLN3 disease likely, microglia target may be benefitial. Cln3 depletion has many faces for example glial dysfunction			

Hope to focus on the treatment towards the core in the future instead of a lot of drugs for example Miglustat.

Thu	13:30	Project Butterfly: A Personalized Antisense Oligonucleotide. A Medicine for an Ultra-rare Form of CLN3 Batten disease	Michelle Hastings, University of Michigan, US & Yael Shiloh-Malawsky, University of North Carolina, US

Notes:Zebronkysen, Project Butterfly. Making a personalized antisense oligonucleotide medicine for cln3 batten disease.

Forebatten foundation founded by the parents to the girls. The girls have a rare mutation. Found a pathway for this mutation. There are many different ultra variants associated with CLN3.

There are two types of ASOS. Zebrokysen is a splice switching ASO.

Clinical study design, dose interval 3 months with a dose escalation. The first dose was given i June 2024. The drug is pretty safe. Outcome measures like walk test, seizures, MRI and more. Primary goal for the study is safety and tolerability, also looking at disease progression as secondary objectives.

Thu	14:00	The caretaker angle: Recruitment, skills, focus and support	Rikke Krause, Duos A/S, DK

Notes: How is to be a caretaker to our children.
Important with a stable team. They cannot be part of the family. Important not to be to involved as a caretaker.

DUOS is a company in Denmark that help more than 5000 citizens every year.
The industry is struggling with lack of employees. High churn for the employees who are in the industry.

Mentally burdensome due to that caregivers are working closely with the relatives

14:25 Group Picture followed by Coffee break			
Thu	15:00	Childhood dementia in education	Bengt Elmerskog & Anne-Grete Tøssebro, NO

Notes: Childhood dementia is a problem in the school to handle especially when the children also is blind.

Children with dementia have potential for action but need support to maintain skills. We know of the upcoming dementia and can prepare for the child.
The window of opportunities.

There is a lack of knowledge in the schools about how to handle the childrens dementia.

The children move to different schools and we need to train new staff and this is very demanding and not good for the child due to that it takes time for the staff to learn how to take care of the child in the best way. Often when everything is in place it's time for the child to change school.

Vision – educational structure with varies competence.

Thu	15:25	Cognitive and adaptive outcomes in CLN3 Batten disease	Heather Adams, University of Rochester Medical Ctr., US

Notes: National history study is one of the things they have worked with.

Cognition and what is happening with the childrens in different ages. Early in the disease you can see a change when measured and in relation to pears.

Important with proactive teaching.

Wechsler intelligence scale for children, a change had been made to WISC-5 a never scale.

The old scale is very similar to the new in measuring.

CLN 3 staging system, staging should be based on core features that most impact disability and that can be easily assessed.

Does cognitive progression overlap with CLN3 staging system?

You can see the same patterns regarding the cognitive progression.

Females experience a more severe disease course in batten disease. Progression is faster compared to the males also regarding measuring cognition.

With the Vineland you cannot see that specific difference between males and females regarding adaptive function.

Thu	15:50	Memorial bank: Professional usage to assist quality of life	Anette & Line, Caretakers, DK
Notes: A young mans life in his third stage, 29 years old. Structure and recognizability is very important. The structure is based on what he is used to from earlier in life. A memory bank can be like notes on a keychain, every note representing something he recognizes. Five times a year he travels to meet with his friends with similar conditions. Everything he does he has done before. The goal for the caregivers is to give him quality of life. To learn a few simple signs early in life will be a benefit as the disease progresses (yes, no, pain, toilet). Even though his vocabulary is gone his sounds also give important information to caregivers who know him well.			
16:05 Mini break			
Thu	16:15	Latest update on NCL laboratory research	Jon Cooper, Washington University, St Louis, US
Notes: NCL is not just one disease, but a collective term of conditions sharing some similarities. How does what is missing affect the body and the brain? And therefore, where and when to give therapies. Treatment will be different to the different CLN varieties, with also gene therapy also in development. Resent research has given more understanding to CLN3 function in the cells. Pre-clinical studies are done in mice and pigs including testing pre-clinical therapies. Some things are known about what is happening in the brain, like knowing which cells are dying. Two types of treatments: ERT (enzyme replacement therapy) vs. gene therapy. Researchers are moving from mice to larger animals. CLN1 and CLN2 gene therapies in mice and sheep (CLN 1) are promising. Other parts of the body are also affected, and efforts are made to understand this better. Gene therapy to neuromuscular junctions in CLN3 has given results (sensitivity to pain). The nerval system in the bowel causing it to slow down is also affected and promising studies in mice are ongoing (CLN1, 2 and 3). Results will be published shortly. Simultaneously treatment of brain and bowel in mice are ongoing. Swallowing problems are being investigated.			
17:00 Wrap up of the day, followed by dinner at 19:00			

