ANNUAL REPORT FOR AGM HELD FEBRUARY 16, 2025

Australian NPC Disease Foundation Inc

ABN: 87 767 010 514

PRESIDENT'S REPORT

Prepared by Mandy Whitechurch

As we reflect on the past year, it is my pleasure to present the President's Report, an in-depth overview of our achievements, challenges, and strategic vision for the future. This report encapsulates the collaborative efforts of our team, the dedication of our stakeholders, and the unwavering commitment to members of the Australian NPC Disease Foundation (ANPDF).

Achievements

Financially

- Sponsoring Reus Valley Meeting held in Switzerland in October 2024
- Contribution to Fran Platts Laboratory for the Catwalk update project
- Engaged Deanna Carpino as General Manager in a paid contract position (minimal hours)
- Engaged Ellie Van Velsen as Project Coordinator for the National Care and Guidelines Project
- A generous donation was received by the late Mala Singh's family as per her wish
- Continuous quarterly contributions to The Florey Institute for Dr. Ya Hui Hung's MRNA gene therapy research.

Development of the NPC Care guidelines

Ellie has worked tirelessly on putting an Australian Niemann-Pick disease type C Guidelines for Care document together. To deliver a guideline for clinicians and reference document for families,

- a Medical Editor was engaged to assist in this project,
- regular medical advisory meetings occurred, and
- regular patient community meetings occurred. Patient families were asked to contribute to Surveys and provide feedback for the guidelines.

Community Engagement

We believe in giving back to the communities that support us. This year, our community engagement efforts have included:

- The engagement of a volunteer through Genetic Counselling/Genomics and Health for student community placement from Melbourne University. David played a huge role in assisting with both the 2024 Annual Conference and Cocktail Fundraiser.
- Attendance to the following events:
    - **State of Childhood Dementia** at Parliament House, Canberra, in September 2024 by Deanna Carpino.
    - **Genetic Alliance Forum** at Parliament of NSW in September 2024 by Ellie Van Velsen and Ali Malone.
    - **Lysosomal Storage Disorder Summit** at Melbourne in October 2024 by Deanna Carpino, Andrew Carpino, Ellie Ven Velsen and Sarah Mercuri.
    - **Rare Voices Australia Summit** in November 2024 by Amy Leddick.

Fundraising Events

- The 2024 annual fundraiser, 'Minds in Motion Charity Cocktail' was a huge success at the Timber Yard in Melbourne raising over $50,000
- Ellie held a taekwondo event in Melbourne with a sausage sizzle raising over $2,000
- Mandy held the first annual NPC Poker Tournament in Benalla which rose over $2,000
- The awareness month 'Silver Raffle' sponsored by the Goat Club, raised over $2,000
- Pip's community again held the saddle raffle and event raising great funds again
- The regular monthly donations have seen a slight increase over the year which is great
- The Sims Metal monthly donations have been consistent and helps keep the bank account topped up
- Family and friends of our community continue to use birthday fundraising events on social media has increased

Challenges

While we have achieved much, we have also faced challenges that have tested our resilience and adaptability. Key challenges this year included:

- The support of families maintaining supply of Miglustat through the RMH – This proved successful for the existing patients, however, disappointing that this will not be offered to new patients in Victoria
- Fortnightly visits to city hospitals for patients on the Cyclodextrin trial continue with the first patient now receiving home infusions in Qld (Tommy)
- Time restraints on Volunteers continues to challenge us with the Executive Committee all having paid employment, caring for their NPC loved ones, energy and time
- First time ever we have put out expressions of interest for both Treasurer, Assistant Treasurer and Secretary with a reasonable response
- NDIS changes making patients funding plans extremely difficult to be appropriately funded

Sustainability

To continue to sustain our progress as a foundation, we as a family community living with Niemann-Pick Diseases in Australia, will continue to work towards our mission of finding better treatment options and hopefully one day a cure for those living with NP-C Disease. We will continue to support one another through our journeys and help those in need when we are able to do so. We are predominantly a volunteer-based foundation, with everyone facing enormous emotional stress as they support their loved ones with NPC and navigate the challenges they face.

