PARTNERING FOR PROGRESS

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2025

Annual Ataxia Conference

Research Update

Lauren Moore, PhD

Chief Scientific Officer & VP of Research
National Ataxia Foundation

NAF
National Ataxia Foundation

March 27-29, 2025
Planet Hollywood
Las Vegas, NV

DISCLAIMER

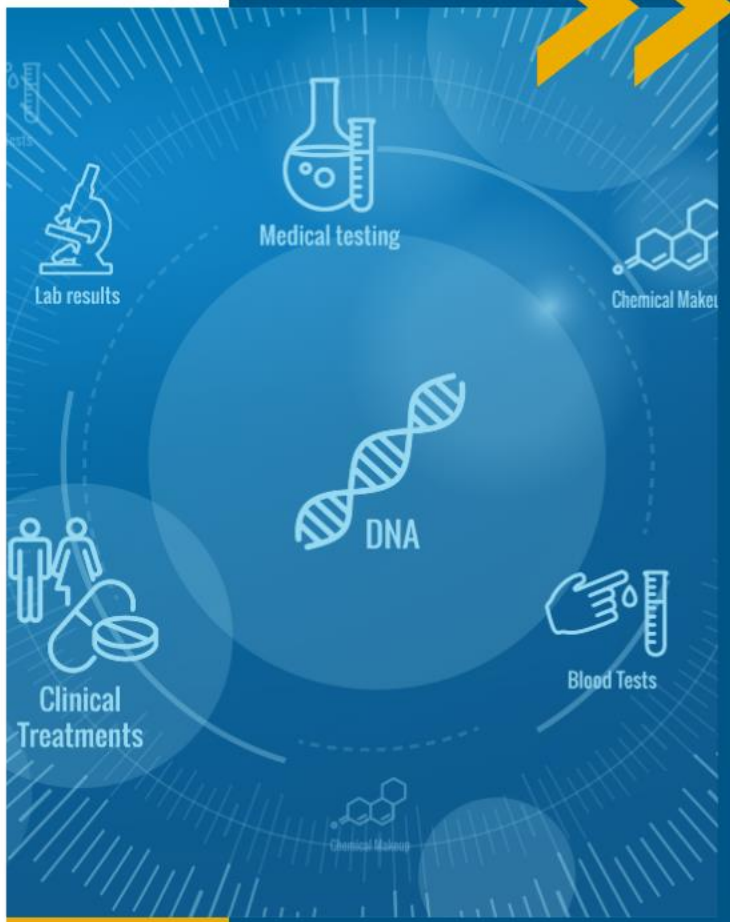
The information speakers provide in any presentation made as part of the 2025 NAF Annual Ataxia Conference is for informational use only.

NAF encourages all attendees to consult with their primary care provider, neurologist, or other healthcare provider about any advice, exercise, therapies, medication, treatment, nutritional supplement, or regimen that may have been mentioned as part of any session.

Products or series mentioned during these sessions do not imply endorsement by NAF.

PRESENTER DISCLOSURES

I am a Full-Time Employee of the National Ataxia Foundation. I have had no further personal financial relationships with commercial interests relevant to this presentation during the past 12 months.



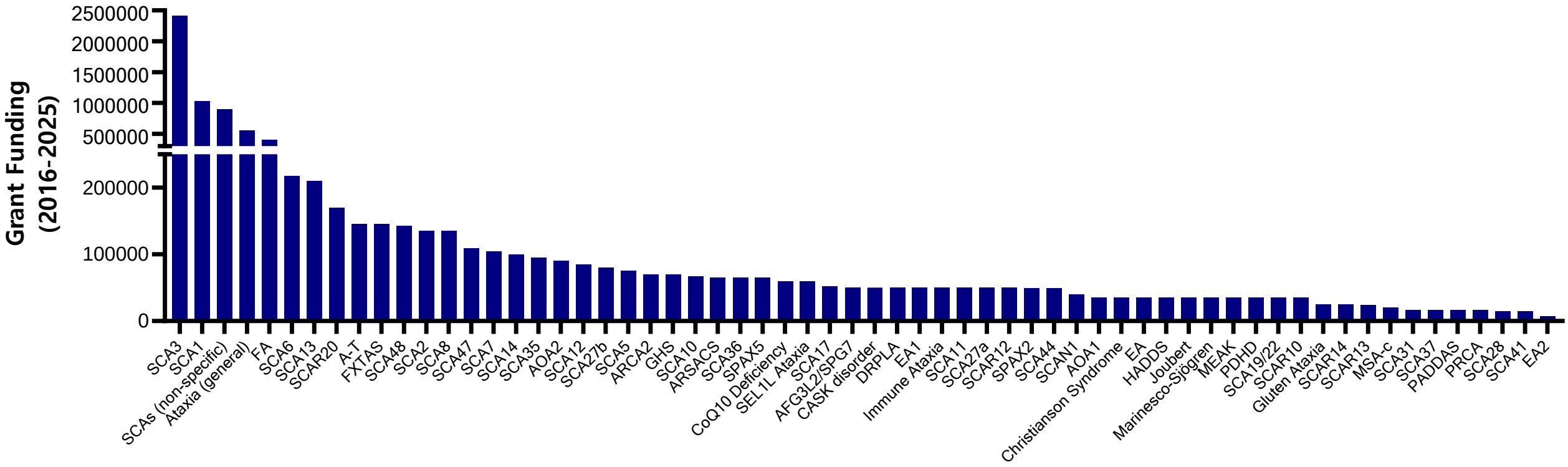
The NAF Impact:
One Decade of NAF Grant Funding

