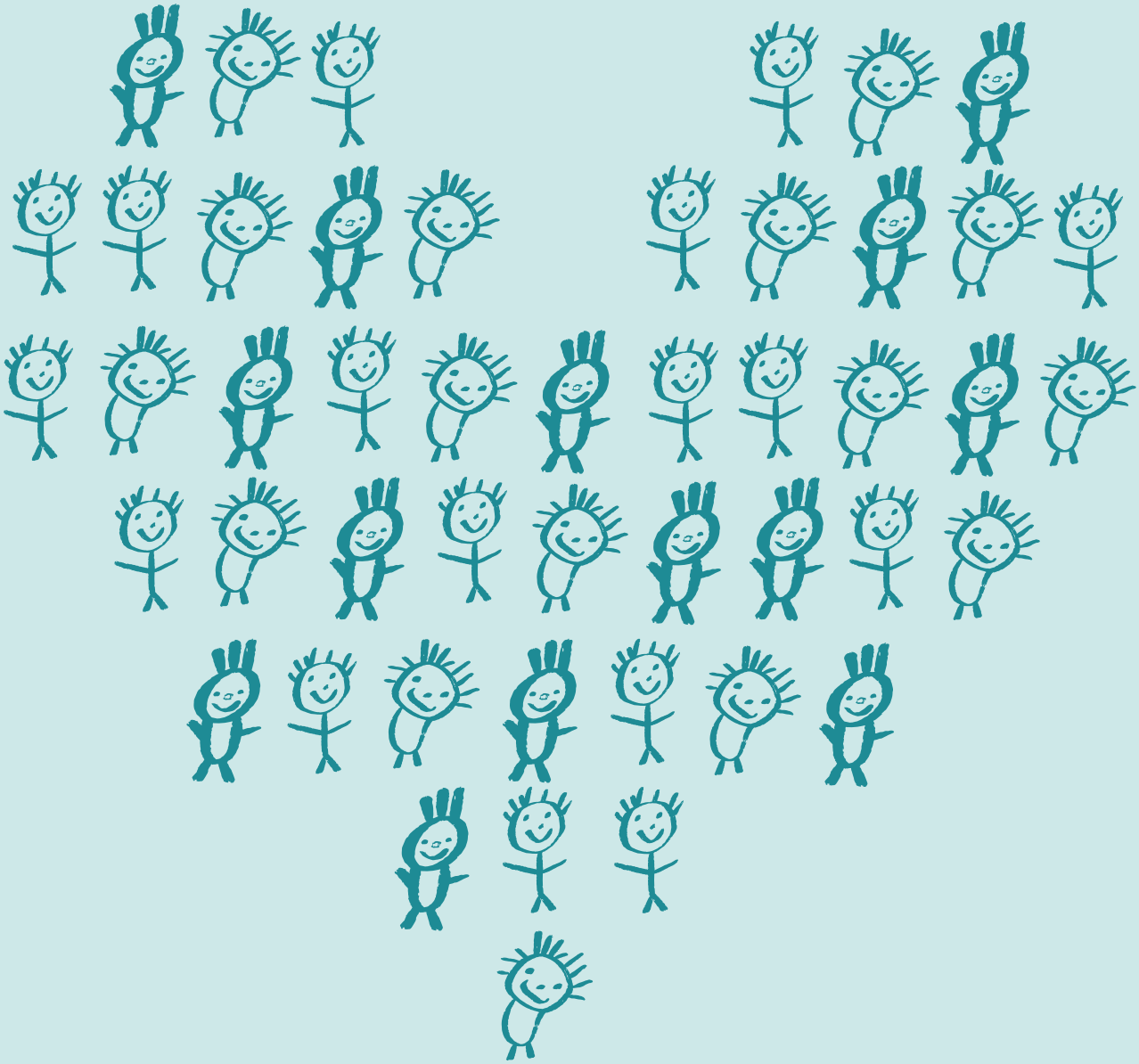
IMPACT REPORT 2021

AGO2

In This Report

AGO2



Message From the President

"We wanted answers to our many questions, to connect with others with a similar experience and the prospect of a treatment for our daugther."