We live with grief before we have lost, grief after we lose, and panic of what to do next when it seems all roads have been tried.

We need to continue to support each other and offer compassion and empathy to those around us respectfully. We need our network to broaden to sustain a successful foundation that will continue to grow and contribute to our community.

In conclusion, I am immensely proud of what we have accomplished this year and excited about the prospects of our organisation. Our success is a testament to the hard work and dedication of our team, the support of our stakeholders, and our unwavering commitment to our mission and values.

As we move forward, we will continue to build on our achievements, address our challenges head-on, and pursue our strategic vision with passion and determination. Together, we will create a brighter and more prosperous future for our organisation and the communities we serve. I trust that we will all contribute to the continuity of our foundation by assisting where we are able.

Many hands make light work as they say, and we only have our General Manager employed for minimal hours a month with volunteers contributing hours on top of that. With the growth of the foundation and our presence being acknowledged around the world, there is always something someone can do to help. We are all here for the one thing in common and that is, someone we love dearly is walking the minefield of living with NPC… it's because of them we do this.

Thank you for your continued support and trust in our leadership.

Sincerely,

Mandy Whitechurch
President
mandy@npcd.org.au

ADULT PATIENT LIAISON REPORT

Prepared by Mandy Whitechurch

What a year 2024 has been for us all.

We have had massive struggles with the Royal Melbourne Hospital (RMH) and Johnson & Johnson maintaining supply of Miglustat to its 8 adult patients. Thankfully due to a pretty hairy ride following lots of conversations between Pip, Mandy, stakeholders and the powers-that-be, together with the wonderful support of Professor Mark Walterfang - we were able to have the RMH approve funding of the drug for its existing patients. Though this is great for these patients, sadly due to the cost of Miglustat now in the hands of Johnson & Johnson as owners, no future patients will be able to have the medication funded. This serves such a blow to our community. One family in Sydney have been trying to survive by self-funding for a period and have now been told they are expected to pay a ridiculous $100K plus to be able to source Miglustat.

Trials for the IB1001 continue to run and most of the patients are now on the real thing following a 12-week rotation including a placebo. Intrabio have progressed with the FDA approvals and hopes that their product will soon be available to all with NPC Disease moving forward.

We have the Cyclo trial still in place with participants travelling to the RMH for treatment on a fortnightly basis. It is hoped that home infusions will be implemented to reduce some of the travel burden to our adult patients with young Tommy already receiving the infusions at home in Qld.

It has come to my attention that the supply of the internationally purchased Tanganil is fading with the product not being available to sell internationally. This again is a blow to those who were using this as an additional treatment to regime.

Sadly, we lost our beautiful Mala Singh on the 4th of February 2024 following her experience of a rapid decline in health. We supported Mala's family throughout her journey and continue to be in contact with the family.

There has been challenges that Maz had had with finding Greg appropriate living options due to his progression and even more so with the standard of care being provided in the environment. Deb is going along well in Queensland and is close contact with Amy as a great support person who really understands. Mark and Deb are currently not on any trials

Matthew has shown significant decline with increased memory loss, swallowing concerns and mobility issues arising over the past 12 months. He suffered his first bout of pneumonia last year.

Timmy nearly went 12 months without a hospital admission for a change. However, in January this year, he was admitted to hospital due to another bout of aspirational pneumonia and has slowly recovered well at home.

The lovely Jessica continues to travel the harrowing red eye flights with her Mum to Melbourne from Perth fortnightly and although has shown slight decline continues to be stable.

Our oldest patient Leonie from Sydney has faced many challenges also with hubby Tim having some health issues throughout the year. They hope to attend the 2025 family conference in Melbourne if Leonie is well enough to travel.

We continue to have regular meetings with all the drug companies including those who are yet to commence trials. We actively make our presence known and continue to build our relationships with the stakeholders and have Australia listed as potential sites for upcoming trials for several medications.

Attending the INPDA face to face meeting again in September this year is imperative to maintain relationships and explore what is on offer for patients living with NPC and advocate for our Australian community to make Australia a place these pharmaceutical companies want to bring their trials to.