2016-2025

NAF has supported advancements in ataxia research for almost **50 years** through our competitive annual grant program.

The following statistics will focus on just the last 10 years of grant funding.

From 2016-2025, NAF has awarded **>$9M** to support **200+ research projects** spanning **60+ forms of Ataxia,** including unknown forms.



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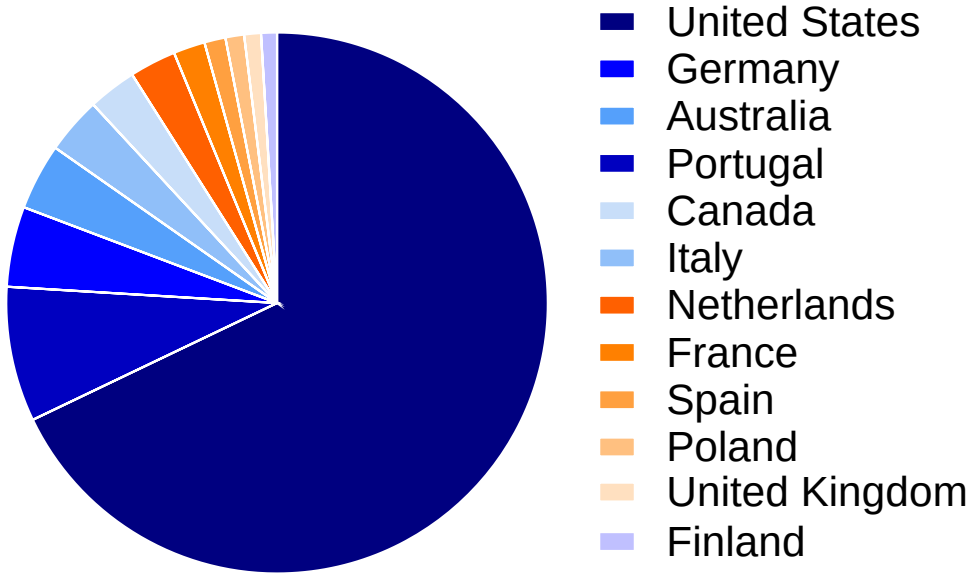
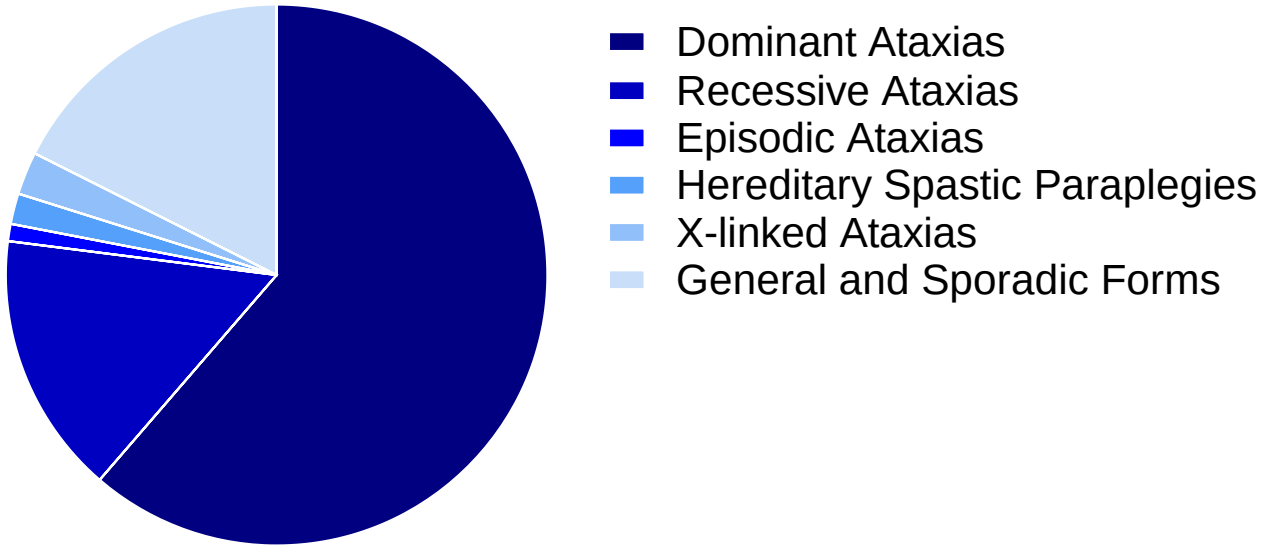
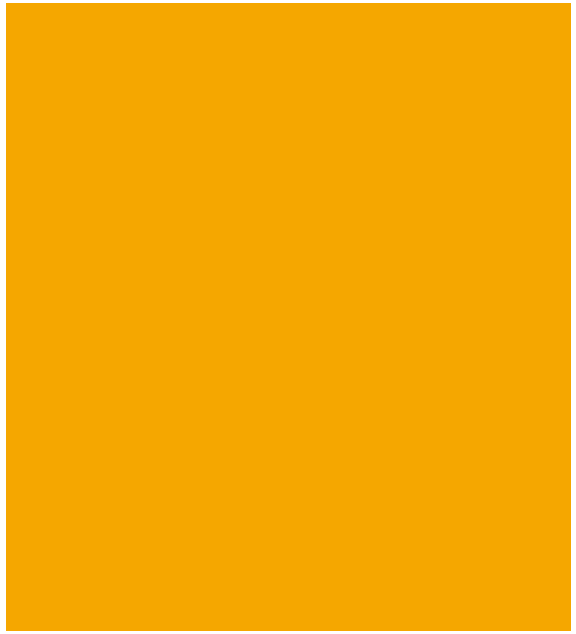
Where are the labs we fund?



