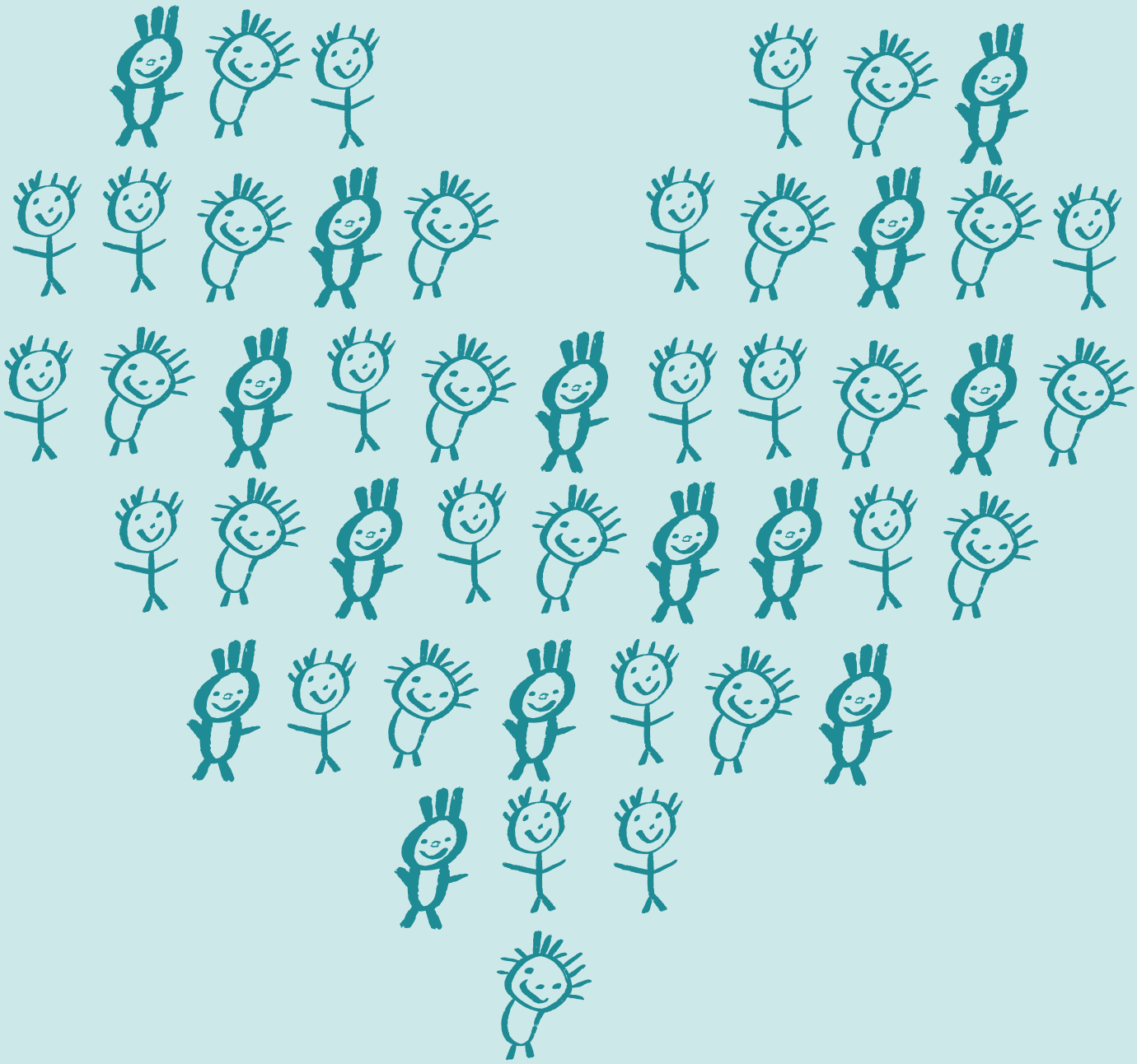
IMPACT REPORT 2022

AGO2

In This Report

AGO2



Message From The President

"I want my daughter and other affected children like her to have a chance to thrive."

- Nora Leonardi, PhD

2022 was the second year of our patient group, and what a year it was!

We organised the first-ever **conference** on Argonaute syndromes with leading scientists Profs. Lessel, Kreienkamp, Piton and Meister. **20% of known patient families joined in person or virtually.** It was a weekend full of emotions, learning and sharing. Jump to page 10 for more.

The **AGO1**-related syndrome was described in late 2021 and given that it is "a similar, if not the same, syndrome" (Profs. Lessel & Piton), we expanded our scope to include AGO1 and welcomed new team and advisory board members. We are planning to change our name this year.

We sincerely thank all supporters and donors for their solidarity and trust. Thanks to your support we could not only conduct crucial projects, but also significantly increase our savings to finance larger projects in the future that push research into a treatment forward.

