Sanfilippo Children's Foundation

Annual Update 20/21

Our Purpose

To drive research for a world without Sanfilippo Syndrome

By funding research, raising awareness and advocating for improved outcomes, we empower families now and find a cure for tomorrow.

What is Sanfilippo?

Sanfilippo is a genetic condition that causes fatal brain damage. It is a type of **childhood dementia** and most patients never reach adulthood.

Over time, brain cells fill up with waste that the body is unable to process. As the brain gets progressively damaged, children experience severe hyperactivity, disordered sleep, loss of speech, cognitive decline, cardiac issues, seizures, loss of mobility, and finally death, usually before adulthood.

There is currently no treatment or cure available to children diagnosed with this devastating disease. Researchers around the world are working hard to develop effective treatments, with several clinical trials already completed or underway.

Our Research

With your help we've committed just over $5.4 MILLION to 33 PROJECTS in the search for treatments and a cure for Sanfilippo

In 2020, six new research projects were funded and one project awarded follow on funding. A total research commitment of $705,786

2020

3 projects looking into novel therapies -

(1) developing drugs to target gene reading, (2) developing chaperones to address the root cause of Sanfilippo B, (3) testing drugs to reduce protein aggregation and reduce inflammation in the brain, slowing the progression of the disease.

2 projects investigating disease mechanisms and new therapeutic targets -

(1) Developing zebrafish models of Sanfilippo types A, B and C to improve understanding of disease processes and test new therapies, (2) Investigating the link between brain cell signalling, inflammation and the cognitive symptoms of Sanfilippo

1 new challenge award bringing together diverse collaborators -

investigating a key inflammation pathway involved in disease progression for Sanfilippo.

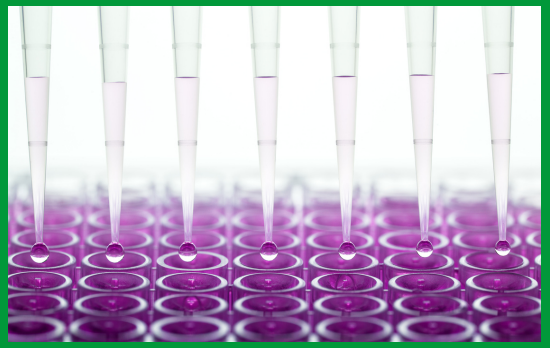
1 project awarded follow on funding to pursue drug candidates -

getting one step closer to potential clinical application.

* includes projects in Australia, Italy and Canada

7 projects funded*

$5.4 million



33 projects

We aim to maximise the impact of our funds by identifying research that has the potential to deliver the greatest benefits and outcomes for our families.

- we are making progress!

The latter months of 2020 and early 2021 saw the completion of 6 research projects. 4 of these were incubator grants designed to develop new insights that improve the understanding of Sanfilippo, with the potential to inform future research.

"New therapeutic strategies for the treatment of behavioural symptoms in Sanfilippo" investigated the behavioural symptoms of the disease to better inform drug development and clinical practice. Despite delays due to the COVID pandemic, the project was completed in February 2021, identifying two drugs that reduced hyperactivity, reduced abnormal repetitive behaviour and increased social interaction in Sanfilippo mice. These are significant outcomes for working towards managing the disease and improving quality of life. Some of the findings were published in Nature Communications in June 2021.

"Generation of 'super active' variants of lysosomal enzymes to treat the CNS in Sanfilippo Syndrome" was aimed at identifying an enzyme variant with enhanced function that could be used for gene therapy and other purposes. Researchers unfortunately experienced issues with the chemistry and the molecule required for the project could not be synthesised in sufficient amounts. The project concluded in April 2021. Valuable information often comes from what we "can't" achieve.

"Creating a MPSIII zebrafish model and brain specific in vivo lysosome reporter for drug screening and in vivo imaging of disease pathology" resulted in the creation of the world's first zebrafish model of Sanfilippo. The project concluded in January 2021 providing a new research tool and insights into the molecular and behavioural aspects of the disease. Initial results from the project were published in May 2021.