What types of diseases do we fund?

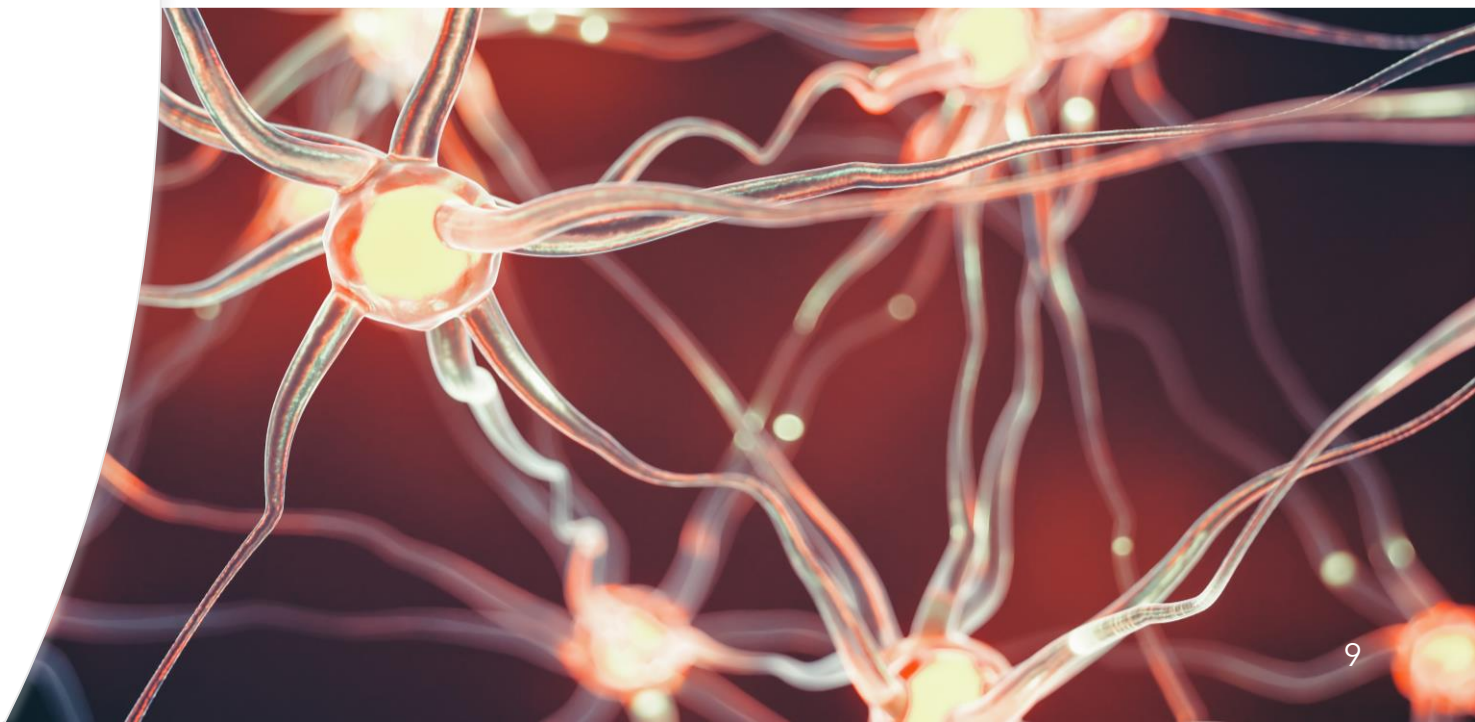


What has been accomplished through NAF Grant Funding?



New Model Systems, Databases, and Clinical Applications for Ataxia Research in Past 3 Years

- **Cell Lines:** SCA3, SCA6, SCA31, TDP1 Ataxia, SEL1L Ataxia, RNF216-associated ataxia, Gluten Ataxia models
- **Mouse Line:** RNF216-associated ataxia
- **New Clinical Assessments:**
  - At home SARA assessment
  - Brain Imaging for Ataxias
- **Genetic Database:** to help identify new ataxia genes
- **Prediction models & assays for drug identification**



Supporting and advancing the next generation of researchers within the Ataxia research field

Alexa Putka
University of Michigan

2024 Recipient of NAF Graduate Research Fellowship

"This investment in my research paved the way for $145,000 in support from the NINDS through (…) a training grant for predoctoral researchers. **NAF's funding played a crucial role in pushing my research forward and emphasizing the importance of ataxia research to the NIH."**

Has authored / co-authored 6 research publications since 2023 that advance our understanding of SCA1 and SCA3 and identify potential new drug targets.

Supporting and advancing the next generation of researchers within the Ataxia research field

Dr. Timothy Balmer
Arizona State University

2022 Recipient of NAF Seed Money Grant