With care, Nora

Co-founder and President of AGO2

Who We Are

Our mission

Improve the lives of children and families impacted by Argonaute syndromes (AGO1 & AGO2 genes) by

1. finding and funding paths to treatment,
2. connecting families,
3. raising awareness.

About us

AGO2 Association is a **family-led patient advocacy group**, founded by Nora Leonardi and Christoph Basten in 2021 after their daughter's diagnosis.

AGO2 Association is registered in Switzerland and partner of Transnational Giving Europe and Rare Village Foundation.

Team

Dr. Nora Leonardi
President

Prof. Christoph Basten
Vice-President

Dr. Silvio Leonardi
Treasurer

Naomi Tudor
Parent Lead USA

Antje Bulmann
Parent Lead Germany

Stefan Kempf
Design & Website

Advisory board

Prof. D. Lessel
University Hospital Salzburg

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

Prof. G. Meister
University of Regensburg

Prof. A. Piton
University Hospital Strasbourg

Highlights 2022

Accelerate development of treatments

Connect families

Raise awareness & educate

We organized the first conference on Argonaute syndromes.

Joined forces across AGO1 and AGO2 genes. Naomi joined our team, and leading AGO1 researcher Prof. Piton our advisory board.

Received an EU grant

EUROPEAN JOINT PROGRAMME RARE DISEASES

Received pro bono support from Costello Medical

Facebook support group grew to 70 members

Received global advocate grant from Horizon Therapeutics.

Joined patient council of ERN-Ithaca, the European Reference Network for Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders

Families received Christmas gifts.

Held virtual patient family meetups and met in person

Spoke on a panel at Rare Disease Showcase 2022

www.ago2.org
31'000 views

100+ subscribers

Launched

“I'm impressed by how far we have come since the first paper on AGO2/ Leskres came out. We've learned quite a bit about the syndrome, you are organized as a patient group, and we had a conference. You are moving very fast.

I have not seen this before in other rare diseases.

Prof. G Meister
University of Regensburg, Germany
Argonaute researcher

Argonaute Syndromes Conference 2022

The **first** conference on AGO1- and AGO2-related syndromes took place in Regensburg, Germany, in August 2022 as a satellite of the first science Meeting on Argonaute Proteins.

The event successfully **united scientists, industry representatives, and 20% of known patient families.** It increased understanding of symptoms, shone a light on real-life challenges and encouraged new research ideas.

We would like to thank Professor Meister, Birgit Clemens and the rest of the Meister lab for their incredible support and cooperation in organising the conference.

Visit our website to read the full report, and our Youtube channel for recordings and a 3-minute highlights video.

We hope to be back in 2024!

What our attendees said


GO2
cting families, and
each their potential


Accelerating research, connecting families, and
educating to help our children reach their potential

The relationships formed through the AGO association among families who truly "understand" [how] to live with AGO provides support beyond measure. This conference has created **long-term connections & hope for our shared cause** which will positively impact children & entire families.

-Ashley

Proud that my son could give a real example for what research is needed.

-Antje, Mum of Finn

"This conference meant a lot for me: as great support to meet parents having also huge number of questions and problems as me, dealing all day long with our AGO2 children. First time I felt like they understand, really understand the point."

Mom to a 10-year-old with AGO2

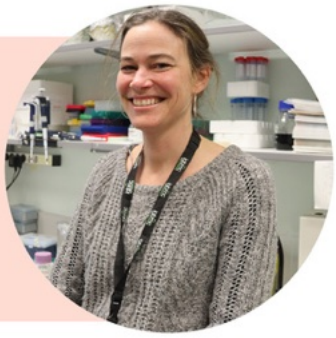
I could develop an understanding of the variability of the disease, I saw that many children have shown progress which suggests strongly that intervention can work.

Lastly, it is always good to remind oneself that **our work is not only interesting but can also potentially make a difference.**

-Marc, Industry Representative

This meeting was very moving for me and has **motivated me even more to try to understand the consequences of mutations in AGO1/AGO2.**

- Prof. Amélie Piton, first to document neurodevelopmental disorders associated with AGO1.