$5.4 million

"Targeting Misfolded Proteins for Therapy of MPSIIIC" aimed to identify potential chaperone drugs to improve the function of the type C enzyme, HGSNAT. This project experienced initial delays, compounded by pandemic related delays in 2020, however, upon it's conclusion in January 2021 two potential chaperone candidates had been identified. The most promising drug was supplied to the drinking water of three-week old type C mice, and these mice showed improved memory performance in two behavioural tests.

The success of the majority of these incubator grants is already informing future research projects. A further research project building on the outcomes of "New Therapeutic strategies for the treatment of behavioural symptoms in Sanfilippo" is committed to for 2022. More on that next year!

The remaining 2 of the 6 completed projects were PhD Top-Up Scholarships awarded to promising researchers with enormous potential for ongoing contribution of expertise in the field of Sanfilippo research.

Andrew Shoubridge of **The University of Adelaide** and **SAHMRI** was granted a 3-year top-up and submitted his PhD in late 2020 after commencing it in 2017. His project was titled "How are the neurons damaged in Sanfilippo and how can it be prevented?" He investigated brain cell structure and function in type A mice and found reduced numbers of dendritic spines, which could contribute to cognitive decline.

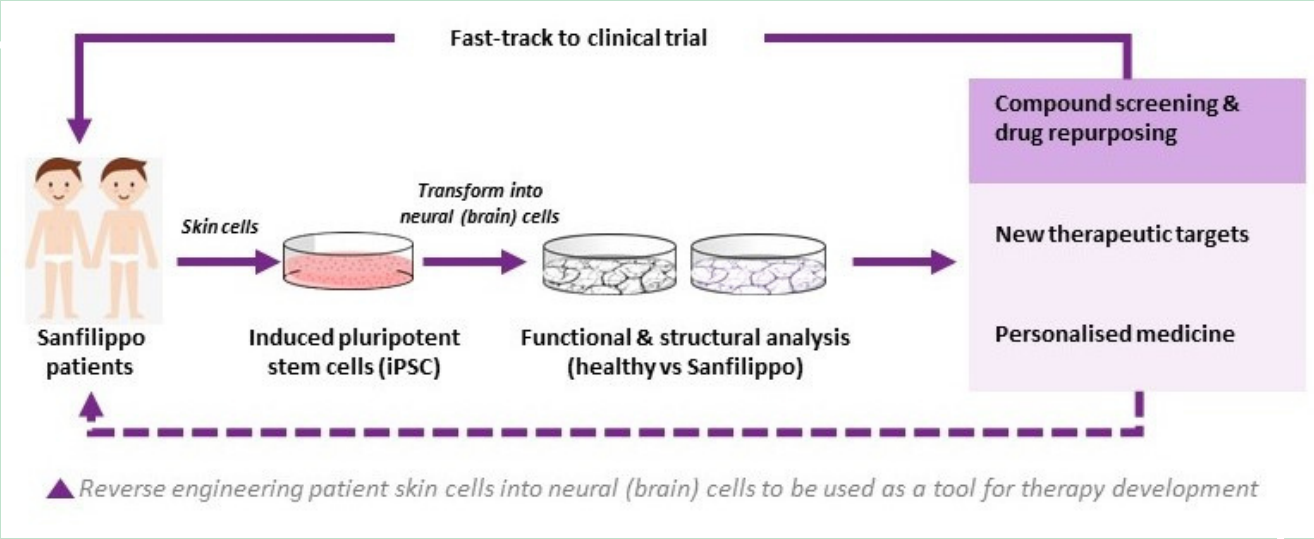
Laura Hewson received a two-year top-up scholarship for her PhD at **The University of Adelaide** titled "Investigating the molecular mechanisms that mediate neuropathology in Sanfilippo Syndrome". Her top-up scholarship commenced in 2018 and a final report for the project was submitted to the Foundation in March 2021.

33 projects

Brain in a Dish

The Brain in a Dish project began in July 2019 with the aim to grow cells in the laboratory from children with Sanfilippo Syndrome that mimic or model what is going on in their brains.

The researchers then compare the cells from children with Sanfilippo with those from healthy children. They study how they look, how well they are able to transmit signals to each other, what genes are being switched on and off and the processes going on inside the cells.



They will then add hundreds of different drugs to the cells to see if any of them can improve the health of the Sanfilippo brain cells.