- Nora Leonardi, PhD

Our daughter Paula was diagnosed with an ultra-rare disease in 2020, which didn't even have a name yet. We were told that nothing could be done.
We felt alone, deeply saddened and powerless. We wanted a treatment for our daughter, high-quality information, and a patient community to share and support one another.

With Dr. Lessel's and Prof. Kreienkamp's support, we founded the first patient organisation dedicated to AGO2 globally in 2021. We focused on getting up & running - tax exemption, accreditation with various bodies, and last but not least a website. We are extremely grateful for the pro bono support by Stefan Kempf of vanilla.ch to launch ago2.org.

We've also had the chance to get to know other patient families, both from our own and other communities. So much warmth and caring!

We sincerely thank all supporters and donors for their solidarity and trust.

Who We Are

AGO2 Association is a patient family-led support group for Lessel-Kreienkamp syndrome, founded by Nora Leonardi and Christoph Basten in 2021 after their daughter Paula's diagnosis.

AGO2 is a non-profit association exempt from taxes in Switzerland and is listed in the commercial register of Zurich, Switzerland.

Our mission

We are dedicated to improving the lives of children and families affected by AGO2/Leskres syndrome by

- finding and funding paths to treatment,
- connecting families,
- raising awareness.

Team

Dr. Nora Leonardi
President

Prof. Christoph Basten
Vice-President &
Treasurer

Antje Bulmann
Patient & Public
Relations

Stefan Kempf
Design & Website

Advisory board

Dr. D. Lessel
Scientist, University
Medical Center
Hamburg-Eppendorf

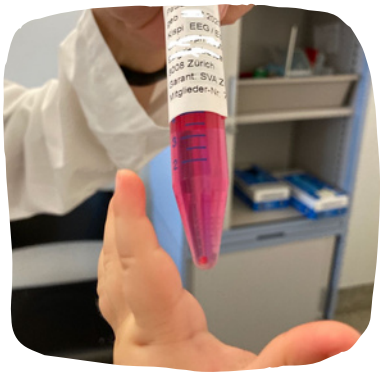
Prof. H.J. Kreienkamp
Scientist, University
Medical Center
Hamburg-Eppendorf

Prof. G. Meister
Scientist, University of
Regensburg

Highlights 2021

Find and fund paths to treatments

Welcomed 3 leading researchers to our scientific advisory board: Dr. Lessel, Prof. Kreienkamp, and AGO2 expert Prof. Meister



Donated patient skin cells to the AGO2 cell bank to establish further stem cell lines

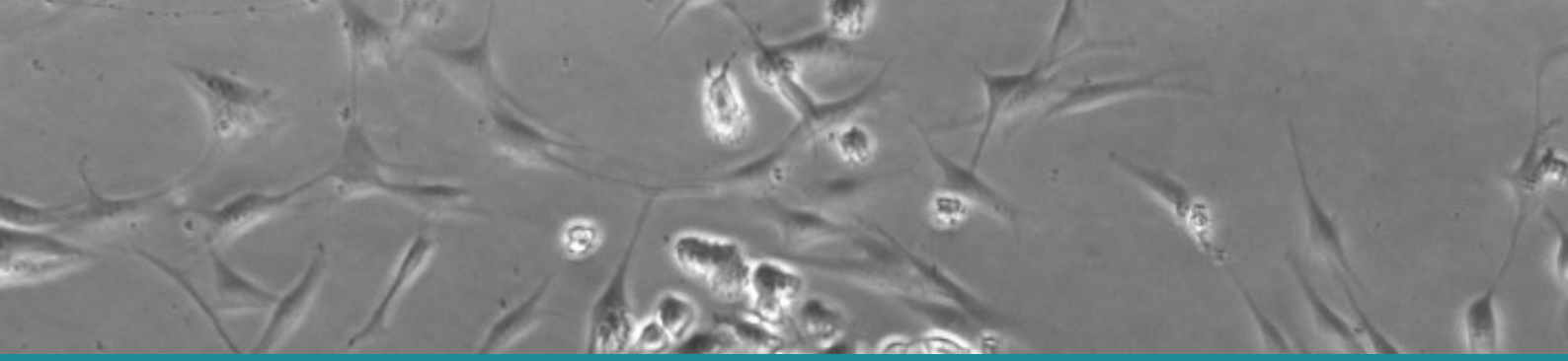
Received our first major donation of 3'000 CHF from the Swiss Re Foundation