We have had our long-term Clinician in Professor Mark Walterfang retire in December 2024 from consulting. This has been a huge shock to all his patients, as there has been over 17 years' service to our community by Mark and finding another Mark will be extremely hard. We are yet to be informed who is actually taking over adult patient consulting and will keep everyone in the loop when we are informed.

I want to acknowledge all our adult patients' parents/partners in the challenges that they face as aging adults ourselves caring for adult loved ones. It's a tough gig and I really hope that time allows us to continue to group together to support one another through our journeys.

Sincerely,

Mandy Whitechurch
Patient Liaison Officer
mandy@npcd.org.au

PAEDIATRIC PATIENT LIAISON REPORT

Prepared by Pip Johnston

Another year has flown by!

With recent exciting news of approval of 2 medications in the USA (Miplyffa and Aqneursa), these continuing developments continue to bring us so much hope for treatments for our children. Thanks to all the dedicated, relentless hard work and effort of all involved.

In Australia, we still have 5 paediatric patients participating in the Cyclo Therapeutics trial, with 3 of them on the OLE (Open Label Extension) part now, meaning they are definitely receiving the drug. It has been a long 2 years to get there, and the other 2 patients will thankfully be on OLE next year. Cyclo Therapeutics is planning for a release of preliminary data soon.

We also have a relatively newly diagnosed young patient in Western Australia, and she has recently been granted access to Cyclo Trappsol so will hopefully be starting those infusions very soon 🤞. The diagnosis of such a young patient has highlighted the lack of data relating to Miglustat-use in younger patients and this has, and will continue to be discussed, as part of the development of Australian guidelines for the management of NPC.

Praying for another year of further developments and hope.

Sincerely,

Pip Johnston
Patient Liaison Officer
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NP-C CONSENSUS GUIDELINES PROJECT – ANNUAL GENERAL MEETING REPORT

FEBRUARY 2025

Summary

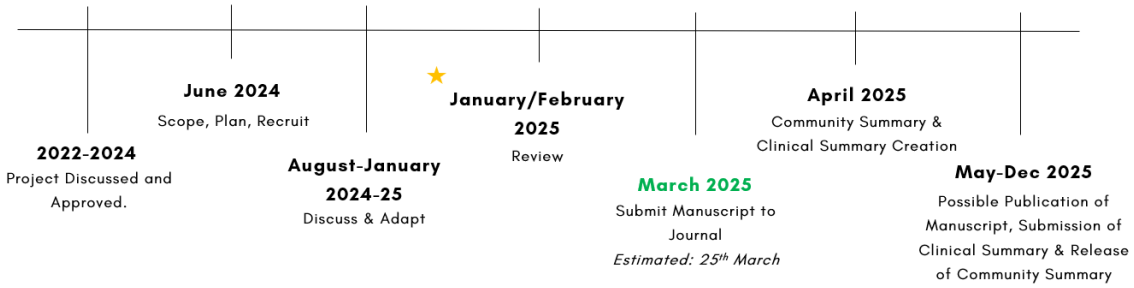
In 2024, the project was able to progress through all scheduled activities as expected, aligning with both budget and timeline expectations. The guidelines are currently in the manuscript review stage, with an expected journal submission date of 25th March 2025. The overall project completion date has been extended from June 2025 to December 2025, to accommodate the creation of an additional clinical guideline summary paper. Despite the additional output and extra time required, the estimated project cost is predicted to be $29,000 in contrast to the original budget of $40,000. Activities for 2025 will focus on the delivery of all outputs and the creation of stakeholder implementation and impact evaluation plans.

For more details on the project plan, please see the project brief.