To date there has been great progress converting skin cells to brain cells:

The project is just over halfway through. Skin samples have been collected from 5 Sanfilippo & 5 age-matched healthy children. Skin cells from 3 patients and 3 healthy children have been converted into stem cells, then immature brain cells and finally mature brain cells. One batch of patient and control brain cells has been growing for 60 days and is "looking beautiful". It's this mature stage that's needed for them to be analysed to look for differences between the Sanfilippo and healthy cells. From here the next steps include analysing the structure and function of the cells using a microscope and innovative biophotonics techniques to reveal biological differences in the cells. Once the analysis is done and all the samples grown into mature brain cells, researchers can begin testing the panel of drugs on these cells.

There's been a few bumps along the way:

The first batch of brain cells "collapsed" before they reached a mature stage. This is not unusual in cell culture, but it takes time to regrow the cells to maturity.

The team identified that some of the materials used to grow the stem cells make the microscope and biophotonics analyses more challenging so they need to identify the best materials to keep the cells healthy, and make the analyses accurate.
While quality control at each step of growing the cells is time-consuming, it ensures the results obtained from the cells are of high quality.

We're excited about what this science can enable:

An exciting opportunity from this project is the chance to expand our collection of skin samples to include individuals with less severe or attenuated forms of Sanfilippo.

Our People

Our team is made up of passionate people committed to driving research towards a world free of Sanfilippo Syndrome.

They bring a collective wealth of energy, enthusiasm and expertise to our cause.

Our Team

Victoria Bowring - CEO
Emma Kirkman - Fundraising Manager
Dr. Lisa Melton - Research Manager
Danielle Cini - Research Program Coordinator
Erene Keriakos - Bookkeeper
Kristina Elvidge - BIAD Project Manager

Our Board

Megan Donnell - Founder/Director
Paul Schoff - Director
Angeline Veeneman - Director
Mark Arnold - Director
Alison Butt - Director

Our Scientific Advisory Board

Professor Ian Alexander
Associate Professor Kim Hemsley
Dr. Nicholas Smith
Dr. Michel Tchan
Associate Professor Sarah Spencer
Associate Professor Karin Borges
Dr Jana Vukovic

Our Founder

Megan Donnell

During the past year our Founder, Megan Donnell, embarked upon a new journey to help the families of **all** rare genetic conditions resulting in childhood dementia. In December 2020, with her legacy in the hands of a new CEO and trusted team, Meg launched the Childhood Dementia Initiative.

Childhood Dementia Initiative is challenging the world to think differently about the childhood dementia disorders, to consider them as a collective and focus on the commonality of presentation (dementia) in order to drive progress in therapeutic development and care and quality of life for all childhood dementia disorders.

The Legacy

"The 7 years I spent running the organisation were professionally the most challenging, but also the most fulfilling. Personally they have been the most heart-breaking, but also the most empowering. So to reflect on this time it is impossible to separate the personal and the professional. After all, I started the Foundation in response to the breathtakingly, heart-searing grief of both my children, Isla and Jude, being diagnosed with Sanfilippo.

From day 1, I was surrounded by the most incredible support to make a difference for kids with Sanfilippo. From fellow families who also love a child with this dreadful disease, to complete strangers who were able to imagine for a moment what it is like.

From Doctors and researchers who have dedicated their lives to Sanfilippo, to celebrities who understood the power their following had in generating support. Each and every one wanted to make a difference.

I have been supported by dedicated employees, generous donors, creative fundraisers, tireless volunteers and an unflappable Board. Everyone has given, and continues to give, both personally and professionally. This is the essence of the Sanfilippo Children's Foundation.

While I am no longer involved in the day-to-day operations of the Sanfilippo Children's Foundation I have not gone far, as I remain on the Board of the Foundation. I am excited by the opportunities that exist for both organisations, individually and collaboratively, and as always **I am looking forward to a world without Sanfilippo**."

Isla and Jude

Our Community

With thanks to the generosity of our community - Sanfilippo families, sponsors, donors and philanthropists - we have been able to fund over $5.4 million of research to strive for a world without Sanfilippo.

The McCoombes

Oliver McCoombes was diagnosed with Sanfilippo at the beginning of 2020. The McCoombes family shares their heartbreaking journey to diagnosis and their hopes for funding future research in honour of Oliver.