"The great majority of your funding has supported a remarkable PhD student , Harsh Hariani. Harsh has a medical degree from India (MBBS), a master's degree in neuroscience from Loyola University, worked at a biotech startup for 2 years, and joined the Balmer laboratory last Fall.

Supporting the training of the next generation of neuroscientists that may go on to a career studying the cerebellum and ataxia may be the most significant achievement of your funding."

Connecting Researchers and Fostering a Productive and Collaborative Community

Dr. Roderick Maas
Stichting Radboud Universitair Medisch Centrum

2023 Recipient of NAF SCA3 Pioneer Grant

"I have initiated an international collaboration, including groups in Germany, Brazil, and Italy, which resulted in a comprehensive review article on cerebellar tDCS, transcranial magnetic stimulation, and deep brain stimulation in degenerative ataxias.

One of the aims of this collaboration was to identify gaps in our current knowledge and avenues for future research in the field.

We are currently discussing possibilities for a shared project on cerebellar tDCS in ataxia patients."

Multiplying impact on Ataxia research through seeding additional funding

Dr. Hannah Shorrock, University at Albany

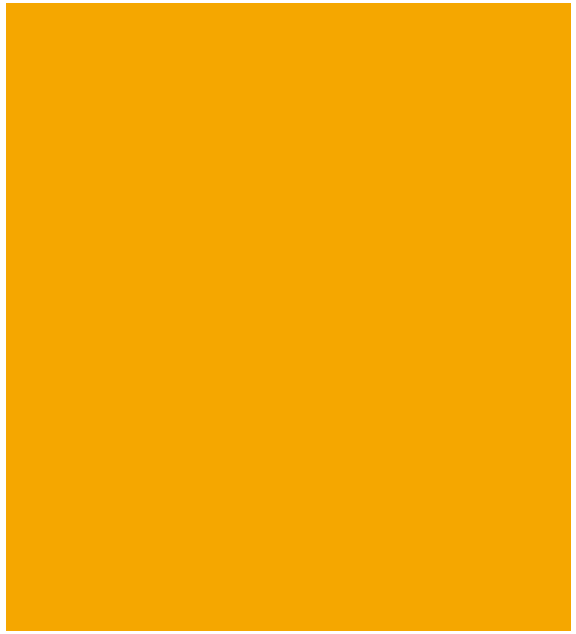
Advanced to an Assistant Professorship, continuing her work on identifying ataxia therapies and mentoring the next generation of ataxia researchers.