Overview

Objective: Create and Publish Australian Diagnosis and Disease Management Consensus Guidelines for Niemann-Pick Type C Disease

Timeline:



Estimated Completion Date: 30th June – 30th December 2025*

**Dependent on journal acceptance, review and publication times. Completion of the project would include delivery of the 3 total project outputs described below.*

Key Outputs (titles not formalised):

- Australian Consensus Care Guidelines for Niemann-Pick type C disease (open-access journal publication)
- NPC Care & Guidelines – A Community Summary (ANPDF website publication)
- [New]: Australian Care Guidelines for Niemann-Pick type C disease – A Clinical Summary (open-access journal publication)

Involved Contractors & Members:

- Paid contractors include a project coordinator and medical writer
- Members:
    - Lead Medical Team: 4
    - Community Advisory Group: 6 & Community Liaison: 1
    - Medical Advisory Group: 30

Medical Advisory Group Geographical Spread	
State	**No. Members**
VIC	16
NSW	6
QLD	5
WA	1
SA	1
UK	1

Project Cost

Project Budget: $40,000

Cost to Date: $12,773

Projected Total Cost: $29,000

- Includes:
    - Project coordinator's work hours. Due to a change in circumstance, the workdays of the project coordinator decreased from 2024 to 2025 with no significant impact on operations due to the progressed stage of the project.
    - Medical writing fees for Hazel Palmer (Scriptix) for a total of $8000.
    - $5000 journal submission fee. This is a conservative estimate and may be reduced based on ANPDF charity status or author university affiliations.

Difference: $11,000 surplus

Progress Metrics

Completed activities:

- Recruitment of a medical lead team, advisory board members, and a medical writer.
- A full revision of 39 statements and materials from the 2018 international guidelines via surveys and monthly meetings with advisory members.

- Total meetings to date: 5 Medical Advisory Group, 4 Community Advisory Group, and 3 Lead Team.

Results:

- 75% average survey response rate across all groups
- Average meeting attendance was 53% for the medical group (many reported time-clashes with clinic days), and 77% for the community group.
- Consensus decisions regarding statements, figures and tables from 2018 international guidelines:

Decision	N
Keep	6
Adapt	33
Remove	5
Total	44

Future Activities

- Formulation and review of the primary manuscript. Submission to a journal for acceptance and peer review
    - Journals considered: Biomedical Journal (BMJ) – Neurology, Medical Journal of Australia (MJA), and Orphanet (a rare disease journal)
- Adaptation of the primary manuscript into a summary for the community. Release on ANPDF website.
- Adaptation of the primary manuscript into a summary for clinicians. Submission to a journal for acceptance and peer review.
- Development and execution of a plan to support the implementation of the guideline papers by key stakeholders.
- Development and execution of an evaluation to assess awareness, implementation and impact of the guidelines.

***Prepared by**: Ellie Van Velsen, Project Coordinator*

***Date**: 6/2/2025*

Australian NPC Disease Foundation Inc
Research. Cure. Persevere.
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SAB Report

Prepared by Ya Hui Hung

SAB members for 2024:

* **Brendon Boot** (Australia) IP Group Pty Ltd; Kookaburra Bio Consulting; Harvard Medical School
* **Ashley BUSH** (Australia) Oxidation Biology Group, The Florey Institute of Neuroscience and Mental Health
* **Caroline HASTINGS** (USA) UCSF Bienoff Children's Hospital
* **Ya Hui HUNG** (Australia) Oxidation Biology Group, The Florey Institute of Neuroscience and Mental Health
* **Pip JOHNSTON** (Australia) Tenterfield Vet Clinic
* **Sharmila KISS** (Australia) Royal Children's Hospital
* **Felicity MUNRO** (Australia) Future Directions Fitness
* **Tina SOULIS** (Australia) Alithia Life Sciences
* **Ellie VAN VELSEN** (Australia) student, The University of Melbourne
* **Mark WALTERFANG** (Australia) Royal Melbourne Hospital

- Only one meeting in 2024. This was a hybrid meeting (in-person: The Florey; online: Zoom) held prior to the annual Australian NP-C conference on 20 June 2024.
    - SAB membership renewal:
        * All appointments to the SAB have been renewed for the next 3 years.
        * Ya Hui Hung re-appointed as the chair of SAB.
    - Australian Clinical Guideline project. Items discussed:
        * Ellie Van Velsen has been employed as project coordinator.
        * An overview of the project plan was presented and discussed.
    - ANPDF website:
        * Ellie Van Velsen prepared a 60-page draft for the website refresh
    - Florey research update:
        * Ya Hui Hung provided a brief update of the Florey research activities on developing an mRNA gene therapy for the treatment of NP-C.
- Attachments: 2024 SAB meeting minutes and the Australian Clinical Guidelines project plan outline.