When Oliver started kindergarten, his development slowed down but the behavioural issues we were seeing really ramped up – he had become very hyperactive! We'd noticed he was also constantly chewing his hands.

We had been seeing a speech therapist and doing occupational therapy and although Oliver was making some progress, it was extremely slow and he was not where he should have been.

He never made much progress with his speech and we started to wonder if there was an underlying cause. We shared our concerns about Oliver's development with the paediatrician, and it was this, coupled with him noticing certain facial features in Oliver, that prompted genetic testing.

Discovering that Oliver had Sanfilippo Syndrome was devastating. To go from having what we thought was just a developmental delay to having a terminal disease, a syndrome that will slowly rob him of everything, made our world come crashing down.

"He's such an affectionate and active little boy, so being told he won't be like that forever is one of the worst things a parent can possibly hear. Oliver's laugh and smile are infectious, and he's always talking to everyone when we go out. "

Since diagnosis we've had our ups and downs. There's not a day that goes by that you don't think about Sanfilippo but at the same time we want to treasure the time we do have with Oliver and create happy memories. Home life has become a bit more hectic with Oliver having many more doctors and specialist appointments.

Our hopes and dreams for Oliver are that we will get to see him grow up, and that he won't have to suffer. Oliver deserves every chance at life.

Stepping Up

We were amazed and humbled at the number of families, carers, friends and colleagues who stepped up to support each other and Sanfilippo Children's Foundation in an unusual and challenging year.

Steps 4 Skye

"In August, two amazing carers set themselves a challenge. Teghan Henderson and Bree Pellow, who care for 10-year-old Skye Robson who has Sanfilippo, rallied 15 walkers to each walk 15,000 steps per day for an entire month.

Steps for Sanfilippo

Our village stepped up last November for our virtual event. An enthusiastic 89 steppers set themselves a goal to complete as many steps as they could in a month. We were excited and grateful for everyone's commitment to stepping 100s and 1000s of steps

Noah's K9 Fun Run

On April 24 over 100 people and their K9 friends, came to Sandgate in Brisbane to step it out in Noah's K9 Fun Run. This fantastic event was organised by the beautiful Bevan family in honour of their son Noah.

Larapinta Hike For Hope

In 2020 Covid-19 turned the world not inside out, but outside in. After continuous lockdowns, cancellations of events, delays in research and many other challenges, we were able to finish the year with the ultimate challenge of a positive kind. A group of 16 amazing humans came together for different reasons but with a common purpose - to hike the Larapinta Trail for 5 days to raise much needed funds and awareness. They braved icy cold waters and climbed Mt Sonder in the darkness to watch the sun (and hope) rise. Every step they took was a step closer to a world without Sanfilippo Syndrome.

no mountain too high

A Heartfelt Thankyou

We are so grateful to the following **Trusts and Foundations** for the significant ongoing support of our research and also to those who wish to remain anonymous.

- Vinva Foundation
- Petersen Family Foundation
- Ripple Foundation
- Lady Fairfax Charitable Trust
- Ha Ke Na Foundation
- St George Foundation

Sanfilippo Children's Foundation wishes to acknowledge our endless appreciation to the following individuals and organisations for providing **Pro-bono Professional Services.**

- Jane Ann Gray, PWC - Legal Services
- Bentleys NSW - Auditing

We would also like to thank our **Board of Directors** and **Scientific Advisory Board Members** for the time, knowledge and expertise that they so generously give to our organisation. All members of these Boards participate in a completely voluntary capacity and are the foundation of our success.

Our Financials

Giving is not just about making a donation. It is about making a difference.