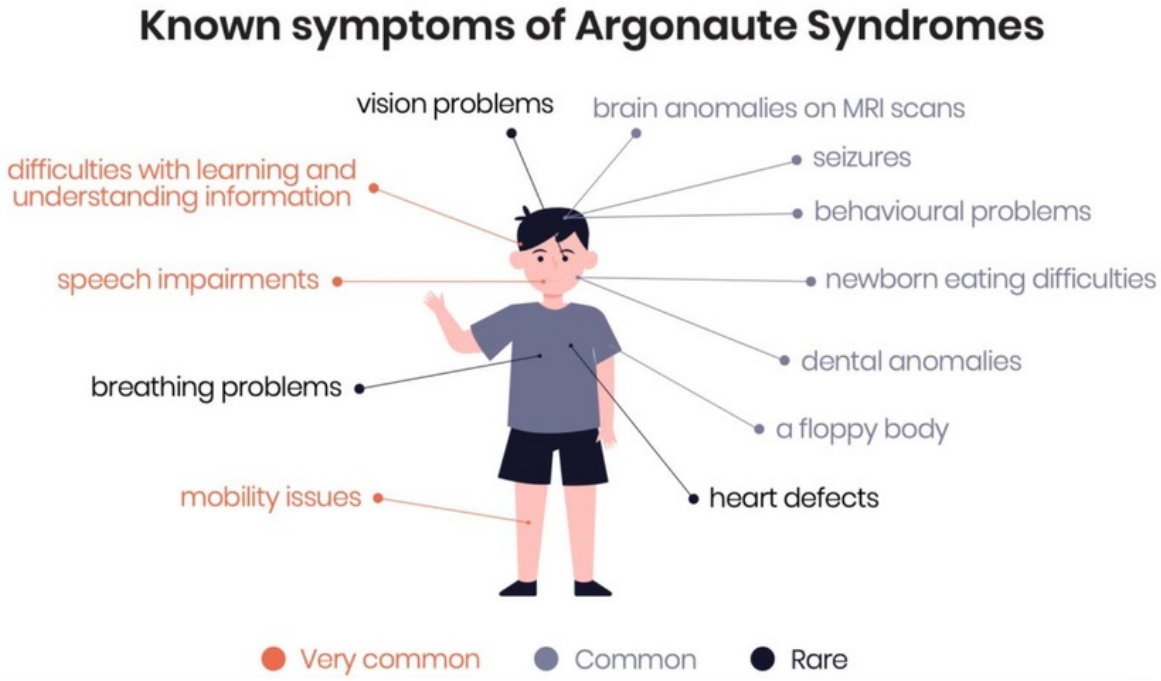


What are Argonaute syndromes?

Worldwide, ~85 people have been diagnosed with Argonaute syndromes

Changes to the AGO1 and AGO2 genes cause rare conditions with similar symptoms, AGO1-related syndrome and Lessel-Kreienkamp/LesKres syndrome respectively, that can collectively be referred to as Argonaute syndromes.

Argonaute syndromes are extremely rare. However, as these syndromes have only been recently discovered, as many as 1 in 16,000 children may be affected.



Lessel et al., Nature Comm 2020; Schalk et al., Journal Med Genet, 2021; Lopez-Rivera et al., Brain 2020

What is a rare disease?

In Europe, a disease is considered rare when less than 1/2,000 individuals are affected.

There are more than 10,000 rare diseases.

Only about 5-10% have at least 1 approved therapy.

Research, diagnosis, appropriate care are a challenge, and a lack of awareness can lead to a lack of understanding & a feeling of isolation.

3 in 4 have a genetic cause

1 in ~25 people are affected by a rare disease

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, former Director of NIH NCATS Office of Rare Diseases Research

Sources: bag.admin.ch;
Wakap et al. European Journal of Human Genetics 2020
Haendel, M. et al. How many rare diseases are there? Nat. Rev. Drug Discov. 19, 77–78 (2020)

A Letter from Johannes, 6, Austria

Hello dear Argonaute friends,

My name is Johannes and I was born in August 2013, so in the AGO2 stone age. I was small and slender, but breathing was no problem, however sucking was very difficult for me. It was only thanks to the endless patience of my mother that I took in enough breast milk. Maybe the doctors already suspected that "something was wrong", but nobody said anything. After a week I was allowed to leave the hospital.

The next six months were probably the most beautiful and happiest for the three of us. My parents always saw me through "rose-colored glasses", they didn't see or didn't want to see that something was off.

> "My journey took me to many doctors, through many clinical exams, blood draws, genetic tests, but no one could find anything."

At the age of six months, during a routine check-up, our pediatrician told us that there must be something "wrong" with me. Thus began my journey as an Argonaute, unnoticed, incognito. My journey took me to many doctors, through many clinical exams, many blood draws, many genetic tests, but no one could find anything.

In the first years, my **low muscle tone was the leading symptom**, I couldn't sit alone, couldn't eat alone, even the bottle had to be held by my parents. Once a week an early interventionist came to the house, then I started physiotherapy, occupational therapy, logotherapy....

Besides these problems I became a vampire. I was awake at night, screaming as if possessed by demons.

When I was about 2.5 years old, I had a focal **seizure for the first time**. In kindergarten, I was cared for by my own pedagogue, and had many mats around me and always my emergency medication.