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Florey Research Report

Prepared by Ya Hui Hung

mRNA-based gene therapy for Niemann-Pick Disease Type C1

mRNA-based gene therapy aims to introduce functional NPC1 protein into NP-C1 cells using mRNA. This strategy represents one of the most effective treatment options for a genetic disease such as NP-C. In 2019 we showed normalisation of cellular cholesterol in NP-C1 patient cells *in vitro* after *NPC1* mRNA treatment. Following on from this promising result, research efforts have focused on optimising *NPC1* mRNA to make it more suitable as a therapeutic.

Research activities in 2024:

- Therapeutic *NPC1* mRNA design and optimisation
  - Identified a design that resulted in sustained NPC1 protein expression in an NP-C1 patient cell line.
  - New collaboration with newly established Australian Centre for AI in Medical Innovations (ACAMI) to develop a generative AI model for therapeutic mRNA and delivery system designs.
- mRNA delivery:
  - optimisation of loading of *NPC1* mRNA into extracellular vesicles – this has been more challenging than expected due to the large mRNA size. We are continuing to investigate solutions to achieve efficient loading of *NPC1* mRNA into extracellular vesicles.
  - commenced *in vivo* testing of *NPC1* mRNA in a benchmark lipid nanoparticle formulation provided by MIPS mRNA Core and Colin Pouton as a part of the MRFF grant collaboration.
  - Setting up collaboration with CSIRO to investigate new lipids they have developed in new lipid nanoparticle formulations.
- Completed re-establishment of the *Npc1* mouse colony and froze new embryo stock for storage.

Publications and manuscripts submitted/in preparation:

- Wongsodirdjo, P., Caruso, A.C., Yong, A.K., Lester, M.A., Vella, L.J., **Hung, Y.H.**, and Nisbet, R.M. (2024). mRNA encoded antibody approach for targeting extracellular and intracellular tau. Brain Communications, fcae100.
- Purnianto, A., Mawal, C., Kulkarni, M.M., Su, H., Koukoulis, T.F., Wongsodirdjo, P., **Hung, Y.H.**, Ayton, S., Bush, A.I., Barnham, K.J., and Vella, L.J. (2024). Small extracellular vesicles contain metals and transfer metal intercellularly. Journal of Extracellular Biology *3*, e70012.
- Blades, B., **Hung, Y.H.**, Belaidi, A.A., Volitakis, I., Schultz, A.G., Cater, M.A., Cheung, N.S., Bush, A.I., Ayton, S., and La Fontaine, S. (2024). Impaired cellular copper regulation in the presence of ApoE4. J Neurochem *168*, 3284-3307.
- Le Roux, L., Walterfang, M., Bush, A.I., **Hung, Y.H.** (in preparation). Current state of therapeutic developments for Niemann-Pick Disease Type C.

Grant applications:

- Successful:
    - Ya Hui Hung | 2024 | Financial assistance to enable Niemann-Pick Disease Type C patients and carers to participate at the 2025 Australian Niemann-Pick Disease Type C Conference | National Disability Conference Initiative 2024 – 2025, Australian Government Department of Social Services | AUD$9,999
- Unsuccessful:
    - mRNA Victoria Research Acceleration Fund, Round 3 (CIA: Ya Hui Hung; CDI, Kim Hemsley, Nicholas Smith, and Anthony Cook)
    - 2024 Perpetual IMPACT Philanthropy Application Program (CIA: Ya Hui Hung; Daniel Scott)
    - KHIDI & mRNA Victoria Research Collaboration (EOI; CIA: Ya Hui Hung)
    - 2024 NHMRC Ideas Grant (CIA Ya Hui Hung; Mark Walterfang, Akram Zamani, and Brittney Gurda)
    - 2024 CUREator+ Dementia & Cognitive Decline (CIA Ya Hui Hung; Ashley Bush, Fazel Shabanpoor, Colin Pouton, Emilio Werden, Haydn Wright, and Christina Sparbier)
    - 2024 CRE – Centre of Research Excellence for Next Generation Dementia Therapeutics (CIA: Rebecca Nisbet; Ya Hui Hung, Laura Vella, Douglas Pires, Fazel Shabanpoor, Juergen Goetz, Anthony White, Kevin Barnham, Charles Reutens, Chien-Hsiung Yu)
    - MRFF – 2023 National Critical Research Infrastructure Initiative (CIA Rebecca Nisbet; Ya Hui Hung; Laura Vella, Fazel Shabanpoor, Scott Ayton, Douglas Pires, Emilio Werden, Ashley Bush)

Research presentations:

- **Hung, Y. H.** NeuMessenger: mRNA gene therapy innovations for childhood dementia | 2024 | AusBiotech 2024: Early-stage innovation forum (Melbourne, Australia)
- **Hung, Y. H.** Message for the brain: mRNA gene therapy for Niemann-Pick Disease Type C1 | 2024 | 2024 Reuss Valley NP-C Meeting (Rotkreuz, Switzerland)
- **Hung, Y. H.** An update on the Florey mRNA gene therapy project for Niemann-Pick Disease Type C1| 2024 | 2024 Australian NP-C Conference (Melbourne, Australia)
- **Hung, Y.H.** mRNA gene therapy: A new approach to treat Niemann-Pick Disease Type C and rare genetic disorders | 2024 | Solving Sanfilippo Symposium (Adelaide, Australia)
- **Hung, Y.H.** Message for the brain: mRNA gene therapy for childhood dementia | 2024 | Parkville Neurodegeneration Seminar Series, The Florey Institute of Neuroscience and Mental Health (Melbourne, Australia)
- **Hung, Y.H.** Treating childhood dementia with mRNA gene therapy | 2024 | Soroptimist International of Victoria, Region Meeting (Melbourne, Australia)
- Le Roux, L., Purnianto, A., Vella, L., and **Hung, Y. H.** Optimization of mRNA loading into extracellular vesicles for *in vivo* therapeutic delivery | 2024 | ISEV 2024 (Melbourne, Australia) – student poster presentation

Other activities:

- Student recruitment:
  - 2024:
    * 2x PhD students
    * 2x Master of Biomedical Sciences students, The University of Melbourne
    * 1x Master of Biotechnology student, The University of Melbourne – completed. Currently employed as a casual RA while waiting for scholarship.
    * 1x 3rd Year work placement students, Deakin University – completed.
    * 1x Monash Engineering Co-op Education Program intern/RA1 – completed.
  - 2025:
    * 1x continuing PhD student.
    * 1x PhD students (awarded ATSE Elevate Scholarship), The University of Melbourne – commencing 24th Feb 2025.
    * 1x PhD student (in application/awaiting scholarship), The University of Melbourne – currently employed as a casual RA.
    * 2x continuing Master of Biomedical Sciences student, The University of Melbourne.
    * 1x discontinued PhD student due to challenges with co-supervisor. Currently employed as a casual RA to assist with experiments.

Projected research activities for 2025:

- Continuing with testing new *NPC1* mRNA therapeutic designs *in vitro* in NP-C1 patient cell lines.
- Continuing with optimisation of *NPC1* mRNA loading into extracellular vesicles.
- Proof of concept pilot study of *NPC1* mRNA-LNP treatment in Npc1 mice.
  - Investigation of different LNP formulations with potential to cross the blood-brain barrier against a benchmark LNP formulation (not capable of crossing the blood-brain barrier).
  - Investigation of mRNA-LNP delivery directly to brain cells by intracerebroventricular injection.
  - Determine dosing regimen of *NPC1* mRNA-LNP.
  - Commence chronic treatment toxicity study and outcomes to assess *NPC1* mRNA therapeutic efficacy.