Financial Year 19/20

Income

Our total consolidated income was **$702,610**

Expenditure

Our total expenditure was **$2,186,624**

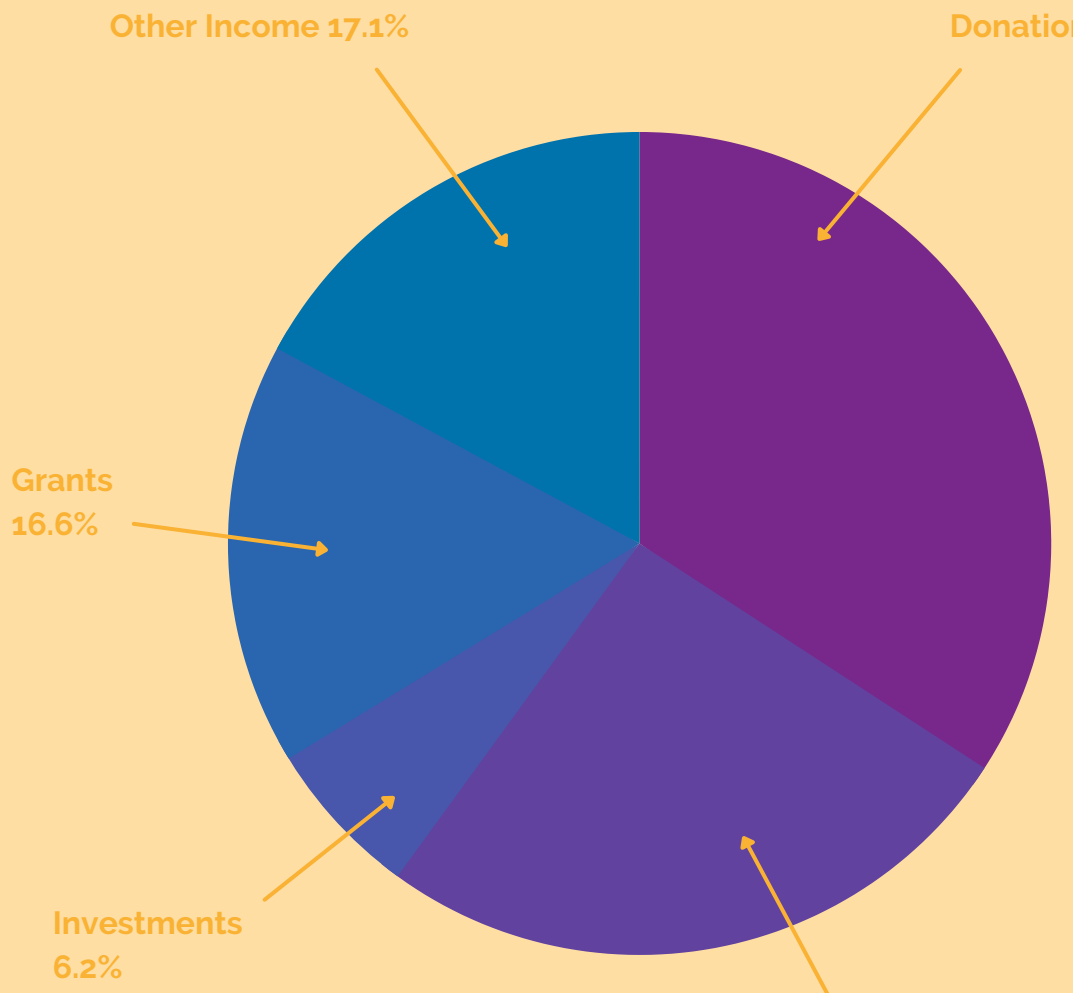
Research & Program Investment

Our investment in research and programs was **$1,602,437**

Research & Program Committment

Funds allocated to ongoing research and programs is $**2,972,222**

Income Sources



* For a full copy of our audited financial report please email info@sanflippo.org.au

Financial Year 19/20

Our Gratitude

2021 began with the hope of life returning to a "new normal" with fewer challenges and less anxiety about what the future holds. Yet we continue to navigate the chaos and uncertainty of a world seemingly beyond our control, finding ways to adapt, adjust and innovate in order to continue our vision to drive research for a world without Sanfilippo.

Despite these challenges we remain committed to this vision and our work here at Sanfilippo Children's Foundation, and whilst we are making progress, there is still much to do. Now more than ever we need to collectively utilise our limited resources to ensure that we maximise our impact. It is through the unwavering generosity and support of our incredible community of researchers, clinicians, donors, sponsors, families, volunteers and fundraisers that we are able to do this.

Thank you to each and every one of you for believing in us and showing us such incredible support. It is this that drives both our research and the resolve of our team!

With gratitude and hope from the bottom of our hearts,

" The SCF Team "