2020
Awarded NAF
Post-doc Fellowship
$35k

Alternative splicing & development of small molecule therapeutics in CAG expansion SCAs

2023
Awarded NIH Grant
for **$2.9M**

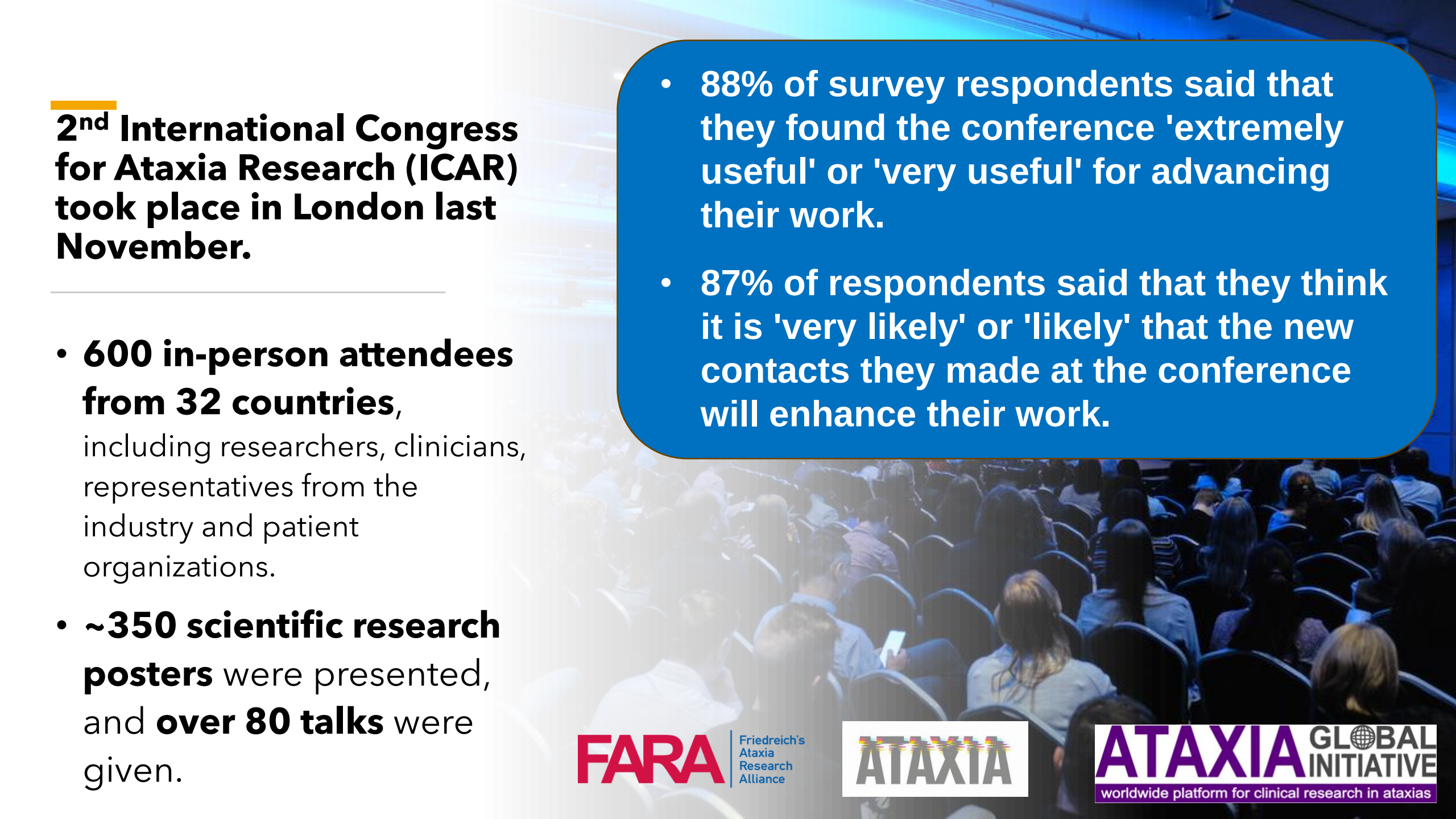
NAF Research Impact: Beyond Grants



2nd International Congress for Ataxia Research (ICAR) took place in London last November.

- **600 in-person attendees from 32 countries**, including researchers, clinicians, representatives from the industry and patient organizations.
- **~350 scientific research posters** were presented, and **over 80 talks** were given.