Swiss Re Foundation

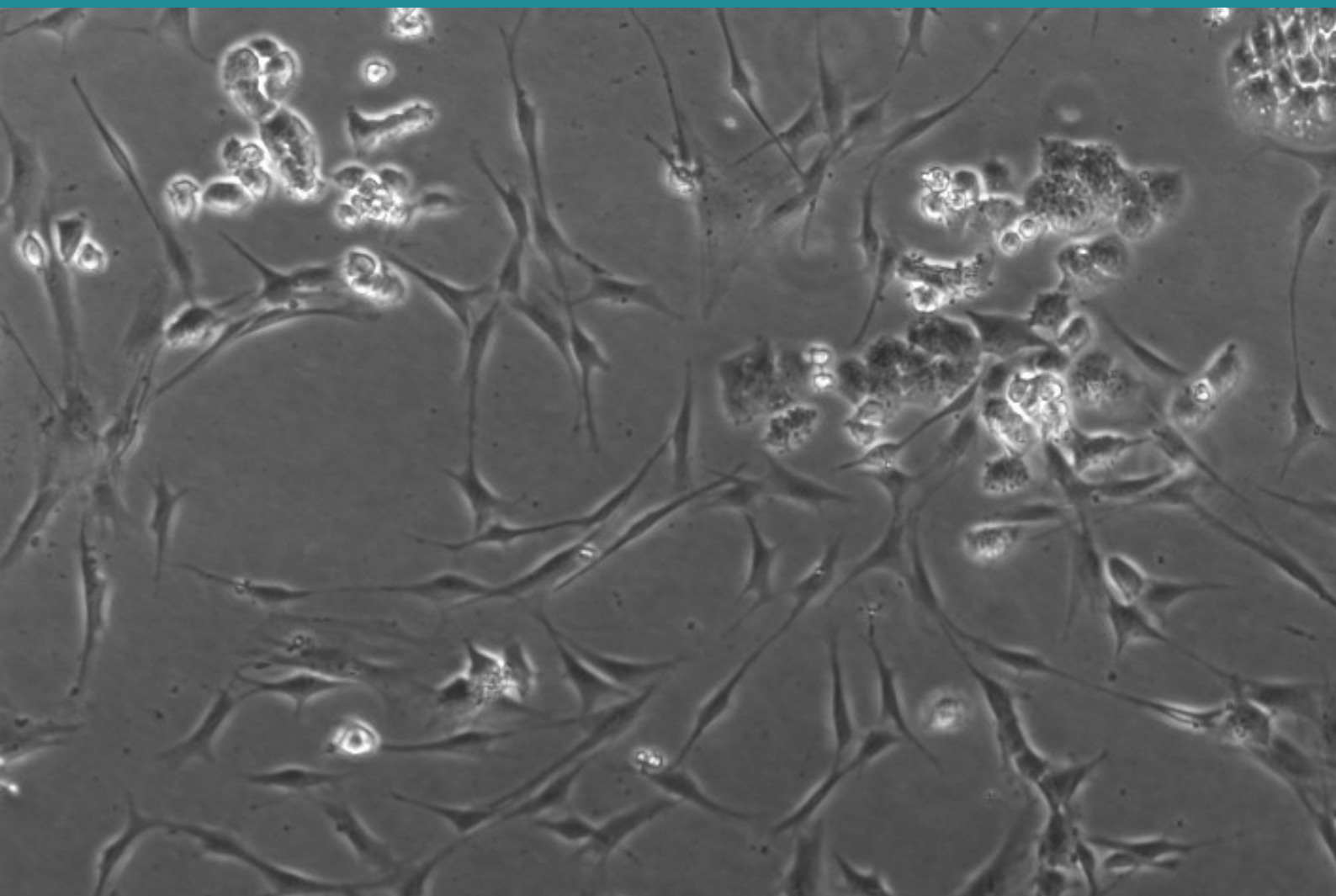
Developed our long-term research roadmap to therapies