My parents, however, did not let their heads hang down. We regularly went on trips. No matter whether it was an Italian sandy beach, Croatia or Corsica. **With the "Wandertragerl" on my dad's back I explored the world. It wasn't easy, but we had fun and really grew together as a family.** For walking I was still much too weak in the beginning.

I began to develop absences. I would twist my eyes upwards and be unresponsive for a short time. From then on I was given regular medication; it was not easy for my parents to explain to a 3-year-old who can't speak or understand that he should swallow a bitter medicine. It helped that my father knows a lot about medicines, especially those for sleeping.

My seizures were well controlled and I also **started to walk** with help.

"When I was about 7 years old, I gave my parents and the kindergarten a special present as I took my first steps - alone!"

Unfortunately, this joy lasted only for a short time. My absences became more frequent again and, above all, I completely lost my muscle tone with every seizure. I fell to the ground unchecked, which gave me a lot of bumps and bruises. **On bad days I have over 100 seizures.**

My parents now work part-time, so they have more time for me, but also more time for themselves to regain strength.

I have become a stately young man, and even if I still can't speak, I can assert my head. I have to be fed food most of the time, but drinking works very well. Either I sit in my stroller or an adult holds me tightly by the hand.

At a check-up at the end of 2021 my physician finally told me that something came up during a repeated genetic examination and I revealed myself as an Argonaute.

Yours,
Johannes

"I am looking for other Argonautes whom I can share experiences with, meet and play with."

Say Hello to Our New Mascot Archie!

Our genes were named Argonaute (AGO) because a plant with a mutation in AGO1 looked like an octopus... Here is our very own!

Out of 9 hand-made octopuses, our families voted for their favourite.
Thanks to artist Alexander!

Kneading helps Alexander (AGO1) to calm down and is one of his favourite hobbies.

A designer then created Archie.

Our Partners

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Allianz Seltener Krankheiten – Schweiz
Alleanza Malattie Rare – Svizzera

MEMBER OF EURORDIS
RARE DISEASES EUROPE

beacon
for rare diseases

Swiss Re Foundation

the orphan disease center

TGE
Transnational Giving Europe

Financial Report 2022
Balance Sheet

	31.12.2022 (in CHF)	31.12.2021 (in CHF)
Assets		
Liquid assets	32 140	15 375
Deferred income	14 360	467
Total assets	46 500	15 842
Liabilities		
Association assets	15 828	14
Profit	30 672	15 824
Total liabilities	46 500	15 842

Financial Report 2022
Profit & Loss

	31.12.2022 (in CHF)	31.12.2021 (in CHF)
Revenue		
Patron contributions	33 847	3 000
Private donations	28 612	13 039
Legal entity donations	555	500
Total revenue	63 014	16 540
Expenses		
Project expenses incl. conference	27 819	0
Administration	3 919	245
• Salaries, Compensation	2 826	0
• Bank fees, currency differencies	661	20
• Memberships, Education, IT	432	235
Extraordinary expenses	604	457
Total expenses	32 342	712
Profit		
Profit (savings)	30 672	15 828

We would like to thank Costello Medical, the Swiss Re Foundation and Vanilla for their combined pro bono support of approximately CHF 15 000.

Salaries & compensation expenses were covered by donations from our board.
In 2022, the board volunteered a total of 600 hours.

Our surplus revenues will be used for developping our association and in large part saved to finance future projects.

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

Hanna-Laura Mock
Hanna_Laura@hotmail.com
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INDEPENDENT AUDITOR'S REPORT

To the general meeting of AGO2, Zurich

Report on the Financial Statements

I have audited the financial statements of AGO2, which comprise the balance sheet as at December 31, 2022 and the statement of Profit & Loss for the year then ended.

My responsibility is to express an opinion on these financial statements based on my audit. I examined whether the balance sheet items were supported by evidence, invoices tie to journal entries on a sample basis and the accounting records are clear and understandable.

In my opinion, the accounting records and financial statements comply with Swiss law and the company's articles of incorporation.

I recommend that the financial statements submitted to you be approved with a profit of CHF 30'672.

Zurich, May 22, 2023

Hanna-Laura Mock

A Look Ahead Into 2023

At the conference, our familiies shared their dreams for

- awareness & earlier diagnoses,
- support through education & networks to share experiences,
- treatments that improve day-to-day lives

We will continue to work towards these dreams in 2023, as a joined-up and stronger group across Argonaute genes. Look out for a name change.

We plan to collaborate with researchers on a **natural history and burden of disease study** to collect data on our patient population and improve our understanding of the phenotypic spectrum and disease progression.

We look forward to hearing updates from Argonaute researchers who attended the 2022 conference as this moves us towards pre-clinical research.

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

With care, Nora

Co-founder and President of AGO2

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.

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