- **88% of survey respondents said that they found the conference 'extremely useful' or 'very useful' for advancing their work.**
- **87% of respondents said that they think it is 'very likely' or 'likely' that the new contacts they made at the conference will enhance their work.**



FARA Friedreich's Ataxia Research Alliance

ATAXIA

ATAXIA GLOBAL INITIATIVE
worldwide platform for clinical research in ataxias

NAF sponsors the CRC-SCA, the largest and longest running Natural History Study for Spinocerebellar Ataxias.

- Over 1000 individuals have enrolled at 16 sites in US and Canada, over 350 visits completed last year.
- Why does the CRC-SCA matter?
  - Provides infrastructure to validate improved clinical assessments and biomarkers
    - Fluid-based assessments, wearable technologies, brain imaging
  - "**Real World Evidence**" from Natural History Studies is being used as a comparator in clinical trials

Progress in Ataxia Diagnosis

Newly Identified Ataxia Genes

Multiple new ataxia-causing mutations have been discovered in recent years:

- CANVAS/ RFC1-Ataxia (2022)
- SCA49 (2022)
- SCA50 (2022)
- SCA27B (2022)
- SCA51 (2023)
- SCA4 (2024)

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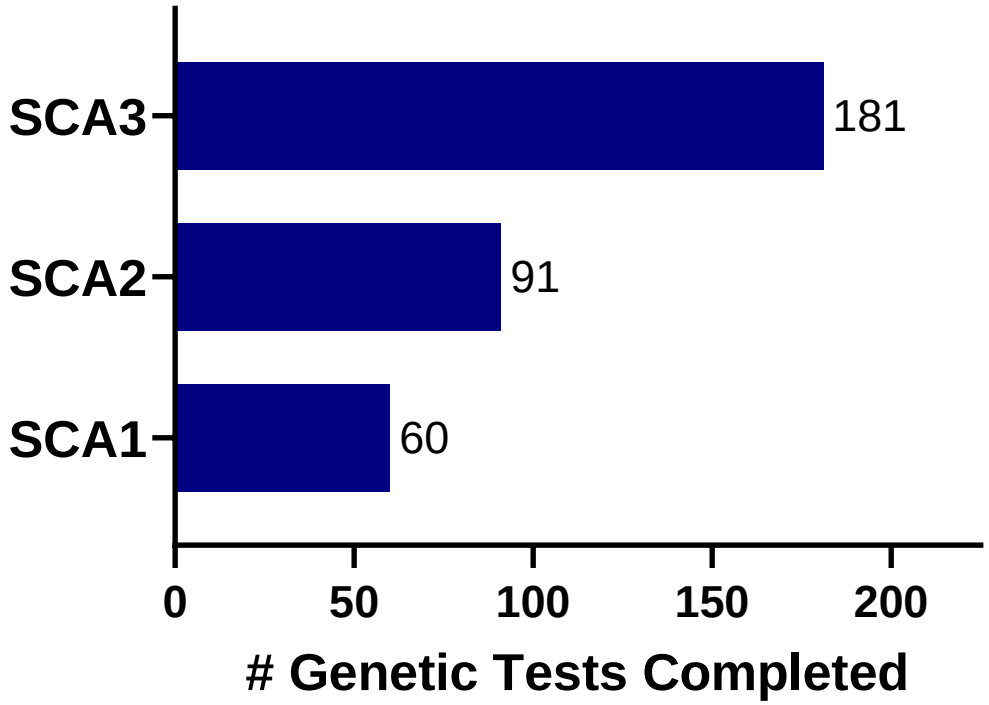
- **SCA27B (2022)**
- SCA51 (2023)
- SCA4 (2024)

In just 2 years, over >700 individuals have been diagnosed with SCA27B.