Funded tax-exempt association in Switzerland and registered in commercial register in Zurich

Partnered with Transnational Giving Europe and Rare Village Foundation to enable tax-deductible donations beyond Switzerland



> To define ultra-rare Mendelian disorders there is an increasing need for a close interdisciplinary collaboration between families/legal representatives of the affected individuals, clinicians, diagnostic and research laboratories.
>
> - Dr. D. Lessel, discoverer of AGO2/Leskres syndrome



Highlights 2021

Connect families

Held our first virtual patient family meetup

Welcomed 10 new members in our private Facebook support group from all over the world and took advantage of the in-built translation features

Raise awareness & educate

> **Knowledge is power!**
>
> - Patient family

Launched ago2.org with information on the syndrome, our research roadmap, and patient stories.

Shared our first newsletter with patient families, donors and professionals

Listed patient group on leading portals Orphanet and InfoDisease Search

Joined umbrella organisation Global Genes Rare Foundation Alliance

Stichting Suze

What Is AGO2/Leskres Syndrome?

AGO2/Leskres (Lessel-Kreienkamp) syndrome is an **ultra-rare neurodevelopmental disorder associated with mutations in the gene AGO2** and has no identified specialist treatment.

The syndrome was discovered by Dr. Lessel and Prof. Kreienkamp and was first described in November 2020. It was later named "Lessel-Kreienkamp syndrome".

Symptoms

Symptoms typically appear in infancy and, while outcomes vary, patients may suffer from delayed motor development, intellectual disability, speech problems, seizures, a floppy body, newborn eating problems, dental anomalies, brain anomalies, heart defects, vision problems, autistic behaviour, hyperactivity and breathing problems.

Prognosis

As the condition is so new, we don't know much yet about its prognosis.

Known patients

Worldwide, around 50 patients have been diagnosed though, given the recency of the syndrome, many patients are likely undiagnosed.

AGO2 gene

AGO2 belongs to the Argonaute protein family and is critical for the regulation of gene expression via RNA interference. This regulation may be faulty in children with mutations in AGO2.

AGO2 silences the expression of other genes by destroying their target RNA

What Is a Rare Disease?

In Europe, rare diseases are defined as diseases that affect **fewer than 1 in 2'000 people**. But rare diseases are only rare in isolation. Many are life-threatening or result in chronic invalidity. The rarity makes it challenging to research, diagnose and provide appropriate care. And lack of awareness can lead to a lack of understanding & a feeling of isolation.

6'000-8'000 rare diseases

1 in ~25 people are affected by a rare disease

3 in 4 have a genetic cause

70% start in childhood

> **"Only about 10% of rare diseases have an FDA-approved therapy. There is an urgent need for more research, and earlier and more accurate diagnoses of and interventions for these disorders"**
>
> - Anne Pariser, Director of NIH NCATS Office of Rare Diseases Research

Sources: bag.admin.ch;
Wakap et al. European Journal of Human Genetics 2020


Hocoma
Hocoma
Hocoma

Patient 1: Finn - How It All Began

I am Antje. I kitesurf, sail, rock climb and travelled the world with my backpack. I have a fantastic job in Tech Innovation and truly believe the world is a fascinating and exciting place. When I got pregnant with Finn at 36 I thought the world would keep moving at the same extraordinary pace - how wrong I was.