Agenda and speakers Friday 15 November

Day	Time	Subject	Presenter
Fri	08:20	Introduction to the day	Mette Behnke, DK
Notes:			
Fri	08:30	Clinical Trial Update	Ineka Whiteman, BDSRA, AUS (Virtual)
Notes: Pipeline updates CLN1 RUSH study, a 7 year old child got the therapy last year and it is currently pending evalution. CLN2: Biomarin is conducting the study, that they now call Phase 4, and it is over a 10 year follow up. There are also several different study for gene therapy in retina. One conducted by Nationwide Childrens hospital and a second by Brineura. There is another in Phase ½ by Regenxbio/Tern. Some hickups on the way but recently they announced a merge with Tern.			

Individual Patient IIT in Brazil: Single dose injection. First reports improvements in motor skills and frequency of seizures.

CLN3:
Nationwide Childrens hospital.
Ongoing assessements. No effeciancy data published so far. The program is back from Amicus to NCH.

ASO Zebronkysen was mentioned. The same study that Michelle presented yesterday.

Batten-1 we know that the treated patients have a good safety profile and the effeciancy has been presented as reported lowering of NFL numbers and motor skill progression reduction.

The 6 patients are getting access to compassionate use through the program.

Increase of offlabel use of Miglustat, and data is currently being collected. It is considered if the protocol can be improved by looking at the data from the patients that is on offlabel Miglustat.

CLN5: Neurogene, recently announced that FDA denied the therapy application of AAV9 gene therapy NGN-101.

BDSRA is trying to work on ways to make this program to move forward.

Ineka also talked about that they developeda practical management approach to behaviour and symptoms. Working together with dementia support firm in Australia they have collaborated and built a support service for families. It is not solely for batten disease but also for other diseases with similiar dementia symptoms and problems.

NCL2025 will be held in Australia next year Oct 28 – Nov 1, 2025

Fri	09:00	Kick-start of work-shops 1 & 2:	Mette Behnke, NCL Denmark, DK
Notes:			
Fri	09:05	Intro Workshop 1: Psychoeducation and how to talk with children with CLN3	Yvonne Kruithof, Bartimeus, NL
Notes: They are working on a school with children that have visual impairment in common. Children are often realising that they are different and are often missing out of non-verbal education. Making children aware of their inabilities helps them to better handle their day-to-day challenges.			

She is talking about that there is a theory and research proving that by following their program and methods is showing positive impact.

They have measured the effect of a study that they conducted around these methods.
Academic skills improved and also their wellbeing.

She gives different examples of how you can speak to your child. What can be helpful for the children, and how you can explain different subjects in a pedagogic way.

Fri	09:05	Intro Workshop 2: Biomarkers & NCL's	Tom Wishart, University of Edinburgh & NTU, GB

Notes: Biomarkers could be both structural and behavioral changes that we can measure. Blood or tissues can be used for measure or the UBDRS scale.

It should be able to answer if a therapy could change the cause or progression of the disease.

A biomarker is something that we can measure objectively athat tells us about disease progression and if it is altered by treatment.

You can divide biomarkers in levels of utility – how useful they are, in terms of detecting different things.

Tom was showing examples of how proteins were affected in the different variants of CLN in animal models and talked about how we in the future could draw conclusions of how far the disease has progressed and evaluate different treatment and use them as biomarkers.