NAF No-Cost Genetic Counseling and Testing Initiative

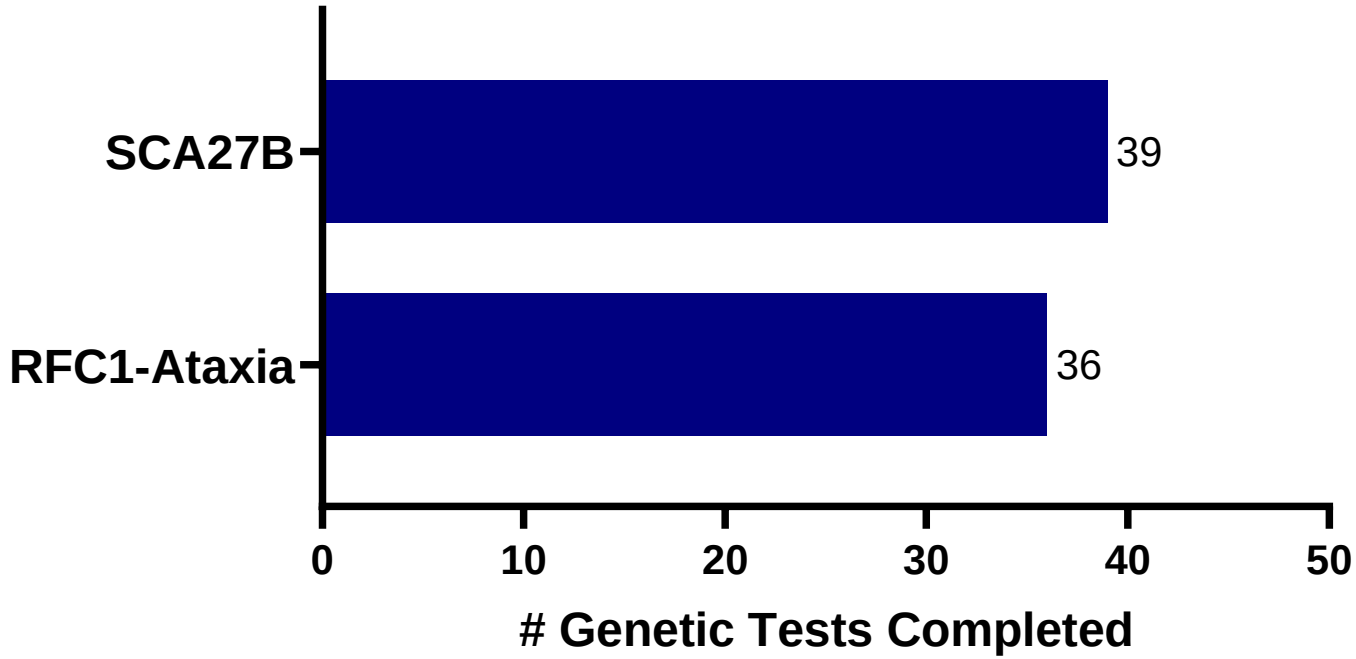
NAF has offered a public no-cost counseling and testing program for individuals at risk for SCA1, 2 and 3 since 2022.



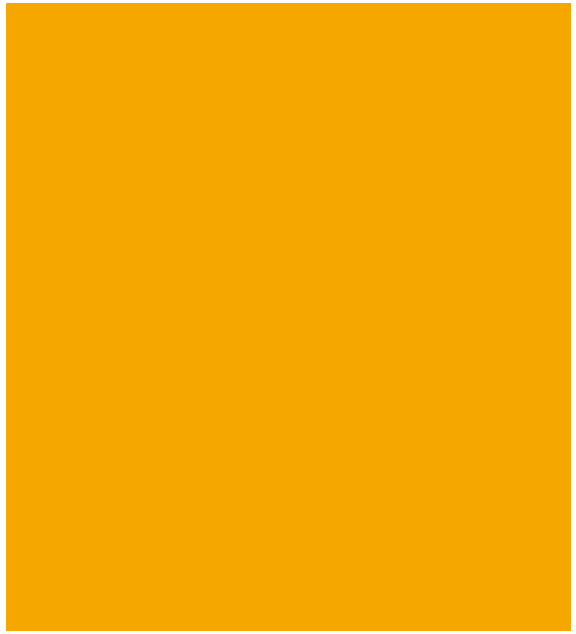
After a short pause, this program has relaunched & is accepting new participants.

Additional NAF Genetic Testing Efforts

In 2024, NAF received external funding to provide no-cost genetic counseling and testing for individuals suspected of SCA27B and RFC1-Ataxia at a limited number of sites.



Towards a Cure:
Progress in Ataxia Drug Development



Drug Companies with Publicly Disclosed Therapeutic Programs for an Ataxia-related Disorder

Progress Towards Expanded Access to Skyclarys for the Treatment of Friedreich Ataxia.

- Skyclarys received FDA approval for the treatment of FA (age 16+) in the US in 2023.
- Approved by European Commission in 2024 and Health Canada in 2025.
- Open-label Phase 1 Study launched to evaluate in participants ≥2 to <16 years of age with FA

Preclinical studies are also assessing whether Skyclarys may be beneficial for other forms of ataxia, such as ARSACS.

Biogen

SKYCLARYS® (omaveloxolone) 50 mg capsules

Two New Drug Applications (NDAs) for experimental ataxia treatments are under review by the FDA, with expected decisions in Q3 2025.