On the 4th day the baby was overdue, we went to the hospital to induce it. When the CTG got critical the doctors decided to ramp up the cocktail and it still took us 14h to get the little baby into our arms. But that wasn't for long. In the arms of his Papa, Finn stopped breathing and turned blue. I will never forget how I panicked and called the nurses back. Someone came running, grabbed the baby and ran away with him....

> "In the arms of his dad Finn stopped breathing and turned blue."

Our journey to a diagnosis

Luckily we had decided for a level one hospital with intensive care for birth. The next time I saw Finn was in the intensive care unit with lots of doctors around. They explained how they reanimated him and that he needed to be on oxygen support for a while. He was very weak and they recommend further investigations.

The next day he had a brain scan to check if it had suffered from the lack of oxygen. Again a couple of doctors and a psychologist came to talk to us to explain the result. Finn's connection between both brain halves (Corpus Callosum) is interrupted. “We cannot tell you how, but this normally goes along with an overlaying problem or disease”, the doctors said. “It is an indication for a bigger problem that your son has, you can talk to the psychologist about it.” The psychologist was about half my age and the first thing she told us was to take good care of each other as 80% of parents of disabled children get divorced. Here we go, the first time ever I heard the word disabled in connection to my son.

The first months with Finn were very busy. After 4 weeks he could leave the hospital with an oxygen alarm attached to his little toe, and this alarm sound was our daily companion for the first year. **A huge diagnostic journey started** and the doctors tried hard to find out what was wrong. All chromosomes were good, the metabolism also and no syndrom fit him. Then they decided to go for whole exome sequencing. In 2016 this was not very common and we were happy to get more clarity. This was the first time we heard about AGO2 and I recall sitting with Dr Lessel and trying to follow his explanations.

The new normal

The new normal was spending a lot of time in therapies, **living in absolute uncertainty of what was going to happen** and pictures in our head on how the future may look like. No one knew the AGO2 gene, no one could tell us what it meant to be affected on this gene. All the more grateful we were for the exchanges with Dr Lessel and to be involved in the latest tests he did.

> "We lived in absolute uncertainty of what was going to happen."

With 2 years Finn developed seizures that kept us busy and brought several hospital nights. They came mostly with fever but very regularly.

Finn still could neither sit nor crawl but developed strategies to overcome his hypotonia. His way to relocate was lying on his back and moving slightly sidewards.
He was also diagnosed mild deafness and got hearing aids. We started with signals and tried to get him into interaction. At the kindergarden the physiotherapist put him on his feet as much as possible. When he was 2.5 years he could sit but was for a long time not able to sit up on his own.
“Verticalization is key for his brain development” they said and we trained with all kinds of physical aids. He got physiotherapy two times a week to strengthen his muscles and once a week we took him to a school to learn signals.
We see the cardiologist every 6 month as his heart has only two instead of three heart valves.

We also see the neurologist every year and **every time I ask the same question: "What can we do to improve?" and every year I get the same answer: "You can go horse riding and swimming."** Did I mention that work in Tech Innovation in aerospace? I simply could not believe that this is true as I see so much great tech popping up every day.

> "You can go horse riding and swimming." I simply could not believe this was all that we could do to help Finn.

Then one day I got the opportunity to apply for a program in Cologne, Germany, that is specialised in kids unable to learn walking. Their training is mainly based on the Galileo vibration therapy and that really worked for us. Finn cannot steer his muscles very well from his brain but the vibrations force the muscles to train without using the brain. A fantastic shortcut without which Finn probably would still be in a wheelchair.