09:50 Coffee Break (incl. check-out)			
10:20 Break-out in Workshops			
Fri	10:20	Workshop 1: Meeting children with NCL3: Challenges and approaches	Moderators: Kristine Stadskleiv, OUH, NO & Yvonne Kruithof, NL
Notes:			
Fri	10:20	Workshop 2: What are the roadblocks for developing a therapy?	Moderators: J. Cooper, M. Nickel & I. Whiteman
Notes:			
Fri	11:30	Feedback from Workshops	

Notes:			
12:00 Lunch			
Fri	12:50	Anticipatory grief	Marlene Ramsberg, Løvemamaerne, NO
Notes: Marlene introduced her family and talked about the challenges of having a husband with RP, children with disabilities. One child was born deaf, and her daughter Novalie has been diagnosed with INCL. The feeling to know that your child will probably not live to their eleventh birthday is horrible and from that moment you start to grief. This is defined as anticipatory grief. Preparation for future grief by high level of support is proven to help you go through the sorrow when your child has passed away. She also talks about the feeling of guild of giving up and to see a future that will be easier without your sick child. At last, she read a beautiful poem that she wrote to her daughter when they got the diagnosis.			
Fri	13:05	Openness about the disease – Syver's journey	Øyvind Blindheim, NO
Notes: Øyvind started to tell us that they told his son last year about the CLN3 diagnosis that he has. Syver turns 13 next year. They want to contribute to the batten community by being open and spreading information about childhood dementia. Besides that, they have done several fundraising activities. To be able to raise awareness they have chosen to talk about childhood dementia instead of NCL which is not known to the public. A positive thing about being open with childhood dementia was that Syver doesn't feel alone anymore due to the fact that he has met many other people with different dementia diagnosis. Among many things there have been a newspaper articles and Syver even met the King in Norway, so now he knows too... They are currently filming a documentary "Pappas kamp før Syver".			
Fri	13:25	Childhood dementia in Denmark; A status	John Østergaard, AUH, DK
Notes:			

John started to say that they were inspired by Øyvind and thought that we need to try and do something too. Giving it a name like childhood dementia puts a label on the disease that is understandable.

Now they are trying to find a place where they can spread knowledge about it, and first tries to get attention from the Danish National center of expertise in dementia failed and then they turned to the Alzheimers organization instead. They responded positively and are willing to have continued dialogue around childhood dementia and what they can learn from each other.
Common thing is behavioral and emotional expressions when feeling discomfort, maybe seen as a mirror of consciousness-raising events taking place during crucial episodes in ones' life.

Fri	13:35	NCL organoids - disease modelling and preclinical testing	Magnar Bjørås, Oslo University hospital, NO

Notes:
Magnar started with a background of different organoids that they are working with, like brain, retina and heart.

Magnar's lab is working with some different technologies around organoids.

Organoid technology is uncovering pathomechanisms and testing treatment modalities.
By using single cell technology, you can then analyse every single cell in the treated organoid.

The process is that you take a skin tissue and take a small sample called fibroblast, reprogram them to stem cells. After that you differentiate the stem cells into different types of cells. And that is then grown in the lab to an organoid.

Findings, that mitochondrial activity increased in CLN3 astrocytes. But mitochondrial function has been reported to decrease in CLN3 neurons, and to answer this finding of how the mitochondria is functioning in the brain and how it relates to astrocytes and neuronal death they are working with brain organoids.

With collaboration with Johnathan Coopers lab, they have started to create neuromusclar organoids because John has found that it places an important part in CLN3 disease.

He went on to show images of retinas that they cultivated in the lab, and details about photoreceptors and rods and cones could be seen.

There is no one that can produce this kind of result in such a short time with such good result in the world. That is why they were chosen by an Australian company to help them get approval for a gene therapy trial for RP.

The reproduceable organoids are the key to be able to reliable result and a key to be able to test out dosage.

Magnar showed initial results on models treated with miglustat. No toxicity was found, and single cell analysis is currently ongoing.

Fri	14:10	Evaluation	
Notes:			
14:30 Coffee Break & wrap up			
15:00 End of Conference			