Troriluzole (BHV4157)

- 1st NDA ever under review for the treatment of adult patients with spinocerebellar ataxia (SCA)
- NDA included "real world data" from the CRC-SCA and another natural history study as "external control arms"

biohaven

Vatiquinone

- 2nd FA NDA (after Skyclarys)
- Also utilized "real world data" from FA natural history studies
- If approved, would be the first therapy for pediatric patients with FA

PTC THERAPEUTICS™

A Safety and Pharmacokinetics Trial of VO659 in SCA1, SCA3 and HD

Phase I/II Study Launched in 2024

- *Experimental treatment:* Intrathecal delivery of VO659, designed to silence expression of toxic polyglutamine-expanded proteins in the central nervous system
- *Status:* Dose studies are ongoing; Actively recruiting individuals with SCA1 and SCA3
  - See full list of eligibility criteria on clinicaltrials.gov
- Study sites located in Europe and Asia

(NCT05822908)

Study of ARO-ATXN2 Injection in Adults With Spinocerebellar Ataxia Type 2

Phase I Study Launched in 2025

- *Experimental treatment:* Intrathecal delivery of ARO-ATXN2, designed to silence expression of the toxic ATXN2 protein in the central nervous system
- *Status:* Actively recruiting individuals with SCA2
  - See full list of eligibility criteria on clinicaltrials.gov
- Study sites located in Canada, Australia, and New Zealand
  - US residents may be eligible to participate at international sites

(NCT06672445)

SCA27B: Gene Discovery to a Clinical Trial

- *(Reminder)* SCA27B gene discovered 2022, genetic test available in 2023, today >700 patients diagnosed
- Just yesterday, Solaxa therapeutics announced plans to conduct a registrational clinical trial evaluating its investigational therapy, SLX-100, for spinocerebellar ataxia type 27B (SCA27B).
- Trial will be funded in part by a $7.3 million dollar grant awarded to Dr. Perlman by the Congressionally Directed Medical Research Program.

Progress in Stem Cell Therapies for Ataxia

- **There are no FDA approved stem cell therapies for Ataxia.**
- Two companies (Steminent, Reprocell) are working towards clinical development of Stemchymal® IV Cell Therapy for SCA.
- Stemchymal® phase II randomized, double-blinded, placebo-controlled clinical trials for treating SCA (including SCA2, SCA3, SCA6) have been completed in Taiwan (n=56) and Japan (n=59).
- Phase II analysis ongoing & may lead to pursual of conditional approval in Japan and Taiwan.
- There is an open IND that could enable a US Phase IIb trial. However, timeline for a potential US trial not yet available.

More Progress in FA

Lexeo

(LX2006)

Phase I/II trials ongoing testing gene replacement / delivery as a treatment for FA cardiomyopathy.

Larimar

Nomlabofusp (CTI-1601)

Phase II open label extension ongoing.

On track to initiate Phase III study by mid-2025.

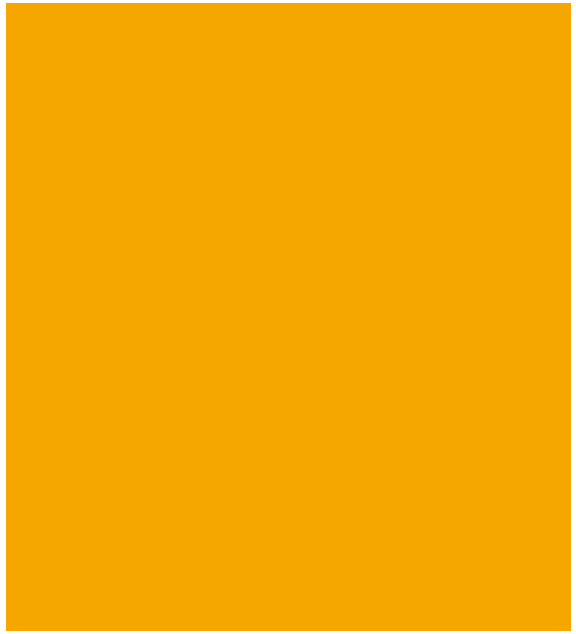
Solid Biosciences

(SGT-212)

IND clearance for first-in-human clinical study utilizing a dual route of administration.

Dosing of first participant anticipated in the second half of 2025.

Take Home Message



Recent boom in pharma investment in ataxias could not have been possible without decades of dedication by **academic ataxia researchers** & importantly, **funding** to support them.

Progress in genetics, biology, technology, informatics, drug design, etc. is being applied in labs around the world across **hundreds of ataxia disorders**.

There will be successes and setbacks in drug development, but the momentum is undeniable -- and it is on the **side of the patients.**