After the storm

The storm settled and we decided to live our life as normal as possible. When Finn was 1.5 years old I restarted work and we went back to travelling. Cuba, South Africa, South East Asia and took Finn with us sailing. At the start always with the oxygen alarm attached and later with emergency treatment for seizures.

Getting back to normal also meant deciding for a sister for Finn, which was the best decision ever and Finn is a great big brother.
With 3.5 Finn made his first steps in a walker and since then we train and train to strengthen his legs and muscles. With 4.5 he made his first step alone, which we celebrated a lot. He went to a kindergarten for children with special needs and has a fantastic team around. Anyway, **a good team is probably the best thing you can have.** Physiotherapists that work with him on his dyspraxia and hypotonia, logopedia to work on his mouth and capabilities to interact and then the doctors that take care of the right aids, his heart, his hips and all the little and big issues we are confronted with.

Today Finn is 6 years old, he goes to a special school and is a happy boy. He still cannot say a single word, he is very difficult to handle as he turns around and runs away as soon as you leave his hand, he falls and still cannot stand up alone. I still do not want to believe that horse riding and swimming is all we can do to help and keep investigating solutions to help our son be better off with the world.

To all researchers out there: this is an amazingly rare disease and a great opportunity to make a real difference for every single child affected.

Our Partners

TGE
Transnational Giving Europe

rare
village
FOUNDATION

Global Genes®
RARE Foundation Alliance

beacon
for rare diseases

the
orphan
disease center

Financial Report 2021

Revenue

3'000	Patron contributions
13'039	Private donations
500	Legal entity donations
1	Other income
16'540	Total revenue

Expenses

26	Print material, postage
431	Incorporation costs
235	Internet costs
20	Bank fees
712	Total expenses

Profit

15'828	Profit

Our expenses were covered by donations from our founders.

Financial Report 2021

Assets

15'375	Liquid assets
467	Deferred income
15'842	Total assets

Liabilities

14	Deferred expenses
15'828	Profit
15'842	Total liabilities

AGO2 is a non-profit organisation and pursues neither commercial nor self-help purposes. Our financial books are externally examined.

Dr. Silvio Leonardi
Friedheimweg 21 | CH-3007 Bern

08.02.2022 Re. Examination of AGO2's accounting

AGO2 Verein
Dr. Nora Leonardi
Balgriststrasse 82
8008 Bern

Dear Madam

As statutory auditor, I have examined the accounts of AGO2 Association for the financial year 2021 ending 31 December 2021.

I examined the accounts, which were prepared in accordance with the double-entry accounting method, on the basis of spot checks of the journal and account statements. All enquiries were answered to my complete satisfaction.

The final balance sheet and income statement agree with the journal and account statements. According to my assessment, the accounting records comply with legal and statutory requirements.

The balance sheet for the year 2021 closes with a profit of CHF 15'828.34, including deferred income of CHF 466.65 and deferred expenses of CHF 12.85.

I propose that the General Assembly approve the balance sheet and income statement.

Kind regards

Silvio Leonardi

Annexes: -
CC: -

A Look Ahead Into 2022

We could never have predicted 2021, so please do not hold us to this.

We will organise the first ever **science and family conference on Argonaute syndromes** together with AGO1 patient families, researchers and clinicians. We will meet in Regensburg and look forward to the closer collaboration with the AGO1 syndrome community.

We plan to launch a **patient registry** to collect data on our patient population and further our understanding of the phenotypic spectrum and disease progression.

We hope to meet more patient families, either virtually or in person.

And we are planning a trip to space (psst)...

On a personal note, we hope that our daughter Paula continues on a good developmental path despite the odds, and wish all families much warmth, happy moments and no health emergencies.

We Thank You For Your Support

Acknowledgements

Our heartfelt thanks to our supporters, donors, scientific advisors, and all those who worked hard behind the scenes. In particular, Stefan Kempf for our website, and Silvio Leonardi for the revision and tireless support.

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